C. ELEGANS LIFE SPAN EXPERIMENTS REPLICATED AND EXTENDED 2
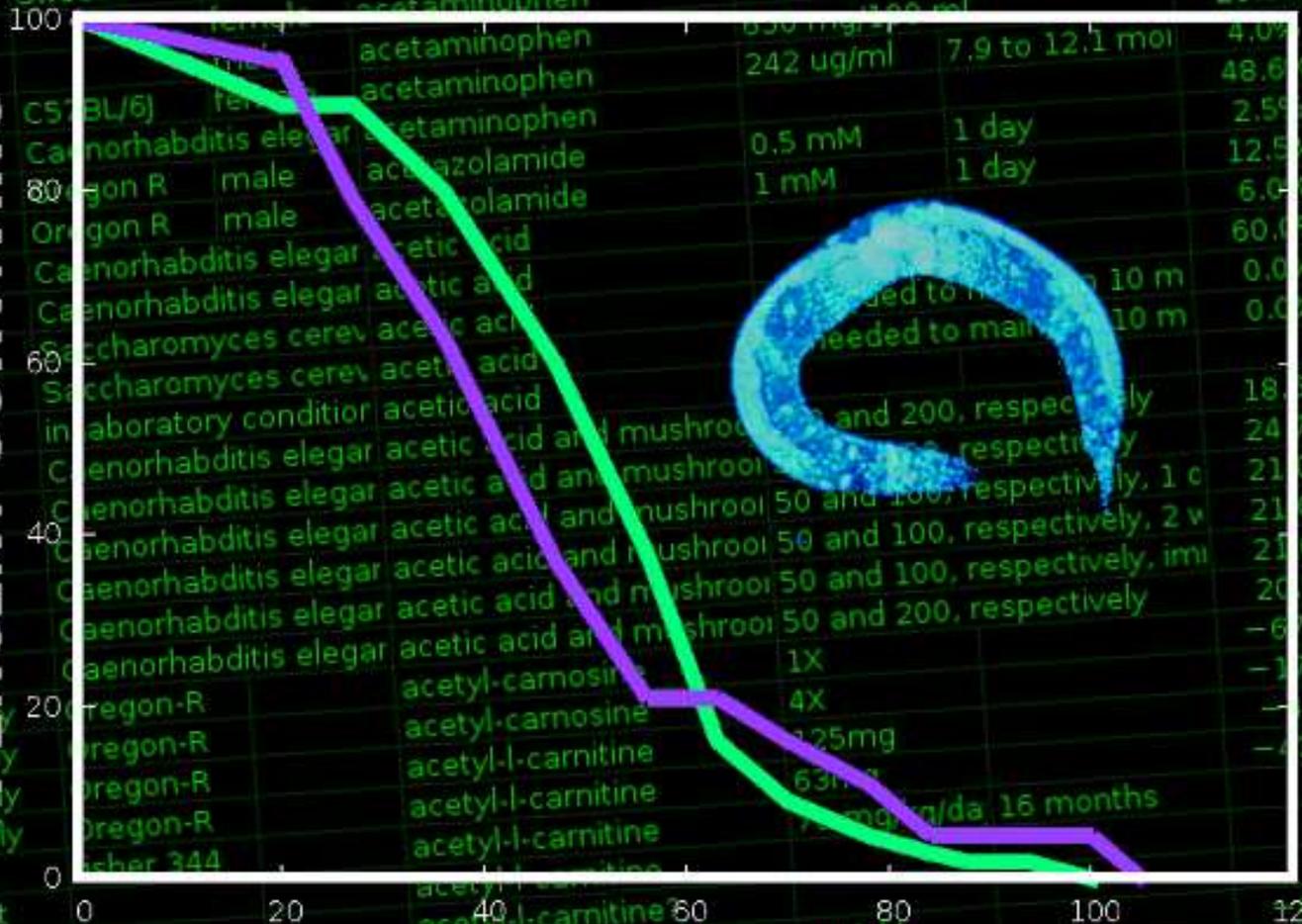
Kingsley G. Morse Jr., B.Sc., MBA
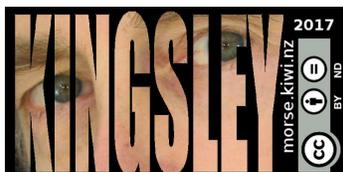
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Contents

1 Abstract

The effects of 10 compounds on the life spans of over 60,000 worms were previously tested and published[1].

I replicated most of their calculations.

Then I extended them by calculating how much mean and maximum life spans changed, and their corresponding statistical p-values.

Some changes are statistically significant.

It seems to me that a dye named "Thioflavin T" worked best.

You know what that means.

A dye delayed (wait for it...) dying.

2 Methods

2.1 Replicating Calculations

The worm researchers published their raw-ish data and summaries1.

They basically look like...

Supplementary Data 9: CITP raw lifespan data (with compounds)											
Lab	Experimenter	Compound	Species	Strain	Trial	Plate	DeathAge	Censor	Dead	DeathNo	LogDeath
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	7	1	0		
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	9	0	1	9	2.1972245773362196
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	9	1	0		
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	9	1	0		
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	14	0	1	14	2.6390573296152584
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	14	0	1	14	2.6390573296152584
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	14	1	0		
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	14	1	0		
DRISCOLL	DB	ALPHA_KETO	C. BRIGGSAE	AF16	2015-Apr-13	DS_041315_BO_AF16_A-KETO-3	14	1	0		
DRISCOLL			BRIGGSAE	AF16			14				
	DG					DS_091415_SG_JU7...				21	3.0445224...
	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775...		0	1	21	3.044522437723423
DRISCOLL	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775 PRP_GAL-1.1	23	0	1	23	3.1354942159291497
DRISCOLL	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775 PRP_GAL-1.1	23	0	1	23	3.1354942159291497
DRISCOLL	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775 PRP_GAL-1.1	23	0	1	23	3.1354942159291497
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DRISCOLL	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775 PRP_GAL-1.1	23	0	1	23	3.1354942159291497
DRISCOLL	DG	PROPYL_GALLATE	C. ELEGANS	JU775	2015-Sep-14	DS_091415_SG_JU775 PRP_GAL-1.1	23	0	1	23	3.1354942159291497

and

Supplementary Data 4: Summary and statistics of all chemical intervention lifespan data by trial											
Compound	Species	Strain	Lab	Trial	Final N	Censored	Mean Longevity	SEM	Kaplan-Meier Median	Lower 95%CI	Upper 95%CI
ALPHA_KETO	C. BRIGGSAE	AF16	DRISCOLL	2015-Apr-13	61	44	27.01485935	0.6994016517	28	25	28
ALPHA_KETO	C. BRIGGSAE	AF16	DRISCOLL	2015-Jun-22	37	28	25.554258616	0.9692220551	25	23	28
ALPHA_KETO	C. BRIGGSAE	AF16	LITHGOW	2015-Mar-23	22	18	25.965864528	1.0879026321	25	25	30
ALPHA_KETO	C. BRIGGSAE	AF16	LITHGOW	2015-Mar-27	46	31	27.56701344	0.6659197858	28		
ALPHA_KETO	C. BRIGGSAE	AF16	LITHGOW	2015-Jul-27	45	64	28.351632506	0.951421105	28	25	30
ALPHA_KETO	C. BRIGGSAE	AF16	PHILLIPS	2015-May-29	32	73	23.166301775	1.0489461889	24	21	28
ALPHA_KETO	C. BRIGGSAE	AF16	PHILLIPS	2015-Jun-05	41	64	...005	0.7973480338	26	21	28
ALPHA_KETO	C. BRIGGSAE		COLL	2015-Apr-13			34.786618...	0.5553925508	32		
ALPHA_KETO	C. BRIGGSAE			2015-Jun-22			34.786618...	...7690...			
ALPHA_KETO	C. BR...	HK104	PHILL...	2015...		27	36.008581749		38		38
...KETO		HK104	PHILLIPS		63	44	33.494325479	0.83654...	35	33	38
VAL...	...IGGSAE	JU1348	DRISCOLL	...pr-13	68	22	21.129698357	0.6151595581	21	18	23
VALPRO...ID	C. BRIGGSAE	JU1348	DRISCOLL	2015-Jun-22	24	11	23.908256656	1.3620162842	23	21	25
VALPROIC_ACID	C. BRIGGSAE	JU1348	LITHGOW	2015-Mar-23	19	20	21.384375	1.1577256355	21	16	25
VALPROIC_ACID	C. BRIGGSAE	JU1348	LITHGOW	2015-Mar-27	44	26	21.556811498	0.8024867652	24	19	24
VALPROIC_ACID	C. BRIGGSAE	JU1348	LITHGOW	2015-Jul-27	49	59	23.143070573	0.8203877511	23	21	25
VALPROIC_ACID	C. BRIGGSAE	JU1348	PHILLIPS	2015-May-29	51	55	22.202092482	0.7595001457	21	19	24
VALPROIC_ACID	C. BRIGGSAE	JU1348	PHILLIPS	2015-Jun-05	71	37	20.048543592	0.6268805442	21	17	24
VALPROIC_ACID	C. BRIGGSAE	JU1348	PHILLIPS	2015-Jun-19	68	37	22.103152005	0.6441925849	21	19	24
VALPROIC_ACID	C. ELEGANS	JU775	DRISCOLL	2015-Apr-13	96	5	15.137678571	0.3864769547	14		

I wrote software that used their raw data to replicate their summary calculations of

1. the numbers of animals that died[1],

2. the numbers of animals that were censored,

3. mean longevities,

4. SEMs (sort of) and

5. Kaplan-Meier medians.

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[1]They called it "Final N".

2.2 Extending Calculations

The original paper reported mean and median[2] life spans.

That's good.

Other commonly reported statistics are changes in mean and maximum life span[3], and p-values[4].

After replicating their mean and median life spans, I was confident I could

1. match data for

   (a) animals receiving a certain compound to
   (b) their corresponding control animals

2. and then calculate

   (a) how much compounds changed life spans and
   (b) the corresponding p-values[5].

So I did.

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[2]Kaplan-Meier

[3]When I calculated maximum life span, I considered how long the oldest 10% of animals lived.

[4]Statisticians and scientists use "p-values" to measure how "significant" differences are. Many think p-values under 0.05 indicate a significant difference.

[5]I calculated p-values using Mann Whitney's U test. It works even with data that's not normally distributed. The logrank and cox methods may have worked well too.
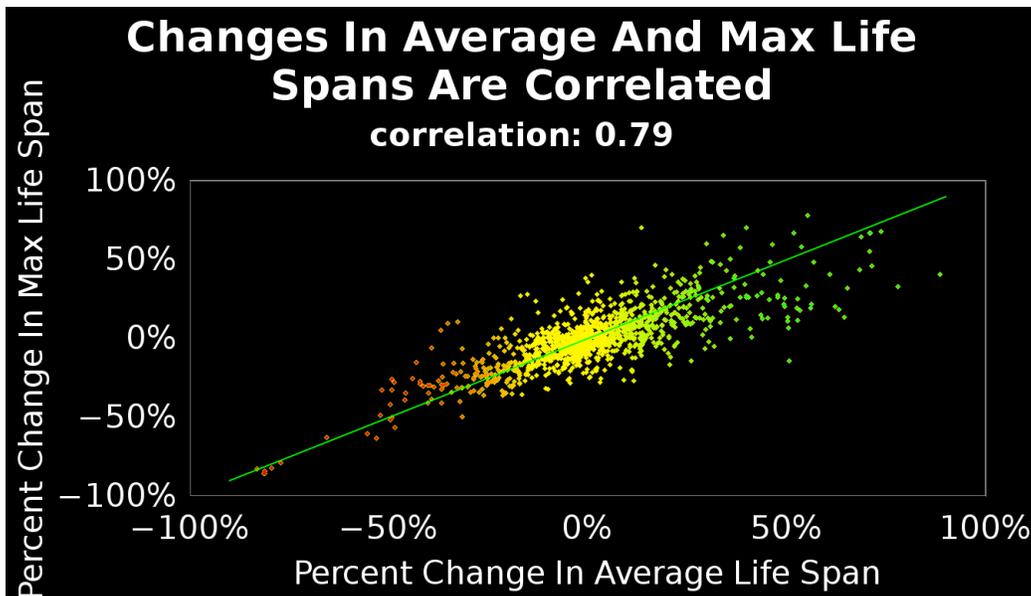
3 Results
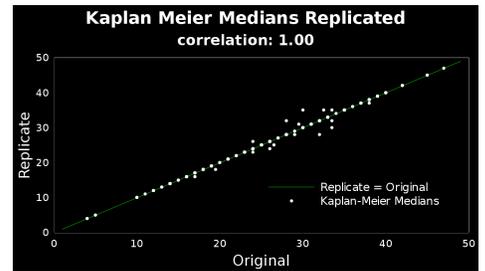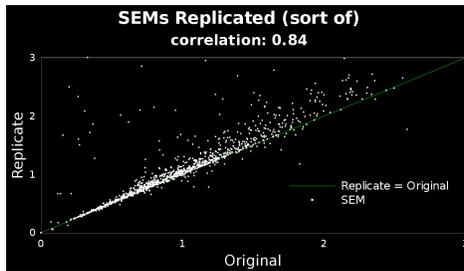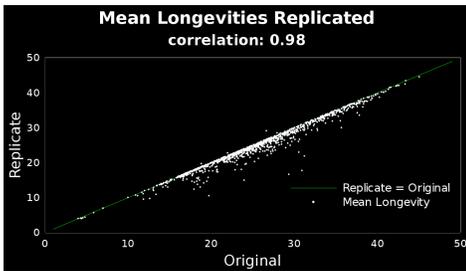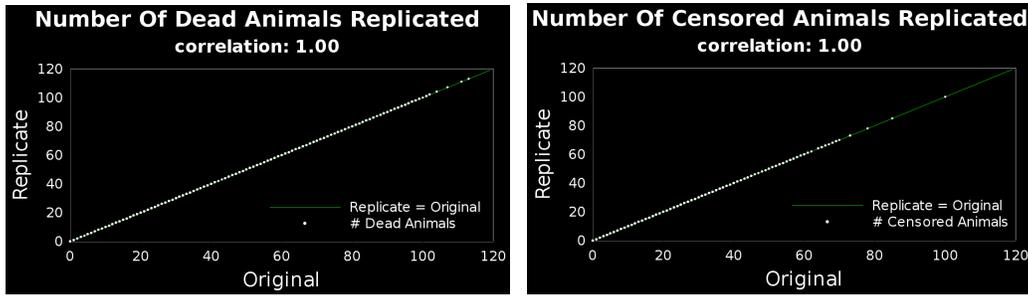
I replicated most of the original researchers' statistics with correlation coefficients of a perfect 1.00, or close[6].

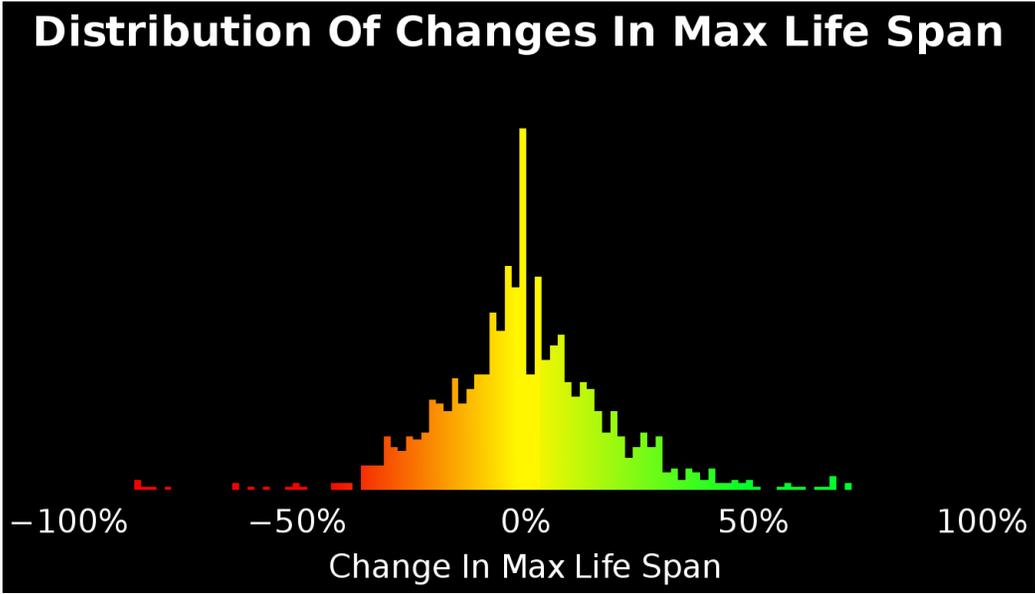But the correlation coefficient between our SEMs isn't as good as I'd like[7].

Changes in mean and max life span are mildly correlated[8].

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[6]That's good.
[7]It's only 0.84
[8]That correlation coefficient is 0.79.

Distribution Of Changes In Max Life Span

Some changes in life span seemed significant.

Top 10: It's All Thioflavin T

INTERVENTION	PERCENT CHANGE IN MEAN LIFE SPAN	MEAN P VALUE	PERCENT CHANGE IN MAXIMUM LIFE SPAN	MAX P VALUE	STRAIN
Thioflavin T	88.6%	0.000	40.5%	0.077	my16
Thioflavin T	78.1%	0.000	32.6%	0.044	my16
Thioflavin T	73.8%	0.000	67.5%	0.139	my16
Thioflavin T	71.6%	0.000	45.8%	0.047	my16
Thioflavin T	71.2%	0.000	66.7%	0.096	my16
Thioflavin T	71.0%	0.000	66.7%	0.096	my16
Thioflavin T	70.9%	0.000	55.2%	0.006	my16
Thioflavin T	68.8%	0.000	64.1%	0.000	my16
Thioflavin T	68.4%	0.000	43.5%	0.03	ju775
Thioflavin T	65.4%	0.000	31.5%	0.128	my16

4 Discussion

I wrote a paper similar to this[4].

These results are consistent with it, and with those from analyzing my ginormous spread sheet of life span experiments[9].

I'm basically satisfied, but "in this the best of all possible worlds"[10], our SEMs would be closer.

I guessed the original researchers used "SEM" as an abbreviation of "Standard Error of the Mean".

If they meant something else, that might explain why we got different SEMs.

I hope Thioflavin T is tested in mammals, and for safety in people.

Ideally, soon.

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[9]It's the world's biggest collection of normalized results from life span experiments[5,6].
[10]Candide

5 Questions For The Original Researchers

1. Was "SEM" an abbreviation for Standard Error of the Mean?

2. What doses were used in the "Supplementary Data 9: Raw lifespan (chemicals) dataset"[7]?

3. Would it be OK to publish the raw data for the 30,000 screened compounds[8]?

6 Conclusion

Many of the original researchers statistics are replicable.

It seems to me that a dye named Thioflavin T is the big winner.
At least in the "MY16" strain of C. Elegans.

You know what that means.
A dye delayed dying.
;-)

7 Funding

8 References

1. Lucanic, M. et al. Impact of genetic background and experimental reproducibility on identifying chemical compounds with robust longevity effects. Nat. Commun. 8, 14256 doi: 10.1038/ncomms14256 (2017).
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2. C. Elegans Life Span Experiments Replicated and Extended
   `http://morse.kiwi.nz/kingsley/lib/exe/fetch.php?media=:science:c_elegans_experiments_replicated_and_extended.pdf`

3. C. Elegans Life Span Experiments Replicated and Extended
   `http://morse.kiwi.nz/kingsley/lib/exe/fetch.php?media=:science:c_elegans_experiments_replicated_and_extended.pdf`

4. C. Elegans Life Span Experiments Replicated and Extended
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5. Kingsley's Big Spread Sheet Of Life Span Experiments
   `http://morse.kiwi.nz/kingsley/lib/exe/fetch.php?media=:science:opportunity.6.pdf`

6. Results from data-mining Kingsley's Big Spread Sheet o' Life Span Experiments
   `http://morse.kiwi.nz/kingsley/doku.php?id=science:kingsleys_big_spread_sheet_of_life_span_experiments`

7. Lucanic, M. et al. Impact of genetic background and experimental reproducibility on identifying chemical compounds with robust longevity effects. Nat. Commun. 8, 14256 doi: 10.1038/ncomms14256 (2017), Supplementary Data 9: Raw lifespan (chemicals) dataset
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