AGING AND LONGEVITY CONTROL OF BIOLOGICAL SYSTEMS VIA DRUGS – A RELIABILITY MODEL

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The treatments in bio-systems correspond to respective repairs known in reliability. Some treatments may make the biological objects younger; others may make them older, or not deteriorate their current age. Such kind of "maintenance" has some analogous failure/repair models in reliability. We use it to incorporate some results of reliability and bio modeling for the quantitative studies of the aging and resistance of bio-systems to environmental stress factors. We call "calendar age" the age of a bio-object which does not use treatments, or uses it without age improvement, or deterioration. All bio-objects, which are using treatments of same strength and direction of effect, have "virtual age". We explain here what the virtual age is, and how is it related to age correcting factors. We illustrate our common results about the virtual ages on the example of the Gompertz-Makenham law of mortality, and discuss the relations of the longevity, mechanism of aging and age affecting control. As a consequence, a concept of age determination is proposed. Numeric and graphical examples are provided.

1. Introduction

This study has been induced by the number of presentations and articles presented at the First French-Russian Conference on Longevity, Aging and Degradation Models in Reliability, Public Health, Medicine and Biology (LAD'2004), hosted by the Saint Petersburg State Polytechnic University, Russia in June 5-11, 2004 [1], [5], [6]. It has been a demonstration that probability and statistical methods cover an enormous ground of research and can successfully handle most of situations involving uncertainty in any area of human activity. One of these is the study of biological systems, particular case of which is every kind of live organisms.

1.1 Bio-Systems as Devices

Bio-systems can be considered as a specifically organized devices constructed to perform some preset functions, according to their genetic programs. These functions are performed in the presence of a great number of random factors (environmental conditions). Following Koltover [5], we may schematically consider any operation bio-system as a multi-dimensional time-dependent random vector $\mathbf{Y}(t) = (Y_1(t), Y_2(t), ...)$ each component of which corresponds to a relevant functional parameter of the device. There exists a relevant subset $\boldsymbol{S}$ of points in the space where $\boldsymbol{Y(t)}$ belongs which corresponds to the feasible (admissible) values (limits) of the functional parameters. If $\boldsymbol{Y(t)} \in \boldsymbol{S}$, then the device (bio-system) is defined as having normal operation at the time t. Whenever $\boldsymbol{Y(t)}$ passes beyond the limits of $\boldsymbol{S}$, then the device gets a failure. Sometimes $\boldsymbol{S}$ may also depend on time, or may be a random set. It is assumed $\boldsymbol{Y(0)} \in \boldsymbol{S}$. Life time of the device as a whole is defined by the random variable

$$\tau = \max\{t : t \geq 0, \mathrm{Y}(t) \in S\}. \qquad (1)$$

It represents the time of non-failure operation of the bio-system. The life time distribution is presented by the function

$$F(t) = P(\tau \le t)\,. \tag{2}$$

1.2 Reliability of Bio-Systems

Reliability of the bio-system is the probability of non-failure operation within the interval of time (0,t), i.e.

$$R(t) = P(\tau > t)\,. \tag{3}$$

For bio-systems it is known as *survival function*, and denoted by $S(t)$

Consequently, all the statistical procedures used in reliability theory can be used in evaluation of the reliability function *R (t)* from many independent copies, *N,* of independently operating bio-systems as the ratio *N (t)/N*. Here *N(t)* is the number of those bio-systems which are alive (do normally operate) at the instant *t.* Also, the mortality rate function

$$\lambda(t) = -\frac{d}{dt}\ln R(t) = -\frac{R'(t)}{R(t)} = \frac{f(t)}{1-F(t)} \tag{4}$$

appears as an analogue to the failure rate function, used in technical reliability. The *f(t)* here is probability density function of the life time distribution. The time *t* just survived by a bio-system is called its calendar age. Therefore, the same mathematical theory of reliability is essentially applicable to the mathematics of mortality. Our article is a step in this direction.

2. Main Models and Results

The specification of components of the random vector ***Y(t)*** for bio-systems, the use of random modeling and analysis helps to understand how the improvement of its reliability can be attained, and how to keep a better control on the survival of such systems. There are lots of analogies as well a number of specific differences in modeling and studies of reliability of technical devices and for the bio-systems. For instance, bio-systems are obviously subject of wearing and aging. Bio-systems have a proven life-span (something like a maximal value of the life time τ beyond which no copy of the bio-system can pass). Life span for people is, for instance, 120 years. Life spans have also most of the functional components of the bio-systems. Life span for people's brain is 250 years. For technical devices the exponential, the Weibull, the Gamma, and even the Norman distributions frequently fit for modeling the life times. For the bio-systems, despite of their complexity, there exists some "universal kinetics of the growth of mortality with the age", expressed by the Gompertz-Makenham law of mortality

$$\lambda(t) = \beta + \alpha e^{\gamma t}\,. \tag{5}$$

Here the parameters α, β, and $\gamma > 0$ are independent on time. The Gompertz – Makenham mortality law has been confirmed for people and for other mammals, flies, mollusks [5] with specific values of its parameters. From [5] we find that for people parameter $\beta \neq 0$ if the age is less than 35 years, and $\beta = 0$ if the age is greater than 35. We treat this parameter β as a collaterals mortality rate (e.g. accidentals, casualties), and guess that its numerical value may vary for different countries and species. For our numeric and graphic examples later we take the value of $\beta = .0025$. Values of parameters $\alpha \approx 42.827 \pm 8.85$ years, and $\gamma \approx .094 \pm .0014$ years^{-1} are assumed (evaluated) for ages above 35 and less than 95, according to [5].

We consider here the effects of drug use that may slow down, or accelerate the aging for people in a proportional fashion as it is modeled and used for technical items in [2] and [3]. Then we study graphically the effects on mortality rates and the life span on people as functions of the age reducing, or age accelerating effects depending on the dosage of medication or treatment. Numerical examples are using values seeming reasonable for the people.

3. The drug use effects

The most convenient description should be given in terms of the mortality rate function $\lambda(t)$ and the related to it hazard function $\Lambda(t) = \int_0^t \lambda(u)du$. There is a convenient relationship between the probability characteristics of the original lifetime X of an individual and these functions.

Let the initial life time, X, be a continuous random variable (r.v.) with c.d.f. $F(x) = P(X \le x)$, and have a p.d.f. $f(x) = \frac{d}{dx}F(x)$. Then its hazard function is

$$\Lambda(t) = -\ln[1 - F(t)] \text{ for } t \ge 0\,, \tag{6}$$

and its mortality rate function is

$$\lambda(t) = \frac{d}{dt}\Lambda(t) = \frac{f(t)}{1 - F(t)}. \tag{7}$$

In reliability works is shown that the temporary failures which do not affect the failure rate after recovery (known as minimal repairs), have Poisson distribution with mean $\Lambda(u + v) - \Lambda(u)$ for their total number within any time interval $[u, u + v)$, $u, v > 0$.

Drug use activities may improve the performance of the individuals and give them a ``new life". The specifics of the drugs, its intake amount of labor, recovery time, or money invested in the health care may have significant impact on the health improvement, which directly affects the longevity of life. If assume that health improvement prolongs the life of such individuals by certain percentage δ, we call it an age- reducing factor. Fig. 1 a) and the model (8) below explain how it happens with actions made on the individual mortality rate.

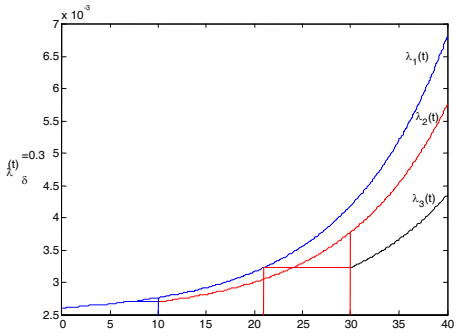

Fig.1 a) Individual mortality rate under age-reducing factor

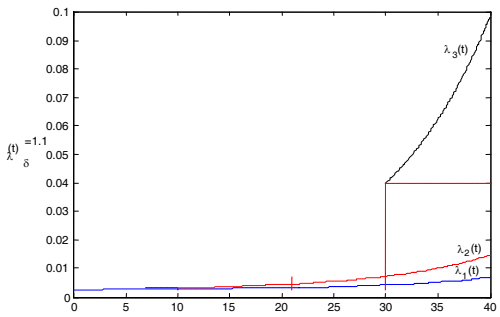

Fig.1 b) Individual mortality rate under age-accelerating factor

Fig. 1. Changes in the individual mortality rates in time with an age affecting factor

We consider also drug abuses (analogous to the reliability maintenance under imperfect repairs) that may shorten the life. Such actions affect the future performance of the individual, and are related to an age-accelerating factor δ, which is equivalent to reducing the overall life of such individuals by certain percentage δ. Fig. 1 b) and the model and the theorem below explain how it happens changes in the individual mortality rate.

Let X_i denote time intervals between successive epochs of drugs intake that affect the individual. Assume that δ_i denote the lack of perfection the life system of an individual may get as a result of the *i*-th action. The values

$$T_0,\ T_i = T_{i-1} + X_i\delta_i\ ,\ \ I = 1, 2, 3, \ldots \tag{8}$$

are understood as *virtual ages* of the individual right after the *i*-th action. When $\delta_i = 1$, then no improvement or deterioration of the virtual age of the individual occurs at the *i*-th epoch of action. When $\delta_i < 1$ (or if $\delta_i > 1$), then an improvement (or a deterioration) of the virtual age of the individual occurs at that epoch.

The model described here is also known in Reliability as Kijima's model II [4].

We consider this model with the assumption that $\delta_i = \delta \neq 0$, and call this δ an *age-correcting factor*. If $\delta < 1$, we call it *age-reducing factor*, and if $\delta > 1$, we call *age- accelerating factor*.

Assume instantaneous effects, continuous non-decreasing virtual hazard function $\Lambda^*(t)$ as a function of the time parameter *t,* and having right derivative $\lambda^*(t) = \frac{d}{dt}\Lambda^*(t)|_{t+0}$. The subscript here indicates that the value of $\Lambda^*(t)$ is considered immediately after an occasional age-reducing action is completed.

Consider the sequence $T_0 < T_1 < T_2 < \ldots < T_n < \ldots$ of times representing the virtual product age after the *n*-th coincident action. Assume that X has a c.d.f. $F(x)$ with $F(0)=0$ and $F(x)<1$ for all $x > 0$. Denote the survival function by $\overline{F}(t) = 1 - F(t) = P\{X>t\}$.

We derive the following expressions.

The *n*-th step transition probability function is

$$P\{T_{n+1} > t \ \big| T_1,\cdots,T_n\} = P\{X > \frac{t}{\delta}\ \big| X > \frac{T_n}{\delta}\} = \frac{\overline{F}(\max[\frac{T_n}{\delta}, \frac{t}{\delta}])}{F(\frac{T_n}{\delta})}\ , \tag{9}$$

for $n = 1,2, \cdots$. The initial distribution is

$$P\{T_1 > t\} = P\{X_1 > \frac{t}{\delta}\} = \overline{F}(\frac{t}{\delta})\ . \tag{10}$$

From (9) and (10), by induction, we get that for any non-negative measurable function $g(t_1,\cdots,t_n)$ and for any *n* it is true that:

$$\boldsymbol{E}[\, g(T_1,\cdots,T_n)\,] =$$

$$\int_0^\infty (\overline{F}(\frac{t_1}{\delta}))^{-1}\int_{t_1}^\infty (\overline{F}(\frac{t_2}{\delta}))^{-1}\int_{t_2}^\infty (\overline{F}(\frac{t_3}{\delta}))^{-1}\cdots\int_{t_{n-2}}^\infty (\overline{F}(\frac{t_{n-1}}{\delta}))^{-1}\int_{t_{n-1}}^\infty g(t_1,\cdots,t_n)dF(\frac{t_n}{\delta})\cdots dF(\frac{t_1}{\delta})\,. \tag{11}$$

Let $\{N_t^v, t \geq 0\}$ be the counting process corresponding to the point process $\{T_n\}_{n=0}^\infty$ defined by

$$N_t^v = \sum_{n=0}^{\infty} I_{[0,t)}(T_n),$$

where $I_B(\cdot)$ is the indicator function of the set *B*.

Theorem 1: The random process $\{N_t^v, t \geq 0\}$ is a non-homogeneous Poisson process with a leading function

$$\Lambda^v(t) = -\log[1 - F(\frac{t}{\delta})] = \Lambda(\frac{t}{\delta}), \tag{12}$$

where $\Lambda(t) = -\ln[1 - F(t)]$ is the leading function of the NPP associated to the life time *X* of this individual.

The proof can be found in [3].

Equation (12) shows that the transformation between the calendar and the virtual time scales is $t \to \frac{t^v}{\delta}$, i.e., if the virtual age of the individual is t^v its corresponding calendar age *t* is t^v / δ. Therefore, we may expect that when the calendar age of an individual acting under age correcting factor δ is *t*, then its virtual (we would say, actual) age is δt.

Denote by *T* the r.v. representing the virtual lifetime of the individual. The c.d.f. of *T* is $F_T(t) = 1 - e^{-\Lambda^v(t)}$. Equation (12) also shows that $P(T \leq t) = F_T(t) = F_X(\frac{t}{\delta}) = P(X \leq \frac{t}{\delta})$. Therefore, $P(T \leq t) = P(\delta X \leq t)$, and this means that **the virtual lifetime *T* and the multiplied by δ calendar lifetime *X* are equal in distribution**, i.e.

$$T =^d \delta X. \tag{13}$$

When the individual is at calendar age *x* its virtual age measured at the calendar age scale is δx. At calendar age *x* an individual maintaining himself under age-correcting medication of factor δ, lives as a new individual at age δx. Thus

$$\lambda^*(x)dx = \lambda(\delta x)dx$$

i.e., the probability to have a failure of the individual from the original population within the interval $[x, x + dx)$ is the same as the probability to have a failure from the population of individuals, maintained by age-affecting actions of factor δ, within the interval $[x, x + \delta\, dx)$.

The relation

$$\Lambda^*(x) = \int_0^x \lambda^*(u)du, \text{ and } \Lambda(x) = \int_0^x \lambda(u)du,$$

leads to

$$\Lambda^*(x) = \frac{1}{\delta}\Lambda(\delta x). \tag{14}$$

Theorem 2: The virtual failure rate $\lambda^*(x)$ at calendar age *x,* and the original failure rate are related by the equality

$$\lambda^*(x) = \lambda(\delta x), x \geq 0, \delta \neq 0; \tag{15}$$

The virtual hazard rate $\Lambda^*(x)$ and the original hazard rate $\Lambda(x)$ are related by equation (14).

An age-reducing factor δ slows down the aging process of the individual by 100(1-δ) %.

Example 1 The *Gompertz-Makenham life-time distribution with an age-affecting factor.*

Consider the Gompertz-Makenham life-time distribution, $X \in Gompertz(\lambda(t,\beta,\alpha,\gamma))$, which is proven to fit the cells and most mammal's life [5]. From relationships (10) – (12) we get

$$F(t) = P\{T_1 \le t\} = 1 - e^{-\int_0^t (\beta + \alpha e^{\gamma u})du} = 1 - e^{-\beta t - (\alpha/\gamma)(1-e^{\gamma t})}, \tag{16}$$

and

$$f(t) = (\beta + \alpha e^{\gamma t}) e^{-\beta t - (\alpha/\gamma)(1-e^{\gamma t})},$$

with λ(t) given by equation (10), and

$$\Lambda(t) = \beta t + \frac{\alpha}{\gamma}(1 - e^{\gamma t}), \ t \ge 0.$$

Here β is a constant rate parameter, α is a secondary time-scaling parameter, and γ is an aging rate parameter.

If the individual has the Gompertz-Makenham life-time distribution with parameters β, α, and γ, and is maintained under age-affecting factor δ > 0, then its virtual failure rate and virtual hazard rates are given by the equations (14), (15), namely

$$\lambda^*(t) = \beta + \alpha e^{\gamma \delta t}, \ t > 0, \delta \ne 0, \tag{17}$$

and

$$\Lambda^*(t) = \beta t + \frac{\alpha}{\delta\gamma}(1 - e^{\gamma \delta t}), \ t \ge 0. \tag{18}$$

Figure 2 illustrates the behavior of the two functions $\lambda^*(t)$ and $\Lambda^*(t)$ under various values of the age-affecting parameter δ. For values of the parameters α, β, and γ are taken the numbers: β=.0025 when $t \le 35$, and β = 0 for $t \ge 0$. For both cases α = 42.827, and γ = .094 as proven to be valid for the human beings with an age between 35 years and 94 years, according to [5]. And respective graphs also are for the ages between 35 and 120 years. For ages between 0 and 35 we assume β=.0025

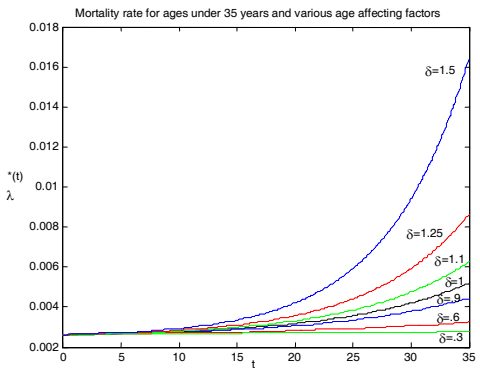

Fig. 2.a.1. Age below 35 years

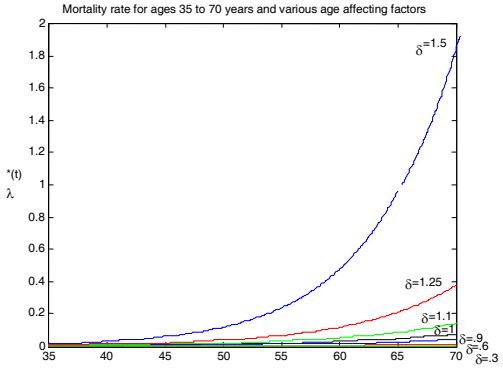

Fig. 2.a. 2. Age above 35 years

Fig. 2 a. Mortality rates $\lambda^*(t)$ for various δ.

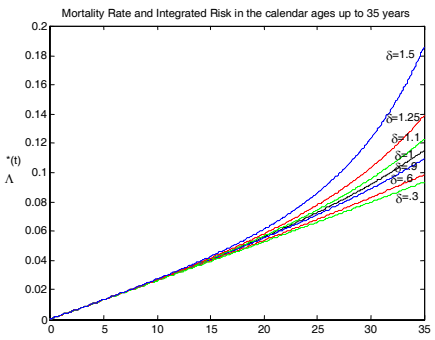

Fig. 2.b.1. Age below 35 years

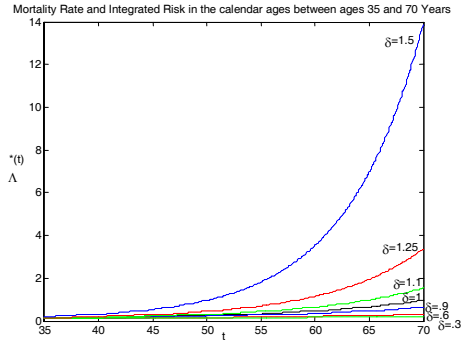

Fig. 2.b.2. Age above 35 years

Fig. 2.b. Integrated mortality rate (hazard rate, integrated risk) $\Lambda^*(t)$ various δ.

Fig. 2. Mortality Rates and Integrated Risks in the calendar ages

4. Comparative ages between different groups

Now we illustrate one possible use of the results obtained in Section 3 by considering again the Gompertz-Makenham life-time distribution. We will think in terms of the human beings as belonging to various groups (or populations) determined by the values of the age-correcting factor δ. As we noticed before, even being at a same calendar age t the individuals from different populations would have different virtual (or as we say, actual) age. Since the only convenient time scale is the calendar age, it makes sense to speak about comparable or equivalent ages between the individuals from different groups. Using the relationships (6), (16) and (18) we find the life-time distribution function for each population determined by the value δ of its age-correcting factor:

$$F_\delta(t) = 1 - e^{-\beta t - \frac{\alpha}{\delta\gamma}(1-e^{\delta\gamma t})}. \tag{19}$$

Equation (19) represents the probability that an arbitrary selected individual from the population with age-correcting factor δ will not survive the calendar age t. The function

$$S_\delta(t) = 1 - F_\delta(t) = e^{-\beta t - \frac{\alpha}{\delta\gamma}(1-e^{\delta\gamma t})} \tag{20}$$

is known as the survival function for the individuals in this population. Its meaning is the same as for reliability expressed by equations (1)-(3). We abandon the notation $R(t)$ and leave it for cases of technical issues.

Definition: We say the age T_{δ_1} of the individual from the population with age-correcting factor δ_1 is equivalent to the age T_{δ_2} of the individual from the population with age-correcting factor δ_2, if it is fulfilled

$$S_{\delta_1}(T_{\delta_1}) = S_{\delta_2}(T_{\delta_2}). \tag{21}$$

In the sense of this Definition, every age of one of the two populations has equivalent comparable age to the other population. Ages are equivalent when the probabilities to survive these respective values T_{δ_1} and T_{δ_2} are equal. When we pick δ = 1, we see to what calendar age of the

normal human population and individual from the population with age-correcting factor δ will be equivalent. Since this is the only available age information, when we know δ we may see what the true age of an individual from the respective population.

However, we notice that equations (21) may be quantified, since these are probabilities. If we select any probability level $p \in (0, 1)$, we will get all the equivalent ages T_δ (p) at this level for all the populations just as solutions of the equations

$$S_\delta(T_\delta) = p.$$

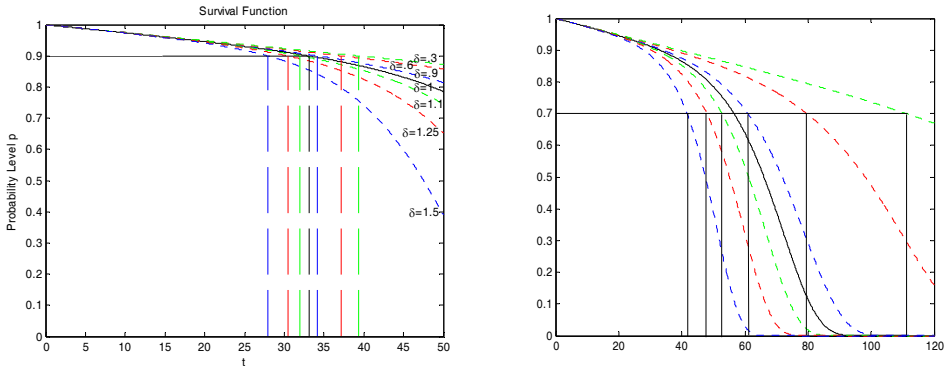

Fig. 3. The survival functions and equivalent ages for the individuals from the population with age-correcting factor δ.

Fig. 3 illustrates the equivalency between the ages of several δ-populations at the survival probability levels $p = .9$ and $p = .7$. The continuous black line traces the "normal population" where δ = 1. The meaning of the numbers is following: At level .9 the age of the normal population is, say, 33. The age-accelerated population with δ = 1.5 will look like this 33 years old people already being at age 28. Similarly, looking on the graph for the equivalent ages at probability level .7, we notice that the end of life for average individual from the normal population is about 95 years, while for these from the age-accelerated population with δ = 1.5 it will be about 64.

We evaluated the equivalent ages for several probability levels, and the results are shown on next table. In bold black digits are shown the respective ages for the normal population at the corresponding level of survival. In the same line of the level are shown the ages in the other populations, at which an average individual would look (have the age) like this in the normal population. One may see some unreal numbers which we also need to comment. For instance, at level .25 individuals in the normal population have properties as 75 years old, while same properties would be in possession by the average individuals at 82 years age if they reduce their ages regularly by a factor δ = .9 (an improvement by 10 % compare to the normal). In the same line we see that the same properties would have the 114 year old people in the population who got 40 % improvements regularly. Finally, we see that as a 75 year old normal individual would have been an individual at age 197 if it was possible to reduce the age regularly by 70 %. Numbers in the last column are somewhat unreal, because they represent a mystic dream for such high level of age reduction.

Table 4.1. Equivalent ages under various age correcting factors at different levels of survival.

p \ δ	1.5	1.25	1.1	**1**	.9	.6	.3
.9	28	30	31	**33**	34	37	39
.7	42	45	50	**58**	61	80	112
.5	48	55	61	**66**	72	98	158
.25	53	62	69	**75**	82	114	197
.1	57	66	75	**81**	89	125	220

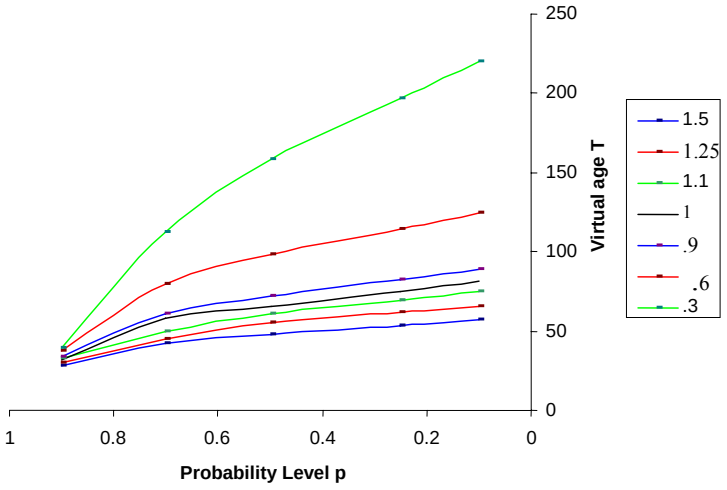

Fig. 4. Equivalent ages for various values of age correcting factor and various values of the age-correcting factor.

On Fig. 4 we show the same numbers in the table as a graph of the equivalent ages that can be approximate to get equivalent ages at any survival level. This graph could be used as a chart for a number of useful comparisons. The black middle line shows the calendar age of the normal population. If one chooses an age, let say, 50 within his population, and draws a vertical line at the heights of the points of intersection with the other graphs one may find at what calendar age the individuals from other populations are, which is equivalent to his. Taking an individual from the normal population at any age in the same way it can be shown to what age he would have been if he was using age corrections as do the individuals from the other populations.

We believe that there is a fresh idea about how to treat age related questions, how to compare ages among different populations, and even, how to work out an approach towards the accelerated life testing based on the above considerations. And this discussion we postpone for another article.

5. Life supporting (insurance) costs associated with an individual during some assigned time

Certainly, there are some costs associated with any improvement or deterioration. Denote by $C_r(u,\delta)$ the cost of an age-affecting action of factor δ at calendar age u of the individual. A natural assumption is that $C_r(u,\delta)$ satisfies the inequalities

$$C_m(u) \le C_r(u,\delta) \le C_c(u),$$

where $C_m(u)$ is the cost for the minimal support of the individual at calendar age u, and $C_c(u)$ is the cost of the complete (radical) loss of the individual at age u. In the sequel we develop a radical modeling for comparing of the expected expenses associated with the life support of individuals under regular life-supporting "maintenance", and these with age-affecting factors. As a matter of fact, the comparison of the virtual ages of individuals at the same calendar age T indicates that those who have used an age affecting action of factor δ differ from what this calendar age is. These are based on comparing the values of the survival functions given by equations (20), Table 4.1 and Fig. 4 shown in the previous section. Struggle to keeping a constant age-correcting factor we call *maintenance policy* for the life style. Hence, the life supporting costs depend on the insurance agreement and the maintenance policy.

We assume that an individual is covered by insurance for some calendar time of duration T, according to a certain policy agreement.

Consider cost modeling from insurer's point of view. The insurer covers all, or a portion of the expenses associated with the needs and supports of the individual starting at age t_0, until the expiration of the insurance coverage, or until the death of this individual. In occasion of a death at age u the insurer pays the amount $C(u, \delta)$, if the case is within the time of the action of the insurance agreement.

5.1. Expected insurance costs for a policy with limited validity

Consider an insurance policy, which starts at age t_0 of an individual, and will last time of duration W, i.e. the insurance policy is valid during the calendar age $[t_0, t_0 + W]$ of that individual. On the other hand this individual has been maintained, and will maintain his life under an age-affecting factor δ. Assume, that the original life time X of the population at this site has failure rate function $\lambda(t)$. During the coverage no partial claims are possible.

The effect of the initial age t_0 of the individual at the start of the insurance coverage is also a parameter of interest, which may affect the expected insurer's expenses. The collected premiums usually are proportional to the elapsed time, u, and may depend on the initial age t_0 when the policy starts, and the supposed age-affecting factor δ. Therefore, the collected premium on the interval $[t_0, t_0 + u)$ equals $C(t_0, \delta)u$. If the failure is beyond the assigned insurance period, the insurer incurs no expenses. If the death occurs at a moment on the interval $[t_0, t_0 + u)$, the insurer refunds the insured by the amount $C(u, \delta)$, thus his expenses are determined according to

$$C(u) = C(u, \delta) - C(t_0, \delta)u .$$

Particular forms of these functions are assumed. Most common seems

$$C(u, \delta) = C = const, \text{ and } C(t_0, \delta) = c_0 + c_1 t_0 + c_2(\delta - 1), \qquad (19)$$

so that if the individual maintains the regular way of life he pays no addition or gets no discount expressed by the third component.

Lemma 1 The expected insurance cost associated with an age correcting factor δ for an individual insured at age t_0 with coverage of duration W is given by

$$C_W(t_0,\delta) = \int_0^W \{C(t_0+u,\ \delta) - C(t_0,\ \delta)u\}\,\lambda(\delta(t_0+u))\ e^{-[\frac{1}{\delta}\Lambda(\delta(t_0+u))-\Lambda(\delta t_0)]}du\ , \qquad (20)$$

where $\lambda(t)$ and $\Lambda(t)$ are the original failure rate and hazard rate functions associated with the life time X of an individual in the population.

Example 2 *The Gompertz-Makenham life-time distribution with an age-affecting factor*

Assume, that the contract prices $C(u, \delta)$ and $C(t_0, \delta)$ for an individual insured at age t_0, are given by the equations (19). Then as a Corollary of Lemma 1 and the previous discussion we get:

Corollary 1. Under the conditions of Lemma 1, and (17)-(19), the expected incurred insurance costs are given by the expression

$$V\ C_W(t_0,\delta) =$$

$$C[e^{-\beta t_0-(\alpha/\gamma)(1-e^{\gamma\delta t_0})} - e^{-\beta(t_0+W)-(\alpha/\gamma)(1-e^{\gamma\delta(t_0+W)})}] - [c_0 + c_1 t_0 + c_2(\delta-1)] \int_{t_0}^{t_0+W} u(\beta+\alpha e^{\gamma\delta u}) e^{-\beta u-\frac{\alpha}{\delta\gamma}(1-e^{\gamma\delta u})} du\ .$$

We work on graphical illustrations of the dependence of $C_W(t_0,\delta)$ on the individual's age t_0 at the time of enrolment into the insurance, for the Gompertz-Makenham lifetime distribution with parameters as for human beings, and for different values of the coverage period W in years.

The effects of increase or decrease of the insurance premiums and costs should be justified. The dependence of the costs and premiums on the calendar age t_0 of individuals and its interaction with the age correcting factors might be reviled.

6. Conclusions

Age-affecting actions on live individuals may have feasible models, and the life supporting (insurance) cost for some natural policies can be analyzed by making use of approaches similar to those in reliability maintenance and warranty cost analysis.

It is shown that the failure rate function and hazard function provide more convenient tools to age-dependent life modeling than the approaches based on the direct use of probability distributions of the individual's life times.

Numerical and graphical examples illustrate the use of the proposed models with Gompertz-Makenham mortality rates and respectively distributed life times with an age- correcting factor for comparing ages between individuals.

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