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short communication

The Stochastic Determinism of Aging and Death

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Abstract

Background. *We have studied human life expectancy in Croatia.*

Materials and Methods. *Local daily papers reported obituitairies for 447 men and 366 women who died in a month period. The data were analyzed with the median derivative power function model.*

Results. *The median age of death was 76 and 81 years for men and women, respectively. Cummulative mortality increases at a constant rate after the age 60 y and 65 y for men and women, respectively (r^2 = 0.99 and 0.98).*

Conclusions. *Individual life span is a stochastic (random) biological event within the deterministic frame of cumulative mortality.*

INTRODUCTION

We may be still missing the true answer to what life is *(1)*, but we may define the crucial steps in a common life cycle, i.e., conception, birth, growth & development, maturity, senescence, and death. Evidently, the life cycle is a time limited affair unless one believes in resurrection (Christianity), reincarnation (Buddhism), and transformation (Taoism) of his/her eternal soul. As the world population is living longer, the number of older people is also growing and centenarians are not exceptionally rare today *(2)*. Presently, geriatry is a recognized medical discipline on its own as it became evident that the health and disease of senescent (aged) population forms a distinct medical entity *(3)*.

Senescence is characterized by the involution of all the body organs, the shrinking of their size and decrease of their functional capacity *(4)*. Indeed, the brain is shrinking *(5)*, hormone production is being reduced *(6)*, hair follicles are decaying *(7)*, muscle are losing mass *(8, 9)*, skin is losing its quality *(10)*, bones are becoming brittle *(11)*, genetic expression is slowing down *(12)* ... – it is like Kubrick's HAL 9000 (Heuristically Programmed Algorithmic Computer) from „2001 A Space Odyssey," a movie where the entire space ship, and not only its artificial intelligence, is decaying, and where the rate of decaying of different components of the system may not be uniform. Today, special attention is payed to the mobility of senescent patients, their gait and vigour of movements, and cognitive capacity – all in order to help sustain their self-reliance. Indeed, the involution of the muscle-skeletal system in the senescent persons due to muscle mass loss (sarcopenia)*(8, 9)* and bone loss (osteoporosis)*(11)* make senescent people more prone to falling and bone fractures. Apparently, regular physical activity is essential for health of senescent people, at the least as long as such a capacity for mobility is sustained *(13)*. Adequate diet also should be included *(14,*

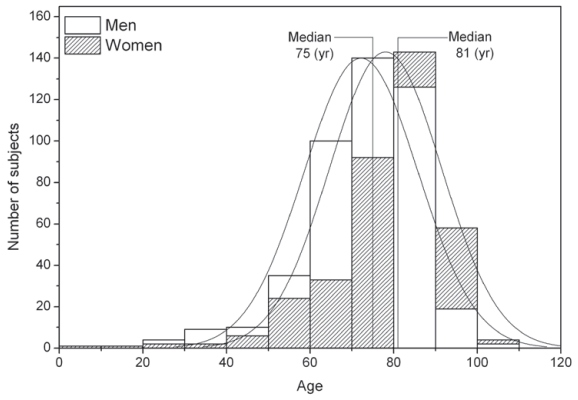

Figure 1. *Medians and mortality frequency distribution for men and women*

15). At present, there is no available scoring system of validation which can reliably assess and grade the physical status of the aging people and their fraility *(16).*

The first author's personal encounter with senescence came when he was refused a travellers health insurance because he was over 71 years old. Since everybody's biological and chronological age may differ, that refusal stimulated him to look at human life expectancy, and to uncover how reliable insurance company profit rules may be. In other words, why do the insurance companies think that they would loose more money then they would make, if they insure one person at the age of 71. Indeed, and for the record, the first author encounter with senescence was when his Institute retired him at the age of 65 y. This study clearly demonstrated that such life span time boundaries are a *sancta simplicita* bureaucratic delusion of not differentiating between the biological and chronological age, respectively.

SUBJECTS AND METHODS

During the summer months August 15 till September 15, 2013, the first author of this paper followed the obituaries published in a daily newspaper Večernji List (edition

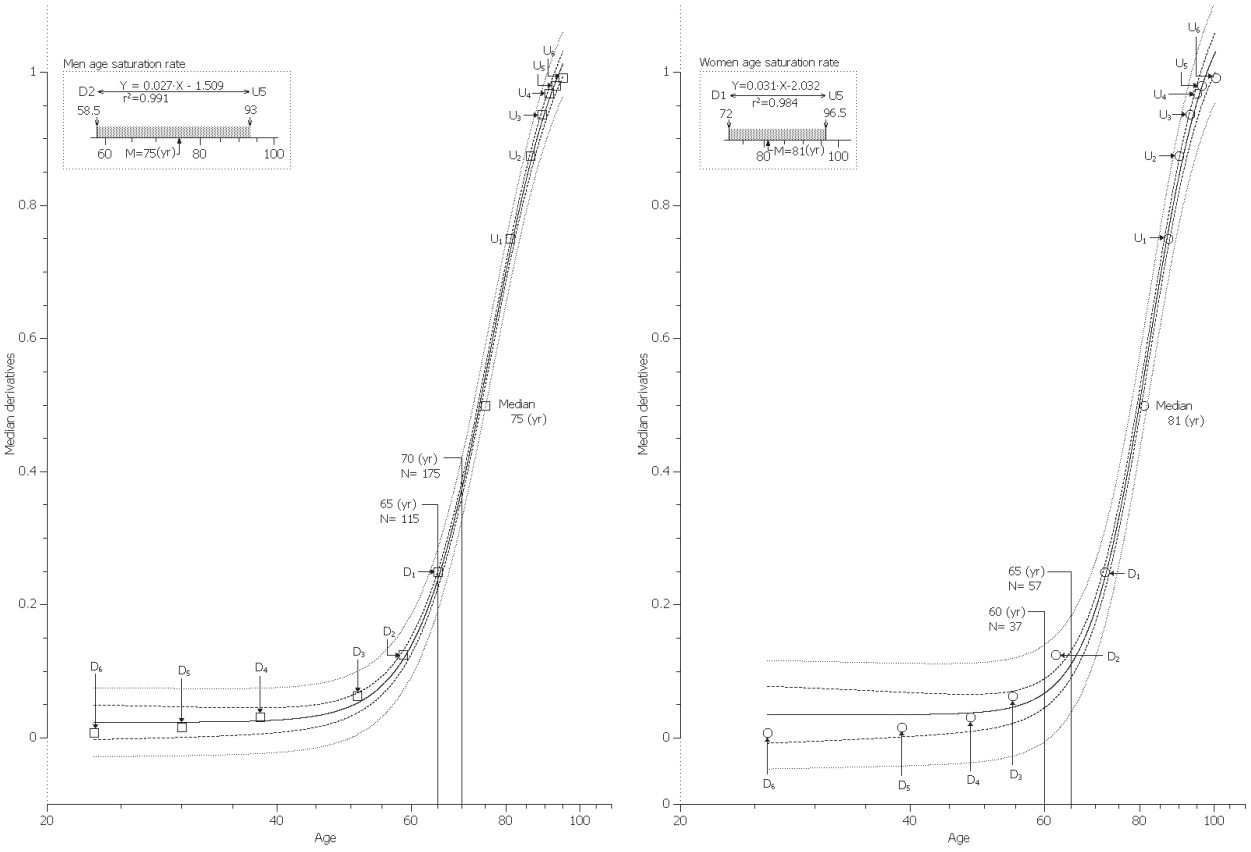

Figure 2. *The power function of the mortality median derivative frequency distribution: Men=477 (□) and Women=366 (○). D, U Men downward (D) and upward (U) median derivatives, d,u Women downward (d) and upward (u) median derivatives.*

––– Logistic function: $A_2 + (A_1 - A_2)/(1 + (X/X_0)^p)$,

––– 0.95 confidence limit, ··· 0.95 prediction limit

Men: $Y = 1.15 + (-0.02 - 1.15)/ [1 + X/76.43)^{9.00}]$

Women: $Y = 1.14 + (-0.03 - 1.14)/ [1 + X/82.14)^{11.13}]$

(see Appendix for model and Table 1. for input values)

for Primorsko-goranska županija, CROATIA). There were 813 obituaries reported (447 men and 366 women), showing their birth and death dates or total life span in years; there were also 54 more subjects of both sexes whose obituaries did not provide enough data to calculate their length of life. Since the data were publically displayed, and since their names or other whereabouts were not used, there were no ethical considerations involved in this study that would require an informed consent or implementation of the Declaration of Helsinki *(17)*.

Traditionally, the mortality rates are calculated by Gompertz attrition model of actuarial statistics and its numerous variants (18). This method oversimplifies and ignores the non-linear aspects of mortality frequency distribution curve (mortality tables); regardless of its limitations the method is the founding stone of the insurance business in the world today. To scrutinize mortality frequency distribution, we used the median derivative model (Appendix 1) to fit the sigmoid logistic regression analysis function for life span and mortality frequency of men and women separately

$$A_2 + (A_1 - A_2) / [1 + (x/x_0)^p]$$

where A_1 is initial value (lower horizontal asymptote), A_2 is final value (upper horizontal asymptote), x_0 is centre (point of inflection, in our case it is the median M_0), p is power (the parameter that affects the slope of the area about the inflection point). The Qtiplot Data Analysis and Scientific Visualisation program was used for this analysis (www.soft.proindependent.com/qtiplot.html). We used this model for assessing the respective environmental silver body exposure and iodine nutritional status *(19, 20)*.

RESULTS AND DISCUSSION

The median life expectancy of men was approximately six years lower than that of women; it was approximately 75 years for men and 81 years for women (Fig.1). When the data on the age of death (Table 1) were presented as a median derivative power function (Appendix 1), a sigmoid saturation curve was generated having a long linear segment of cumulative mortality. The sigmoid curves with their linear segments are presented separately for men (Fig. 2a) and women (Fig. 2b). Evidently, the scythe of death was reaping human lives at a steady exponential rate, indicating that presently half of all the living men and women won't make their 75' or 81' birthday, respectively. The chance of a man of my generation 42' to became a centenarian, is less than one percent.

That the number of living persons is decreasing with the increased age is not a surprise. However, it is disturbing, that already at the age of 50 the life expectancy started to diminish at an accelerated rate. Indeed, half of men and women would not make it to live up till the age of 75 y for men and age 81 y for women. That fact of life, e.g. that there is a human population having a short life span, is usually neglected. Apparently, some humans may have a decisive determinant that their candle of life, or vital breath, or whatever, is going to run out short, and leave them in oblivion at an early age. This process of dying is certainly deterministic, because we will all die some time, but it is also stochastic (random) because we still do not know who will be the one called out from the stream (flow) of life *(21)*. Our results point to the sobering fact that the average life expectancy is our statistical mental construct suitable for actuarial statistics of the insurance companies *(18)*. However, this analysis also shows how senescence and mortality, although related phenomena, are distinct entities. After the age of 60 y for men, and 65 y for women, the human population, i.e., the human population biomass („bioplasma"), is decaying (dying) at an impressive constant rate (r^2 = 0.99 and 0.98 for men and women, respectively). The fact that we all belong to some geneticaly defined group of life forms, e.g., humans in this particular case, and hence we all have some common features discernible by statistical analysis (mortality), it is still far away from determining what actually induces individual rates of aging and death, i.e., your or my life span.

The key element of senescence appears to be the loss of our viable cells across the tissues and organs of the body, so that the cellular matrix, like a coral reef, remains after

Table 1. *Mortality median derivative frequency distribution (MDFD): Men (D_1–D_6 downward MDFD, U_1–U_6 upward MDFD) and Women (d_1–d_6 downward MDFD, u_1–u_6 upward MDFD).*

	MEN	Median$(M_0)_{n477}$ = 75 yr					WOMEN	Median$(M_0)_{n366}$ = 81 yr			
MDC	n	Age	MDC	n	Age	MDC	n	Age	MDC	n	Age
D_1	224	65	U_1	224	81	d_1	183	72	u_1	183	87
D_2	112	59	U_2	112	86	d_2	92	62	u_2	92	90
D_3	56	51	U_3	56	89	d_3	46	55	u_3	46	93
D_4	28	38	U_4	28	91	d_4	23	48	u_4	23	95
D_5	14	30	U_5	14	93	d_5	12	39	u_5	12	97
D_6	7	23	U_6	7	95	d_6	6	26	u_6	6	101

Common Median $(M_0)_{n813}$ = 77 yr

its inhabitants, the living cells or corals, have already gone. What is that built-in transforming power that terminates our body-state of 10^{12}-10^{16} united cells *(22)*, and now replicated in some $7{\cdot}10^{9}$ human beings living around the world today, remains to be elucidated. Our life span may be related to apoptosis *(23)*, free radicals *(24)*, telomere shortening *(25)*, failure of stem cell regeneration *(26)*, lack of caloric intake restriction (so that the body metabolism operates at an enhanced rate) *(27)*, or something else. Apparently, these undetermined factors affect our lives more than we think. It is pertinent to note here that dietary restriction slows down cancer cell growth *(28, 29)*, and today the "fat based ketogenic diet" (a highly restrictive calories, carbohydrate, and protein diet) *(30)* appears to be a promising new concept in cancer nutrition.

If we now look at odds for an insurance company to make (or lose) money on ensuring aged subjects, then the chance of a man's dying before the age of 65 and/or of 70 would be ≈35% and ≈40%, and for women 60 and 65 years old ≈20% and ≈25%, respectively. The first author's chance of making 72 would be about 55% and insurance company loss chance may be estimated at some 45%, meaning that the odds for insurance company to make money were better. As a matter of fact, by knowing reasonably well the rate of death, the insurance companies could make more money; especially if they add some correction factor that would additionally improve their chances to earn somebodies money. Knowing the chance of accurately assessing life expectancy (the risk factor), may be also of some use to the practicing physician to set his diagnostic and therapeutic goals within a suitable age-dependent time frame. Please, note, that we are not advocating the idea of penalizing aged people for being old and living too long by some insurance company actuarial accounts. Or any other gambling „Casino game" of the insurance companies. As a matter of fact, the provided statistical data may guide our Public Health authorities on how to provide a reliable and sustainable system of health protection to provide a decent end of life to its senior citizens beyond „the right to die". Moreover, since senescence is a process with a different rates of change for the participating decaying individuals, there is a fallacy in reasoning that all the people lose their capacity, like working capacity, at the same chronological age. Indeed, there is no iron-clad „one size fits all" age, that would force all women and men to retire at the age of 60 and 65, respectively. Some of them would be already dead, but some of them would carry on in this „Casino game" of life.

The riddle of human life and death *(31)* will surely be an intriguing and challenging agenda for years to come *(32)*. However, we have to develop new methods to accurately assess the actual status of the aging human body and to find the means on how to keep the frail body of old age as mobile and mentally alert as long as possible. Indeed, the senescent human being can be fragile, but still mobile and mentally alert. With the exploding advancement of the medical science and technology *(33)*, it may be difficult to provide all the needed health services for all the ailing and diseased aged people *(34)*. Indeed, life span and senescence are a complex human biological traits not to be mechanically subsumed under the chronological age.

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Appendix 1. *The median derivatives model (Population Size, PS = 1.000)*

Median ($M_{0,n=870}$ = 0.499 μg·g^{-1})

<–––––––––––––––––––––––––––––––––––>□<–––––––––––––––––––––––––––––––––––>

Median Derivative Downward (Descending) Branch ($D_{0,n=435}$ = PS/2 = 0.500) Descending Median Derivatives		Median Derivative Upward (Ascending) Branch ($U_{0,n=435}$ = PS/2 = 0.500) Ascending Median Derivatives	
$D_1 = D_0/2$	0.250	$U_1 = U_0 + U_0/2$	0.750
<----------□---------->		<----------□---------->	
$D_2 = D_0/4$	0.125	$U_2 = U_1 + U_0/4$	0.875
<----------□---------->		<----------□---------->	
$D_3 = D_0/8$	0.062	$U_3 = U_2 + U_0/8$	0.937
<-----□----->		<-----□----->	
$D_4 = D_0/16$	0.030	$U_4 = U_3 + U_0/16$	0.969
<--□-->		<--□-->	
$D_5 = D_0/32$	0.016	$U_5 = U_4 + U_0/32$	0.983
<□>		<□>	
$D_6 = D_0/64$	0.008	$U_6 = U_5 + U_0/64$	0.992
□		□	

We studied the frequency distribution of hair iodine (H·I) median and its derivatives to assess the iodine deficiency, adequacy and excess. First we assess the median (M_0) hair iodine concentration of our subject population. By definition, one half of the studied population was above the median (upward median branch, U_0), and the other half was below the median (downward median branch, D_0). Hence, the population size (PS) for M_0 is the sum of the respective upward and downward median branches around the central inflection "hinge" M_0, i.e., PS = U_0 + D_0 = 0.5 + 0.5 = 1.0. Both the respective upward and downward median branches can be further divided in the same "median of median" way into a series of sequential median derivatives ($U_{0,1,2,3\ldots n-1,\,n}$ and $D_{0,1,2,3,\ldots n-1,\,n}$). For every median derivative of the population, the actual hair iodine concentration can be identified. Thus, instead of mechanically throwing the preconceived percentile grid upon the observed data, we inferred the median derivative grid out from the data set itself (35).