

## **Rate of Aging of Chinese Oldest-old and its Determinants**

Kuangshi HUANG<sup>1</sup> Zhuo CHEN<sup>1</sup> Xuying ZHANG<sup>1</sup> Jiehua LU<sup>2</sup> Kirk SCOTT<sup>3</sup>

1 Demographic Laboratory, China Population and Development Research Center

2 Department of Sociology, Peking University

3 Center for Economic Demography, Lund University

### **Abstract**

In recent decades, individual rate of aging has become the most exciting and attractive topic and approximately the core of research on aging. Given that most of current literature of the rate of aging focused on the elderly in developed countries, this project will concentrate on the biggest developing country—— China.

This study uses a longitudinal data from the Chinese Longitudinal Healthy Longevity Survey and frailty index to examine the rate of individual aging of Chinese elderly and its determinants. The key finding is that the mean rates of aging for the elderly at different ages are nearly the same, almost between 2 percent and 2.5 percent each year. The regression results showed that most of variables about the early and middle life are statistically insignificantly, including *the birth place, the current residence, the marriage times, the availability of medical service both at around age 60 and in childhood, and the experience of hunger in childhood*. But some variables are significant, including *doing regular exercise, the adequacy of medical service if seriously ill and sufficiency of financial support for daily costs*. Therefore it is possible for humans to slow the rate of aging, albeit with too slight influence of such efforts.

# Table of Contents

<b>1. Introduction</b> .....	3
<b>2. Literature Review</b> .....	3
<b>2.1 rate of aging</b> .....	3
<b>2.2 determinants of the rate of aging</b> .....	5
<b>3. Data and Method</b> .....	7
<b>3.1 Data</b> .....	7
<b>3.2 Method</b> .....	8
<b>3.2.1 Frailty index</b> .....	8
<b>3.2.2 The slope of linear regression</b> .....	9
<b>3.3 Variables</b> .....	12
<b>4. Results</b> .....	13
<b>4.1 Value and direction of rate of aging</b> .....	13
<b>4.2 Change of rate of aging with age</b> .....	16
<b>4.3 Determinants of rate of aging</b> .....	17
<b>5. Conclusion and discussion</b> .....	21
<b>References</b> .....	22

# 1. Introduction

In recent decades, rate of aging has become the most exciting and attractive topic and approximately the core of research on aging. Study on rate of aging will considerably illustrate the studies on aging because it grasps the key questions of aging as follows: how we age? What is the rate of aging for human? Is it constant over ages? Do all humans have the same rate of aging? Why we age? What kinds of factors affect the rate of aging? Which one has the biggest effect on rate of aging? Can we slow or delay the rate of aging? To what extent we can control our rate of aging? How to slow and delay the rate of aging if possible? The answers of these questions will make us truly become masters of our own lives. Given that most of current literature examined the rate of aging of the elderly in developed countries, this project will focus on the biggest developing country——China.

## 2. Literature Review

### 2.1 rate of aging

Practically, most researchers equated “aging process” with “rate of aging” in their studies. Literally, rate of aging points to a kind of speed or acceleration, which is a more quantitative measurement of “aging process”. Different from the vital rates, such as fertility rate, mortality rate and birth rate as well as death rate, rate of aging refers to the change of aging over age or time, rather than a kind of proportion or ratio. It is precisely because this, we use “rate of aging” rather than “aging rate” . Although the meaning of “rate of aging” is quite similar to that of “speed of aging”, it is widely accepted that the “speed of aging” is mostly used in explaining the change of proportion of 65+ in the total population over time while the “rate of aging” is mainly employed in describing the change of something indicative of aging with age or over time.

The dominating use of “rate of aging” in biology is associated with both mortality and fecundity. The idea that the rate of increase of mortality and decrease of fecundity with age can be employed as a measurement of aging rate has been widely used in many empirical studies by biologist (Linda Partridge, Nicholas H. Barton, 1996). Furthermore, this idea can be measured by the product  $l(x)m(x)$  , which could be viewed as a measurement of the extent of aging in the life history (where  $l(x)$  is survival from birth to age  $x$  and  $m(x)$  is fecundity at age  $x$  (Linda Partridge et al.,1996). However, in many circumstances this measure is a spurious indication of aging, especially in the absence of the real decrease in the phenotype with age although there is an apparent decrease in death rate with age. Therefore Linda Partridge (1996) proposed the Fisher’s “reproductive value” as an ideal index of the

rate of aging.

$$v(x) = \int_x^{\infty} \frac{\ell(y)}{\ell(x)} m(y) e^{r(x-y)} dy$$

Here,  $v(0) = 1$  and  $r$  is the asymptotic rate of population growth, usually taken as zero in many cases.

For those who just focus on later life or at old (advanced) ages, they consider the rates of acceleration of mortality as rate of aging (Johnson, 1990; Elisabetta, 2003) and combine the characteristics such as frailty, morbidity, disability in late life or at advanced ages. In 1979, Vaupel J. et al. incorporated the concept of individual susceptibility to death in the analysis of survival data by devising a frailty model for studying mortality (Vaupel et al., 1979). Afterwards, Yashin et al. proposes a correlated frailty model to solve the problems emerging from the frailty model (Yashin et al., 1995). However, these studies still define rate of aging as the rate of increase in the chance of death due to increasing deterioration with age, namely “the pace of increase in mortality with age” (Vaupel, 2010).

With intensive research on the health of elderly, many studies on frailty or senescence or debility, diseases or morbidity, and disability have emerged. These studies center on the real aging process rather than the outcome (death). So the rate of aging is defined as “rate of increase in the chance of death due to increasing deterioration with age (senescence)” (Vaupel, 2010). In this sense, rate of aging means rate of deterioration or rate of debilitation. Operationalization of these concepts further makes the aging more measurable. Several studies define the changes of aging markers as the rates of aging. So these studies use rates of aging rather than rate of aging, because there are many aging markers, such as lens opacity, hearing, grip strength, skin thickness (Aihie Sayer A, Cooper C, Evans JR et al, 1998). However, the dominating method to measure aging is to build a comprehensive index integrating as many indicators of aging as possible and calculate the change of such index over age as the rate of aging. The term frailty is widely used in geriatricians and gerontologists to describe a range of conditions about aging process in older people. Conceptually, frailty is a kind of increasing risks of loss of independence, although not necessary related with the specific disease and disabilities. More specifically, frailty is a systemic indication of age-accelerated physical and cognitive deficits or impairments (Fried et al., 2004; Kulminski et al., 2006; Kulminski, Ukraintseva et al., 2007; Markle-Reid, 2003; Morley, Perry, & Miller, 2002; Rockwood, Mogilner, & Mitnitski, 2004; Yashin et al., 2007). Previous empirically studies provide two most common methods to operationalize frailty: one is the phenotypic approach and the other is the frailty index (Bergman et al., 2007; Kulminski et al., 2008; Levers, Estabrooks, & Ross Kerr, 2006; Rockwood et al, 2007). The former defines frailty by selecting any three items from dozens of conditions, including weight loss, exhaustion, weakness, slowness, or low physical activity (Fried et al., 2001). Alternatively, the frailty index pays less attention to specific deficits of individuals and more attention to the cumulative number of health deficiencies (Kulminski et al., 2006; Mitnitski et al., 2005). Many studies show that the frailty index is more ideal measurement for predicting mortality than

phenotypic method (Kulminski et al., 2006, 2008; Rockwood et al., 2007), because frailty index has three obvious strengths: firstly, frailty index is easy to calculate as the proportion of cumulative health deficits to all possible deficits for a specific person (Rockwood, 2005). Secondly, frailty index is more aggregate measurement by integrating a variety of psychological, physiological, and functional conditions and abilities (Fisher, 2005; Rockwood, Fox, Stolee, Robertson, & Beattie, 1994). Last but not least, as a proxy for biological age, the validity of frailty index has been widely proved in various populations to be a robust predictor of health change, health care utilization, and death (Goggins, Woo, Sham, & Ho, 2005; Janssen, Shepard, Katzmarzyk, & Roubenoff, 2004; Kulminski et al., 2006; Mitnitski, Graham, Mogilner, & Rockwood, 2002; Mitnitski, Mogilner, & Rockwood, 2001; Mitnitski et al., 2005; Puts, Lips, & Deeg, 2005; Song, Mitnitski, MacKnight, & Rockwood, 2004; Yashin et al., 2007).

Conventionally, for humans, the rate of aging will follow the mortality pattern, namely the exponential model: at the early and mid life the rate of aging is very slow and after 40s the rate of aging goes up quickly and linearly increase in later life. However, some studies show that the rate of aging of the force of mortality will slow down at older ages and the rate of aging seems more likely to follow a logistic pattern with deceleration at advanced ages (Vaupel et al., 1979; Horiuchi and Coale, 1990; Manton and Vaupel, 1995; Thatcher et al., 1998). Gu Danan et al.'s observation also indicate that the curve of mean of frailty index by age from 65 to 109 fit better in with logistic distribution than exponential, linear, or quadratic distributions (Gu Danan et al., 2009). However, linear model of rate of aging also have been developed by empirical and theoretical researches on oldest-old people. Kaare Christensen et al. considered the indicators of aging such as grip strength, disability score, cognitive composite score, and depression symptomatology score, as dependent variables and time as independent variable, then employed the linear regression model and put the slope as the rate of aging (Kaare Christensen et al., 2008). In their four waves of a longitudinal study on the Danish 1905-cohort, Kaare Christensen et al. also views the regression coefficient for the total means as a summary measure of aging at the population level and the regression coefficients conditional on the number of waves of participation as the rate of aging at the individual level (Kaare Christensen et al., 2008). James Vaupel also concluded in his study that the rate of deterioration with age seems to be constant across individuals and over time (Vaupel, 2010). Besides, some studies indicate that in contrast to mortality rates increasing exponentially, the human functional decline tends to be linear (Strehler, 1999).

## **2.2 determinants of the rate of aging**

The studies on the determinants of rate of aging were entirely fuelled by determinants of longevity, health and aging. The association between longevity and genes has been repeatedly examined empirically and theatrically, both in the laboratory and in the field. Although many genes reportedly determining longevity have been found but “none has an effect as big as the modest effect of APOE (the apolipoprotein E gene)”

(Vaupel, 2010) and few has been repeatedly proved in studies. There is no evidence proved that identical twins share a heritable maximum lifespan. Some studies showed that genetic variation among individuals can explain only about 25% of the variation in adult lifespan (McGue, 1993; Herskind,1996). The effect of genetic variation on lifespan seems to have a slight increase with age and there is still modest influence even among the elderly. But the impact of genetic variation might be more pronounced at the oldest ages (Perls,2002). Although there is little success for biologists to identify the major longevity genes in humans (Christensen, 2006), more and more studies show that genes just play a modest role in determining how long humans live (Herskind,1996; Perls,2002; Hjelmborg,2006; Christensen,2006).

Many studies uncover that environmental factors play a bigger role in aging. The evolutionary theory elaborates the role of environmental factors in aging. From an evolutionary perspective, aging either comes from the constrained optimization of the life history (Williams 1957, 1966; Charlesworth 1980, 1994; Kirkwood & Rose 1991; Partridge & Barton 1993) or results from mutation pressure (Medawar 1952; Hamilton 1966; Charlesworth 1980, 1994). The rate of aging is related with the impact of external factors on the survival and fecundity of the population (Medawar 1952; Williams 1957; Hamilton 1966; Charlesworth 1980, 1994). Usually, the higher externally imposed death rates of adults would bring about evolution of higher rates of aging for both survival and fecundity (Linda Partridge, Nicholas H. Barton, 1996).

The relationships between early growth and rate of aging are repeatedly proved. Many studies indicated that rates of aging are to some extent related with early growth. The results from animal's studies have shown that the long-term effects of poor early nutrition on aging are obvious because undernutrition in utero will bring about the raised blood pressure(Langley,1994),altered glucose and lipid metabolism (Hales,1991; Barker,1993)which are related with cardiovascular and other degenerative diseases (Aihie Sayer A et al,1998). The study on human has the similar result that in some systems, events in early life have already programmed the rates of aging, because the mechanism of aging process is "the impaired development of repair systems by inadequate early nutrition" (Lucas,1991). Aihie Sayer A et al made the retrospective cohort study and found that lower weight at first year after birth was statistically related with increased lens opacity score, higher hearing threshold, reduced grip strength and thinner skin, although visual acuity, macular degeneration and intraocular pressure were not statistically associated with early growth(Aihie Sayer A et al,1998).These empirical observations further prove the effects of environmental factors rather than genetic variables on rates of aging because nutrient supply rather than genome determines the early growth(Walton,1938; Morton,1955). The effects of events in utero and in childhood (Barker, 2008), such as season of birth (Moore,1997; Doblhammer,2004), on health in old age are observed significantly. A study reports that "babies born in November in Europe around 1900 lived several months longer after age 50 than babies born in May" (Doblhammer,2004). Furthermore, results from twins' studies reveal that childhood environments shared by the twins can explain almost 10% of the variation in adult lifespan (McGue,1993; Herskind,1996).

Lifestyle also plays important role in human aging. The persons who smoke cigarettes, have little exercise and are grossly obese, would have big risk to die earlier or age more rapidly than those who not. Generally, cigarette smoking during adult years exerts rather serious influence on health even decades later, which in turn speeds up the rate of aging. Studies show that the reason, why advance in reducing adult death rates is faster in some countries than in others, can be explained well by the patterns of cigarette smoking (Wang, 2009).

Some types of events later in life also are major determinants of aging. Studies show that the progress in reducing the risk of death rates among the elderly mostly come from the medical advances or economic growth (Kannisto,1994;1996; Rau,2008; Vaupel,1997). Take Germany as example, the rates of death of the old and very old in the former East Germany experienced rapid decline and approached those of the former West Germany, after the reunification of Germany several decades ago (Vaupel, 2003).

There are more and more emphasis on the effects of social environmental factors and individual efforts. Studies show that the extension of lifespan and postponement of aging is entirely owed to the progress being made in medical and public-health services, advancement of living standards, and improvement in education and nutrition as well as betterment of lifestyle (Oeppen,2002; Riley,2001). Studies also show that dietary restriction (Mair,2003; Sohal,1996),public-health efforts for a safer home and outdoor environments and for high-quality health care as well as for more salubrious lifestyles by reducing self hazardous behavior (cigarette smoking, excess alcohol consumption, obesity, lack of exercise and so on), might be effective to delay human aging. Some studies also stressed that for further progress in lengthening lifespan and postponing senescence in the future, it is important to make efforts to improve the health not only of the elderly but also of the young so that they can reach their old ages in better condition (Vaupel, 2010).

Overall, more and more researchers believed that the age process is a comprehensive consequence of multiple factors, including biological differences, preference of life styles, variance of environmental and living conditions as well as economedical factors (Vaupel and Yashin, 1985; Vaupel and Carey, 1993).

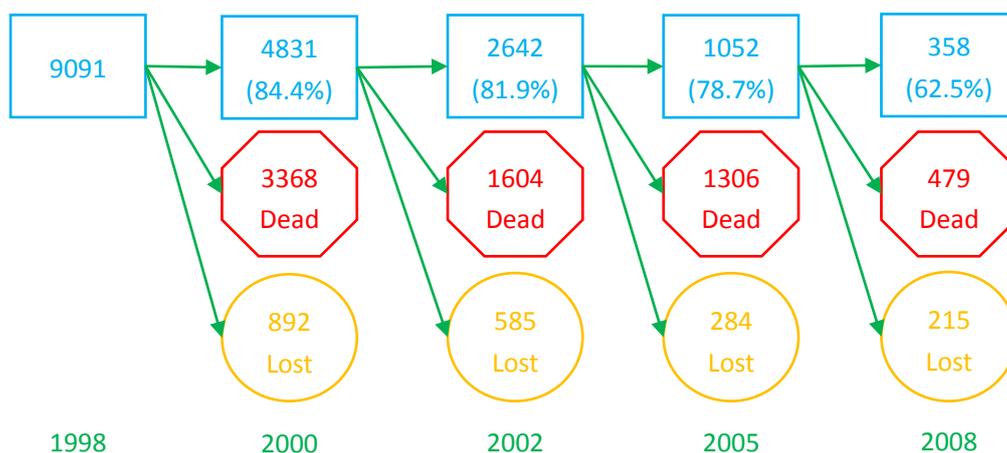
### **3. Data and Method**

#### **3.1 Data**

This study employs the longitudinal data from the Chinese Longitudinal Healthy Longevity Survey (CLHLS), consisted by the 9093 elderlies who are fully interviewed in baseline survey and partially participated in next four follow-up surveys. For simplicity, I deleted the individuals who dropped out in one survey but came back in next survey, so finally I had a sample with 9091 old persons aged

75–125. Of the 9091 participants, 4831 (53.14 per cent) were alive and re-interviewed in the follow-up survey in 2000, 2642(29.06 per cent) in 2002, 1052(11.57 percent) in 2005, and 358(3.94 per cent) in 2008. My analyses are restricted to the 4831 individuals who have two and more surveys because we have no information of aging process for the elderies lost or died in 2000 survey. Of the 4831 participants, 3389 were died and 1084 were lost in next three follow-up surveys. The interview rate in 2002 follow-up survey is 81.9%, 78.7% in 2005, and 62.5% in 2008 (Figure1).

In order to further examine the rate of aging of these interviewees, four survey cohorts can be identified in this longitudinal data. Cohort 1 is the interviewees who are died and lost in 2002 survey, namely who experienced only twice surveys. Cohort 2 is the respondents who are died and lost in 2005. They took part in three follow-up surveys. Cohort 3 is the elderly who were observed by four follow-up surveys, namely died and lost in 2005. Cohort 4 is the older persons who have participated in the previous four wave’s surveys and still survived in 2008 survey. In other words they were investigated by five follow-up surveys.



Note: the square boxes provide the number of interviewees and interview rates.

Figure 1 Flow-chart of four follow-up surveys of 9091 Chinese elderlies interviewed in 1998

## 3.2 Method

### 3.2.1 Frailty index

The study uses the frailty index to measure the aging. Frailty index is an effective summary tool widely used in most studies to capture the cumulative health deficits of an individual (Cohen, 2000; Markle-Reid, 2003; Mitnitski et al., 2005). The formula for the frailty index can be written as

$$F = \frac{\sum_{i=1}^n d_i}{N}$$

Here, F denoted the value of frailty index. N is the total number of possible deficits and  $n$  is the number of indicators in the frailty index. I used 30 indicators of health

including ADLs (Activities of daily living), functional limitations, self-reported and interviewer-rated health status, disability, auditory and visual ability, heart rhythm, and numerous chronic disease, without consideration of the cognitive functioning and IADLs (instrumental activities of daily living) because of difficulties in measurement of cognitive functioning and partial overlap between IADLs and IDLs (see Table 1). However, these items are basically similar to those used in studies from China mainland (Gu et al, 2009), Canada (Mitnitski et al., 2005), the United States (Kulminski et al., 2006), and Hong Kong SAR (Goggins et al., 2005).

Each item was dichotomized by coding 1 if a deficit is present while 0 if not. Following prior research(Goggins et al,2005), I assigned a score of 2 if the interviewees suffered two or more serious illnesses in past two years, coded a score of 1 if once and coded 0 when no. So the total number of possible deficits  $N$  in this study is 31. Therefore the value of individual frailty index should be any value between 0 and 1. Previous empirical assessment of the validity and sensitivity of frailty index showed that the results of different combinations of individual indicators are basically consistent if the major dimensions of health are included in the index such as ADLs and chronic diseases (Gu et al, 2009).

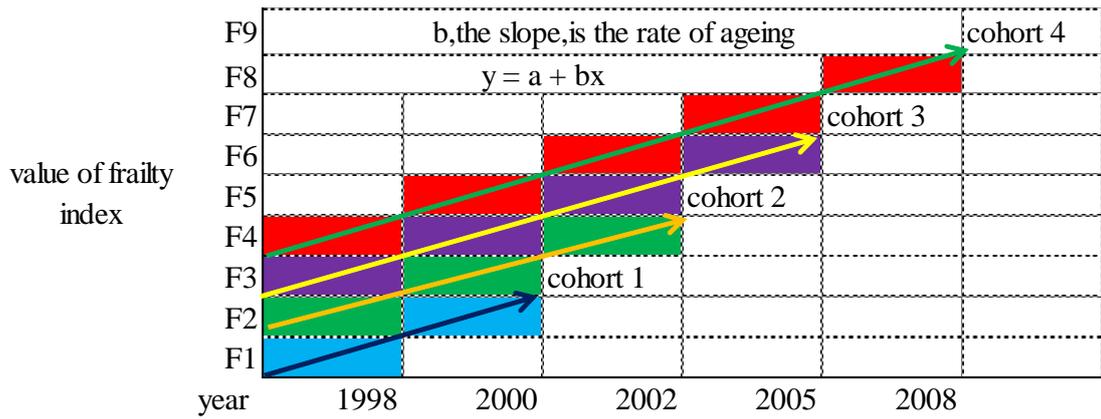
### **3.2.2 The slope of linear regression**

This study assumed that the aging of elderly followed the linear mode and employed the linear regression to estimate the rate of aging. I used the value of frailty index as the dependent variable and the year as the independent variables. The aging model can be expressed as follows:

$$y = a + bx + \varepsilon$$

Here,  $y$  denotes the value of frailty index for a given year  $x$ . The regression coefficient or slope  $b$  is the rate of aging.

This study calculated the rate of aging based on the individual level by regressing individual value of frailty index each year on the number of years. The slope of regression is the rate of aging for each individual. By this method, this study not only can calculate all of the individuals' rates of aging and further have the mean, distribution of total samples as well as sub-samples, but also can make a deeper analysis of the effects of demographic, socioeconomic, medical, and living environmental factors on the rate of aging.



Note: the value of frailty for individuals next year does not necessarily increase. It could decrease or stay at the same value. In other words, the rates of ageing (the slope) of individuals could be negative, zero, or positive.

Figure 2 the rate of aging for 4 sub-cohorts

Table 1 List of Items Included in the Frailty Index and their Codings

No.	Items	coding	No.	Items	coding
1	ADLs: Needs assistance for bathing	code 1 if yes,otherwise 0	16	Abnormal heart rhythm	code 1 if yes,otherwise 0
2	ADLs: Needs assistance for dressing	code 1 if yes,otherwise 0	17	Number of serious illnesses in the past 2 years	code 2 if having 2 and more serious diseases ,1 if only 1, and 0 if zero
3	ADLs: Needs assistance for toileting	code 1 if yes,otherwise 0	18	Suffering from hypertension	code 1 if yes,otherwise 0
4	ADLs: Needs assistance in indoor transferring	code 1 if yes,otherwise 0	19	Suffering from diabetes	code 1 if yes,otherwise 0
5	ADLs: Needs assistance for eating	code 1 if yes,otherwise 0	20	Suffering from heart disease	code 1 if yes,otherwise 0
6	ADLs: Incontinence	code 1 if yes,otherwise 0	21	Suffering from stroke/cerebrovascular disease	code 1 if yes,otherwise 0
7	Functional limitations: Unable to put hand behind neck	code 1 if yes,otherwise 0	22	Suffering from bronchitis, pulmonary emphysema, asthma, or pneumonia	code 1 if yes,otherwise 0
8	Functional limitations: Unable to put hand behind lower back	code 1 if yes,otherwise 0	23	Suffering from pulmonary tuberculosis	code 1 if yes,otherwise 0
9	Functional limitations: Unable to stand up from sitting in a chair	code 1 if yes,otherwise 0	24	Suffering from cataract	code 1 if yes,otherwise 0
10	Functional limitations: Unable to pick up a book from the floor	code 1 if yes,otherwise 0	25	Suffering from glaucoma	code 1 if yes,otherwise 0
11	Functional limitations: Unable to turn around 360° within five steps	code 1 if yes,otherwise 0	26	Suffering from cancer	code 1 if yes,otherwise 0
12	Poor self-rated health	code 1 if yes,otherwise 0	27	Suffering from prostate tumor	code 1 if yes,otherwise 0
13	Poor interviewer-rated health	code 1 if yes,otherwise 0	28	Suffering from gastric or duodenal ulcers	code 1 if yes,otherwise 0
14	Hearing loss	code 1 if yes,otherwise 0	29	Suffering from Parkinson's disease	code 1 if yes,otherwise 0
15	Vision loss	code 1 if yes,otherwise 0	30	Suffering from bedsores	code 1 if yes,otherwise 0

### 3.3 Variables

Based on the well-established literature on determinants of aging, I selected 21 variables coming from two categories: one is about the early and mid life of the elderly shared in different follow-up surveys, while another is about the present life which could be changeable in each follow-up surveys. The former category includes 12 explanatory variables constituting three dimensions: demographics, lifestyle in the past, and economic traits in the past. The latter category contains 9 explanatory variables involving four dimensions: living environment, current marriage status, economic traits in present life, and lifestyle in the past.

This study employed multiple regression method to test effects of these explanatory variables on the rate of aging. I coded all categorical variables into the dummy variables and assigned the most unfavorable variables for rate of aging such as rural, illiterate as reference categories. For the regression of determinants in the past life, I used the following model:

$$y = a_0 + a_1 \text{ age} + a_i \sum_{i=2}^{21} \text{shared variables} + \varepsilon$$

Here,  $y$  is the rate of aging for each older person.  $a_0$  is the constant.  $a_1$  is the coefficient of numerical variables  $\text{age}$ .  $\varepsilon$  denotes the error item.  $a_i$  represent the coefficients of 20 variables about the past life.

Because there is no question about the *household income* in questionnaires of the first two surveys, in other words, we have no information about the household income of cohort 1. Therefore, for cohort 1, I used the following model:

$$y = a_0 + a_i \sum_{i=1}^{11} \text{changeable variables} + \varepsilon$$

Here,  $y$  is also the rate of aging for each older person.  $a_0$  is the constant.  $\varepsilon$  denotes the error item.  $a_i$  represent the coefficients of 11 variables about the present life.

For other three cohorts, I used the following model:

$$y_j = a_{0j} + a_{1j} \text{ household income} + a_{ij} \sum_{i=2}^{12} \sum_j^4 \text{changeable variables} + \varepsilon_j \quad (j = 2,3,4)$$

Here,  $j$  denotes different cohorts ( $j=2,3,4$ ).  $y_j$  is the rate of aging for each older person of different cohorts.  $a_{0j}$  is the constant for each cohort.  $a_{1j}$  is the coefficient of numerical variables *household income* for each cohort.  $\varepsilon_j$  denotes the error item of each cohort.  $a_{ij}$  represent the coefficients of 11 variables about the present life for each cohort.

## 4. Results

### 4.1 Value and direction of rate of aging

Table 2 presents the value and direction of rate of aging for each cohort. On average, cohort 2, cohort 3, and cohort 4 has the almost same mean rate of aging while cohort 1 has exceptionally high mean of rate of aging. After a breakdown of three cohorts, the exceptional high mean in cohort 1 is entirely contributed to the dead samples, whose mean of rate of aging is nearly 0.1. If we subtract the higher part of mean of dead samples in cohort 1 than the average of dead samples from the mean of cohort 1 and add the mean of lost samples, we get the adjusted mean of cohort 1 which is equal to  $0.024(0.062-(0.096-0.058)=0.024)$ . The adjusted mean of cohort is also very close to the mean of other three cohorts. Furthermore, compared with the lost samples and dead samples of cohort 2 and cohort 3, the highly consistent mean of rate of aging provides enough reasons making us believe that the mean of rate of aging for each cohort are the same, more specifically a constant, which roughly is between 0.018 and 0.03. Such range is within the error range. So I am more inclined to believe that the rate of aging for humans is a constant.

Figure 3 is the density distribution of rate of aging for different cohorts. Graphically, such conclusion is further demonstrated in Figure 2 displaying a shape of a closed or combined umbrella in density distribution of cohort 2, cohort 3, and particularly cohort 4. The density distribution looks like a line with high proportion of samples sharing the mean rate of aging. This is to say, the rate of aging fluctuated within a certain range. The range is the error range of mean of the rate of aging. At least, we are sure that overall for octogenarians the rate of aging is more likely to be a constant in next ten year's lives.

The constant mean of rate of aging represents the overall speed of aging, however, individually the rate of aging existed significantly differences. Some have positive rate of aging, while others have zero or negative rate of aging. Table 4 presents that of 2189 elderlies in cohort 1, 21.6% have negative rate of aging and in other three cohorts there are 1.7-2.8% of old persons in each cohort have the negative rate of aging. Of 2189 participants in cohort 1, 3.7% have the zero rate of aging, which means that people get older but do not become aging. The percentages of the elderly whose rate of aging is zero in other three cohorts are much higher than that in cohort 1. In particular, in cohort 4 the percentage of zero rate of aging is 18.7%. At the aggregate level, about 80% of the old persons have the positive rate of aging while 20% of the old persons have zero or negative rate of aging. About 14% averagely have zero rate of aging in cohort 2, cohort 3, and cohort 4, which is very close to the percentages of lost samples in the three cohorts.

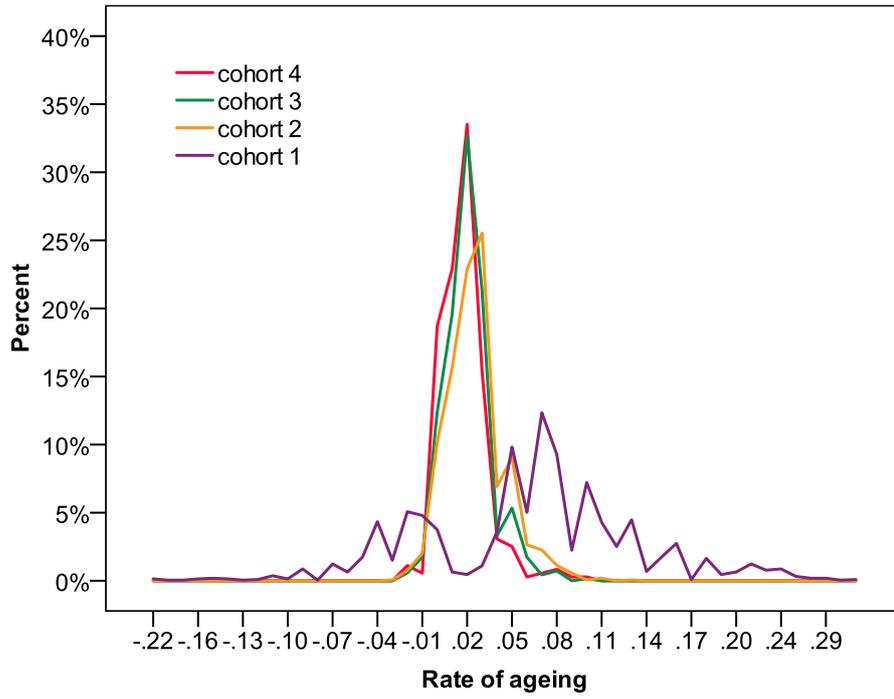


Figure 3 the density distribution of rate of ageing for different cohorts

Table 2 Value and direction of rate of aging for different cohorts and samples

study sample	1998	2000	2002	2005	2008	Total number	quality of ageing(%)		
	means value of rates of ageing (standard deviation)						positive ageing(rate>0)	zero ageing(rate=0)	negative ageing(rate<0)
Cohort 1	0.062(0.073)					2189	74.7	3.7	21.6
Cohort 2	0.026(0.02)					1590	87	10.2	2.8
Cohort 3	0.021(0.016)					694	85.3	12.4	2.3
Cohort 4	0.018(0.016)					358	79.6	18.7	1.7
Total means		0.041(0.054)	0.023(0.018)	0.02(0.016)	0.018(0.016)	4831	80.6	8.2	11.2
Interviewees number		4831	2642	1052	358				
Lost samples of Cohort 1	-0.03(0.041)					585	5.3	14	80.7
Lost samples of Cohort 2	0.023(0.020)					284	81.7	14.1	4.2
Lost samples of Cohort 3	0.020(0.016)					215	82.3	14	3.7
Total means	-0.006(0.041)					1084	40.6	14	45.4
Lost number			585	284	215				
Died samples of Cohort 1	0.096(0.049)					1604	100	0	0
Died samples of Cohort 2	0.026(0.020)					1306	88.1	9.3	2.5
Died samples of Cohort 3	0.021(0.016)					479	86.6	11.7	1.7
Total means	0.058(0.051)					3389	93.5	5.3	1.2
Dead number			1604	1306	479				

## 4.2 Change of rate of aging with age

Figure 4 illustrated clearly the change of mean rate of aging among the four cohorts. Figure 5 showed the change of mean of rate of aging for different subsamples with age. Figure 6 showed the mean rate of aging for different observation durations of dead samples. Graphically, it seems more reasonably to conclude that the rate of aging is a constant over age, both for cohort samples and for dead samples. For the elderly who were observed in their last two or three years of lives, the constant is much higher than those both who were observed in their last four or seven years of lives and who are still alive. In other words, the constant rate of aging will exist in normal process of aging, however such constant will be changed in two or three years before when they achieve their upper limit age, even though the rate of aging during the last two or three years of lives, it is still the same for different ages.

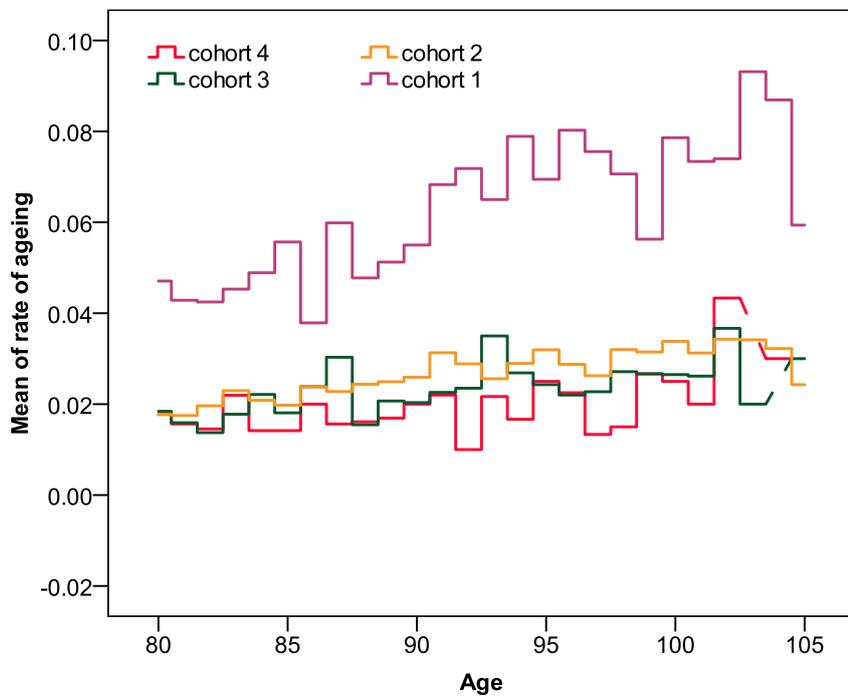


Figure 4 the change of mean of rate of aging for different cohorts with age

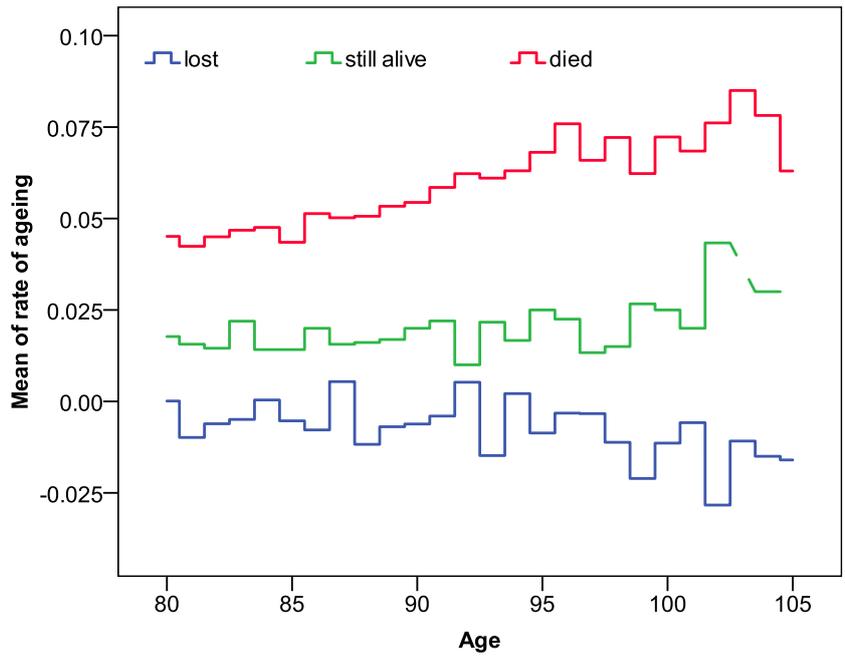


Figure 5 the change of mean of rate of aging for different subsamples with age

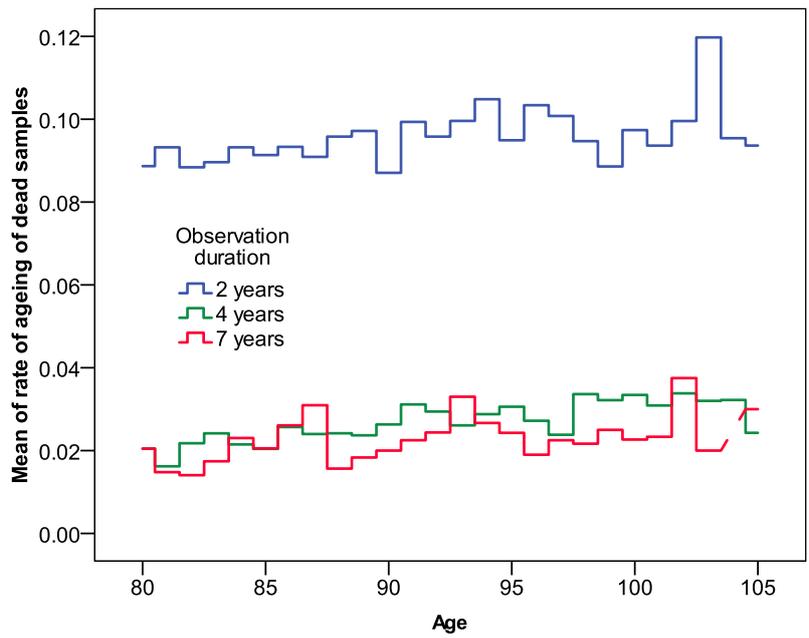


Figure 6 the breakdown of dead samples for different cohorts

### 4.3 Determinants of rate of aging

Table 3 presents the regression results for the effects of variables in past life on the rate of aging. Table 4 presents the cohort samples' regression results for the effects of variables at present life on the rate of aging. Of all variables both early life and

present life, regular exercise is the only variable which can have negative influence on rate of aging. Remarkably, the effects of both adequacy of medical service if seriously ill and sufficiency of financial support for daily costs are significantly negative for rate of aging, while availability of medical service both at around age 60 and in childhood also does not show statistical significance.

Table 3 Regression results for the effects of variables in past life on the rate of aging

Variables(reference group)		Total		Cohort 1		Cohort 2		Cohort 3		Cohort 4
		male	female	male	female	male	female	male	female	total
age		0.0015 ***	0.0016 ***	0.0007 ***	0.0013 ***	0.0006 ***	0.0006 ***	0.0004 ***	0.0004 ***	0.0002
birth place(rural)		-0.0027	0.0000	0.0019	-0.0039	0.0007	0.0012	-0.0016	0.0002	-0.0027
education(illiterate)		0.0024	-0.0011	-0.0047	0.0116 **	-0.0008	-0.0009	-0.0020	-0.0030 ♀	-0.0015
How many times have you been married?(twice and more)		0.0035	-0.0007	0.0035	-0.0012	-0.0004	0.0007	-0.0001	-0.0018	0.0035
<b>Demographic variables</b>	professional and technical personnel	-0.0083 ♀	-0.0025	-0.0224 **	0.0087	0.0003	0.0007	0.0014	-0.0006	0.0093 *
	governmental, institutional or managerial personnel	-0.0082	-0.0209	-0.0287 **	0.0119	0.0006	0.0002	0.0048	0.0074 ♀	0.0041
	industrial worker	-0.0091 *	-0.0005	-0.0172 **	0.0105	-0.0006	0.0006	-0.0023	-0.0025	0.0030
	commercial or service worker	-0.0062	0.0013	-0.0123 *	0.0066	-0.0014	-0.0013	0.0022	0.0015	-0.0003
	military personnel	-0.0055	0.0008	-0.0041	0.0038	-0.0047	-0.0027	0.0172 *	0.0125	0.0081
	houseworker	-0.0148	0.0120	0.0119 *	-0.0065	0.0031 ♀	0.0016	0.0046 *	0.0014	0.0069 **
others		0.0017	0.0004	0.0052	0.0230	-0.0003	0.0005	0.0001	-0.0010	0.0074
<b>lifestyle variables</b>	Did you smoke in the past?(yes)	-0.0006	-0.0016	0.0100 **	-0.0092 *	0.0010	0.0015	-0.0012	-0.0004	0.0041 *
	Did you drink alcohol in the past?(yes)	0.0034	-0.0074	0.0076 *	-0.0017	0.0015	0.0009	0.0012	0.0006	-0.0014
	Did you do exercises regularly in the past?(no)	-0.0016	-0.0042 **	-0.0014	-0.0085 *	-0.0014	-0.0011	-0.0011	-0.0010	-0.0049 *
	Have you done physical labor regularly?(yes)	-0.0004	0.0051	-0.0035	-0.0134 **	0.0014	0.0031 *	0.0028	0.0034 ♀	-0.0005
Could you get adequate medical service when you were sick at around age 60?(no)		-0.0037	0.0034	0.0010	0.0127	-0.0031	-0.0012	-0.0041	-0.0024	-0.0034
<b>eoconiomedic al variables</b>	Could you get adequate medical service when you were sick in childhood?(no)	-0.0057	0.0044	-0.0045	0.0027	0.0004	-0.0001	-0.0019	-0.0026	0.0008
	Did you frequently go to bed hungry as a child?(yes)	0.0000	-0.0025	0.0032	0.0066	0.0009	-0.0005	-0.0011	-0.0025	-0.0008
size of sample		1909	2784	1787	1899	1383	1418	555	592	348
constant		-0.0947 ***	-0.1023 ***	0.0016	-0.0476 *	-0.0292 ***	-0.0320	-0.0122	-0.0095	-0.0048
R Square		0.0550	0.0610	0.0760	0.0510	0.0750	0.0720	0.0830	0.0690	0.0980
F Value		5.5000 ***	9.5000 ***	7.2860 ***	5.0510 ***	5.5250 ***	5.4570 ***	2.4010 ***	2.1280 **	1.7670 *

♀p < 0.1; \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001

Table 4 Regression results for the effects of variables at present life on the rate of aging

variables(reference group)			Cohort 1		Cohort 2		Cohort 3		Cohort 4	
			male	female	male	female	male	female	male	female
Living enviornmental variables	residence(rural)	urban	-0.0033	-0.0026	0.0017	0.0016	0.0011	0.0010	-0.0003	0.0026
	living arrangement(alone)	with household member(s)	0.0252 ***	0.0249 ***	0.0043 ***	0.0047 **	0.0047 *	0.0043 *	0.0021	-0.0043
		in a nursing home	0.0235 **	0.0259 **	0.0061 *	0.0067 *	0.0042	0.0046	0.0116	-0.0083
Current marriage variable	marriage status(widowed)	married and living with spouse	-0.0251 ***	0.0061	-0.0056 ***	-0.0049 ***	-0.0045 **	-0.0053 **	0.0036	-0.0076
		separated	-0.0032	-0.0045	-0.0003	-0.0014	-0.0101 ♀	-0.0161 *	0.0019	-0.0048
		divorced	-0.0262	-0.0088	0.0067	0.0121 *	-0.0191	-0.0071	0.0000	0.0000
economedical variable	Does all of your financial support sufficiently pay your daily costs?(no)	yes	-0.0058	-0.0038	-0.0053 ***	-0.0049 ***	-0.0024	-0.0011	-0.0097	0.0027
	Household income last year				0.0000004 *	0.0000004 *	0.00000001	-0.00000001	0.00000005 **	-0.00000005
lifestyle variables	Can you get adequate medical service when you are seriously ill?(no)	yes	-0.0104	0.0027	-0.0045 **	-0.0053 ***	-0.0015	-0.0016	-0.0064	-0.0109 *
	Do you smoke at the present time?(yes)	no	0.0157 ***	-0.0097 ♀	0.0046 **	0.0043 **	0.0022	0.0001	0.0000	0.0019
	Do you drink alcohol at the present time?(yes)	no	0.0063 ♀	-0.0031	0.0024 ♀	0.0021	0.0037 *	0.0035 *	-0.0020	0.0010
	Do you do exercises regularly at present?(no)	yes	-0.0289 ***	-0.0242 ***	-0.0136 ***	-0.0134 ***	-0.0051 ***	-0.0052 ***	-0.0025	-0.0023
size of sample			1625	1706	1310	1338	560	560	139	214
constant			0.0652 ***	0.0679 ***	0.0257 ***	0.0260 ***	0.0161 ***	0.0185 ***	0.0259 ***	0.0301 ***
R Square			0.114	0.043	0.163	0.153	0.079	0.067	0.144	0.052
F value			18.94 ***	6.98 ***	21.03 ***	20 ***	3.92 ***	3.464 ***	1.943 *	0.998

♀p < 0.1; \* p < 0.05; \*\* p < 0.01; \*\*\* p < 0.001

## 5. Conclusion and discussion

This study employed a cumulative index, namely frailty index, to estimate rate of aging on the individual level for the oldest-old interviewed at least twice or more times and on this basis further examined the effects of external factors such as lifestyle on individuals' rate of aging.

The key finding of this study is that the mean rate of aging for the elderly at different ages is a constant, almost 2-3% per year. This finding that rate of aging for the elderly at different ages is averagely constant was directly concluded based on the conclusions of four aspects: firstly, all cohorts but cohort 1 has almost the same mean rate of aging. After the breakdown of cohort 1, the adjusted mean rate of cohort 1 is also very close to the other three cohorts. Secondly, the density distribution of rate of aging for different cohorts looked like a closed umbrella with high concentration in the mean rate and symmetric dispersion within an error range of mean rate. Thirdly, graphically, the curves of change of mean rate of aging with age for all cohorts with an exception of cohort 1 basically are a flattened line. The curves of change of mean rate of aging with age for dead samples of different cohorts are also a straight line. This result is totally consistent with the James W. Vaupel's hypothesis that the rate of aging is "a basic biological constant" (Vaupel, 2010).

Constant mean rate of aging refers to the average speed of human aging at the aggregate level or at population level, allowing the significant variance on the rate of aging at individual level. Although all of individual rate of aging are mainly distributed around mean rate with a limited fluctuation, as showed in figure 7, individual has obvious differences not only on the quantity of rate of aging but also on the quality of rate of aging, as presented in table 2. This study indicated that about 20% of the elderly have the nonpositive rate of aging, particularly in their 80s and 90s. It is noteworthy that about 14% of the elderly have zero rate of aging which means that they aged without frailty. This finding also shows consistence with previous research (Vaupel, J. W, et al., 2004; Baudisch A., 2005; Baudisch A., 2008). Results also show that most of the lost samples have negative rate of aging, it is precisely because of this that they can migrate. In other words, most of lost samples are not dead but move so that it is too difficult for the survey team to follow them. This finding is completely different from the conclusions that the lost samples have poorer health conditions than participants (Christensen, K., 2008).

The different rate trajectory of aging among individuals sounds good news for individuals because finding determinants of such differences provides possibilities of slowing down or delaying the rate of aging by external efforts. However, the regression results showed that most of variables about the early and mid life of elderly are statistically insignificantly. Of 12 explanatory variables at present life, only the coefficients of *regular exercise* and *living with spouse* are significantly basically for all models of all cohorts. It seems to be true that the rate of aging for elderly is slightly dependent on the external environmental factors.

Most postulated determinants of rate of aging are not tested statistically significantly in this study, including the birth place, current residence, marriage times, availability of medical service both at around age 60 and in childhood, and experience of hunger

in childhood. Some presumably determinants of rate of aging are significant in limited models, such as education, occupation, smoking experience both in the past and at present, drinking alcohol both in the past and at present, regular physical labour, current marriage status, living arrangements, and the adequacy of medical service if seriously ill and sufficiency of financial support for daily costs. In other words, the effects of these variables on rate of aging mostly depend on individual. Only the effect of the variable *regular exercise* on rate of aging proved statistically significant for all models, both about the past life and the present life.

Moreover, of all variables both early life and present life, regular exercise is the only variable which can have negative influence on rate of aging. Such inspiring finding that doing exercise regularly is contributive to the slowing of aging seems to be good news for the elderly. Besides, the meaningful finding that the adequacy of medical service if seriously ill and sufficiency of financial support for daily costs are also helpful for the slowing of aging suggests that economic and medical factors play very important role in healthy aging for the elderly. These findings do not deny the mean constant hypothesis of rate of aging. On the contrary, these findings further prove that it is possible for humans to slow the rate of aging, albeit with too slight influence of such efforts.

## References

- Abrams, P. A. & Ludwig, D.(1995).Optimality theory, Gompertz' law, and the disposable soma theory of senescence. *Evolution*49:1055-1066.
- Aihie Sayer A, Cooper C, Evans JR et al.(1998).Are rates of aging determined in utero? *Age and Aging* 27:579–83.
- Barker DJP, Martyn CN, Osmond C, Hales CN, Fall CHD(1993).Growth in utero and serum cholesterol concentrations in adult life. *Br Med J* 307: 1524-7.
- Barker, D. J. P., Bergmann, R. L. & Ogra, P. L. (eds) (2008).*The Window of Opportunity: Pre-Pregnancy to 24 Months of Age*.Karger.
- Baudisch, A.(2005).Hamilton's indicators of the force of selection. *Proc. Natl Acad. Sci. USA* 102:8263–8268.
- Baudisch, A.(2008). *Inevitable Aging? Contributions to Evolutionary-Demographic Theory* .Springer.
- Bergman H, Ferrucci L, Guralnik J, Hogan DB, Hummel S, Karunanathan S, Wolfson C.(2007).Frailty: An emerging research and clinical paradigm—issues and controversies. *Journal of Gerontology: Medical Sciences* 62A(7):731–737.
- Blarer, A., Doebeli, M. & Stearns, S. C.(1995). Diagnosing senescence: inferring evolutionary causes from phenotypic patterns can be misleading. *Proc. R. Soc. Lond. B* 262:305-312.
- Board of Trustees, Federal Hospital Insurance Trust Fund (1999).*Annual Report of the Board of Trustees of the Federal Hospital Insurance Trust Fund*.Washington: U.S. Government Printing Office.
- Brommer JE, Wilson AJ, Gustafsson L.(2007).Exploring the genetics of aging in a

- wild passerine bird. *Am Nat* 170: 643–650.
- Brommer, JE., Rattiste K. and Wilson, A.(2010).The rate of aging in a long-lived bird is not heritable. *Heredity*104:363–370
- Carey JR.(2003). “Theories of life span and aging”. In: *Physiological Basis of Aging and Geriatrics* (3rd ed.), edited by Timiras PS. Boca Raton, FL: CRC, p85–95.
- Carey, J. R., Liedo, P., Orozco, D. & Vaupel, J. W.(1992).Slowing of mortality rates at older ages in large medfly cohorts. *Science*, Wash. 258:457-461.
- Charlesworth, B.(1980).*Evolutionary in age-structured Populations*.1st edn. Cambridge University Press.
- Charlesworth, B.(1994).*Evolutionary in age-structured Populations*.2nd edn. Cambridge University Press.
- Christensen, K., Doblhammer, G., Rau, R. & Vaupel, J. W.(2009).Aging populations: the challenges ahead. *Lancet* 374:1196–1208 .
- Christensen, K., Johnson, T. E. & Vaupel, J. W.(2006).The quest for genetic determinants of human longevity: challenges and insights.*Nature Rev. Genet.* 7: 436-448.
- Christensen, K., McGue, M., Petersen, I., Jeune, B. & Vaupel, J. W.(2008). Exceptional longevity does not result in excessive levels of disability. *Proc. Natl Acad. Sci. USA* 105:13274–13279.
- Comfort, A.(1964).*Aging: The Biology of Senescence*. Routledge & Kegan Paul, London.
- Curtsinger, J. W., Fukui, H., Townsend, D. & Vaupel, J.(1992).Failure of the limited-lifespan paradigm in genetically homogeneous populations of *Drosophila melanogaster*. *Science*, Wash. 258:461-463.
- Doblhammer, G. (2004).*The Late Life Legacy of Very Early Life*.Springer.
- Dufouil C, Brayne C, Clayton D.(2004).Analysis of longitudinal studies with death and drop-out: A case study. *Stat Med* 23(14):2215–2226.
- Elisabetta Barbi.(2003).Assessing the rate of aging of the human population.MPIDR WORKING PAPER WP:2003-008.MARCH.
- Finch, C. E.(1990).*Longevity, Senescence, and the Genome*.The University of Chicago Press.Chicago and London.
- Fisher AL.(2005).Just what defines frailty? *Journal of the American Geriatrics Society* 53:2229–2230.
- Fried LP, Ferrucci L, Darer J, Williamson J, Anderson G.(2004).Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care.*Journals of Gerontology: Medical Sciences*.59:M255–M263.
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. (2001).Frailty in older adults: Evidence for a phenotype.*Journal of Gerontology: Medical Sciences* 56A:M146–M157.
- Goggins WB, Woo J, Sham A, Ho SC.(2005).Frailty index as a measure of biological age in a Chinese population.*Journals of Gerontology: Medical Sciences*. 60A:M1046–M1051.
- Gu D, Dupre ME.(2008). “Assessment of reliability of mortality and morbidity in the 1998–2002 CLHLS waves”. In: Zeng Y, Poston D, Vlosky DA, Gu D, editors. *Healthy longevity in China: Demographic, socioeconomic, and psychological dimensions (pp. 99–115)* Dordrecht, The Netherlands: Springer.
- Gu D.(2008).“General data assessment of the Chinese Longitudinal Healthy Longevity Survey in 2002”. In: Zeng Y, Poston D, Vlosky DA, Gu D, editors.

- Healthy longevity in China: Demographic, socioeconomic, and psychological dimensions* (pp. 39–59) Dordrecht, The Netherlands: Springer.
- Gu Danan, Matthew E Dupre, Jessica Sautter, Haiyan Zhu, Yuzhi Liu, Zeng Yi, (2009). Frailty and Mortality Among Chinese at Advanced Ages. *The Journals of Gerontology*; Mar; 64B, 2; Academic Research Library: 279
- Hales CN, Barker DTP, dark PMS *et al.*, (1991). Fetal and infant growth and impaired glucose tolerance at age 64. *Br Med J* 303: 1019-22.
- Hamilton, W. D. (1966). The moulding of senescence by natural selection. *J. theor. Biol.* 12: 12-45.
- Herskind, A. M. *et al.* (1996). Untangling genetic influences on smoking, body mass index and longevity: a multivariate study of 2464 Danish twins followed for 28 years. *Hum. Genet.* 98:467–475.
- Hjelmborg, J. vB. *et al.* (2006). Genetic influences on human lifespan and longevity. *Hum. Genet.* 119:312–321.
- Horiuchi Shiro, Coale Ansley, (1990). Age patterns of mortality for older women. *Mathematical Population Studies*, Vol. 2, 4: 245-267.
- Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. (2004). The healthcare costs of sarcopenia in the United States. *Journal of the American Geriatrics Society*. 52:80–85.
- Johnson, T. E. (1990). Increased life-span of *age-1* mutants in *Caenorhabditis elegans* and lower Gompertz rate of aging. *Science* 249:908–912.
- Jones OR, Gaillard J-M, Tuljapurkar S, Alho JS, Armitage KB, Becker PH *et al.* (2008). Senescence rates are determined by ranking on the fast–slow life-history continuum. *Ecol Lett* 11: 664–673.
- Kannisto, V. (1994). *Development of Oldest-Old Mortality, 1950–1990: Evidence from 28 Developed Countries*, Odense Univ. Press.
- Kannisto, V. (1996). *The Advancing Frontier of Survival: Life Tables for Old Age*, Odense Univ. Press.
- Kirkwood, T. B. L. & Austad, S. N. (2000). Why do we age? *Nature* 408:233–238 .
- Kirkwood, T. B. L. & Rose, M. R. (1991). Evolution of senescence: late survival sacrificed for reproduction. *Phil. Trans. R. Soc. Lond. B* 332:15-24.
- Kirkwood, T. B. L. (1999). *Time of Our Lives: The Science of Human Aging*. Oxford Univ. Press.
- Kirkwood, T. B. L. (2005). Understanding the odd science of aging. *Cell* 120: 437–443.
- Kowald A and Kirkwood TB. (1996). A network theory of aging: the interactions of defective mitochondria, aberrant proteins, free radicals and scavengers in the aging process. *Mutat Res* 316: 209–236.
- Kowald, A., and Kirkwood, T. B. (1994). Towards a network theory of aging: a model combining the free radical theory and the protein error theory. *J Theor Biol* 168(1):75-94.
- Kulminski A, Ukraintseva S, Akushevich I, Arbeev K, Yashin A. (2007). Cumulative index of health deficiencies as a characteristic of long life. *Journal of the American Geriatrics Society*. 55:935–940.
- Kulminski A, Ukraintseva S, Kulminskaya IV, Arbeev K, Land K, Yashin A. (2008). Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: Lessons from the Cardiovascular Health Study. *Journal of the American Geriatrics Society*, 56:898–903.
- Kulminski A, Yashin A, Ukraintseva S, Akushevich I, Arbeev K, Land K, Manton K. (2006). Accumulation of health disorders as a systemic measure of aging:

- Findings from the NLTCs data. *Mechanisms of Aging and Development*, 127:840–848.
- Lally Frank, Crome Peter,(2007).Understanding frailty. *Postgrad Med J* :83:16-20.
- Langley SC, Jackson AA.(1994).Increased systolic blood pressure in adult rats induced by fetal exposure to maternal low protein diets. *Clin Sci* 1994; 86: 217-22.
- Levers MJ, Estabrooks CA, Ross Kerr JC.(2006).Factors contributing to frailty: Literature review.*Journal of Advanced Nursing* 56:282–291.
- Linda Partridge, Nicholas H. Barton,(1996).On measuring the rate of aging. *Proceedings: Biological Sciences*, Vol. 263.No. 1375:1365-1371
- Lucas A.(1991).“Programming by early nutrition in man”. In Bock GR, Whelan J eds. *The childhood environment and adult disease*. Ciba Foundation Symposium 156. Chichester John Wiley, 1991: 38-50.
- Mair, W., Goymer, P., Pletcher, S. D. & Partridge, L.(2003).Demography of dietary restriction and death in *Drosophila*. *Science* 301:1731–1733.
- Manton Kenneth G., Vaupel James W. (1995).Survival after the age of 80 in the United States, Sweden, France, England and Japan.*New England Journal of Medicine*, Vol. 333: 1232-1235.
- Markle-Reid M.(2003).Conceptualizations of frailty in relation to older adults. *Journal of Advanced Nursing*. 44:58–68.
- McGue, M., Vaupel, J. W., Holm, N. V. & Harvald, B.(1993).Longevity is moderately heritable in a sample of Danish twins born 1870–1880. *J. Gerontol. A* 48, B237-B244.
- McNamara, J. M. & Houston, A. I.(1996).State-dependent life histories.*Nature*, Lond. 380:215-221.
- Medawar, P. B. (1952). *An Unsolved Problem of Biology*. H. K. Lewis, London.
- Medvedev, Z. A. (1990). An attempt at a rational classification of theories of aging. *Biol Rev Camb Philos Soc* 65(3):375-398.
- Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K.(2002).Frailty, fitness and late-life mortality in relation to chronological and biological age. *BMC Geriatrics*.2:1.
- Mitnitski AB, Mogilner AJ, Rockwood K.(2001).Accumulation of deficits as a proxy measure of aging. *Scientific World* 1:323–336.
- Mitnitski AB, Song X, Skoog I, Broe GA, Cox JL, Grunfeld E, Rockwood K.(2005).Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. *Journal of the American Geriatrics Society*. 35:2184–2189.
- Moore, S. E., Cole, T. J., Poskitt, E. M. E. & Sonko, B. J.(1997).Season of birth predicts mortality in rural Gambia. *Nature* 388: 434–435.
- Morley JE, Perry HM, III, Miller DK.(2002).Something about frailty. *Journals of Gerontology: Medical Sciences*.57A:M698–M704.
- Morton NE.(1955).The inheritance of human birth weight. *Ann Hum Genet*; 20: 125-34.
- Oeppen, J. & Vaupel, J. W.(2002).Broken limits to life expectancy. *Science* 296, 1029–1031.
- Partridge, L. & Barton, N. H. (1993).Optimality, mutation and the evolution of aging. *Nature*, Lond. 362, 305-311.
- Partridge, L., and Mangel, M. (1999). Messages from mortality: the evolution of death rates in the old.*Trends in Ecology and Evolution* 14(11):438-442.
- Perls, T. T. *et al.*(2002).Life-long sustained mortality advantage of siblings of

- centenarians. *Proc.Natl Acad. Sci. USA* 99: 8442–8447.
- Puts MT, Lips P, Deeg DJ.(2005).Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. *Journal of the American Geriatrics Society*. 53:40–47.
- Rau, R., Soroko, E., Jasilionis, D. & Vaupel, J. W.(2008).Continued reductions in mortality at advanced ages. *Popul. Dev. Rev.* 34:747–768.
- Riley, J. C.(2001).*Rising Life Expectancy: A Global History*.Cambridge Univ. Press.
- Rockwood K, Andrew M, Mitnitski A.(2007).A comparison of two approaches to measuring frailty in elderly people. *Journals of Gerontology: Medical Sciences*:62A(7):M738–M743.
- Rockwood K, Fox RA, Stolee P, Robertson D, Beattie BL.(1994).Frailty in elderly people: An evolving concept.*Canadian Medical Association Journal*150:489–495.
- Rockwood K, Mogilner A, Mitnitski AB.(2004).Changes with age in the distribution of a frailty index. *Mechanisms of Aging and Development* 125:517–519.
- Rockwood K.(2005).Frailty and its definition: A worthy challenge. *Journal of the American Geriatrics Society*: 53:1069–1070.
- Rose MR (1991).*Evolutionary Biology of Aging*. Oxford University Press: New York.
- Rose, M. R. (1994), *Evolutionary Biology of Aging* .Oxford Univ. Press.
- Sacher GA.(1982).Evolutionary theory in gerontology.*Perspect Biol Med* 25: 339–353.
- Sierra, F., Hadley, E., Suzman, R. & Hodes, R.(2009).Prospects for life span extension. *Annu. Rev. Med.* 60:457–469.
- Sohal, R. S. & Weindurch, R.(1996).Oxidative stress, caloric restriction, and aging. *Science* 273:59–63.
- Song X, Mitnitski A, MacKnight C, Rockwood K.(2004).Assessment of individual risk of death using self-report data: An artificial neural network compared with a frailty index. *Journal of the American Geriatrics Society*. 52:1180–1184.
- Strehler, B. L. (1999).*Time, Cells, and Aging*. Demetriades Brothers, Larnaca.
- Tatar, M., Carey, J. R. & Vaupel, J. W.(1993).Long-term cost of reproduction with and without accelerated senescence in *Callosobruchusa culatusa*: nalysis of age-specific mortality. *Evolution*47, 1302-1312.
- Thatcher Roger, Kannisto V än ö, Vaupel James (1998).*The force of mortality at ages 80 to 120*.Odense, Monographs on Population Aging, Vol. 5, Odense University Press, 104 p.
- Tissenbaum, H. A. & Johnson, T. E.(2008).Aging Processes in *Caenorhabditis elegans* in “*Molecular Biology of Aging*” (eds Guarente, L.,Partridge, L. & Wallace, D. C.).Cold Spring Harbor Laboratory Press:153–183.
- Vaupel James, Carey James R.(1993).Compositional interpretations of medfly mortality, *Science*,Vol. 269: 1666-1667.
- Vaupel James, Manton Kenneth, Stallard Eric,(1979).The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography*.Vol. 16: 439-454.
- Vaupel James, Yashin Anatoli, (1985).Heterogeneity’s ruses: some surprising effects of selection on population dynamics. *American Statistician*.Vol. 39: 176-185.
- Vaupel, J. W., Baudisch, A., Dolling, M., Roach, D. A. & Gampe, J.(2004).The case for negative senescence. *Theor. Popul. Biol.* 65:339–351.
- Vaupel, J. W., Carey, J. R. & Christensen, K.(2003).It’s never too late. *Science* 301:1679–1681.

- Vaupel, J. W., Wang, Z., Andreev, K. F. & Yashin, A. I.(1997).*Population Data at a Glance: Shaded Contour Maps of Demographic Surfaces over Age and Time*. Odense Univ. Press: 22; 39; 52; 54; 59–63.
- Vaupel, J. W.(2010).Biodemography of human aging. *Nature* 464(7288):536-542.
- Wachter KW and Finch CE.(1997).*Between Zeus and the Salmon*. Washington, DC: National Academy Press.
- Wachter, K. W. & Finch, C. E. (eds) (1997).*Between Zeus & the Salmon*.US Natl Acad. Press.
- Walton A, Hammond J.(1938).The maternal effects on growth and conformation in Shire horse-Shetland pony crosses. *ProcRoy Soc Lond B* 125: 311-35.
- Wang, H. & Preston, S. H.(2009).Forecasting United States mortality using cohort smoking histories. *Proc. Natl Acad. Sci. USA* 106:393–398.
- Williams, G. C. (1957).Pleiotropy, natural selection, and the evolution of senescence. *Evolution* 11:398-411.
- Williams, G. C.(1966).Natural selection, the cost of reproduction and a refinement of Lack's principle. *Am. Nat.* 100: 687-690.
- Wilson, D. L.(1994).The analysis of survival (mortality) data: fitting Gompertz, Weibull, and logistic functions.*Mech Aging Dev* 74(1-2):15-33.
- Yashin AI, Arbeev KG, Kulminski A, Akushevich I, Akushevich L, Ukraintseva SV.(2007).Cumulative index of elderly disorders and its dynamic contribution to mortality and longevity. *Rejuvenation Research*.10(1):75–86.
- Yashin, A. I., Vaupel, J. W. & Iachine, I. A.(1995).Correlated Individual Frailty: an Advantageous Approach to Survival Analysis of Bivariate Data. *Math. Popul. Stud.* 5, 145-160.
- Zeng Y, Gu D.(2008).Reliability of age reporting among the Chinese oldest-old in the CLHLS data sets. In: Zeng Y, Poston D, Vlosky DA, Gu D, editors. *Healthy longevity in China: Demographic, socioeconomic, and psychological dimensions*.Dordrecht, The Netherlands: Springer: pp. 61–78.
- Zeng Yi and James W. Vaupel (2004).Association of Late Childbearing with Healthy Longevity among the Oldest-Old in China.*Population Studies*,Vol. 58, No. 1 Mar., pp. 37-53.
- Zeng, Yi, J. W. Vaupel, Z. Y. Xiao, C. Y. Zhang, and Y. Z. Liu.(2002).Sociodemographic and health profiles of the oldest old in China. *Population and Development Review* 28: 251–273.