

Are We Approaching the Upper Bounds of Human Life Span?

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Prolonging Life Expectancy

- The average life-span has being experienced a significant increase since turning to the 20th century.
- →For example, the life expectancies of U.S. male and female were at the upper 40's in 1900's and reached upper 70's in 2000's.
- →The life expectancies of Taiwan male and female have similar increasing trend.



The Life Expectancy of U.S. and Taiwan



Year

Increments of Life Expectancy (Taiwan Complete Life)



Complete Life Table

Actuaries Increments in Life Expectancy Risk is Opportunity.^{str}

- The life expectancy in U.S. has an increment of 0.3 year annually during the 20th century. The trend in Taiwan is similar but it seems that the slope is steeper.
- →According to U.N., the world has an annual increment of 0.25 year, during the second half of 20th century. The trend is likely to continue, at least for a while.





Impacts of Prolonging Life



- We are experiencing the longest life ever in the history, and this has changed our lives.
- →The life expectancies at age 65 were 12.20 and 14.63 years for Taiwan male and female in 1974, increased to 17.91 and 21.33 years in 2014. It increases about 50% more financial burden for retirement preparation.
- →Taiwan started national pension in 2008, in addition to other social insurance programs.



Soon they may live for 200 years

THE day may come when Roger Dobson and people will celebrate the start of Nina Goswami middle age on their 100th birthday. Some of the world's most the defeat or control of mass eminent experts on ageing have infectious diseases, such as medicied that average life smallness and taberculosis. expectancy in the developed. Over the next century, scienworld could rise to 200 years by tists say genetic advances will the end of the century.

From the end of the 19th atficantly higher. century to the present day, the average life span has almost fessor of medicine at Michigan doubled. In new research some State University, was among scientists predict a jump of the expens who thought life even greater proportions over expectancy could rise to 200 the next 100 years, thanks to years or more. He said "People advances in genetic medicine. haven't realised it, but we are in Out of 60 expents on ageing a similar position to the 1870s who were asked to predict life with regard to stopping the expectancy for a huby born in spread of infectious diseases. 2100, more than half believed it would be more than 100 years, slowly stop sepairing them-Seven who were interviewed in selves. I think we are going to the research project for the Joan- be able to reverse that process sal of Anti-Aging Medicine and through genetic intervenhelieved it could be between tion, will be able to tell the cells 150 and 200.

If such a change were to happes, it would mean a world the study agreed that dramatic dominated by the over-100s advances in genetic research torventure led by American scitetirement age.

of cleaner living conditions and California San Prancisco, said bridge elayed a leading role.

push the average life span sig-

Michael Fessel, clinical pro-"As you get older, your cells

to repair themselves." Other experts interviewed for

and a radical increase in the may unlock the secrets to long entits Dy Cruig Venter and the life in this century. Elizabeth international state-funded hu-In the past century, increases Blackhum, professor of bio- man genome project, in which in life expectancy were a result chemistry at the University of the Sanger Centre in Cam-

The code offers have potenlife expectancy could reach 175 tial in the buttle against openg years in 2100. She said: "In experiments in and research has already shown small animals, when some that transplanted aged skin cells. can be rejuvenated by manipulagenes are mutated away from tion of DNA. Other scientists their natural form, they can

are less convinced, however,

increase life span twofold. We believing the human body has a don't yet have an easy picture of how this might work in fixed limit on life span that it will not be possible to breach. humans, but it's theoretically possible. We know there is a To date, though there is no evidence of life expectancy levgenetic component [affecting elling off. A male been in Engageing] but don't yet know whether it will be a few genes land in the 1850s had a life expectancy of just over 40 or a large number." The sequencing of the human years while a fernale had a life. expectancy of 42. By 2000, a

genetic code - or genome -is the main reason for the predicman's life expectancy was 76 years and a woman's 80. The tions of such dramatic increases. in average life upans. The breakincrease is expected to continue through was made four years over the next few decades. Professor Tom Kirkwood, The sequencing of the human

head of biogerentology at Newgenetic code - or genome castle University's Institute for is the main reason for the predic-Ageing and Health, said many tions of such dramatic increases in the scientific community had in average life spars. The breakbeen surprised that life expectthrough was made four years ancy is still rising. ago by two parallel projects to He said: "Most people would map human DNA: a private-sechave predicted that, with the removal of most causes of premature death through infectious disease. life expectorers would start to reach a plateau. What has taken people by surprise is

that over the past 25 years we ess is undergoing change.

> have already been made and upheavals in history. that there is little prospect of a penetic benkehrough this cen- 60 and over was about 600m tury that will severse ageing. in 2000, compared with about He estimates life expectancy 300en in 1950, By 2050, the will be 90 by the year 2100. He said "Living for 200 pled to 2 billion. yours is unrealistic. To do that In a report last year, the

we would have to wipe out Center for Strategic and Interthings like cancer, heart disease mational Studies, a US think and other major health prob- tank, warned that "countries lens. Despite the billions being will have to race against time spent on these areas, that type to insure their economic and of endication of disease is frus- social fabric against the shock tratingly slow."

increase life span by 30%.

lished last week suggested this could be done by a protein.

Sittl, which controls when cells store or release fat.

If there are dramatic have seen expectancy increase, increases in life expectancy, it which tells us the ageing proc- is likely to mean an even greater burden on the health sys-Kirkwood believes most of tem and pensions. It will also the gains in life expectancy mean one of the greatest social

The great leap Life expectancy in

90 Years

80

70

60

1841

to long life

the againg genes

effects of old age

may be able to

counteract the

DNA Scientists believe interventions in

England and Wales

At birth

(formale)

1930

Unlocking the secrets

At birth (male)

2010

The world's population aged numbers are likely to have tri-

of global ageing".

It is not just genetic advances. Scientists such as Blackthat may boost longevity, wood, however, are excited by Research on animals has shown the possibilities of a longer life. that reducing calorie intake can She said: "How many of as have wanted to do something Scientists are now trying to else in our lives, such as be a develop a "megic ballet" that novelist, but not had the time? could simulate the effect of calo- So much human potential is rie restriction without people untapped. Perhaps with longer having to eat less. Research pub- lives, we could start to tap it."

> Older, bolder and hetter The Magazine, pages 28-36

A significant reduction in calorie intake may be able to increase lifespan by up to 50%. Scientists are now trying to dovise drugs that will mimic the effects of eating less **Beating disease** Human trials are already being conducted on cancer vaccines that stimulate the body to attack cancerous cells. In future decades, it may be possible to reverse heart disease by replacing diseased cells with healthy functioning ones. Stem cell research Doctors last

Nutrition

month announced that within the next decade people may be able to grow new teeth from stem cells. implanted in their gums. As the method develops, faulty organs could be replaced or repaired as the body begins to deteriorate

Bers The longest recorded 187%) Illespan for a human. Jeanne-Louise Calment, a Frenchwoman, was born on February 21, 1875 and died in 1997 at the age of 122 years and 164 days

Andorra in the Pyrenees has the highest life expectancy in the world, at 83 years. Mozambique has the lowest life expectancy in the world, at 31 years



Actuaries 黑弗克極限(Hayflick Limit) Risk is Opportunity.**

過去在學術界瀰漫著「正常脊椎動物的細胞,只要在最適宜的環境下進行培養,將永生不 死」之概念。提出理論的諾貝爾獎得主卡爾 (Carrel),據說他主持的實驗室,成功地培養雞 心臟的纖維母細胞長達34年。

然而,黑弗克在1960年前後的一連串實驗發現,他實驗室裡正常的人類纖維 母細胞,在分裂了50多代之後, 就停止複製、而凋零死亡。

來源:http://blog.roodo.com/thinkfly/archives/2254977.html







Mortality Improvement Continues.....





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Mortality Compression?

Ages of Death Probability for Taiwanese Females

	25%	50%	75%	90%	95%
1979-1981	69	79	86	91	93
1989-1991	72	80	87	92	94
1999-2001	74	83	90	95	98
2009-2011	78	86	92	97	99



Female









Applications

Work Supporting "No Limit"

- Oeppen and Vaupel (2002) predicted a life expectancy of 100 in 2060 in U.S.
- Wilmoth and Robine (2003) found maximum recorded life span has been steadily increasing at least for 140 years in Sweden.
- Robine and Vaupel (2002) reported that a probability of dying at age 110 of 0.52 based on the International Database on Longevity.



Work Supporting "Limit"

- Olshansky et al. (1990) consider that attaining a figure of 100 in 2060 is implausible.
- Decline in the death rate from the major cardiovascular diseases.
- The death rate from cancer increased 24% between 1970 and 2000 (US NCHs, 2004).



Rectangularization and Lifespan

- Regarding the theory of lifespan, there are two opinions: life with or without a limit.
- \rightarrow The rectangularization is a consensus.
- →Premature deaths (including infants) will gradually decrease and some postulates that the distribution of death number will behave like a normal curve.



What is Mortality Compression?

- Mortality Compression is (Fries, 1980)
- \rightarrow Rectangularization of the survival curve
- → A state in which mortality from exogenous causes is eliminated and the remaining variability in the age at death is caused by genetic factors.
- Mortality compression is linked with morbidity compression.





Mortality Compression (Wilmoth and Horiuchi, 1999)



Horizontalization, Longevity Extension, Verticalization



Mortality Compression (Cheung et al., 2005)



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Measuring Compression

- Wilmoth and Horiuchi (1999) proposed 10 measurements and they recommended the Interquartile (IQR).
- Kannisto (2000, 2001) calculated percentiles, IQR, shortest age interval (e.g., C50) on numbers of deaths from 22 countries.
- Cheung et al. (2005) computed SD(M+) for Hong Kong data.
- Thatcher et al. (2010) computed SD(M+) for 6 countries from HMD.





Age of Death is converging!(Sweden Male)





Mode and Standard Deviations (Kannisto, 2000)

Shortest Age Intervals (Kannisto, 2000)

Compression of mortality, Female



3D Measures (Hong Kong data) Risk is Opportunity.⁵⁷⁷

- Cheung et al.(2005) proposed 3-D measures, Horizontalization, Verticalization, and Longevity Extension.
- → They applied the idea to complete life tables in Hong Kong (1976-2001) and found "the increase in human longevity is meeting some resistance."
- Note: The mortality rates of ages 85 to 120 were graduated using logistic curve.



3 Dimensions of Survival Curve Bisk is Opportunity.sm

- Cheung et al. (2005) proposed 3-dimension measurements to describe the survival curve.
- →Horizontalization: *how many survivors can live before aging-related deaths significantly decrease*
- →Verticalization: *how concentrated aging-related deaths are around the modal age at death*
- →Longevity Extension: *how far the highest normal life durations can exceed Mode*



3 Dimensions of Survival Curve (Cheung et al., 2005)



Some Questions

- The calculations rely on values from the life tables, which are being graduated.
- → The elderly mortality rates (and ex) are influenced the most.
- Like in the Gompertz model, the estimation of parameter can be modified.
- → Yue (2002) considered 3 estimation methods for the parameter C, where $\mu_x = BC^x$.



Graduated Mortality Rates (Taiwan Male, 1999-2001)



Age





Motivation Proposed Simulation Study Applications Discussions Neasures of Compression (Kannisto, 2000) Modal Age, M, or the age with the maximal number of deaths. $M^* = x + \frac{f(x) - f(x-1)}{[f(x) - f(x-1)] + [f(x) - f(x+1)]}$

Standard deviation (σ) of the age at death above the mode, SD(M+).

$$SD(M+) = \sqrt{\frac{\sum_{M}^{\infty} f(x)(x-M)^2}{\sum_{M}^{\infty} f(x)}} \text{ or } \sqrt{\frac{\int_{M^*}^{\infty} f(x)(x-M^*)^2}{\int_{M^*}^{\infty} f(x)}}$$



- Proposed Approaches
- Three estimation methods: (Yue, 2002)
- →Maximal Likelihood Estimation (MLE), Nonlinear Maximization (NM), and Weighted Least Squares (WLS).
- →The MLE is expected to produce the most reliable estimates (smallest mean squared error), and the WLS is easy to use.
- →We choose the NM method since it has the best overall performance.



- Proposed Approaches (Conti.)
- The optimization method is model dependent and two distributions are used to verify the NM method.
- \rightarrow Normal distribution (Number of deaths d_x)

$$d_x \propto \frac{1}{\sqrt{2\pi\sigma}} e^{-\frac{(x-M)^2}{2\sigma}}$$

 \rightarrow Logistic distribution (Force of Mortality μ_x)

$$\mu_x \propto \frac{a e^{bx}}{1 + a e^{bx}}$$





About the Estimation

- The parameter estimates are influenced by the number of observations, or the data range *k*.
 → The estimation results using M~M+2*k* and M-*k*~M+*k* are similar, we will show only the results of M~M+2*k*.
 - \rightarrow The data format is "age-last-birthday" and the estimation of M shall be modified.



Motivation

Evaluating the Proposed Approaches

- Computer simulation:
- → The modal age M is 80 and the standard deviation σ is 10. Randomly generate 100,000 deaths from normal or logistic distribution.
 → Comparison criteria: Mean Squares Error (MSE), *Loss function (MSE) = Bias² + Variance*. and the probability of confidence interval covering true parameter (Coverage probability).









k(Range)

k(Range)



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σ² Motivation Proposed Approach Simulation Study Applications Discussions Risk is Opportunity.sm

Coverage Probability of Normal Dist.

	N		
	Integer Age	First Decimal	SD(M+)
М	.951	.952	.969
σ	.956	.937	.000

Note: M = 80 and $\sigma = 10$



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Coverage Probability of Logistic Dist.

	N		
	Integer	First	SD(M+)
	Age	Decimal	
Μ	.948	.924	.893
σ	.956	.927	.000

Note: *a* = 80 and *b* = 0.1336837



Empirical Studies

• We check if the graduation process would influence the estimation.

 \rightarrow Consider the Whittaker graduation

$$F = \sum_{x=1}^{n} w_x (v_x - u_x)^2 + h \sum_{x=1}^{n-z} (\Delta^z v_x)^2$$

→ The age-at-death follows N(80,10²), with 100,000 deaths for 1,000 simulation runs and h = ave. sample (W1) & 1,000×ave. sample (W2).



\sum	Motivation	$\mathbf{>}$	Proposed Approach	$\mathbf{>}$	Simulation Study	$\mathbf{>}$	Applications	Discussions	\rangle
								Risk is Opportunit	y. sm

M Estimates for Raw and Graduated Data

Μ		NM		SD(M+)			
k	Raw	W1	W2	Raw	W1	W2	
5	79.98	80.07	80.38	79.45	79.37	75.02	
6	80.01	79.87	80.37	79.37	79.51	75.02	
7	80.00	79.98	80.50	79.43	79.46	75.02	
8	79.99	79.82	80.60	79.48	79.66	75.02	
9	79.99	80.02	80.58	79.41	79.40	75.04	
10	79.99	80.01	80.57	79.37	79.35	75.04	



\sum	Motivation	$\mathbf{>}$	Proposed Approach	$\mathbf{>}$	Simulation Study	$\mathbf{>}$	Applications	Discussions	>
								Risk is Opportuni	ty. sm

σ Estimates for Raw and Graduated Data

σ		NM		SD(M+)			
K	Raw	W1	W2	Raw	W1	W2	
5	9.99	10.00	9.73	5.47	5.47	5.50	
6	10.00	10.00	9.70	6.34	6.34	6.39	
7	9.99	10.00	9.67	7.10	7.09	7.19	
8	10.00	10.00	9.67	7.71	7.71	7.89	
9	10.00	10.00	9.66	8.31	8.31	8.46	
10	10.01	10.01	9.66	8.69	8.69	8.91	



- Apply the mortality data from the Human Mortality Database and assume the age-at-death follows normal or logistic distribution.
- \rightarrow Using NM or SD(M+) estimation;
- →Several countries are considered and the σ estimates are used to evaluate the mortality compression.















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The Estimate of σ (WLS; Yue, 2012)



Year







Year

Conclusions and Discussions

- \bullet The proposed approaches are more reliable in estimating the modal age M and $\sigma.$
- \rightarrow NM (& WLS) are preferred.
- \rightarrow Raw data are preferred.
- \rightarrow The estimation method is model sensitive.
- The mortality compression is still not clear.
- →Some countries show a decreasing pattern, but some don't. However, the probability of surviving beyond age M+1.96 σ is increasing.



- Conclusions and Discussions (Conti.)
- The normal assumption is questionable.
- →The estimation methods are influenced by the distribution assumption.
- Using the standard deviation as the measure of mortality compression is questionable.
- →Are there alternative measures, such as the IQR and percentile?





Normality Test (Permutation Test)



Group	1	2	3	4	5	6	7	8
Ei	11504	12690	10262	11560	15778	10786	13856	13563

Note: The expected numbers are based on 10,000 simulation runs.







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- Conclusions and Discussions (Conti.)
- The probability of surviving to very high age cannot be ignored and if the life expectancy has a limit is still unknown. (Longevity Risk!)
- Some possible future study topics:
- →Modify the idea of mortality compression and apply it in dealing with longevity risk.
- \rightarrow Apply the extreme value theory.









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