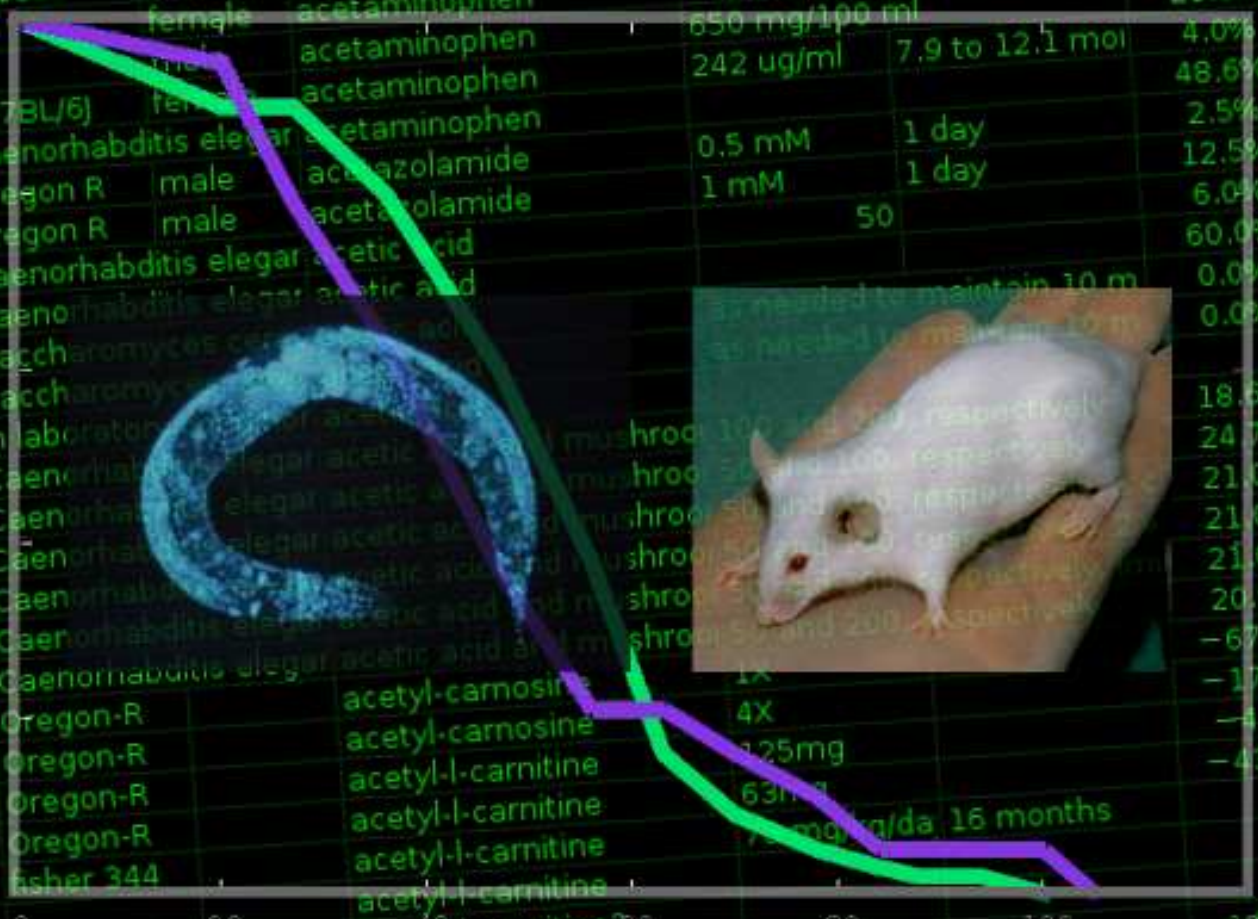


# C. ELEGANS LIFE SPAN EXPERIMENTS REPLICATED AND EXTENDED

PERCENT SURVIVING



TIME



Kingsley G. Morse Jr., B.Sc., MBA

[kingsley@loaner.com](mailto:kingsley@loaner.com)

<http://morse.kiwi.nz>

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# 1 Abstract

Results from testing an impressive 1280 compounds on the average life spans of 126,681 worms (*C. elegans*) were published in 2014[1].

Their good results for nortriptyline, minocycline and biogenic amines have been replicated in mammals.

I replicated thousands of their worm calculations, and extended them to include maximum life span.

Changes in the worms' average and maximum life spans are correlated.

## 2 Methods

### 2.1 Finding Mammal Experiments That Replicated Worm Results

The worm paper very reasonably suggests retesting its good compounds in mammals.

I checked my big spread sheet of life span experiments[2].

Nortriptyline[3], minocycline[4] and biogenic amines[5] also worked in mammals.

compound or class	worm change in average life span	mammal experiments			
		subjects	effect on life span	reference	comment
nortriptyline	+21%	mouse model of amyotrophic lateral sclerosis	longer life	6	
		mouse model of Huntington's disease	no effect	6	
		recent human stroke victims	50% less risk of dying	7	
minocycline	+29%	mouse model of amyotrophic lateral sclerosis	+13% longer on average	8	
		mouse model of Huntington's disease	+12% longer on average	9	
biogenic amines	+10% to +43%	male Jc1:ICR mice	no effect	10	spermine and spermidine
		male Jc1:ICR mice	longer life	10	high dose spermine and spermidine
		mice	no effect	11	spermine, spermidine and putrescine
		mice	12.5%+ longer life	11	high dose spermine, spermidine and putrescine
promethazine	+32%	mouse model of amyotrophic lateral sclerosis	same or shorter life	6	
beta-Estradiol	+7%	male rats	+7% longer life	13	oestrogens
		female rats	+0.3% longer life	13	oestrogens
		men with previous myocardial infarction	no effect	14	high dose estrogen
		men with previous myocardial infarction	3% increased risk of dying	14	low dose estrogen
		postmenopausal women	2% to 18% less risk of dying	15	estrogen

## 2.2 Replicating Worm Calculations

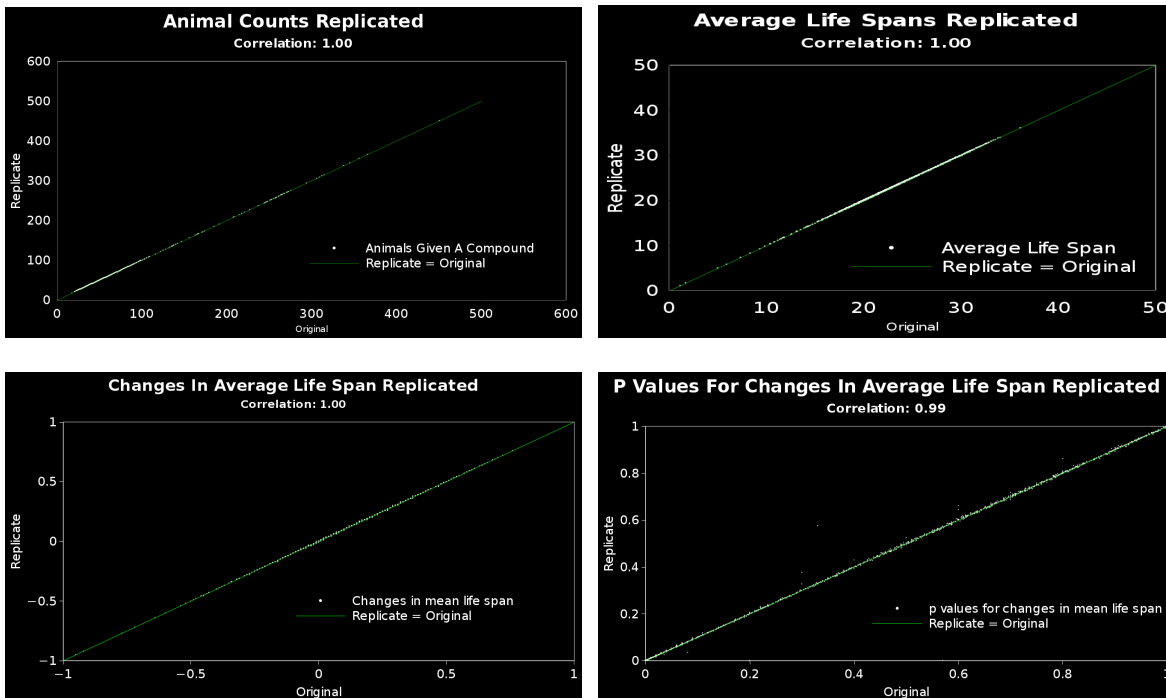
A worm researcher<sup>1</sup> very nicely shared their data.

It basically looks like...

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	this data set contains all the C. elegans lifespan experiments that went into the LOPAC paper														
2	plate	col	row	WellID	date	set	strain	Drug	conc	day	died	alive	class	action	selectivity
3	10	1	D	01001DC102607	102607	C	N2	DMSO	33	21	1	4			
4	10	1	C	01001CB102607	102607	B	N2	DMSO	33	18	1	10			
5	10	1	E	01001EB102607	102607	B	N2	DMSO	33	28	1	1			
6	10	1	C	01001CA102607	102607	A	N2	DMSO	33	28	1	0			
7	10	1	A	01001AA102607	102607	A	N2	DMSO	33	25	1	1			
8	10	1	D	01001DD102607	102607	D	N2	DMSO	33	25	1	1			
9	10	1	E	01001EC102607	102607	C	N2	DMSO	33	25	1	3			
10	10	1	B	01001BB102607	102607	B	N2	DMSO	33	18	1	9			
11	10	1	H	01001HB102607	102607	B	N2	DMSO	33	18	1	6			
126675	10	1	E	00509ED102607	102607	D	N2	trans-Dehydroandrosterone	33	25	1	2	Hormone	Aldosteron	
126676	5	9	E	00509ED102607	102607	D	N2	trans-Dehydroandrosterone	33	25	1	2	Hormone	Aldosteron	
126677	5	9	E	00509ED102607	102607	D	N2	trans-Dehydroandrosterone	33	14	1	7	Hormone	Aldosteron	
126678	5	9	E	00509EB102607	102607	B	N2	trans-Dehydroandrosterone	33	14	1	10	Hormone	Aldosteron	
126679	5	9	E	00509ED102607	102607	D	N2	trans-Dehydroandrosterone	33	21	1	4	Hormone	Aldosteron	
126680	5	9	E	00509EC102607	102607	C	N2	trans-Dehydroandrosterone	33	25	1	1	Hormone	Aldosteron	
126681	5	9	E	00509EA102607	102607	A	N2	trans-Dehydroandrosterone	33	14	1	8	Hormone	Aldosteron	
126682	5	9	E	00509EC102607	102607	C	N2	trans-Dehydroandrosterone	33	21	1	2	Hormone	Aldosteron	
126683	5	9	E	00509ED102607	102607	D	N2	trans-Dehydroandrosterone	33	11	1	9	Hormone	Aldosteron	
126684															
126685															

Part of the raw-looking data

Through a process of coding<sup>2</sup>, trial and error, I replicated thousands of their calculations:



It's reassuring that the big worm researchers<sup>3</sup> correctly calculated thousands of numbers.

<sup>1</sup>Michael Petrascheck

<sup>2</sup>Computer programmers sometimes call software “code”.

<sup>3</sup>There's a rumor that this paper might qualify me as a junior big worm researcher. (OK, I started the rumor. ;-))

## 2.3 Extending Worm Calculations To Include Maximum Life Span

The original paper reported the effect of each compound on average life span.

That's good.

Another commonly reported statistic is how much maximum life span changes.

It's the age of the oldest of the old.

After I replicated their calculations of changes to average life span, I was confident I could match

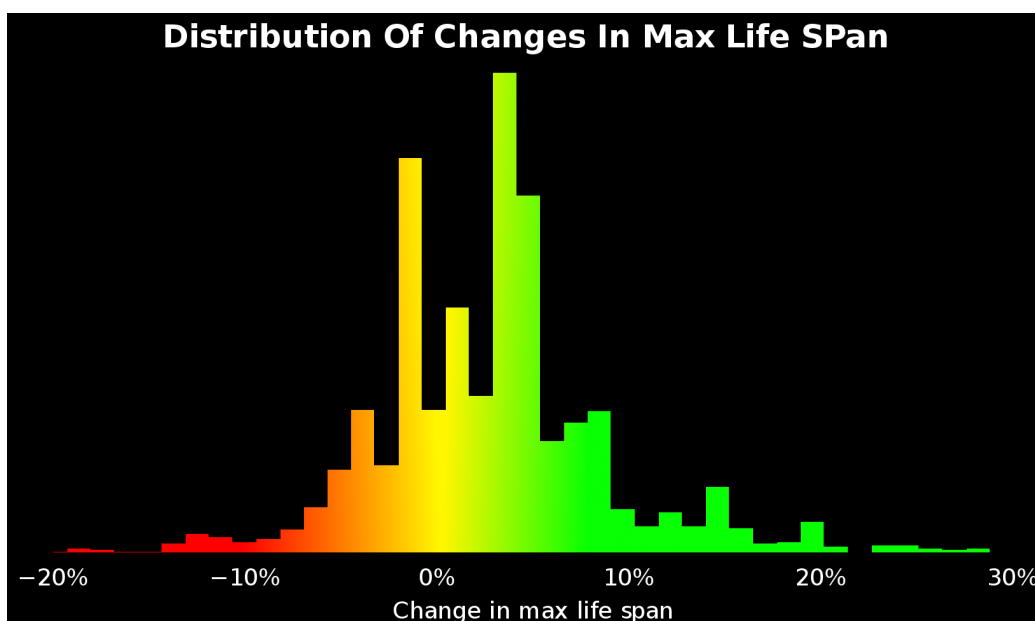
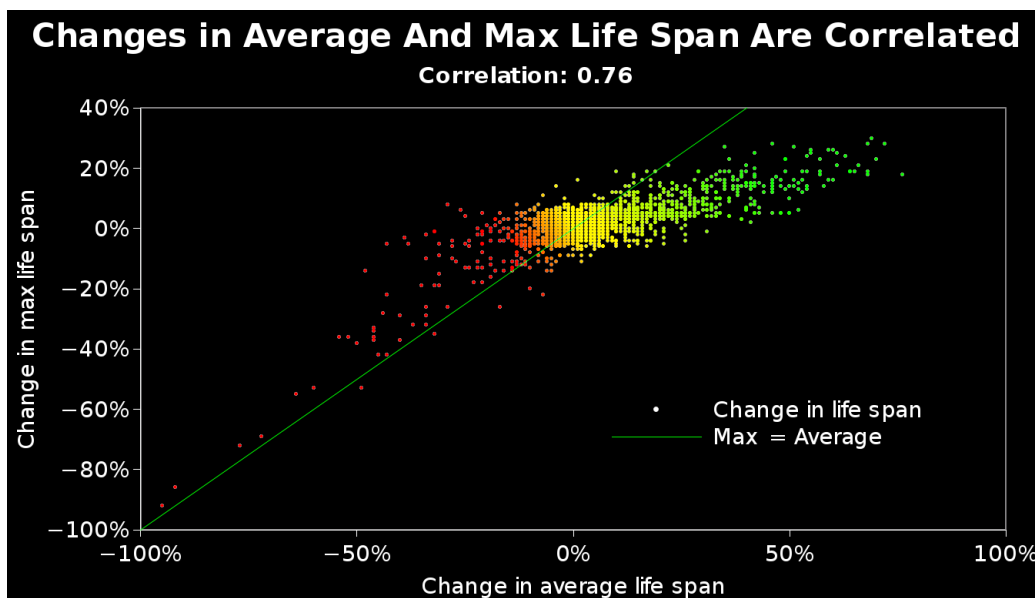
1. data for animals receiving a certain compound to
2. corresponding data for their control animals

and could calculate maximum life spans the same way.

So I did.

I considered how long the oldest 10% lived.

Changes in average and max life span are correlated.



## Changes In Maximum Life Span For The 57 "Hit" Compounds Reported In The Original Paper

Compound/drug	Life Span		p-value
	Average increase	Maximum increase	
Demeclocycline hydrochloride	16%	4%	2E-02
Doxycycline hydrochloride	18%	1%	1E-02
Minocycline hydrochloride	29%	10%	5E-04
3,4-Dichloroisocoumarin	13%	7%	8E-02
Amoxapine	33%	10%	2E-04
Doxazosin mesylate	15%	10%	1E-02
Guanabenz acetate	12%	9%	2E-06
Guanfacine hydrochloride	15%	7%	2E-01
Naftopidil dihydrochloride	14%	9%	1E-01
Nortriptyline hydrochloride	21%	6%	5E-03
(±)-Octoclothepein maleate	38%	14%	2E-04
BTCP hydrochloride	14%	8%	6E-04
Chlorprothixene hydrochloride	33%	16%	7E-09
cis-(Z)-Flupenthixol dihydrochloride	30%	8%	4E-04
Cortexolone maleate	11%	6%	1E-02
Dihydroergocristine methanesulfonate	34%	10%	2E-06
Loxapine succinate	43%	15%	6E-09
Methylethergonovine maleate	28%	8%	5E-03
N-(2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl)-3-methoxybenzamide	35%	14%	3E-09
Pergolide methanesulfonate	37%	13%	9E-04
Propionylpromazine hydrochloride	20%	11%	4E-03
Thioridazine hydrochloride	31%	10%	3E-05
Loratadine	18%	4%	3E-01
Oxatomide	25%	7%	2E-05
Promethazine hydrochloride	32%	6%	3E-04
PAPP/LY-165,163	33%	12%	3E-06
Amperozide hydrochloride	38%	13%	2E-05
BRL 15572	10%	4%	3E-03
Dihydroergotamine methanesulfonate	24%	5%	3E-02
Ketanserine tartrate	13%	2%	4E-01
LY-367,265	34%	10%	7E-04
Metergoline	23%	5%	2E-02
Mianserin hydrochloride	32%	8%	8E-08
Cinnarizine	15%	6%	2E-04
Nicardipine hydrochloride	23%	13%	3E-06
Nitrendipine	25%	10%	3E-04
Hexahydro-sila-difenidol hydrochloride	15%	6%	4E-03
BRL 50481	18%	9%	4E-06
Trequinsin hydrochloride	27%	12%	2E-07
Vinpocetine	15%	4%	4E-05
Vincristine sulfate	12%	2%	2E-01
AMN082	8%	5%	5E-02
Eliprodil	16%	2%	8E-01
(R,R)-cis-Diethyl tetrahydro-2,8-chrysenediol	7%	3%	4E-01
Beta-Estradiol	7%	4%	8E-02
Cyproterone acetate	23%	-3%	9E-02
Danazol	13%	7%	8E-03
Psora-4	42%	14%	7E-10
Quinidine sulfate	12%	5%	7E-02
4-Phenyl-3-furoxan carbonitrile	30%	9%	2E-03
7-Cyclopentyl-5-(4-phenoxy)phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-ylamine	11%	7%	2E-03
Cyclosporin A	18%	9%	1E-02
DAPH	15%	7%	1E-01
Kenpaullone	27%	12%	1E-04
LFM-A13	27%	12%	1E-07
SU 4312	5%	11%	8E-06
Tyrphostin AG 1478	11%	6%	6E-04



### **3 Discussion**

I read that all three of the compounds that worked in worms and mammals affect nerves.

Nortriptyline is an antidepressant[3].

Minocycline evidently penetrates the central nervous system[4].

Biogenic amines include neurotransmitters[5].

Maybe neural control of aging is evolutionarily conserved between worms and mammals.

### **4 Conclusion**

Nortriptyline, minocycline and biogenic amines extended the average life spans of worms and mammals.

Changes in the worms' average and maximum life spans are correlated.

### **5 Funding**

No money was involved.

I donated my time and skillz because I was interested, and it seemed worthwhile.

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