



MAX-PLANCK-INSTITUT MAX PLANCK INSTITUTE FÜR DEMOGRAFISCHE FOR DEMOGRAPHIC FORSCHUNG RESEARCH

The Rise of Longevity

by James W. Vaupel

30th Anniversary

Estonian Demographic Association

Tallinn, 1 June 2016









View 1: Fixed frontier

.....



The fixed frontier of survival in evolutionary theories of aging

Peter Medawar	Mutation accumulation
George Williams	Antagonistic pleiotropy
William Hamilton	Demographic mathematics
Thomas Kirkwood	Disposable soma
Annette Baudisch	Inevitable senescence?

William Hamilton (1966, 1996)

I... show that no life schedule, even under the most benign ecology imaginable, could escape my spectrum of forces of selection.

William Hamilton (1966, 1996)

I... show that no life schedule, even under the most benign ecology imaginable, could escape my spectrum of forces of selection.

...after a few hundred years of draconian eugenic measures...the human lifespan might be stretched out just a little...say [to] 75 instead of... 70.

William Hamilton (1966, 1996)

I... show that no life schedule, even under the most benign ecology imaginable, could escape my spectrum of forces of selection.

...after a few hundred years of draconian eugenic measures...the human lifespan might be stretched out just a little...say [to] 75 instead of... 70.

[Research on] extension of active life seems to me comparable with the alchemists' search....[and] detracts both from unavoidable truth and from realistic social programs.



View 2: Secret of longevity

year	age claimed	possible age
1540	56	56
1557	80	73
1565	95	81

Determinants of Longevity

- Average lifespan in a population
 - Biomedical knowledge, health care system, standard of living, education, healthy behavior, environment
- Variation in lifespans among individuals

Determinants of individual longevity

adult life 65%



Determinants of individual longevity



Determinants of individual longevity









Determinants of individual longevity





Listen to your mother

h	1896	Midne,	tordelade	etter	alder	oci.	todelliar.	
70		B:lo	.+					

N	Z	वं	ante	a: 1	1	0794	92	3	2	044	9			on	9:
1	É	+		-	E Z	14763	12894	1	1	19965	12135	J.	7	28547	26447
0	a	d	SYNE	4334	mar 5	122	129	12	SIL	101	113	Ζ.	¢.	312	340
10.	۲	1			er "	118	105	15		93	112	70	1	318	310
		Ŧ	~		15	138)18		50	113	125		15	337	381
		1			2/	131	114	16	+	118	116	<i>////</i>	24	288	346
		1		-	-74	121	70		49	109	70	21		376	377
1.		ł			11 -	124	116	12	-	105	98	13.	-	340	371
		ł			-73	220	104	H	78	111	92		12	336	389
1	9	4	5333	1831	28.)20) 00	17	~	119	100	17.	21	328	395
					4 12	128	110	40	1	119	99	75.		305	358
	L				c11	119	30 (46	106	130	76	~	298	350
1			1.055	1006	25	105	113	57		140	111	77	19	241	331
1	Г	Т			-70	96	79		45	138	123	1	18	363	336
	L				26.	97	105	57.		144)58	17.	71	309	351
	0		730	634	- 69	108	86		44	135	124	2%	4	288	362
Г	ľ	Т			87	20	69	62		126	131	80	"	232	345
3			466	424	- 68	81	83		43	120	132	10.	15	262	2.121
	Γ	Т			1. Cet	73	99	4 .V.		144	149	e.,	14	23	
	6	3	382	391	00	102	75	1 14	1	164	133	15		2	259
-	ľ			2014	7 66	- 91	110	1	41	137	100	12	13	1	188
3	ł	+	315	240	30	105	105	55		151	128	-	2	5	244
	6	2	2.87	2.87	65	98	103	2	40	152	140	47.	**	1	297
4		1	226	242	3%	92	- 90	25		170	100	16.	10	162	2.74
1	T		0.24	Day	64	99	1 10	J.	23	135	159	1K		120	164
H	•	n	2 27	2.51	10	111	114	5%	24	149	130	87	on	80	143
13			201	217	11	89	101	60	20	176	156	172	08	80	118
1	4	200	166	145	6	13	10,	7	31)60	169	11.	or	14	24
		3	158		34	103	11	3 5		171	14	1 8%	~	22	86
E	1	5	151	136	61	89	11.	5	36	174	172	90.		43	- 69
12	1		152	139	35	196	10	Ja	-	200	183	91	05	35	56
17	1	- 0	116	119	- 60	109		2	-35	100	12	(04	38	61
1	1	81	125	109	-41	110)3	26/	-	184	20	99. G	03	29	59
Ľ		86	133	114	-3	97	. 11		- 34	214	1 24	93.		33	27
1	2	-	24	110	1/10	101	1)	9	33	225	5 21	5 94	02	23	21
1	2	55	87	81	JU.	100	10	76		210	21	1-	10	10))6
H	-	84	88	100	-5	1 100	10	٩Ľ	- 32	203	\$ 22	\$ 95.	00	6	16
Ľ	<u>^</u>	83	\$1	85	37	99	11	30	2	20;	2 20	\$ 96	-		8
1	1.		63	90	- 5	191	10	3-	-31	20:	0 20	97	11		
1		83	88	84	12	94		20	(-	26	2 25	3 01	- 98		ý
É	-	81	94	85	5	1 10	10	1	30	23	\$ 24	9 -	91	1	20
1	5.		81	101	1/1	91	1 20	314	-	28	0 24	91	96	1	
1	5	20	83	106	40	1 10	6 10	2	2	27	4 28	10	0.96		2
H	-	19	12	87	14,)) 0:	2 11	71	2.	25	2 26	3 10	175		2
Ľ	4	78	117)) 0 6	47	10	5 11	1	7-	25	8 25	5)0'	191		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
1	1.	-	35)12	-5	2 101	6 9	5	-2	1 27	1 27	T	-		-
1	10.	(136	113	4	1 1	0 8	9	2	28	6 27	1	1.	- 0.0	1
Ľ					1			+	-		-	1	0	21	20/20
12	36.	1.	14,763	15664	hal	31996	2 1813	5	apt	\$ 58,54	15014	19	a.	38,58	201018

View 3: Advancing frontier

		A DESCRIPTION OF TAXABLE PARTY.	
85	1.1	160	195
00.	10	162	224
00	101	123	164
00.	00	105	164
	07	80	1431
87.		73	119
	08	201	110
88.	-	DO	124
	01	19	27
89	- 1	53	109
%	06	49	86
00	0.0	41	- 69
10-		50	73
H OV	05	25	56
91.		38	61
-	04	02	55
93.		~)	5.5
i i	103	29	30
93		28	26
4	00	13	211
au	1-2	23	21
197.)2	14
1 miles	101	10)6
95		10	16
-	100	0	10
0 96.			
1	-99		D
07	1.1		4
277.	90		4
00	10		7
70.	Tar		8
	171		2
\$ 99	a	1	
3100	096		2
010	195	2	2
		1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
510.	141		
			19.3



Hans Lundström



Discovery of the Advancing Frontier of Survival: The Decline in Octogenarian Mortality

Women, Ages 80-89

Men, Ages 80-89



Source: Calculations by Roland Rau (unpublished) based on Human Mortality Data 429e

The frontier of survival

The explosion of centenarians



Advancing frontier

The explosion of centenarians

What do we know about the physiology of human longevity?

MAJOR DISCOVERY:

The frontier of survival is advancing: old-age mortality is not intractable

SUPPLEMENTAL DISCOVERIES:

1. The frontier of survival is advancing – because senescence is being delayed, not decelerated.

The Postponement of Senescence: Evidence from Sweden

Data from Human Mortality Database. Also see Christensen...Vaupel ,Lancet 2010, 2013.

Current age and age of equivalent mortality 50 years ago.

	Equivalent Age 50 Years Ago							
	Femal	е			Male			
Age	France	Sweden	England & Wales	Japan	France	Sweden	England & Wales	Japan
50	42	40	42	23	44	43	43	39
60	49	52	52	43	51	53	51	50
70	59	62	62	53	59	62	59	57
80	71	72	73	67	71	73	72	70
90	83	85	83	79	84	87	82	81

What do we know about the physiology of human longevity?

MAJOR DISCOVERY:

The frontier of survival is advancing: old-age mortality is not intractable

SUPPLEMENTAL DISCOVERIES:

- 1. The frontier of survival is advancing because senescence is being delayed, not decelerated.
- 2. Life expectancy is rising linearly, with no sign of a looming limit.

The frontier of survival

The Revolution in Record Life Expectancy

Oeppen & Vaupel Science 2002; extended

Life expectancy:

- might rise more slowly than in the past, perhaps approaching a limit that is not much greater than the current best-practice level, with some chance that life expectancy might fall.
- in the countries doing best, might continue to rise at the historical pace of almost 3 months/year for the next several decades and perhaps longer.
- might rise substantially faster than this, because of major biomedical breakthroughs.

- A. Best-practice national life expectancy (for women) has been rising linearly for the past 175 years at a steady pace of about 2.5 years per decade. The record is now above 87. Over the next 50 years do you think that this record will increase:
- 1. Even faster--by more than 3 years per decade, reaching 102 or more;
- 2. At about the same pace--by 2-3 years per decade, approaching 100 or so;
- 3. At a slower and slower pace—declining from 2.5 years per decade to roughly 1 year per decade, reaching perhaps 95 or so;

4. At a much slower pace, reaching a plateau, a life-expectancy limit, not much higher than the current record of 87—perhaps 90 or so;

5. At a negative rate, falling to a value below 87.

- A. Best-practice national life expectancy (for women) has been rising linearly for the past 175 years at a steady pace of about 2.5 years per decade. The record is now above 87. Over the next 50 years do you think that this record will increase:
- 1. Even faster--by more than 3 years per decade, reaching 102 or more; 6%

2. About the same pace, by 2-3 years per decade, approaching 100 or so; 9%

3. At a slower and slower pace—declining from 2.5 years per decade to roughly 1 year per decade, reaching perhaps 95 or so; 22%

4. At a much slower pace, reaching a plateau, a life-expectancy limit, not much higher than the current record of 87—perhaps 90 or so; 59%

5. At a negative rate, falling to a value below 87. 3%

B. What do you think the probability is that record life expectancy will increase at about the same pace as in the past or somewhat faster—by at least 2 years per decade on average over the next 50 years, reaching a level of 97 or more?

1. Likely: at least 50% chance.

2. Possible but not likely: more than 25% but less than 50% chance.

3. Unlikely: more than 5% but less than 25% chance.

4. Very unlikely: less than 5% chance.

B. What do you think the probability is that record life expectancy will increase at about the same pace as in the past or somewhat faster—by at least 2 years per decade on average over the next 50 years, reaching a level of 97 or more?

1. Likely: at least 50% chance.

2. Possible but not likely: more than 25% but less than 50% chance. 56%

27%

- 3. Unlikely: more than 5% but less than 25% chance. 16%
- 4. Very unlikely: less than 5% chance. 2%

C. What do you think the probability is that record life expectancy will increase slowly or maybe even decline over the next 50 years, reaching a level less than 90.

1. Likely: at least 50% chance.

2. Possible but not likely: more than 25% but less than 50% chance.

3. Unlikely: more than 5% but less than 25% chance.

4. Very unlikely: less than 5% chance.

C. What do you think the probability is that record life expectancy will increase slowly or maybe even decline over the next 50 years, reaching a level less than 90.

1. Likely: at least 50% chance.

2. Possible but not likely: more than 25% but less than 50% chance.

4%

45%

3. Unlikely: more than 5% but less than 25% chance. 39%

4. Very unlikely: less than 5% chance.

The Sorry Saga of Looming Limits to Life Expectancy Oeppen and Vaupel Science 2002

The Future will be different from the past

Since 1840, future progress in extending life expectancy has been different from past progress.

- The country with the longest life expectancy has shifted from Sweden to Japan
- The causes of death against which progress has been made have shifted from infectious diseases to chronic diseases
- The ages at which mortality has been reduced have shifted from childhood to old age

Age-Specific Contributions to the Increase of Record Life Expectancy among Women 1850 to 2009 in %

Ag gro	ge oup	1850- 1901	1901- 1925	1925- 1950	1950- 1975	1975- 1990	1990- 2009
	0	14	32	15	21	10	4
1	-14	55	8	16	12	4	2
15	-49	25	38	39	20	7	4
50	-64	3	13	19	17	20	11
65	-79	2	8	11	24	41	37
	30+	0	1	0	6	17	41
То	tal	100	100	100	100	100	100

Data Source: Calculations based on Human Mortality Database by Roland Rau and James Vau 22(29) (published)

The Future Will Be Different from the Past

- In next decade or two, progress against cancer and dementia and in developing genotype-specific therapies
- Then progress in regenerating and eventually rejuvenating tissues and organs
- Accompanied by progress in replacing deleterious genes (CRISPR)
- Aided by nanotechnologies (nanobots)
- Perhaps in a decade or two, probably later, progress in slowing the rate of aging (as opposed to further postponing aging).

Postponement vs. Deceleration of Senescence:

D. Consider the lifespans of the cohort of infants born in England & Wales in 2016.What is the chance the average lifespan for this cohort will exceed 100?

- 1. Likely: 50% or more.
- 2. Possible but not likely: more than 25% but less than 50%.
- 3. Unlikely: more than 5% but less than 25%.
- 4. Very unlikely: less than 5%.

D. Consider the lifespans of the cohort of infants born in England & Wales in 2016.What is the chance the average lifespan for this cohort will exceed 100?

- 1. Likely: 50% or more. 40%
- 2. Possible but not likely: more than 25% but less than 50%. 46%
- 3. Unlikely: more than 5% but less than 25%. 14%
- 4. Very unlikely: less than 5%. 1%

E. Consider the lifespans of the cohort of infants born in England & Wales in 2016.
What is the chance the average lifespan for this cohort will exceed 120?

- 1. Likely: 50% or more.
- 2. Possible but not likely: more than 25% but less than 50%.
- 3. Unlikely: more than 5% but less than 25%.
- 4. Very unlikely: less than 5%.

E. Consider the lifespans of the cohort of infants born in England & Wales in 2016.What is the chance the average lifespan for this cohort will exceed 120?

- 1. Likely: 50% or more. 2%
- 2. Possible but not likely: more than 25% but less than 50%. 25%
- 3. Unlikely: more than 5% but less than 25%. 32%
- 4. Very unlikely: less than 5%. 40%

Forecasting Cohort Life Expectancy

For birth cohorts, life expectancy may increase by 4 months per year.

If so, most people born in long-lived populations since 2000 will celebrate their 100th birthdays.

Oldest Age at which at least 50% of a Birth Cohort is

Still Alive Christensen, Doblhammer, Rau & Vaupel Lancet 2009, extended

Year of Birth:	2000	2005	2010
France	102	104	105
Germany	100	101	103
Great Britain	102	103	105
Japan	105	107	108
Sweden	101	102	104
USA	101	103	105

Data are ages in years. Baseline data were obtained from the Human Mortality Database and refer to the total population of the respective countries.

The Rise in Record Life Expectancy at Age 65

Data Source: Calculations based on Human Mortality Database from Roland Rau and James Vaupel (unpublished)

Consider the remaining life expectancy of people in England and Wales at age 65, currently about 20 years. How much will this value increase over the next 30 years?

- 1. 5 years or more.
- 2. More than 2 but less than 5 years.
- 3. More than 6 months but less than 2 years.

4. Close to zero: less than 6 months and perhaps the value might even decline.

Consider the remaining life expectancy of people in England and Wales at age 65, currently about 20 years. How much will this value increase over the next 30 years?

- 1. 5 years or more. 50%
- 2. More than 2 but less than 5 years. 44%
- 3. More than 6 months but less than 2 years. 6%

4. Close to zero: less than 6 months and perhaps the value might even decline.

Year	Born	e65	Ave. lifespan
2012 period		23	88

Year	Born	e65	<u>Ave. lifespan</u>
2012 period		23	88
cohort	1947	27	92

Year	Born	e65	Ave. lifesp	an
2012 period		23	88	
cohort	1947	27	92	
cohort*	5	28	93	

*Rate of ageing slowed at a rate of 2%/year after 2030

Year		Born	e65	Ave. lifespan
2012	period		23	88
	cohort	1947	27	92
	cohort*		28	93
2030	cohort	1965	30	95

Year		Born	e65	Ave.	<u>lifespan</u>
2012	period		23	88	
	cohort	1947	27	92	
	cohort*		28	93	
2030	cohort	1965	30	95	
	cohort*		38	103	

*Rate of ageing slowed at a rate of 2%/year after 2030

Year		Born	e65	Ave. I	<u>ifespan</u>
2012	period		23	88	
	cohort	1947	27	92	
	cohort*		28	93	
2030	cohort	1965	30	95	
	cohort*		38	103	
2060	cohort	1995	38	103	

Year	Born	e65	Ave. lif	espan	
2012 period		23	88		
cohort	1947	27	92		
cohort*		28	93		
2030 cohort	1965	30	95		
cohort*		38	103		
2060 cohort	1995	38	103		
cohort*		67	132		
*Rate of ageing slowed at a rate of 2%/year after 2030					

Year		Born	e65	Ave	<u>. lifespan</u>
2012	period		23	88	
	cohort	1947	27	92	
	cohort*		28	93	
2030	cohort	1965	30	95	
	cohort*		38	103	Risk
2060	cohort	1995	38	103	
	cohort*		67	132	Big Risk
*Rate of ageing slowed at a rate of 2%/year after 2030					

The Failure of Expert Imagination

Mortality forecasts based on expert judgment have been less accurate than extrapolation.

The Best Forecasting Strategy

At present the best way to forecast life expectancy is to extrapolate long-term historical trends from countries with high life expectancy.

And then to ask: why might progress be faster? Why might it be slower?

Q: Will the postponement of senescence continue, leading to reductions in mortality after age 100?

Q: Will the rate of ageing be slowed down, leading to even greater improvements?

How important is the Human Mortality Database to your work?

- 1. Very important and I would strongly favor improving it to include more up-to-date statistics, data for other populations, corrections of problematic data, etc.
- 2. Important but substantial improvements are not needed.
- 3. Of some value.
- 4. Of little or no value.

How important is the Human Mortality Database to your work?

- Very important and I would strongly favor improving it to include more up-to-date statistics, data for other populations, corrections of problematic data, etc. 59%
- 2. Important but substantial improvements are not needed. 15%
- 3. Of some value. 25%
- 4. Of little or no value.2%

Max-Planck Odense Center on the Biodemography of Aging

FÜR DEMOGRAFISCHE FOR DEMOGRAPHIC FORSCHUNG RESEARCH

MAX-PLANCK-INSTITUT MAX PLANCK INSTITUTE

Key publications

James W. Vaupel and Hans Lundström (1994) "Longer Life Expectancy? Evidence from Sweden of Reductions in Mortality Rates at Advanced Ages" in David A. Wise (editor) <u>Studies in the Economics of Aging</u>, U. of Chicago Press, pp. 79-94. This chapter presented the twin discoveries about the advancing frontier of human survival that Vaupel made in 1992 based on Swedish data compiled for him by Hans Lundström at Statistics Sweden. Unfortunately the research was presented in 1992 to a group of health and labor economists who did not understand the significance of the discoveries and the research was published in 1994 in a rather obscure book of the proceedings of the 1992 workshop.

An article by Vaupel et al. in Science introduced a much wider audience to the research breakthroughs: J.W. Vaupel et al. (1998) "Biodemographic Trajectories of Longevity", Science **280**, pp. 855-860.

Jim Oeppen and James W. Vaupel (2002) "Broken Limits to Life Expectancy", Science **296**, pp. 1029-1031. Although demographers knew that life expectancy was tending to increase in most countries, it was not realized until this article was published that an astonishing regularity underlay the progress: in the populations doing best, life expectancy has increased from a bit over 45 for Swedish women in 1840 to more than 87 for Japanese women today. The rise has been linear—3 months per year.

James W. Vaupel (2010) "Biodemography of Human Ageing", Nature **464**, pp. 536-542. This comprehensive review describes Vaupel's discoveries and their implications for research and for society.

James W. Vaupel (2005) "The Biodemography of Aging" in L.J. Waite (editor) Aging, Health, and Public Policy: Demographic and Economic Perspectives, Population Council, New York, pp. 48-62 (Population and Development Review; **30**, 2004, Suppl.). This is an earlier account by Vaupel of his research; the material in it is a lightly-edited transcript of impromptu remarks Vaupel made to a group of students.

James R. Carey,..., James W. Vaupel (1992) "Slowing of Mortality Rates at Older Ages in Large Medfly Cohorts", Science **258**, pp. 457-461.

James W. Curtsinger,..., James W. Vaupel (1992) "Biodemography of Genotypes: Failure of the Limited Lifespan Paradigm in *Drosophila melanogaster*", Science **258**, pp. 461-463.

Key publications continued

James W. Vaupel, Annette Baudisch et al. (2004) "The Case for Negative Senescence", Theoretical Population Biology **65**, pp. 339-351.

Annette Baudisch and James W. Vaupel (2012) "Getting to the Root of Aging", Science **338**, pp. 618-619. This short article summarizes why Hamilton was wrong: senescence is not inevitable.

Owen R. Jones,..., James W. Vaupel (2014) "Diversity of Ageing across the Tree of Life", Nature **505**, 169-173.

Ralf Schaible,..., James W. Vaupel (2015) "Constant Mortality and Fertility over Age in *Hydra*", PNAS December 2015.

Fernando Colchero,..., James W. Vaupel (2015) "Lifespan Equality and Life Expectancy in Humans and Other Primates", Science, under review.

A fuller list of Vaupel's publications can be found at user.demogr.mpg.de/jwv. This website provides electronic access to most of his articles. The website also provides access to several non-technical descriptions, published in the Lancet and elsewhere, of Vaupel and his research.