Fac
Direct
A
CFP

Faculty/Presenter Disclosure

- **Faculty:** G Michael Allan

- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** None
  - **Other:** None

Science can seem,…

The Back Page

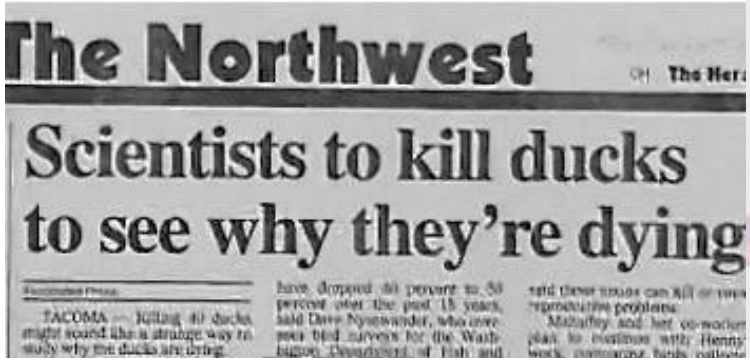
State population to double by 2040; babies to blame

TOM PHILP
Clatchy News Service

SACRAMENTO — In their first attempt at projecting California population in the year 2040, officials Tuesday unveiled a future state with twice as many people

Area Counties

Northern San Joaquin Valley counties with their 1990 populations and projections



The Northwest

Scientists to kill ducks to see why they're dying

TACOMA — Killing 40 ducks might sound like a strange way to study why the ducks are dying

Science can seem,…

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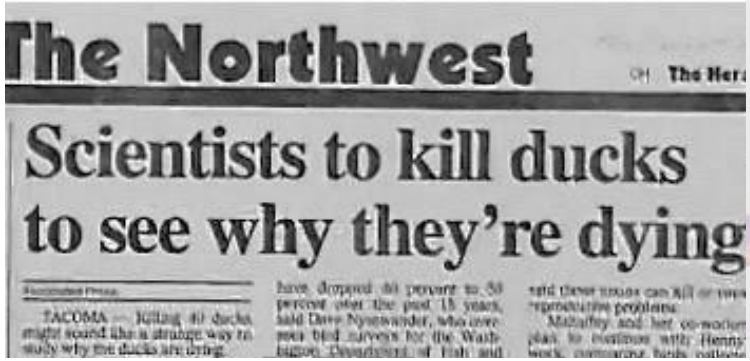
Review: Varenicline increases risk for serious adverse cardiovascular events in tobacco users

Clinical impact ratings: GM ★★★★★★☆ C ★★★★★★



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Clinical impact ratings: GM ★★★★★★☆ C ★★★★★☆☆

Missing what really matters!

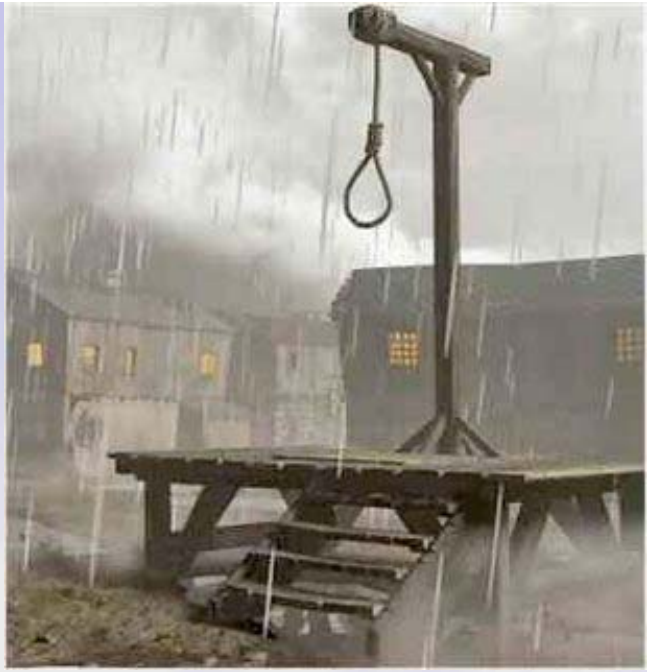
A Medical Tale:
The Surrogate Heart

- Once upon a time,..
- In a Kingdom Far, Far away,…
- It was noticed abnormal beats follow Heart Attacks
- More beats = ↑ risk of Sudden Death
- The King said: “Give a potion to decrease extra beats and thou shalt increase survival”
- And So they did,…

A Medical Tale:
The Surrogate Heart

- And it was good,… until
- A Jester asked: “Are we saving life's?”

A Medical Tale:
The Surrogate Heart



- After the execution, the King asked his people to solve the riddle
- So, they gave the magic potion to some and not to others
- After 10 months

A Medical Tale: The Surrogate Heart

	X (730)	Y (725)
Mortality	56 (7.7%)	22 (3.0%)
arrhythmia death or cardiac arrests	33 (4.5%)	9 (1.2%)

i. NEJM 1989; 321(6): 406-12

A Medical Tale: The Surrogate Heart

- The Number Needed to Harm (kill) 1 extra patient was only 21.

	Treatment (730)	Placebo (725)
Mortality	56 (7.7%)	22 (3.0%)
arrhythmia death or cardiac arrests	33 (4.5%)	9 (1.2%)

i. NEJM 1989; 321(6): 406-12

Outcomes: Surrogate, Subjective, Objective

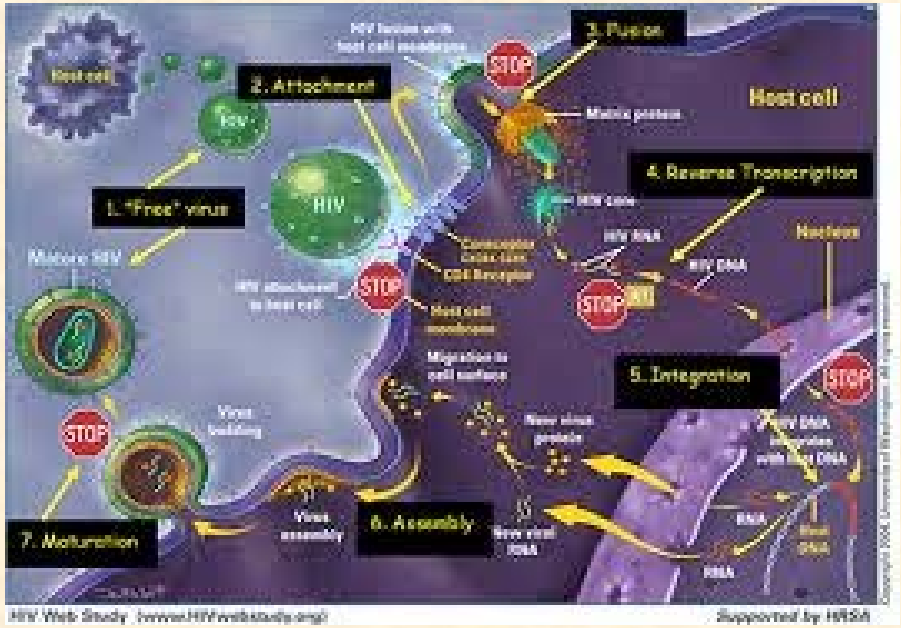
- Ask yourself: Can a patient feel the outcome?
- If No; it is a surrogate marker

Surrogates: The Never-ending Story

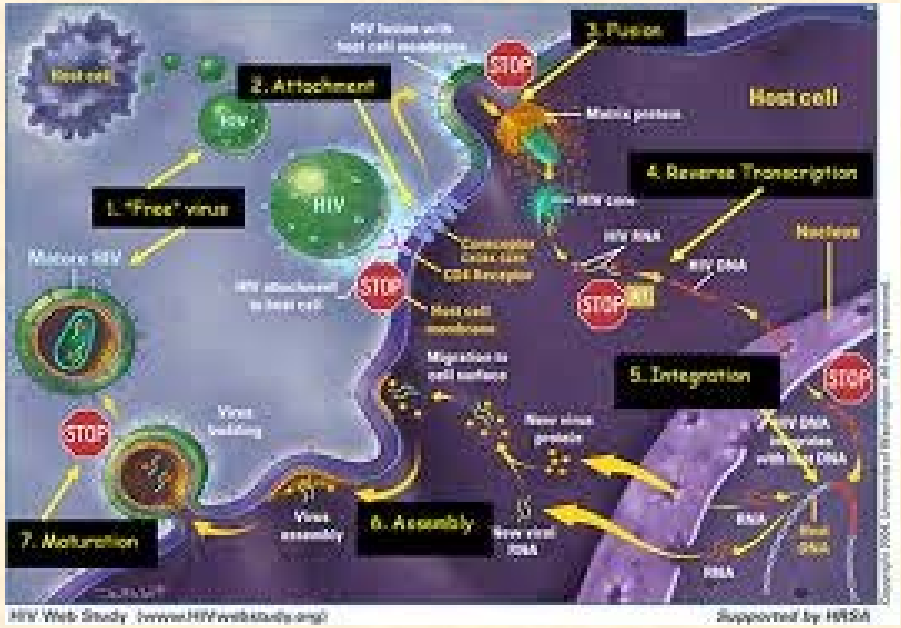
The Marker	The Treatment
•HDL	•Torcetrapib •Niacin
•LDL	•Non-statins
•BP	•Atenolol •Doxazosin •Aliskerin
•A1C	•Rosiglitazone •Almost any diabetes medications except Metformin
•CRP in CVD	•Vitamin E, Rosiglitazone, etc.

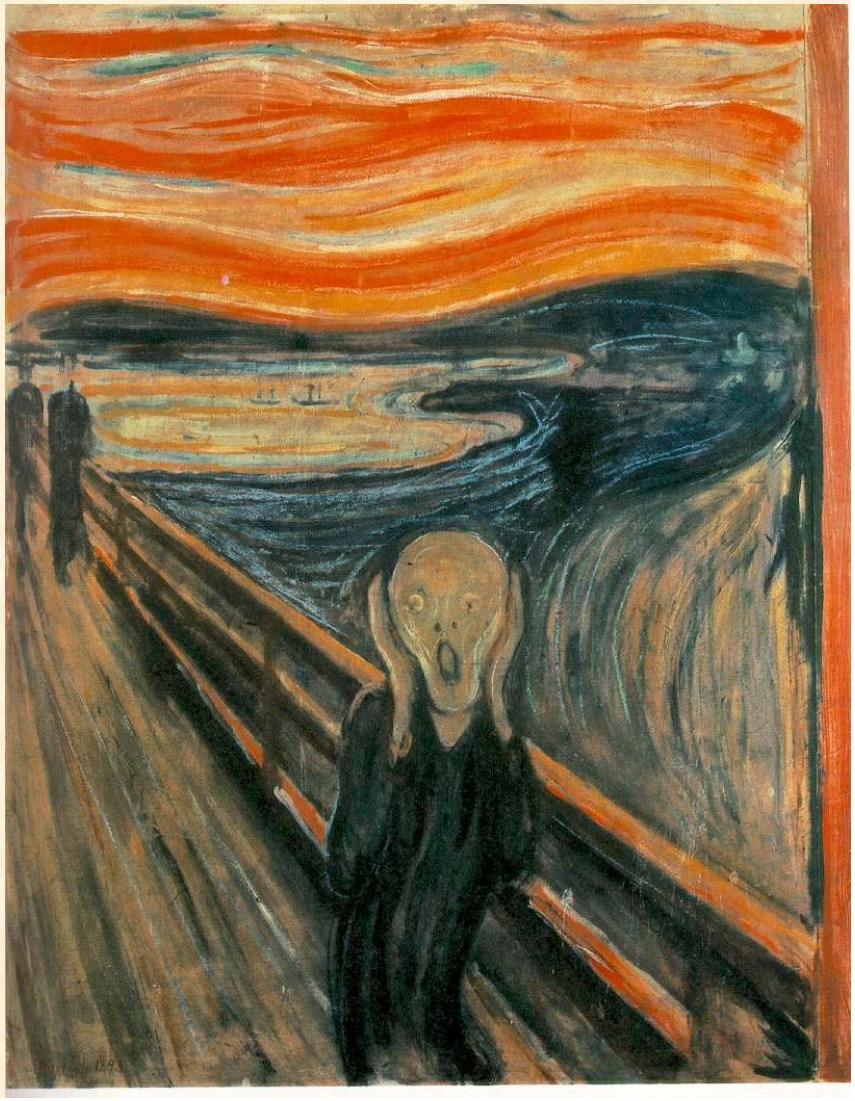
HDL: N Engl J Med 2007;357:2109-22. November 5, 2012, at NEJM.org. Niacin: N Engl J Med. 2011;365(24):2255-67. Ezetimibe: Tools for Practice, March 29, 2010. Atenolol: Lancet 2004; 364: 1684–89. Doxazosin: JAMA 2000; 283: 1967- 1975. Aliskerin N Engl J Med. 2012 Dec 6;367(23):2204-13.Rosi: Tools for Practice October 4, 2010. CRP: PLoS Med 2010; 7(2): e1000196

How Drugs Work?

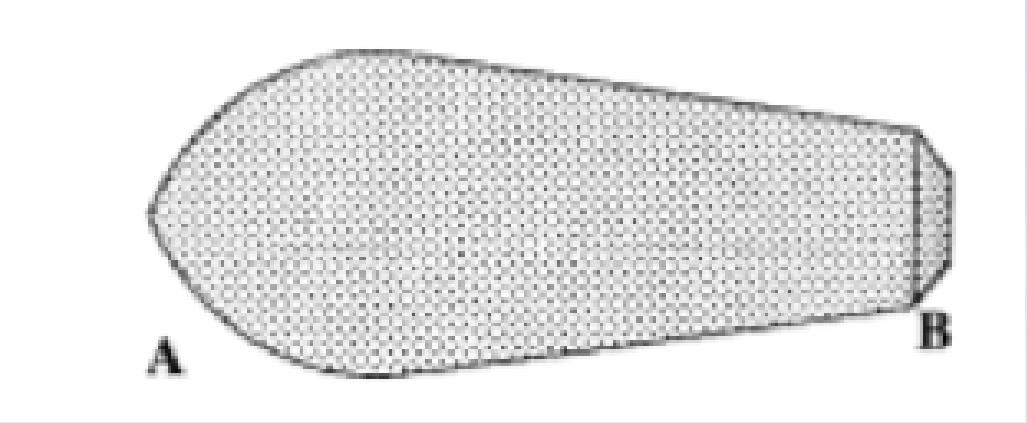


How Drugs Work?





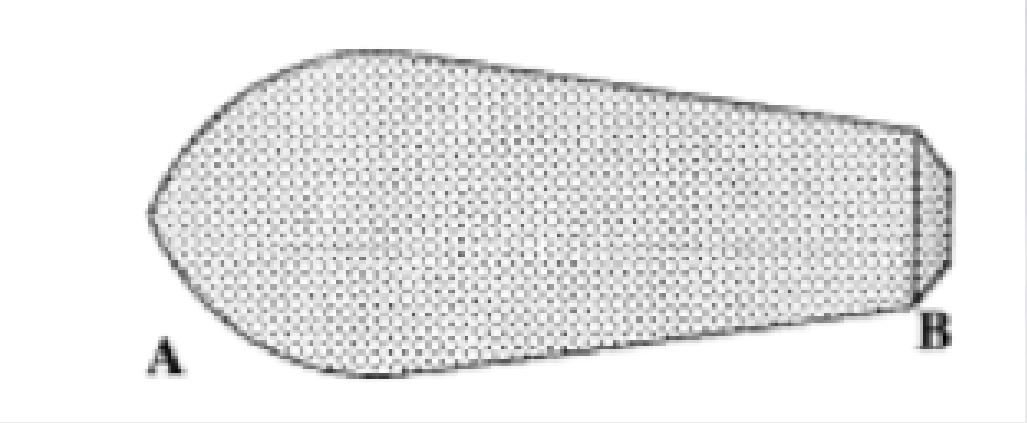
WHERE DO SUPPOSITORIES FIT IN?



DO YOU INSERT THE A OR B END FIRST?

Lancet 1991;338:798-800

WHERE DO SUPPOSITORIES FIT IN?



DO YOU INSERT THE A OR B END FIRST?

A = 83% needed to introduce finger - 3% expulsion

B = 1% needed to introduce finger - 0% expulsion - 98% found this method easier

Lancet 1991;338:798-800

We have no real idea why,…

This stuff works

- Lithium for Bipolar
- Vitamin D for Falls
- Nitro patches for tendinopathy
- Nifedipine for renal stones
- Most drugs really

We have no real idea why,…

This stuff works

- Lithium for Bipolar
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- Most drugs really

This stuff doesn't

(Other wrong theories)

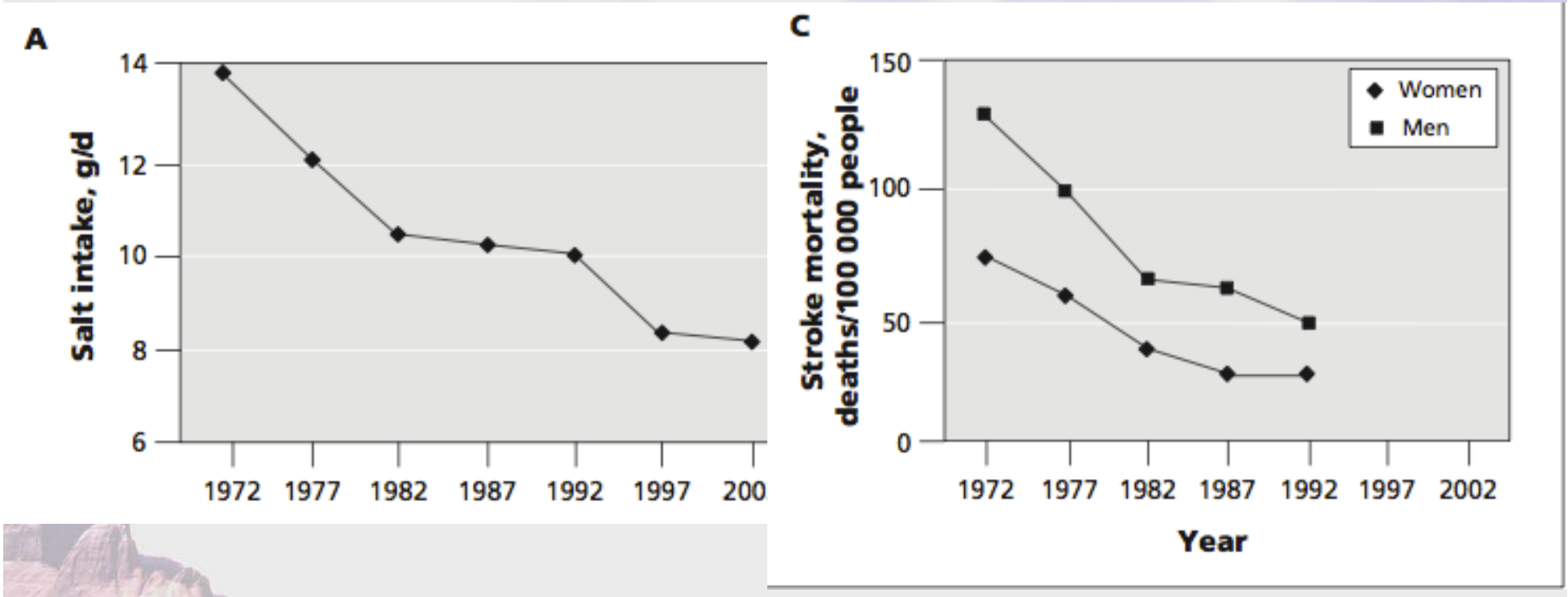
- Oral HRT for incontinence
- Anti-oxidants
- Cough Meds in kids
- Febrile seizure antipyretics
- Plus the non-drug theories
  - Analgesia in Abdo pain
  - Lubricant on a speculum

Look alikes Not always alike

CMAJ

ANALYSIS

Effective population-wide public health interventions to promote sodium reduction

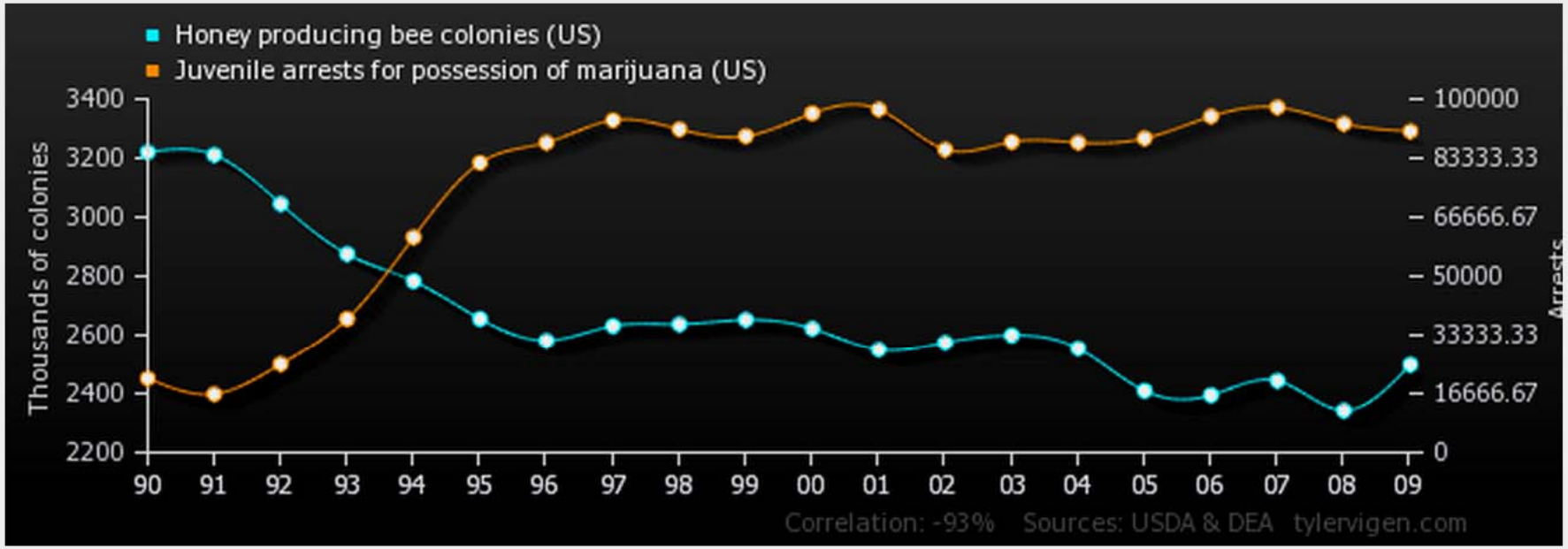


CMAJ 2009. DOI:10.1503/cmaj.090361

Honey producing bee colonies (US)

inversely correlates with

Juvenile arrests for possession of marijuana (US)



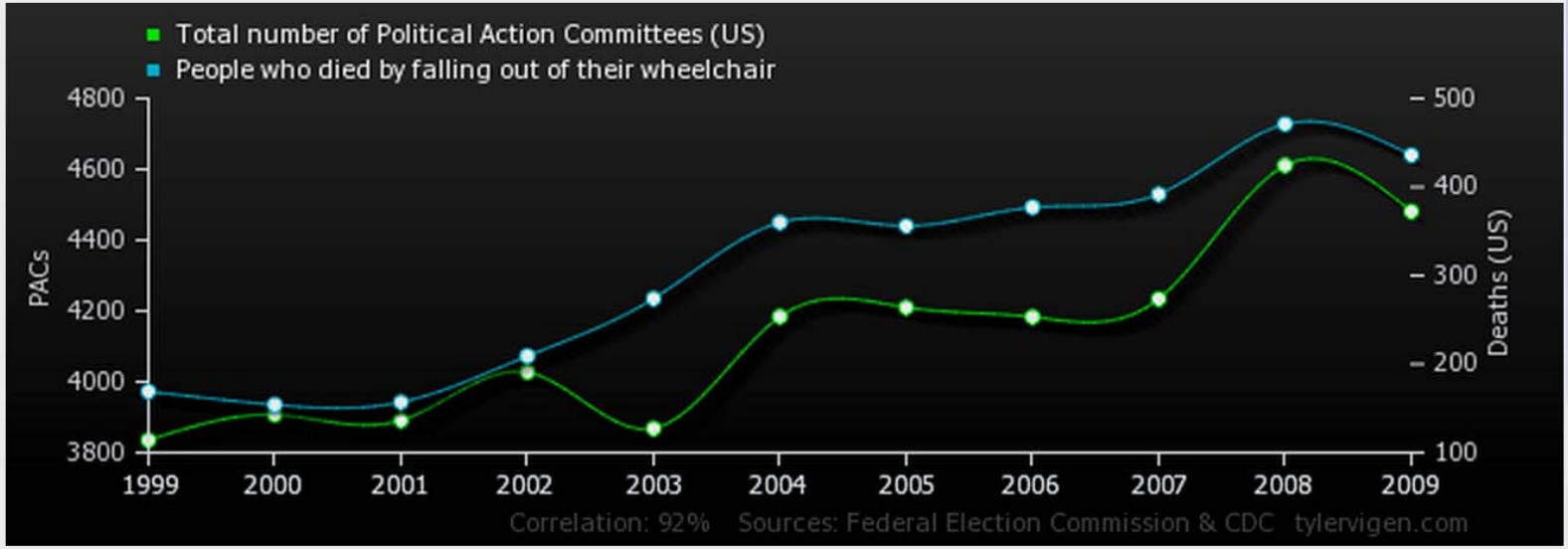
Honey producing bee colonies (US) *Thousands of colonies (USDA)*	'90: 3,220; '91: 3,211; '92: 3,045; '93: 2,875; '94: 2,783; '95: 2,655; '96: 2,581; '97: 2,631; '98: 2,637; '99: 2,652; '00: 2,622; '01: 2,550; '02: 2,574; '03: 2,599; '04: 2,554; '05: 2,409; '06: 2,394; '07: 2,443; '08: 2,342; '09: 2,498
Juvenile arrests for possession of marijuana (US) *Arrests (DEA)*	'90: 20,940; '91: 16,490; '92: 25,004; '93: 37,915; '94: 61,003; '95: 82,015; '96: 87,712; '97: 94,046; '98: 91,467; '99: 89,523; '00: 95,962; '01: 97,088; '02: 85,769; '03: 87,909; '04: 87,717; '05: 88,909; '06: 95,120; '07: 97,671; '08: 93,042; '09: 90,927

Correlation: -0.933389

Total number of Political Action Committees (US)

correlates with

People who died by falling out of their wheelchair



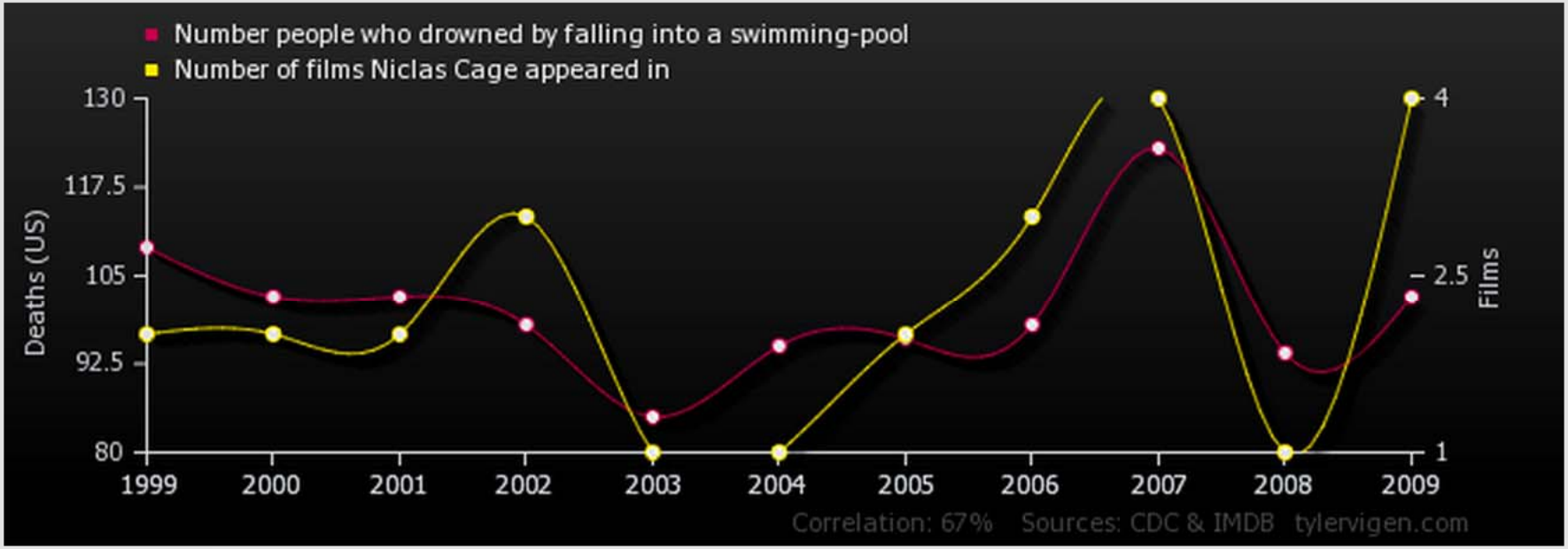
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Total number of Political Action Committees (US) *PACs (Federal Election Commission)*	3,835	3,907	3,891	4,027	3,868	4,184	4,210	4,183	4,234	4,611	4,481
People who died by falling out of their wheelchair *Deaths (US) (CDC)*	169	154	157	209	274	360	356	377	392	471	436

Correlation:
0.915876

Number people who drowned by falling into a swimming-pool

correlates with

Number of films Nicolas Cage appeared in

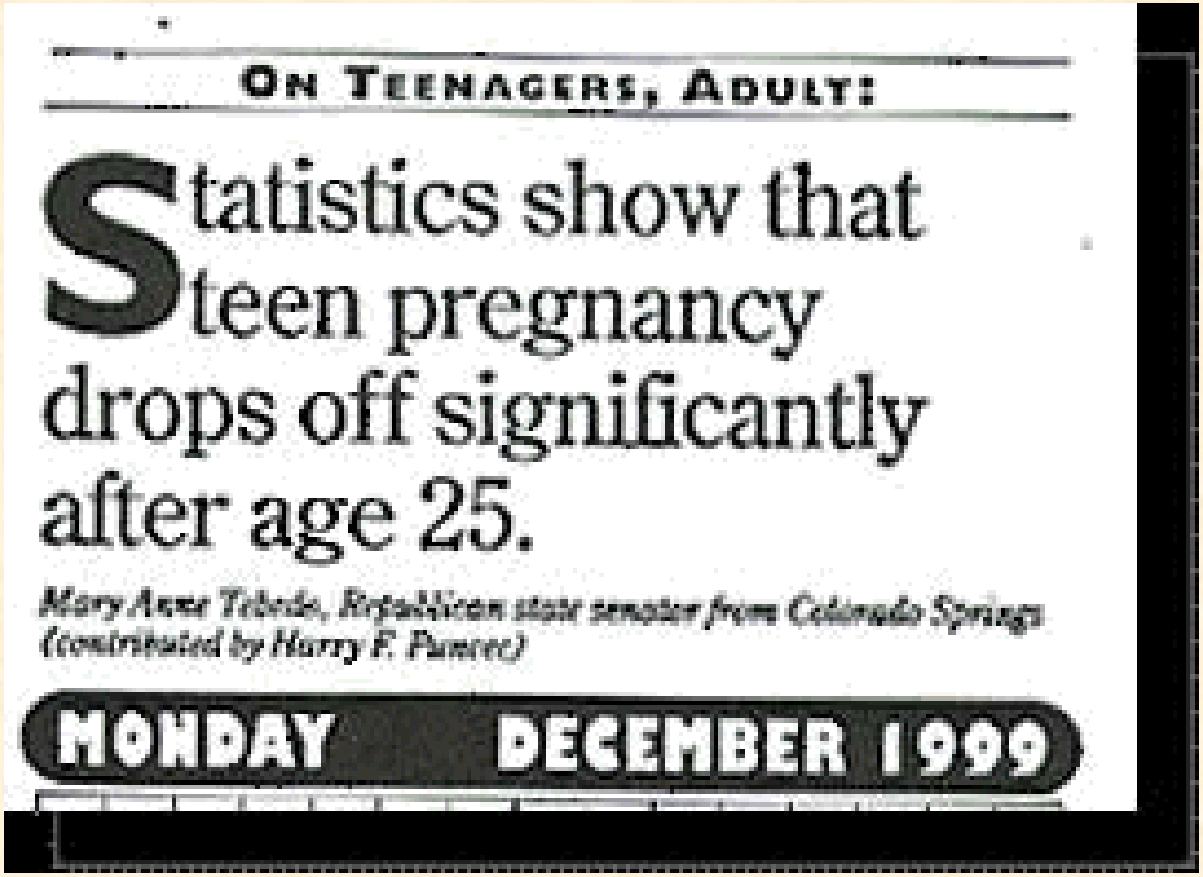


	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Number people who drowned by falling into a swimming-pool Deaths (US) (CDC)	109	102	102	98	85	95	96	98	123	94	102
Number of films Nicolas Cage appeared in Films (IMDB)	2	2	2	3	1	1	2	3	4	1	4

Correlation: 0.666004

Understanding Statistics?

Understanding Statistics?



ON TEENAGERS, ADULT:

Statistics show that teen pregnancy drops off significantly after age 25.

Mary Anne Tebedo, Republican state senator from Colorado Springs (contributed by Harry F. Pancec)

MONDAY DECEMBER 1999

Risk: Relative, Absolute & NNT

- If you don't know where you start, it's hard to know where you finish.
- Zoster Vaccine reduces shingles up to 70%

Study	Placebo	Zoster Vac	Benefit	NNT (3 yrs)
Age 50-59 (3 yrs)	2.03%	0.62%	1.41%	71
Age ≥60 (3 yrs)	3.42%	1.67%	1.75%	58

Bottom-Line: Over 3 years, one in 60-70 patients will avoid shingles due to the vaccine

- **One in 350 for post-herpetic neuralgia.**

Tools for Practice Nov 12, 2012.

Meta-Analysis: Don’t swallow Mystery Meat?

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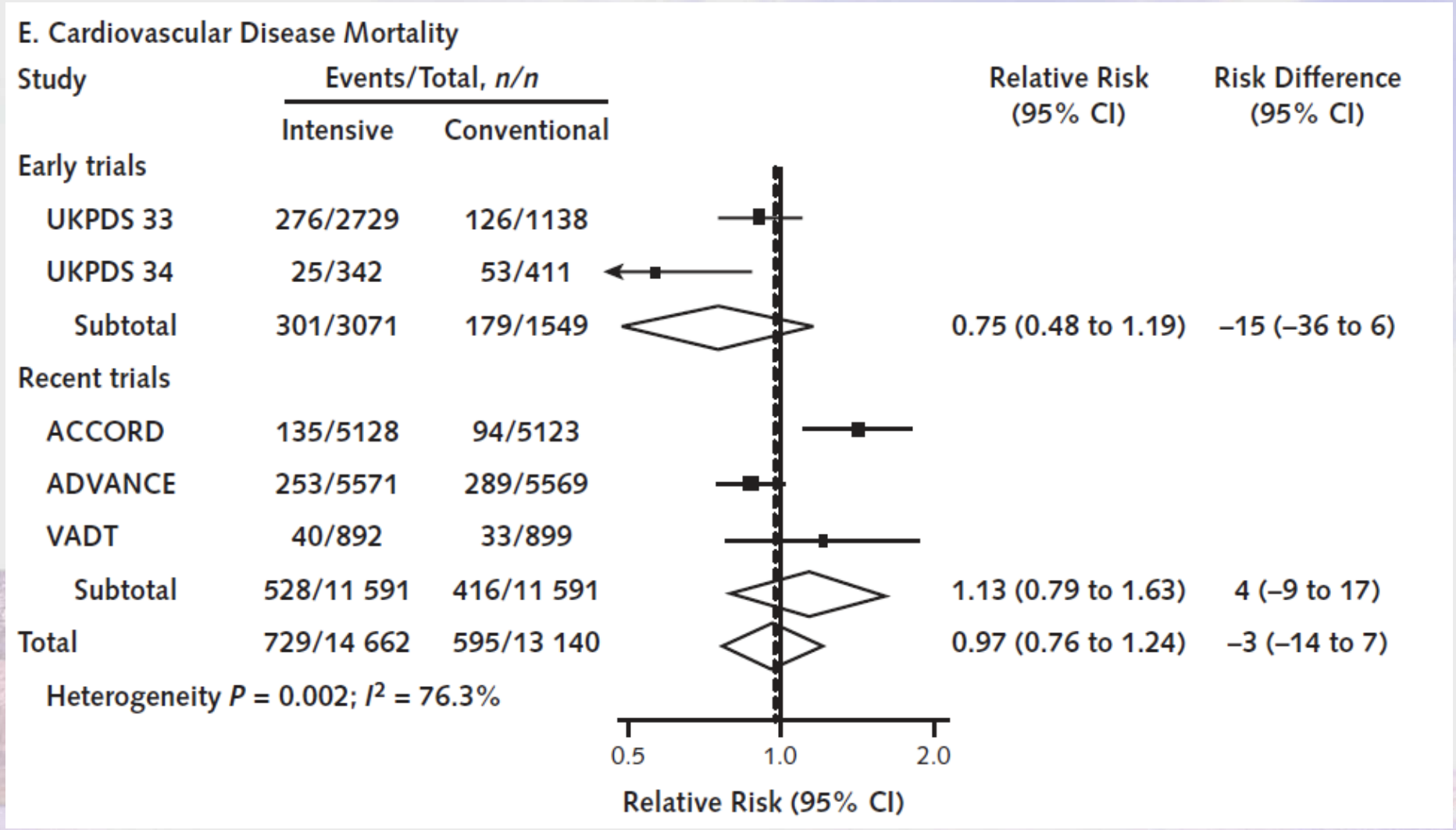
Diabetes: Apples and Oranges



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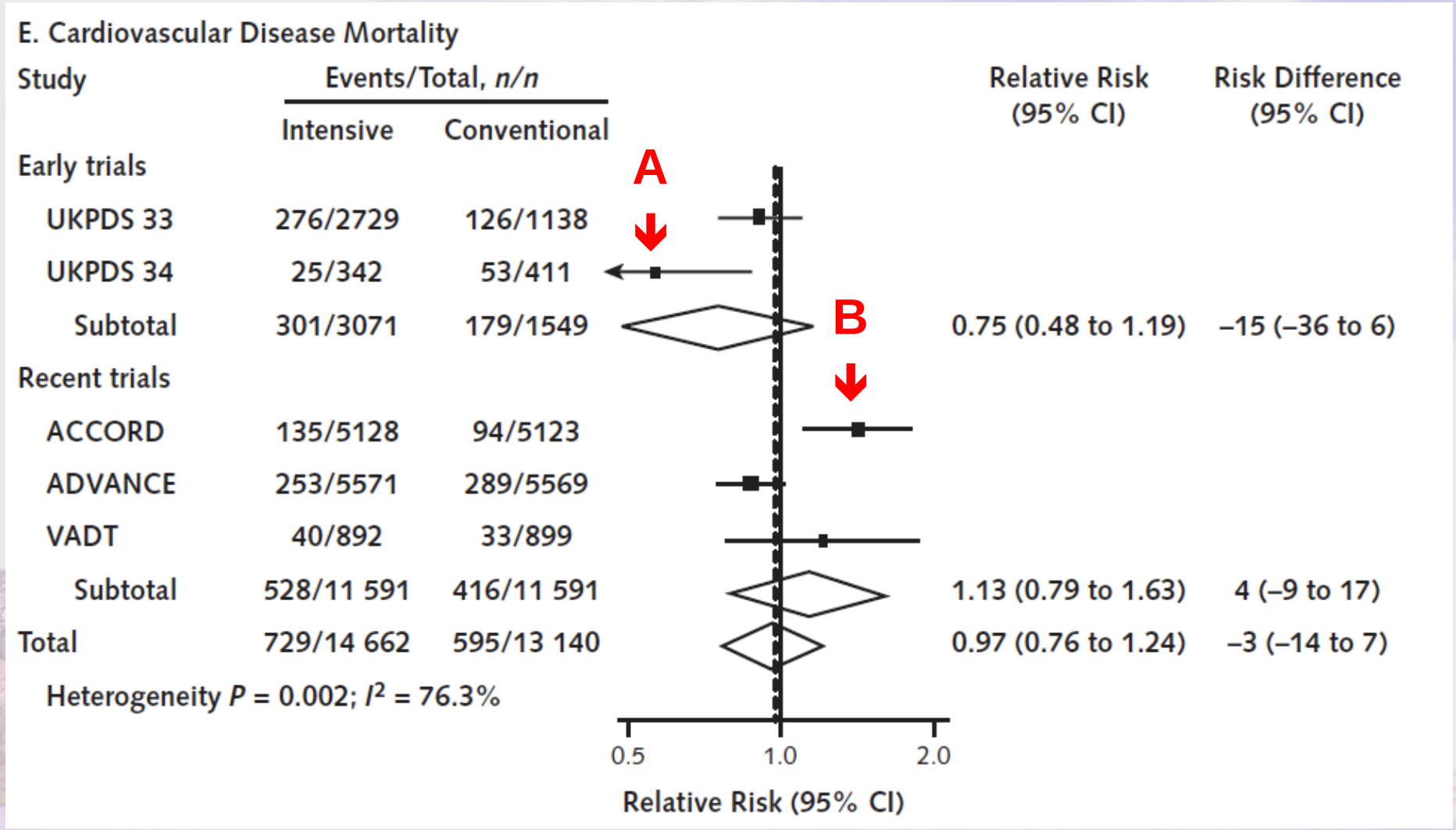
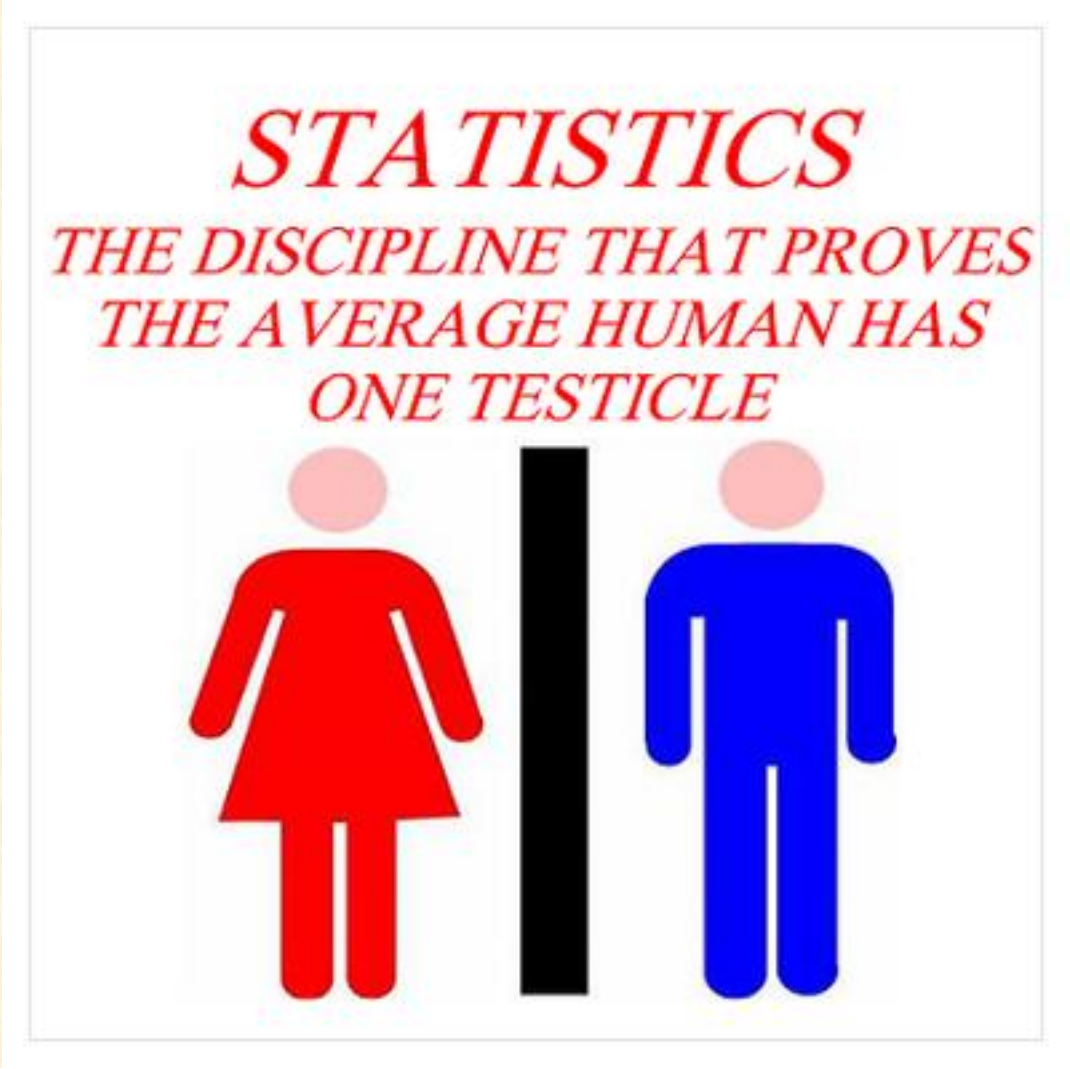


Statistical Significance & Confusion Intervals.



Novel Anti-Coagulant

- “ARISTOTLE: A major win for apixaban in AF”
- “the most positive yet”
- “first of the three new oral anticoagulants to show a clearly significa reduction in all-cause mortality”

http://www.theheart.org/article/1268723.
2009;361:1139-51. Apixaban: N Engl

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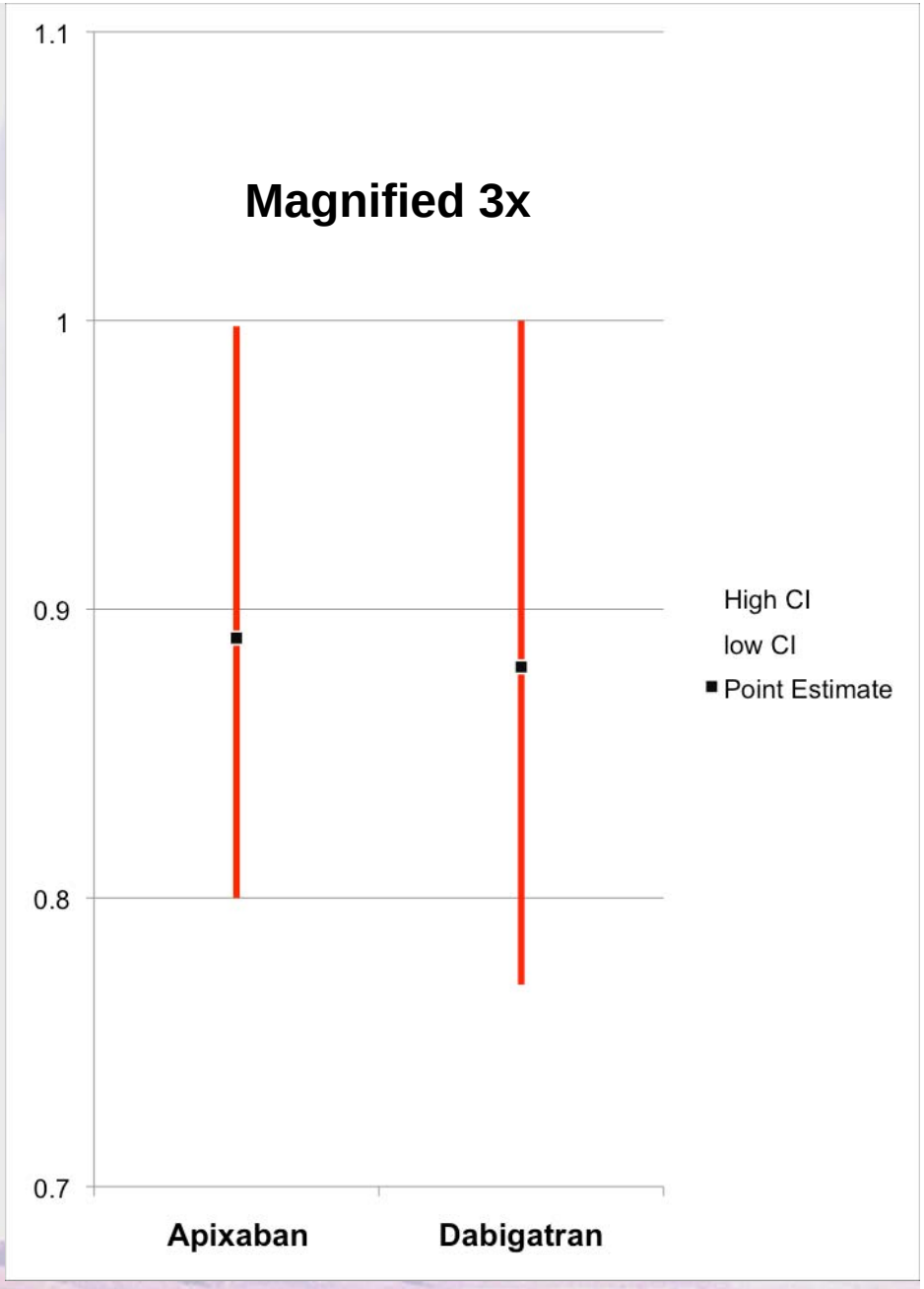

http://www.theheart.org/article/1268723.do, Dabigatran (150mg): N Engl J Med 2009;361:1139-51. Apixaban: N Engl J Med. 2011;365(11):981-92

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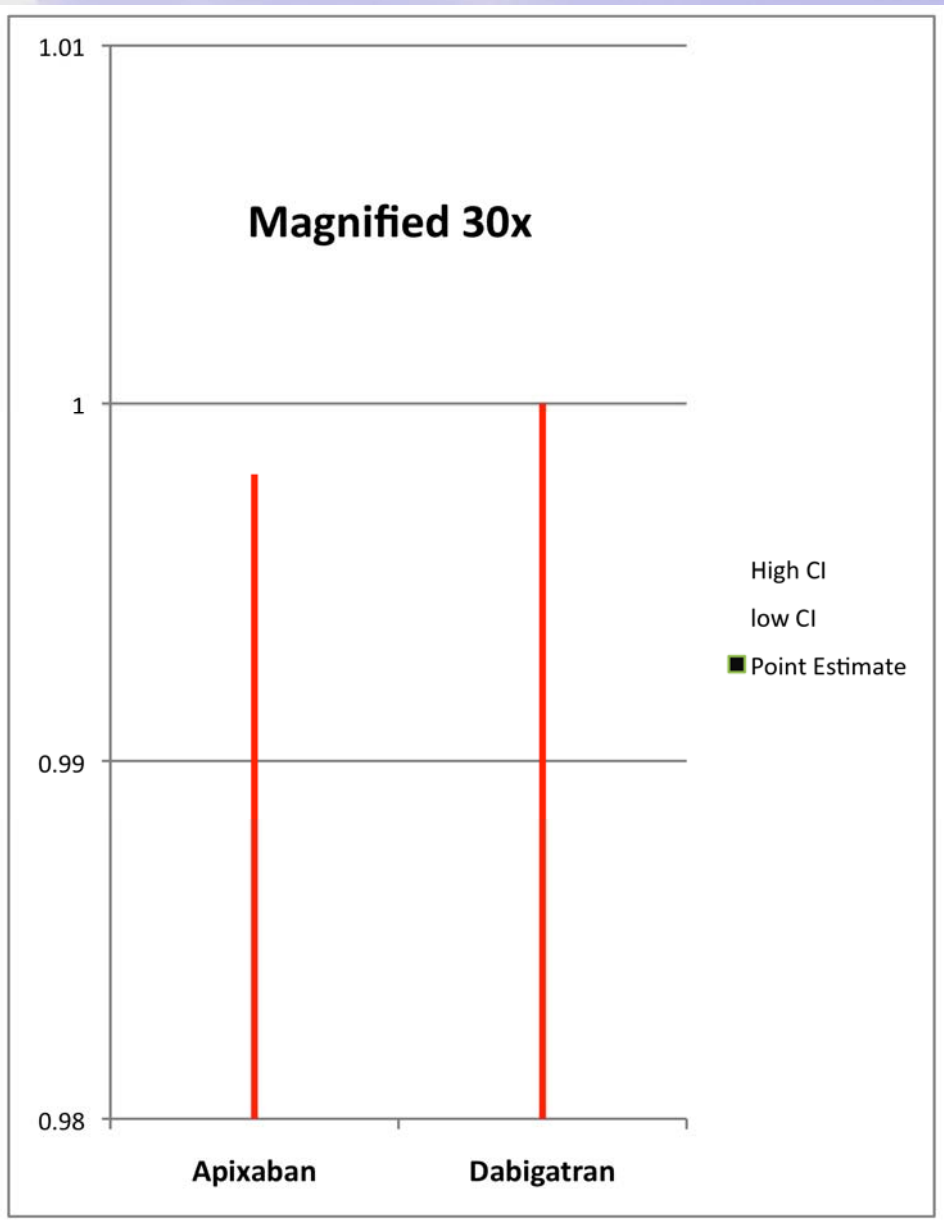
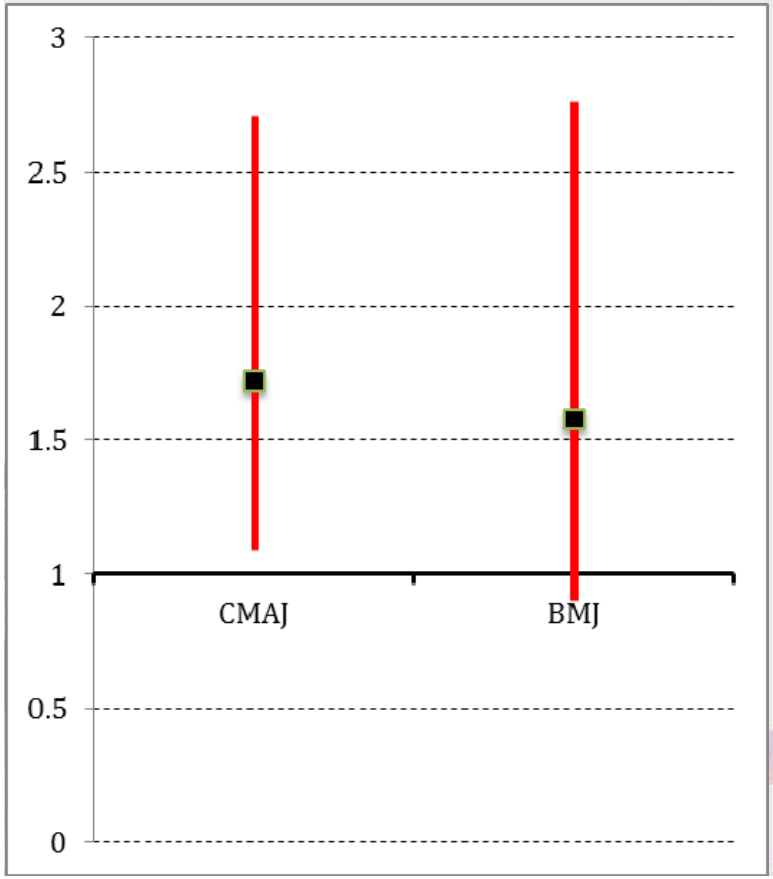


http://www.theheart.org/article/1268723.do, Dabigatran (150mg): N Engl J Med 2009;361:1139-51. Apixaban: N Engl J Med. 2011;365(11):981-92

Varenicline & CVD Risk

- 2 meta-analysis: CMAJ[1] Yes, BMJ No[2]
  - Odds ratio: CMAJ 1.72 (1.09-2.71) & BMJ 1.58 (0.90-2.76)



- NNH = 60 – 600+
  - Depend on baseline risk
- If high risk, may consider other options first

1) CMAJ. 2011;183:1359-66. 2) BMJ. 2012;344: e2856. 3) Ann Intern Med. 2011; 155(4): JC 4-5.

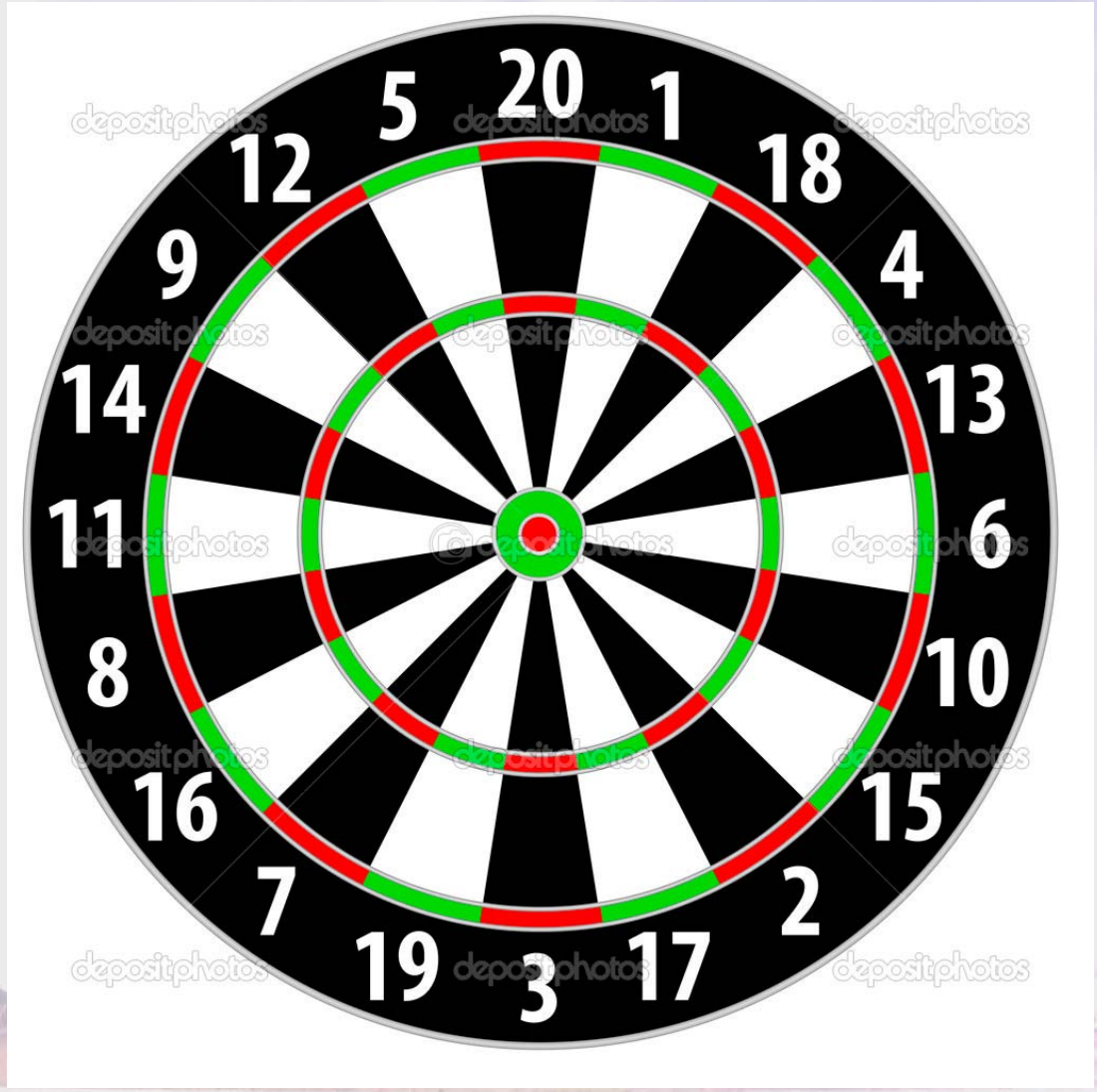
Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

PLoS Med: 2005

A Thousand Monkeys,…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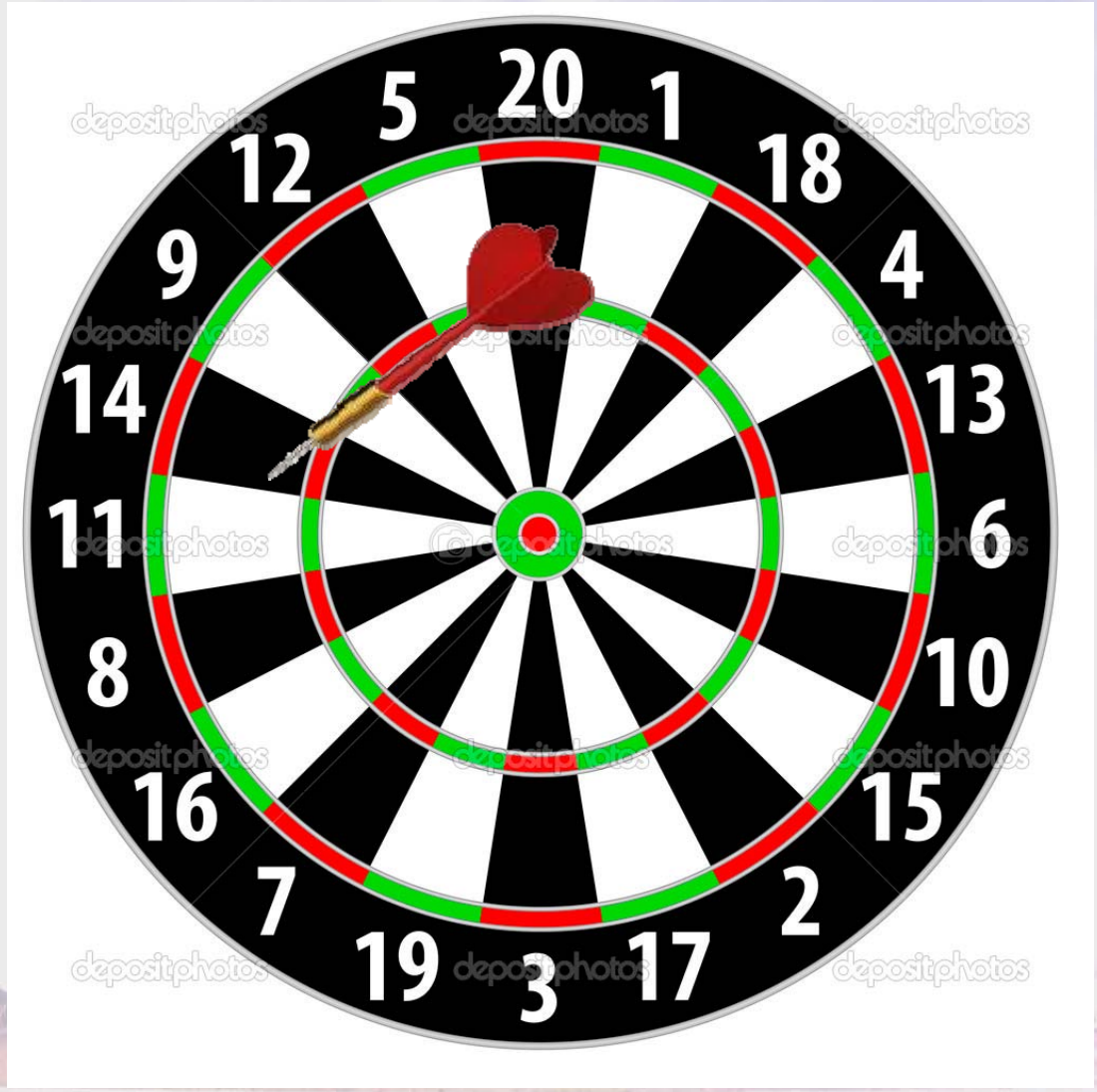
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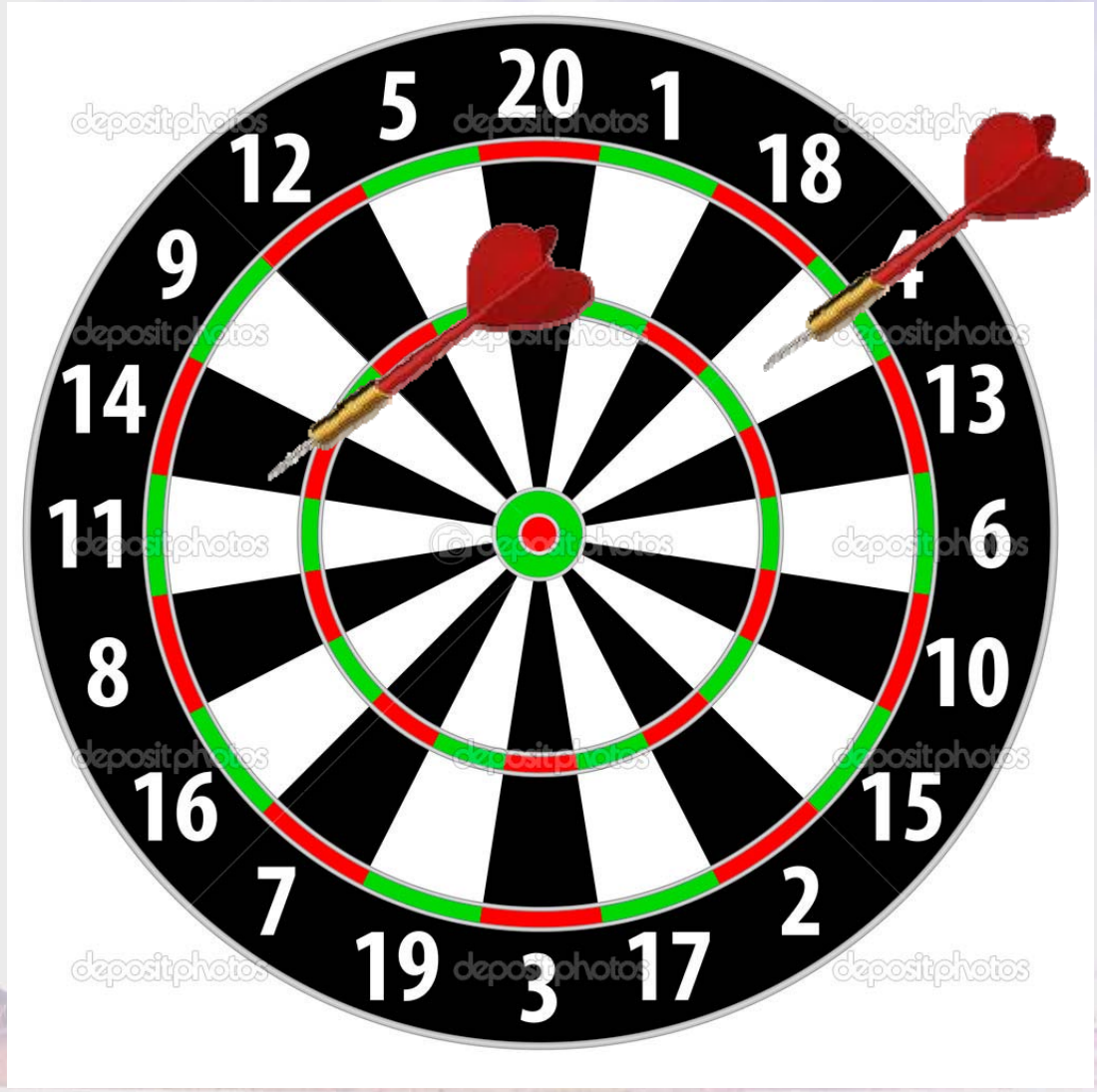
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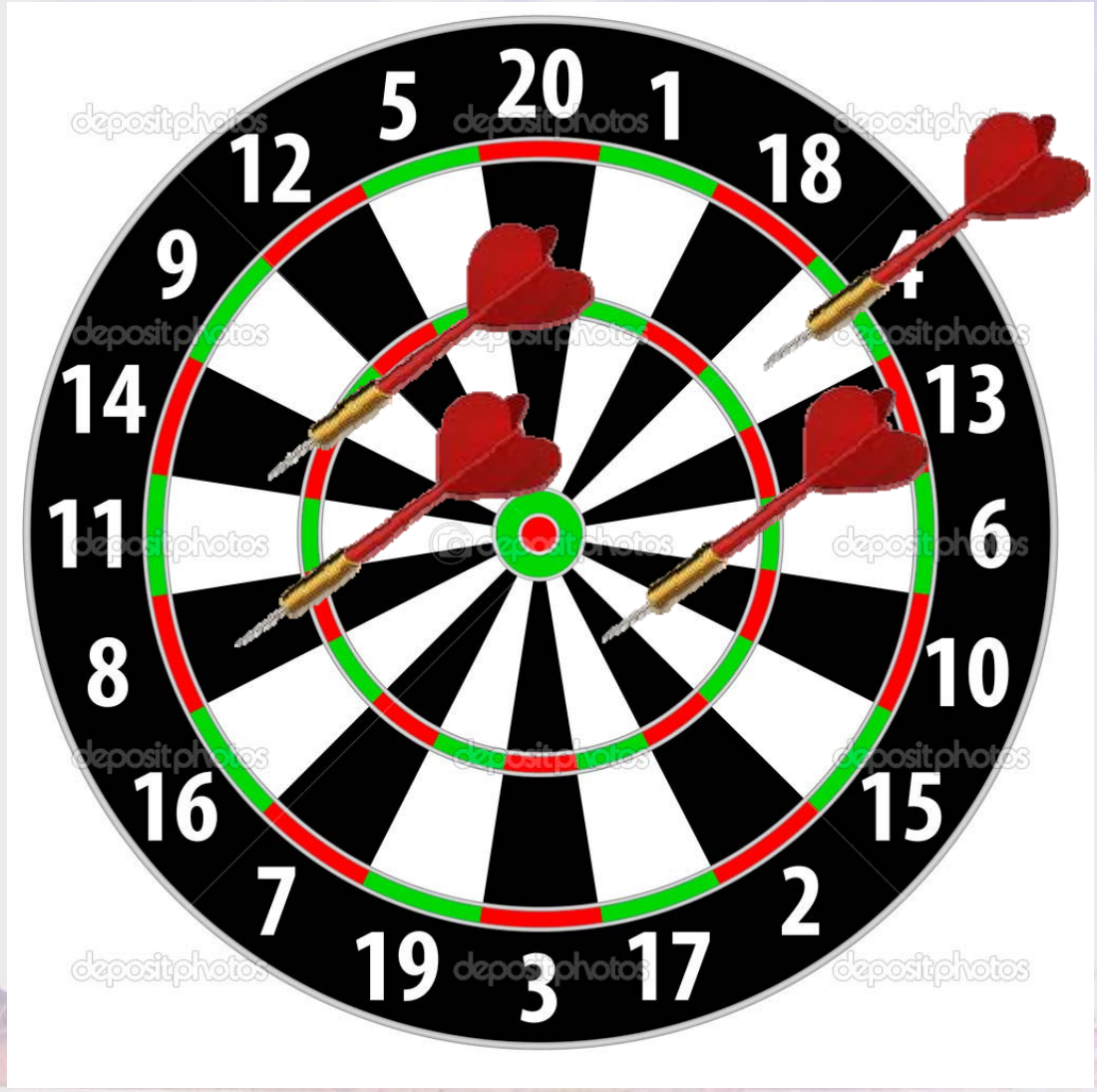
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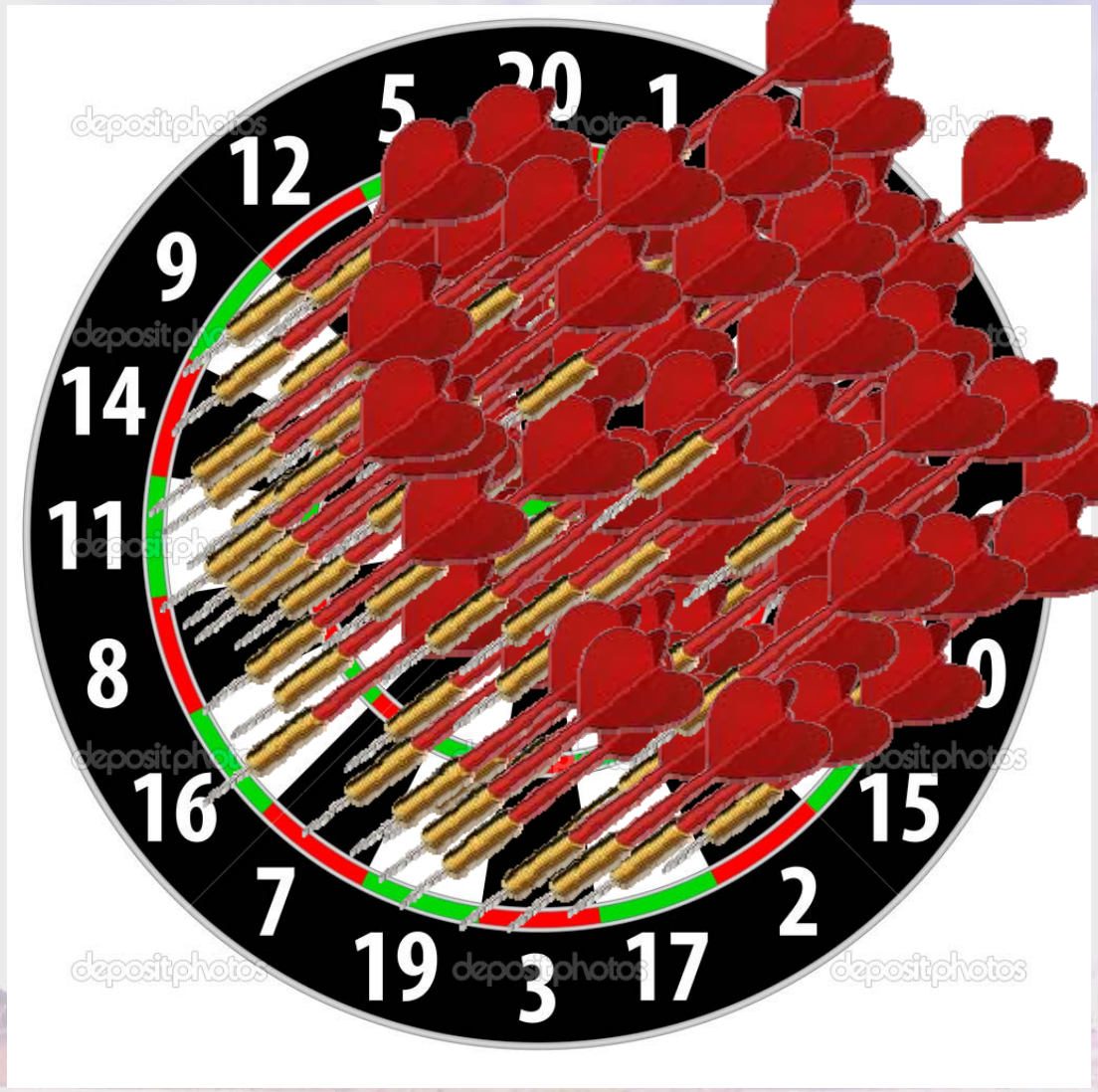
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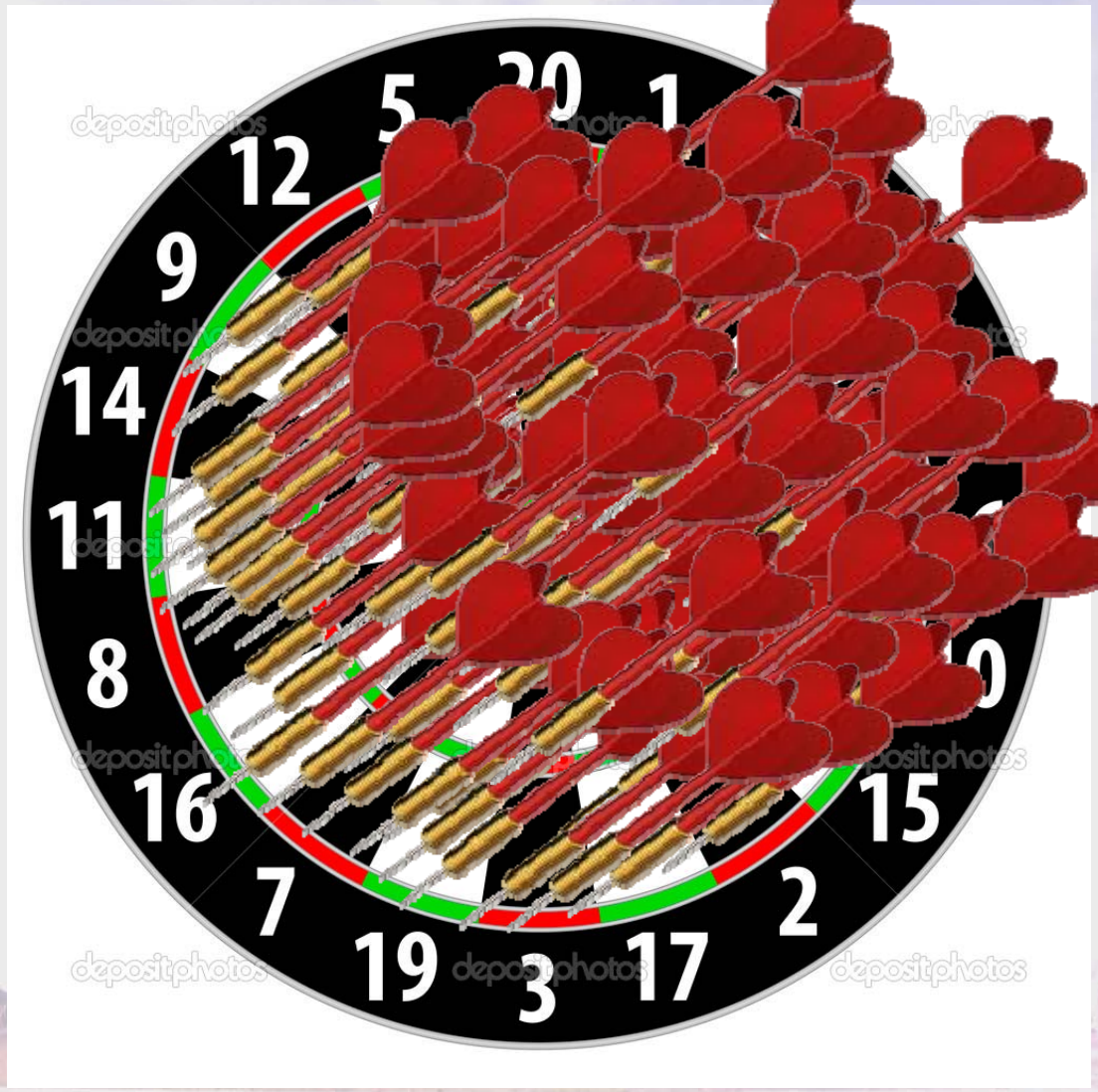
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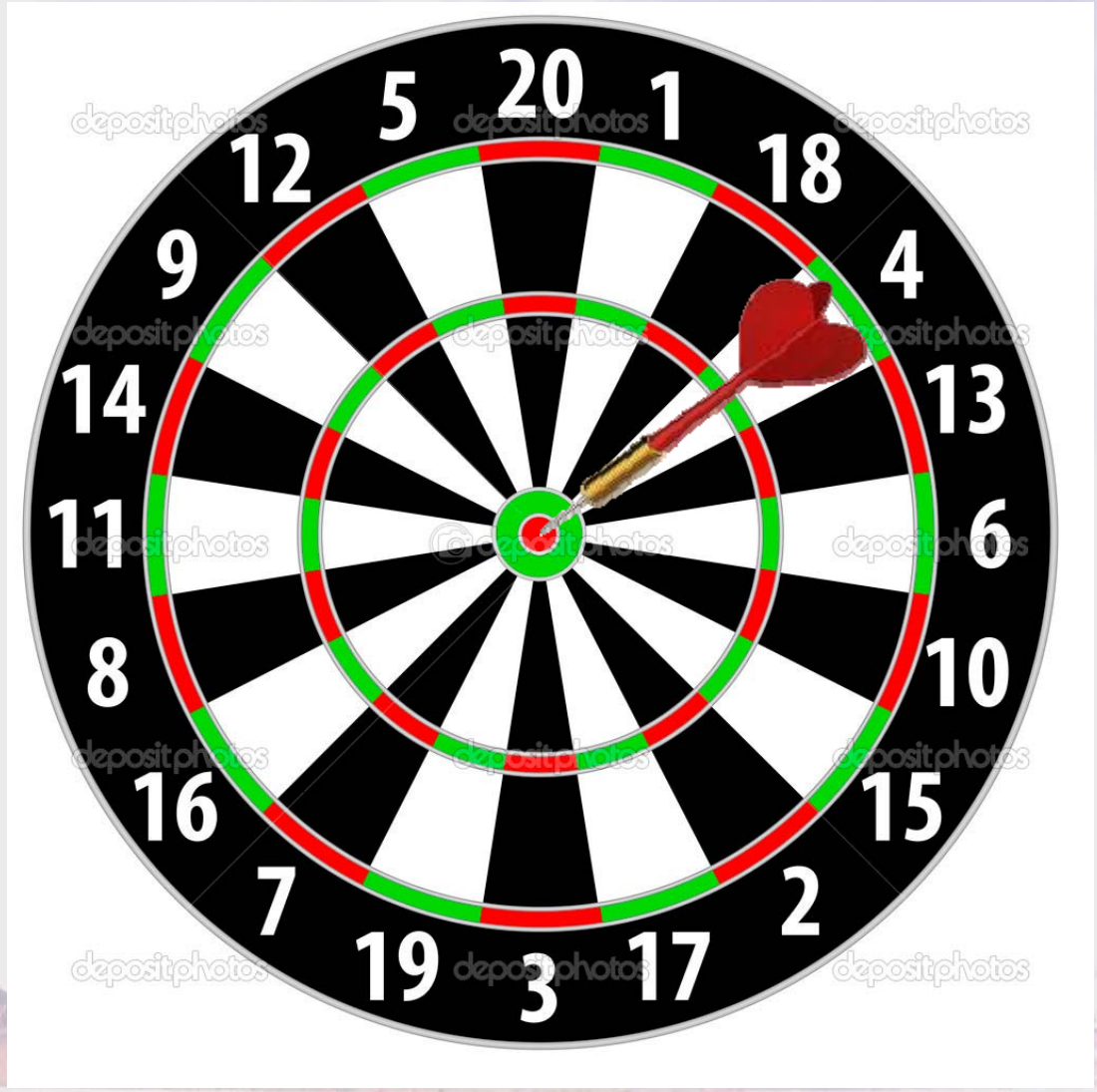
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6 tests

	Years From HT Initiation Among Women With No Prior Use of HT					
	<2		2–4		≥5	
	HR	95% CI	HR	95% CI	HR	95% CI
Coronary heart disease						
CEE	1.12	0.55, 2.24	0.99	0.49, 2.00	0.60	0.35, 1.04
CEE/MPA	1.42	0.76, 2.65	1.37	0.71, 2.67	1.24	0.61, 2.50

Am J Epidemiol. 2009 Jul 1;170(1):12-

24 tests

	Years From HT Initiation Among Women With No Prior Use of HT					
	<2		2–4		≥5	
	HR	95% CI	HR	95% CI	HR	95% CI
Coronary heart disease						
CEE	1.12	0.55, 2.24	0.99	0.49, 2.00	0.60	0.35, 1.04
CEE/MPA	1.42	0.76, 2.65	1.37	0.71, 2.67	1.24	0.61, 2.50
Stroke						
CEE	1.49	0.68, 3.28	2.45	1.06, 5.65	2.46	1.29, 4.70
CEE/MPA	1.58	0.69, 3.66	2.17	0.99, 4.80	3.48	1.36, 8.96
Venous thromboembolism						
CEE	1.12	0.40, 3.17	0.80	0.30, 2.15	0.99	0.46, 2.14
CEE/MPA	6.44	2.79, 14.85	3.15	1.47, 6.74	2.69	1.28, 5.63
Invasive breast cancer						
CEE	1.44	0.54, 3.84	1.15	0.57, 2.32	1.00	0.54, 1.84
CEE/MPA	1.05	0.56, 1.97	2.18	1.31, 3.63	3.15	1.90, 5.20

114 tests

	Years From HT Initiation Among Women With No Prior Use of HT						Years From "Current" HT Episode[a] Among Women With Prior Use of HT					
	<2		2–4		≥5		<2		2–4		≥5	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Coronary heart disease												
CEE	1.12	0.55, 2.24	0.99	0.49, 2.00	0.60	0.35, 1.04	1.26	0.64, 2.46	1.52	0.81, 2.86	0.86	0.48, 1.52
CEE/MPA	1.42	0.76, 2.65	1.37	0.71, 2.67	1.24	0.61, 2.50	2.70	1.11, 6.52	1.10	0.46, 2.63	2.18	0.77, 6.19
Stroke												
CEE	1.49	0.68, 3.28	2.45	1.06, 5.65	2.46	1.29, 4.70	1.43	0.61, 3.39	1.56	0.81, 3.03	2.39	1.25, 4.56
CEE/MPA	1.58	0.69, 3.66	2.17	0.99, 4.80	3.48	1.36, 8.96	1.73	0.53, 5.59	1.05	0.45, 2.45	1.48	0.51, 4.29
Venous thromboembolism												
CEE	1.12	0.40, 3.17	0.80	0.30, 2.15	0.99	0.46, 2.14	4.09	1.28, 13.11	2.19	0.97, 4.95	1.56	0.73, 3.31
CEE/MPA	6.44	2.79, 14.85	3.15	1.47, 6.74	2.69	1.28, 5.63	1.65	0.70, 3.89	2.37	0.88, 6.43	1.64	0.41, 6.59
Invasive breast cancer												
CEE	1.44	0.54, 3.84	1.15	0.57, 2.32	1.00	0.54, 1.84	1.63	0.68, 3.91	0.82	0.42, 1.57	0.91	0.49, 1.69
CEE/MPA	1.05	0.56, 1.97	2.18	1.31, 3.63	3.15	1.90, 5.20	1.79	0.84, 3.83	4.02	2.03, 7.98	3.14	1.46, 6.75
Invasive colorectal cancer												
CEE	1.42	0.45, 4.52	1.91	0.44, 8.37	2.12	0.55, 8.16	0.95	0.32, 2.82	0.44	0.12, 1.66	4.43	1.13, 17.38
CEE/MPA	0.54	0.16, 1.77	0.46	0.16, 1.36	0.50	0.16, 1.58	0.53	0.13, 2.22	0.27	0.06, 1.28	0.71	0.17, 3.07
Invasive endometrial cancer												
CEE/MPA	1.50	0.21, 10.67	1.60	0.40, 6.45	1.97	0.54, 7.13	0.33	0.04, 2.87	0.56	0.14, 2.31	0.82	0.17, 3.90
Hip fracture												
CEE	0.46	0.04, 4.88	0.53	0.11, 2.51	0.69	0.19, 2.56	0.60	0.11, 3.24	0.13	0.02, 1.08	0.54	0.16, 1.76
CEE/MPA	0.35	0.10, 1.17	0.33	0.10, 1.10	0.22	0.07, 0.71	0.94	0.19, 4.58	0.26	0.05, 1.25	0.43	0.09, 2.07
Death from other causes[d]												
CEE	1.26	0.42, 3.81	1.04	0.43, 2.53	1.88	0.90, 3.93	1.29	0.51, 3.21	0.82	0.41, 1.63	3.16	1.53, 6.55
CEE/MPA	0.96	0.43, 2.14	0.70	0.34, 1.42	0.87	0.40, 1.88	0.18	0.02, 1.47	0.69	0.30, 1.61	0.75	0.26, 2.13
Global index[e]												
CEE	1.26	0.86, 1.83	1.23	0.87, 1.75	1.18	0.89, 1.57	1.29	0.90, 1.85	1.03	0.76, 1.39	1.53	1.15, 2.03
CEE/MPA	1.53	1.14, 2.05	1.56	1.18, 2.06	1.89	1.42, 2.49	1.28	0.86, 1.91	1.32	0.94, 1.85	1.43	0.96, 2.11

168 tests

	Years From HT Initiation Among Women With No Prior Use of HT						Years From "Current" HT Episode[a] Among Women With Prior Use of HT						5-Year[b] Increase in Gap Time		Ratio[c] of HR in Observational Study to HR in Clinical Trials	
	<2		2–4		≥5		<2		2–4		≥5					
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	Ratio	95% CI
Coronary heart disease																
CEE	1.12	0.55, 2.24	0.99	0.49, 2.00	0.60	0.35, 1.04	1.26	0.64, 2.46	1.52	0.81, 2.86	0.86	0.48, 1.52	0.98	0.85, 1.12	1.05	0.63, 1.76
CEE/MPA	1.42	0.76, 2.65	1.37	0.71, 2.67	1.24	0.61, 2.50	2.70	1.11, 6.52	1.10	0.46, 2.63	2.18	0.77, 6.19	1.01	0.84, 1.22	0.76	0.41, 1.42
Stroke																
CEE	1.49	0.68, 3.28	2.45	1.06, 5.65	2.46	1.29, 4.70	1.43	0.61, 3.39	1.56	0.81, 3.03	2.39	1.25, 4.56	1.01	0.89, 1.15	0.46	0.25, 0.84
CEE/MPA	1.58	0.69, 3.66	2.17	0.99, 4.80	3.48	1.36, 8.96	1.73	0.53, 5.59	1.05	0.45, 2.45	1.48	0.51, 4.29	0.91	0.72, 1.14	0.33	0.14, 0.78
Venous thromboembolism																
CEE	1.12	0.40, 3.17	0.80	0.30, 2.15	0.99	0.46, 2.14	4.09	1.28, 13.11	2.19	0.97, 4.95	1.56	0.73, 3.31	1.12	0.95, 1.33	0.61	0.30, 1.26
CEE/MPA	6.44	2.79, 14.85	3.15	1.47, 6.74	2.69	1.28, 5.63	1.65	0.70, 3.89	2.37	0.88, 6.43	1.64	0.41, 6.59	1.01	0.83, 1.23	0.62	0.32, 1.20
Invasive breast cancer																
CEE	1.44	0.54, 3.84	1.15	0.57, 2.32	1.00	0.54, 1.84	1.63	0.68, 3.91	0.82	0.42, 1.57	0.91	0.49, 1.69	0.85	0.73, 0.98	1.07	0.60, 1.93
CEE/MPA	1.05	0.56, 1.97	2.18	1.31, 3.63	3.15	1.90, 5.20	1.79	0.84, 3.83	4.02	2.03, 7.98	3.14	1.46, 6.75	0.80	0.69, 0.93	1.06	0.66, 1.71
Invasive colorectal cancer																
CEE	1.42	0.45, 4.52	1.91	0.44, 8.37	2.12	0.55, 8.16	0.95	0.32, 2.82	0.44	0.12, 1.66	4.43	1.13, 17.38	0.90	0.67, 1.21	0.32	0.09, 1.17
CEE/MPA	0.54	0.16, 1.77	0.46	0.16, 1.36	0.50	0.16, 1.58	0.53	0.13, 2.22	0.27	0.06, 1.28	0.71	0.17, 3.07	1.21	0.88, 1.68	1.85	0.68, 5.01
Invasive endometrial cancer																
CEE/MPA	1.50	0.21, 10.67	1.60	0.40, 6.45	1.97	0.54, 7.13	0.33	0.04, 2.87	0.56	0.14, 2.31	0.82	0.17, 3.90	0.72	0.48, 1.09	1.13	0.35, 3.67
Hip fracture																
CEE	0.46	0.04, 4.88	0.53	0.11, 2.51	0.69	0.19, 2.56	0.60	0.11, 3.24	0.13	0.02, 1.08	0.54	0.16, 1.76	1.01	0.77, 1.31	0.96	0.28, 3.32
CEE/MPA	0.35	0.10, 1.17	0.33	0.10, 1.10	0.22	0.07, 0.71	0.94	0.19, 4.58	0.26	0.05, 1.25	0.43	0.09, 2.07	1.29	0.94, 1.78	3.10	1.20, 7.98
Death from other causes[d]																
CEE	1.26	0.42, 3.81	1.04	0.43, 2.53	1.88	0.90, 3.93	1.29	0.51, 3.21	0.82	0.41, 1.63	3.16	1.53, 6.55	1.01	0.90, 1.14	0.38	0.18, 0.76
CEE/MPA	0.96	0.43, 2.14	0.70	0.34, 1.42	0.87	0.40, 1.88	0.18	0.02, 1.47	0.69	0.30, 1.61	0.75	0.26, 2.13	1.09	0.91, 1.31	0.97	0.48, 1.95
Global index[e]																
CEE	1.26	0.86, 1.83	1.23	0.87, 1.75	1.18	0.89, 1.57	1.29	0.90, 1.85	1.03	0.76, 1.39	1.53	1.15, 2.03	0.97	0.91, 1.03	0.70	0.53, 0.91
CEE/MPA	1.53	1.14, 2.05	1.56	1.18, 2.06	1.89	1.42, 2.49	1.28	0.86, 1.91	1.32	0.94, 1.85	1.43	0.96, 2.11	0.92	0.85, 0.99	0.86	0.67, 1.11
Total invasive cancer																
CEE	1.72	1.04, 2.83	1.07	0.68, 1.69	1.17	0.80, 1.70	1.12	0.70, 1.81	0.74	0.49, 1.11	1.40	0.96, 2.02	0.91	0.83, 0.99	0.77	0.54, 1.11
CEE/MPA	1.14	0.78, 1.67	1.49	1.08, 2.07	1.82	1.31, 2.53	1.01	0.64, 1.61	1.48	0.99, 2.22	1.42	0.90, 2.25	0.88	0.80, 0.97	1.06	0.79, 1.43
Total mortality																
CEE	1.62	0.75, 3.53	1.26	0.66, 2.41	1.35	0.82, 2.24	2.19	1.08, 4.47	1.06	0.62, 1.83	1.92	1.16, 3.19	0.97	0.88, 1.07	0.53	0.33, 0.86
CEE/MPA	0.83	0.43, 1.60	0.89	0.50, 1.60	1.13	0.59, 2.16	0.55	0.18, 1.63	0.84	0.43, 1.66	0.90	0.38, 2.14	1.09	0.93, 1.27	0.76	0.43, 1.37

250+ tests

	Use of Conjugated Equine Estrogens					Use of Conjugated Equine Estrogens/ Medroxyprogesterone Acetate				
	Time From Menopause to First Use of HT, years				P for Gap Time Interaction[a]	Time From Menopause to First Use of HT, years				P for Gap Time Interaction[a]
	<5		≥5			<5		≥5		
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
ıary heart disease										
prior HT[b]	—[c]		0.89	0.67, 1.20	0.40	0.99	0.49, 1.98	1.19	0.91, 1.57	0.42
ır HT	1.22	0.89, 1.67	1.04	0.58, 1.86		1.57	0.99, 2.50	1.45	0.69, 3.06	
prior HT	—		1.64	1.12, 2.41	0.96	0.92	0.38, 2.24	1.31	0.96, 1.79	1.00
ır HT	1.36	0.98, 1.90	0.56	0.20, 1.28		1.20	0.71, 2.03	1.10	0.46, 2.68	
ıs thromboembolism										
prior HT	—		1.07	0.65, 1.76	0.65	2.26	1.00, 5.10	2.59	1.81, 3.71	0.45
ır HT	1.71	1.12, 2.60	1.37	0.64, 2.95		1.78	1.05, 3.02	1.07	0.40, 2.81	
ve breast cancer										
prior HT	1.12	0.39, 3.21	0.58	0.36, 0.93	0.20	1.77	1.07, 2.93	0.99	0.74, 1.31	0.03
ır HT	1.00	0.66, 1.51	0.77	0.33, 1.80		2.06	1.30, 3.27	1.30	0.57, 2.99	
ve colorectal cancer										
Prior HT	—		1.10	0.61, 1.99	0.34	—		0.72	0.42, 1.16	0.42
ır HT	1.43	0.82, 2.51	—			0.35	0.13, 0.94	—		
ve endometrial cancer										
prior HT	—		—		—	—		0.57	0.26, 1.22	0.97
ır HT	—		—			0.80	0.31, 2.11	—		
acture										
prior HT	—		0.87	0.48, 1.60	0.58	—		0.81	0.53, 1.24	0.04
ır HT	0.54	0.30, 0.99	—			0.25	0.09, 0.74	—		
from other causes[d]										
prior HT	1.15	0.50, 2.69	0.91	0.70, 1.19	0.14	0.66	0.31, 1.40	1.05	0.80, 1.37	0.21
ır HT	1.27	0.99, 1.63	0.76	0.45, 1.30		0.69	0.44, 1.11	0.79	0.36, 1.76	
l index[e]										
prior HT	0.90	0.53, 1.53	0.98	0.83, 1.16	0.05	1.13	0.84, 1.53	1.12	0.99, 1.28	0.93
ır HT	1.22	1.04, 1.43	0.71	0.50, 1.00		1.11	0.90, 1.37	1.09	0.77, 1.55	
invasive cancer										
prior HT	1.72	1.00, 2.94	0.84	0.66, 1.07	0.07	1.07	0.73, 1.55	0.90	0.76, 1.07	0.25
ır HT	1.07	0.85, 1.33	0.48	0.27, 0.84		1.17	0.90, 1.52	1.08	0.69, 1.67	
mortality										
prior HT	1.15	0.50, 2.69	0.91	0.70, 1.19	0.14	0.73	0.38, 1.39	1.05	0.84, 1.33	0.36
ır HT	1.27	0.99, 1.63	0.76	0.45, 1.30		0.83	0.57, 1.21	0.95	0.51, 1.76	

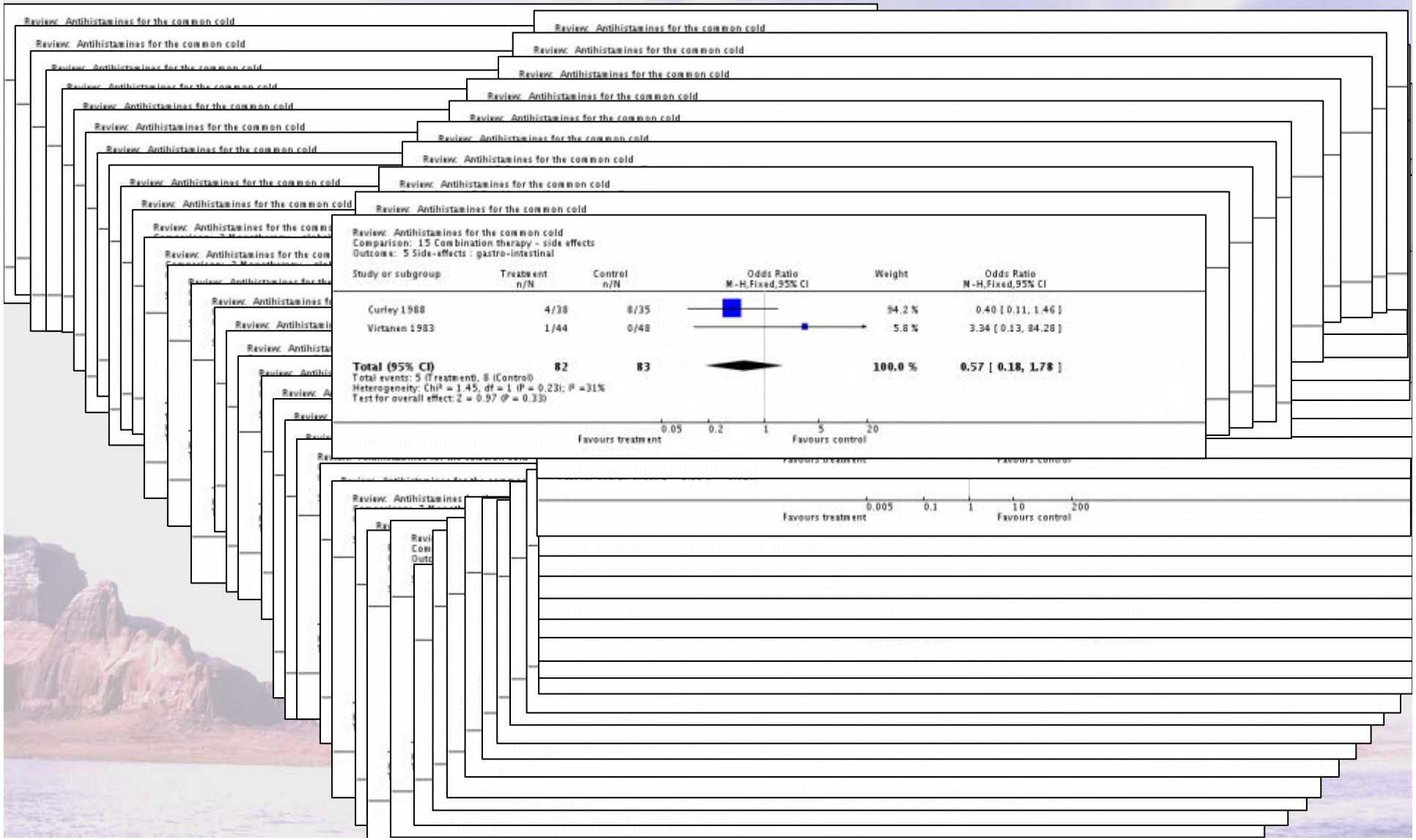
urrent" HT Episode[a] Among With Prior Use of HT				5-Year[b] Increase in Gap Time		Ratio[c] of HR in Observational Study to HR in Clinical Trials	
2–4		≥5					
R	95% CI	HR	95% CI	HR	95% CI	Ratio	95% CI
52	0.81, 2.86	0.86	0.48, 1.52	0.98	0.85, 1.12	1.05	0.63, 1.76
10	0.46, 2.63	2.18	0.77, 6.19	1.01	0.84, 1.22	0.76	0.41, 1.42
56	0.81, 3.03	2.39	1.25, 4.56	1.01	0.89, 1.15	0.46	0.25, 0.84
05	0.45, 2.45	1.48	0.51, 4.29	0.91	0.72, 1.14	0.33	0.14, 0.78
19	0.97, 4.95	1.56	0.73, 3.31	1.12	0.95, 1.33	0.61	0.30, 1.26
37	0.88, 6.43	1.64	0.41, 6.59	1.01	0.83, 1.23	0.62	0.32, 1.20
32	0.42, 1.57	0.91	0.49, 1.69	0.85	0.73, 0.98	1.07	0.60, 1.93
02	2.03, 7.98	3.14	1.46, 6.75	0.80	0.69, 0.93	1.06	0.66, 1.71
14	0.12, 1.66	4.43	1.13, 17.38	0.90	0.67, 1.21	0.32	0.09, 1.17
27	0.06, 1.28	0.71	0.17, 3.07	1.21	0.88, 1.68	1.85	0.68, 5.01
56	0.14, 2.31	0.82	0.17, 3.90	0.72	0.48, 1.09	1.13	0.35, 3.67
13	0.02, 1.08	0.54	0.16, 1.76	1.01	0.77, 1.31	0.96	0.28, 3.32
26	0.05, 1.25	0.43	0.09, 2.07	1.29	0.94, 1.78	3.10	1.20, 7.98
32	0.41, 1.63	3.16	1.53, 6.55	1.01	0.90, 1.14	0.38	0.18, 0.76
89	0.30, 1.61	0.75	0.26, 2.13	1.09	0.91, 1.31	0.97	0.48, 1.95
03	0.76, 1.39	1.53	1.15, 2.03	0.97	0.91, 1.03	0.70	0.53, 0.91
82	0.94, 1.85	1.43	0.96, 2.11	0.92	0.85, 0.99	0.86	0.67, 1.11
74	0.49, 1.11	1.40	0.96, 2.02	0.91	0.83, 0.99	0.77	0.54, 1.11
48	0.99, 2.22	1.42	0.90, 2.25	0.88	0.80, 0.97	1.06	0.79, 1.43
06	0.62, 1.83	1.92	1.16, 3.19	0.97	0.88, 1.07	0.53	0.33, 0.86
84	0.43, 1.66	0.90	0.38, 2.14	1.09	0.93, 1.27	0.76	0.43, 1.37

400+ tests

	Use of Conjugated Equine Estrogens					Use of Conjugated Equine Estrogens/ Medroxyprogesterone Acetate				
	Time From Menopause to First Use of HT, years				*P* for Gap Time Interaction[a]	Time From Menopause to First Use of HT, years				*P* for Gap Time Interaction[a]
	<5		≥5			<5		≥5		
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
ıary heart disease										
prior HT[b]	—[c]		0.89	0.67, 1.20	0.40					
ır HT	1.22	0.89, 1.67	1.04	0.58, 1.86						
ə										
prior HT	—		1.64	1.12, 2.41	0.96					
ır HT	1.36	0.98, 1.90	0.56	0.20, 1.28						
ıs thromboembolism										
prior HT	—		1.07	0.65, 1.76	0.65					
ır HT	1.71	1.12, 2.60	1.37	0.64, 2.95						
ve breast cancer										
prior HT	1.12	0.39, 3.21	0.58	0.36, 0.93	0.20					
ır HT	1.00	0.66, 1.51	0.77	0.33, 1.80						
ve colorectal cancer										
Prior HT	—		1.10	0.61, 1.99	0.34					
ır HT	1.43	0.82, 2.51	—							
ve endometrial cancer										
prior HT	—		—		—					
ır HT	—		—							
acture										
prior HT	—		0.87	0.48, 1.60	0.58					
ır HT	0.54	0.30, 0.99	—							
from other causes[d]										
prior HT	1.15	0.50, 2.69	0.91	0.70, 1.19	0.14					
ır HT	1.27	0.99, 1.63	0.76	0.45, 1.30						
l index[e]										
prior HT	0.90	0.53, 1.53	0.98	0.83, 1.16	0.05					
ır HT	1.22	1.04, 1.43	0.71	0.50, 1.00						
invasive cancer										
prior HT	1.72	1.00, 2.94	0.84	0.66, 1.07	0.07					
ır HT	1.07	0.85, 1.33	0.48	0.27, 0.84						
mortality										
prior HT	1.15	0.50, 2.69	0.91	0.70, 1.19	0.14					
ır HT	1.27	0.99, 1.63	0.76	0.45, 1.30		0.83	0.57, 1.21	0.95	0.51, 1.76	

	Years From HT Initiation Among Women With No Prior Use of HT						Years From "Current" HT Episode[a] Among Women With Prior Use of HT					
	<2		2–4		≥5		<2		2–4		≥5	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Coronary heart disease												
CEE	1.12	0.55, 2.24	0.99	0.49, 2.00	0.60	0.35, 1.04	1.26	0.64, 2.46	1.52	0.81, 2.86	0.86	0.48, 1.52
CEE/MPA	1.42	0.76, 2.65	1.37	0.71, 2.67	1.24	0.61, 2.50	2.70	1.11, 6.52	1.10	0.46, 2.63	2.18	0.77, 6.19
Stroke												
CEE	1.49	0.68, 3.28	2.45	1.06, 5.65	2.46	1.29, 4.70	1.43	0.61, 3.39	1.56	0.81, 3.03	2.39	1.25, 4.56
CEE/MPA	1.58	0.69, 3.66	2.17	0.99, 4.80	3.48	1.36, 8.96	1.73	0.53, 5.59	1.05	0.45, 2.45	1.48	0.51, 4.29
Venous thromboembolism												
CEE	1.12	0.40, 3.17	0.80	0.30, 2.15	0.99	0.46, 2.14	4.09	1.28, 13.11	2.19	0.97, 4.95	1.56	0.73, 3.31
CEE/MPA	6.44	2.79, 14.85	3.15	1.47, 6.74	2.69	1.28, 5.63	1.65	0.70, 3.89	2.37	0.88, 6.43	1.64	0.41, 6.59
Invasive breast cancer												
CEE	1.44	0.54, 3.84	1.15	0.57, 2.32	1.00	0.54, 1.84	1.63	0.68, 3.91	0.82	0.42, 1.57	0.91	0.49, 1.69
CEE/MPA	1.05	0.56, 1.97	2.18	1.31, 3.63	3.15	1.90, 5.20	1.79	0.84, 3.83	4.02	2.03, 7.98	3.14	1.46, 6.75
Invasive colorectal cancer												
CEE	1.42	0.45, 4.52	1.91	0.44, 8.37	2.12	0.55, 8.16	0.95	0.32, 2.82	0.44	0.12, 1.66	4.43	1.13, 17.38
CEE/MPA	0.54	0.16, 1.77	0.46	0.16, 1.36	0.50	0.16, 1.58	0.53	0.13, 2.22	0.27	0.06, 1.28	0.71	0.17, 3.07
Invasive endometrial cancer												
CEE/MPA	1.50	0.21, 10.67	1.60	0.40, 6.45	1.97	0.54, 7.13	0.33	0.04, 2.87	0.56	0.14, 2.31	0.82	0.17, 3.90
Hip fracture												
CEE	0.46	0.04, 4.88	0.53	0.11, 2.51	0.69	0.19, 2.56	0.60	0.11, 3.24	0.13	0.02, 1.08	0.54	0.16, 1.76
CEE/MPA	0.35	0.10, 1.17	0.33	0.10, 1.10	0.22	0.07, 0.71	0.94	0.19, 4.58	0.26	0.05, 1.25	0.43	0.09, 2.07
Death from other causes[d]												
CEE	1.26	0.42, 3.81	1.04	0.43, 2.53	1.88	0.90, 3.93	1.29	0.51, 3.21	0.82	0.41, 1.63	3.16	1.53, 6.55
CEE/MPA	0.96	0.43, 2.14	0.70	0.34, 1.42	0.87	0.40, 1.88	0.18	0.02, 1.47	0.69	0.30, 1.61	0.75	0.26, 2.13
Global index[e]												
CEE	1.26	0.86, 1.83	1.23	0.87, 1.75	1.18	0.89, 1.57	1.29	0.90, 1.85	1.03	0.76, 1.39	1.53	1.15, 2.03
CEE/MPA	1.53	1.14, 2.05	1.56	1.18, 2.06	1.89	1.42, 2.49	1.28	0.86, 1.91	1.32	0.94, 1.85	1.43	0.96, 2.11
Total invasive cancer												
CEE	1.72	1.04, 2.83	1.07	0.68, 1.69	1.17	0.80, 1.70	1.12	0.70, 1.81	0.74	0.49, 1.11	1.40	0.96, 2.02
CEE/MPA	1.14	0.78, 1.67	1.49	1.08, 2.07	1.82	1.31, 2.53	1.01	0.64, 1.61	1.48	0.99, 2.22	1.42	0.90, 2.25
Total mortality												
CEE	1.62	0.75, 3.53	1.26	0.66, 2.41	1.35	0.82, 2.24	2.19	1.08, 4.47	1.06	0.62, 1.83	1.92	1.16, 3.19
CEE/MPA	0.83	0.43, 1.60	0.89	0.50, 1.60	1.13	0.59, 2.16	0.55	0.18, 1.63	0.84	0.43, 1.66	0.90	0.38, 2.14

Ways of Measuring A Runny Nose



The Worst
Part of
Censorship
is

It’s on a Need to Know Basis

Understanding Funding Bias

- However, Funding gives an OR of 4-5.3 that,[2]
  - Study outcomes favor therapy studied
  - Therapy is recommended as Treatment of Choice
  - Odds Ratio: 5.0 (2.1-12.0) (my research)

- How do they do it? And an example.

1) BMJ, 2003; 326: 1167-70 Ann Intern Med. 1996 Mar 1;124(5):485-9. 2) JAMA, 2003; 290(7): 921-8. BMJ, 2003; 326: 1167-70. CMAJ 2004;170(4): 477-83.

Even Objective Outcomes are Subjective: Seeing with Rosi-coloured Glasses

Figure 4: K-M Plot of Time to First GSK MI

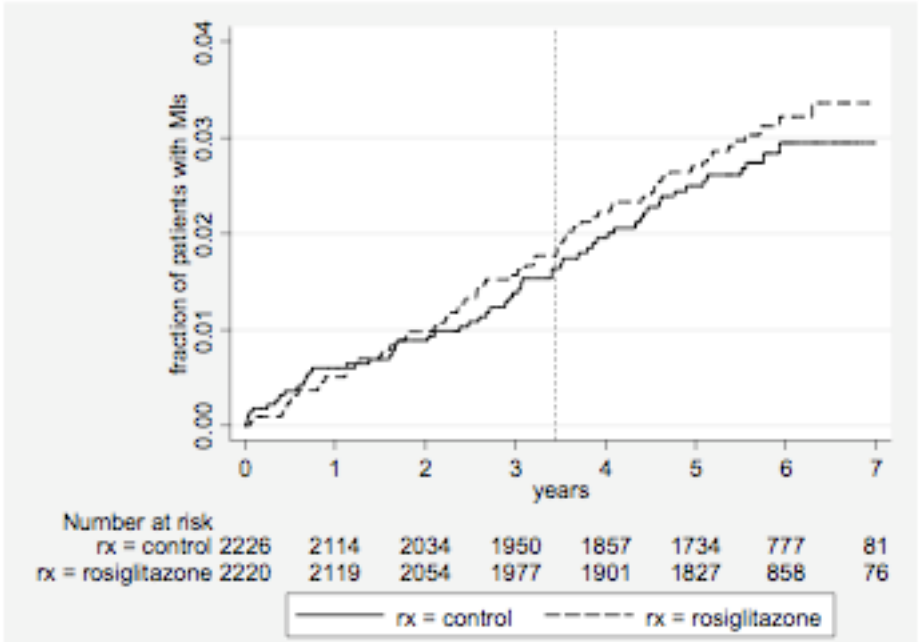
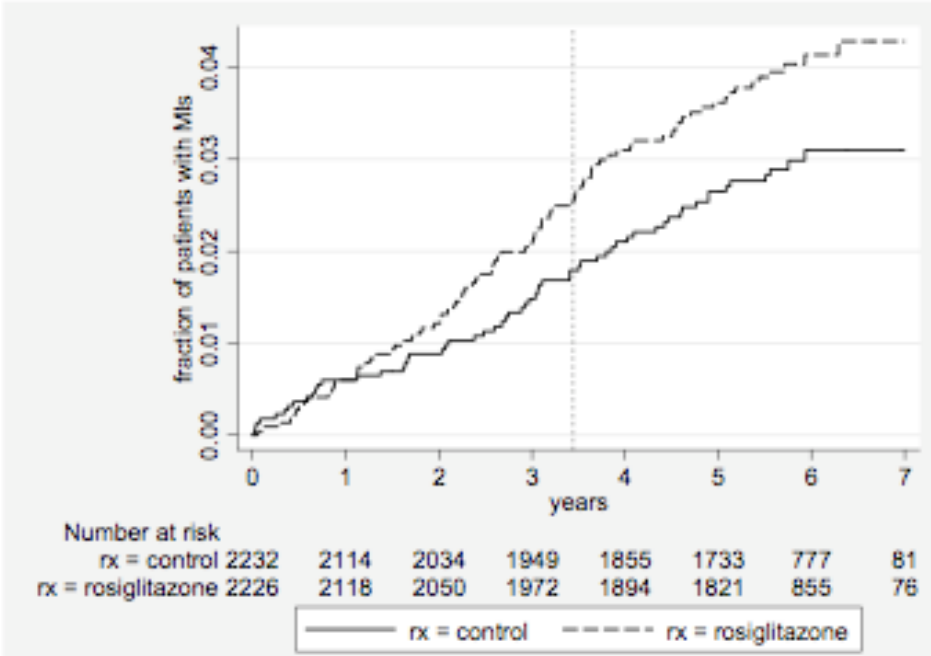


Figure 3: K-M Plot of Time to First FDA MI



Food and Drug Administration. Briefing document: July 13-14, 2010 meeting of the Endocrinologic and Metabolic Drugs Advisory Committee. (Accessed August 6, 2010)

SSRI: Super Selective Release of Information

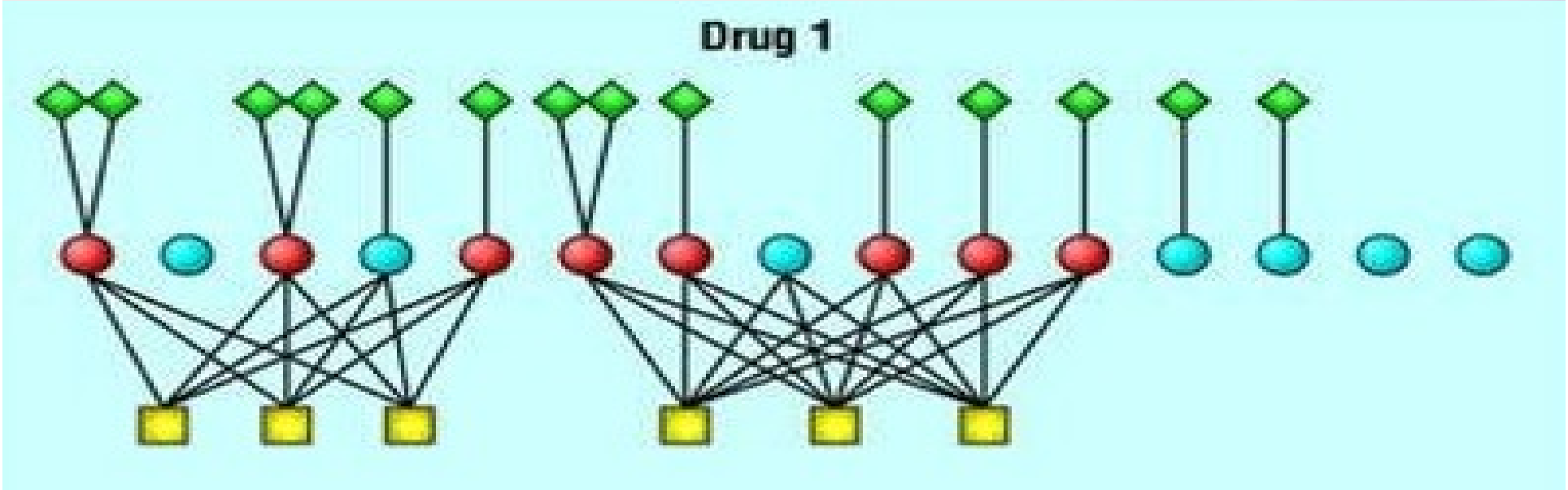
- 94% of all published SSRI trials are positive.

- So why do they not work as well in practice,….
- Step 1, Hide Bad Trials
- Of 74 Trials SSRI/SNRI trials submitted to FDA:
  - 38 Positive: 37 published
  - 36 Negative: 14 published (11 as positive).

NEJM 2008; 358: 252.

SSRI: Super Selective Release of Information

- Step 2: Re-publish the good!
  - Three Trials find their way into 12 publications (5 each)

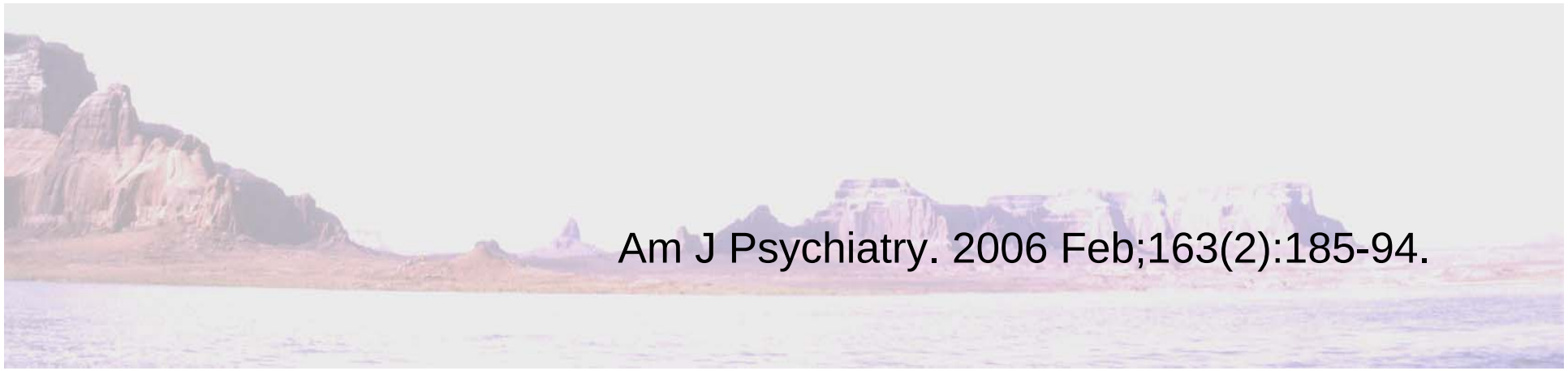


Melander H, Ahlqvist-Rastad J, Meijer G, Beermann B. Evidence b(i)ased medicine--selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications. BMJ. 2003 May 31;326(7400):1171-3.

That’s how we end up here

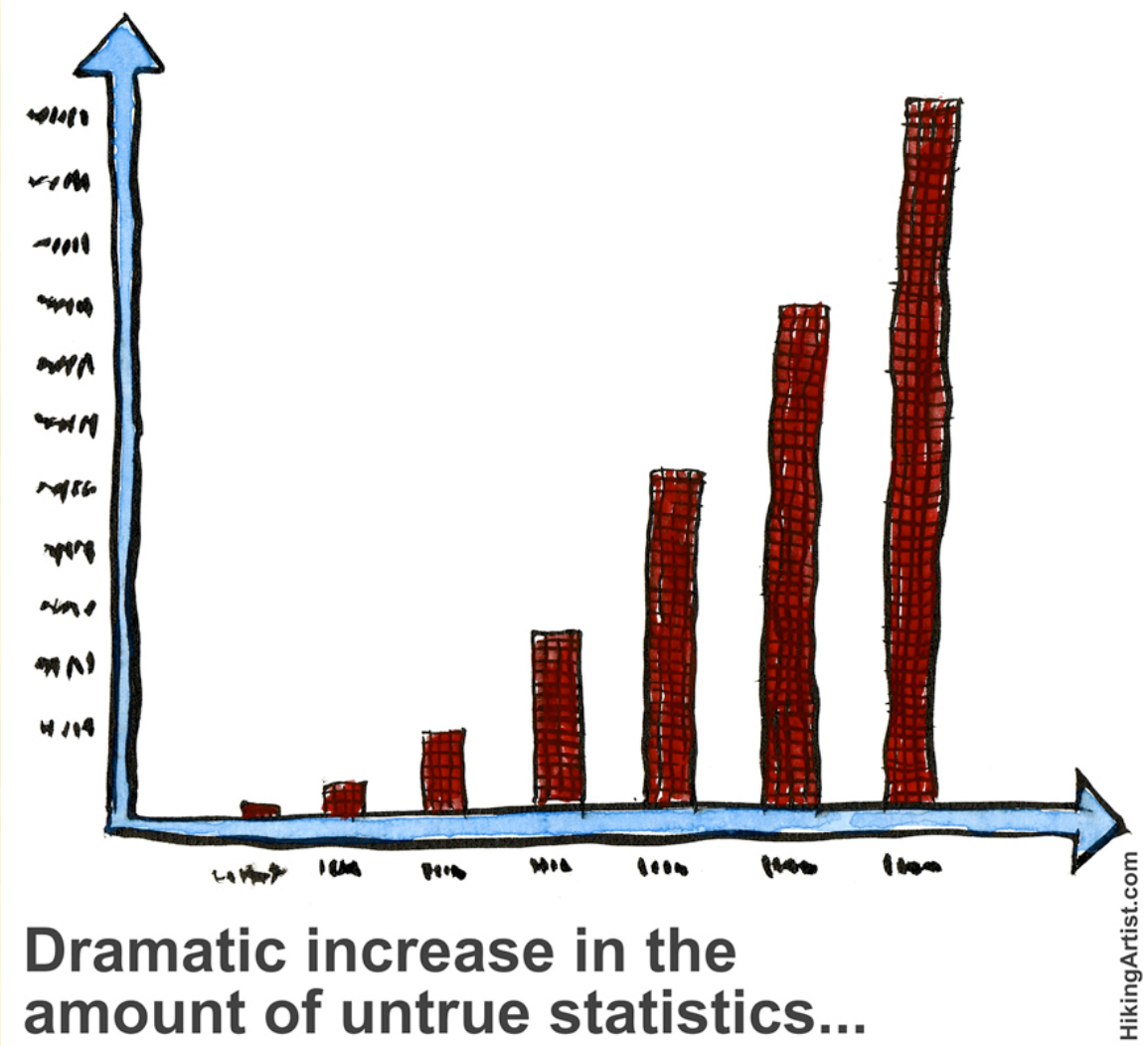
Reviews and Overviews

Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics



Am J Psychiatry. 2006 Feb;163(2):185-94.

Using Scales to confuse



Liars, Damn Liars & Scales

- Continuous variables can be reported many ways; and each can look different
- Scales = lots of numbers
- ↑ numbers = ↑ odds Statistical significance
- Statistical Significant ≠ clinical significance

“Facts are Stubborn but Statistics (*Scales*) are Pliable” (Mark Twain)?

- Example cholinesterase inhibitors
  - Recommend by
    - Alberta Clinical Practice Guidelines Program, Scottish Guidelines, Canadian consensus Group, American Academy of Neurology, etc.[1]
  - Not recommended by
    - NICE: UK’s National Institute of Clinical Excellence, Therapeutics Initiative,[2] etc

1) www.topalbertadoctors.org/informed_practice/cpgs/cognitive_impairment_part2.html. Int J Geriatr Psychiatry 2006; 21: 14–16. Am Fam Phys 2003; 68: 1365-72. 2) BMJ 2005; 330: 495-6. Therapeutics Letter 2005; 56:1-4.

Liars, Damn Liars and Scales

- Problems with trials, Quality of Life unchanged & No hard data
- But much of the confusion is in the scales
  - ADAS-cog diff of 4 (5.7%) clinical significant
-

	Donepezil	Galantamine	Rivastigmine	All
ADAS - Cog	3% less Decline	4% less Decline	3% less Decline	3.9% less Decline
ADAS – Cog of 4		NNT 6	NNT 14	
Glob Clin State	NNT 10	NNT 6*	NNT 15	NNT 12
AE Drop-out	NNH 27	NNH 12	NNH 7	NNH 9

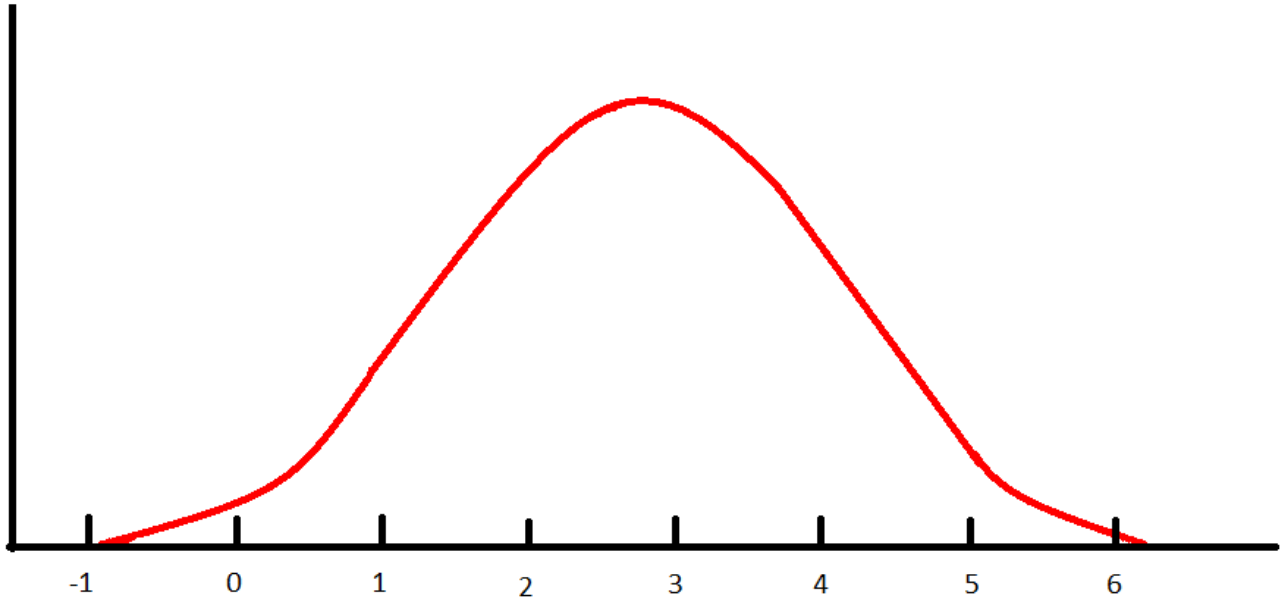
* Not significant if ITT analysis

Cochrane. 2006;(1):CD001190. Cochrane 2000;(4):CD001191. Cochrane 2009(2):CD001191. CMAJ 2003; 169: 557-64.

Means vs How Many Get Better

Example: Donepezil for Dementia

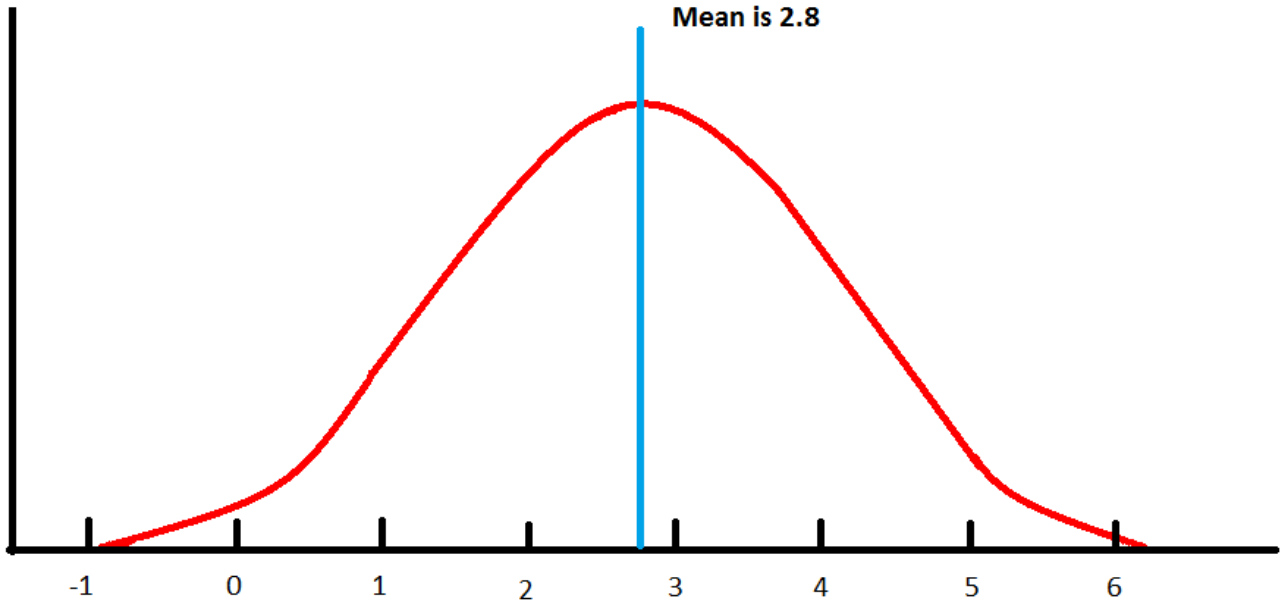
ADAS-Cog score change at the bottom.



Means vs How Many Get Better

Example: Donepezil for Dementia

ADAS-Cog score change at the bottom.



Means vs How Many Get Better

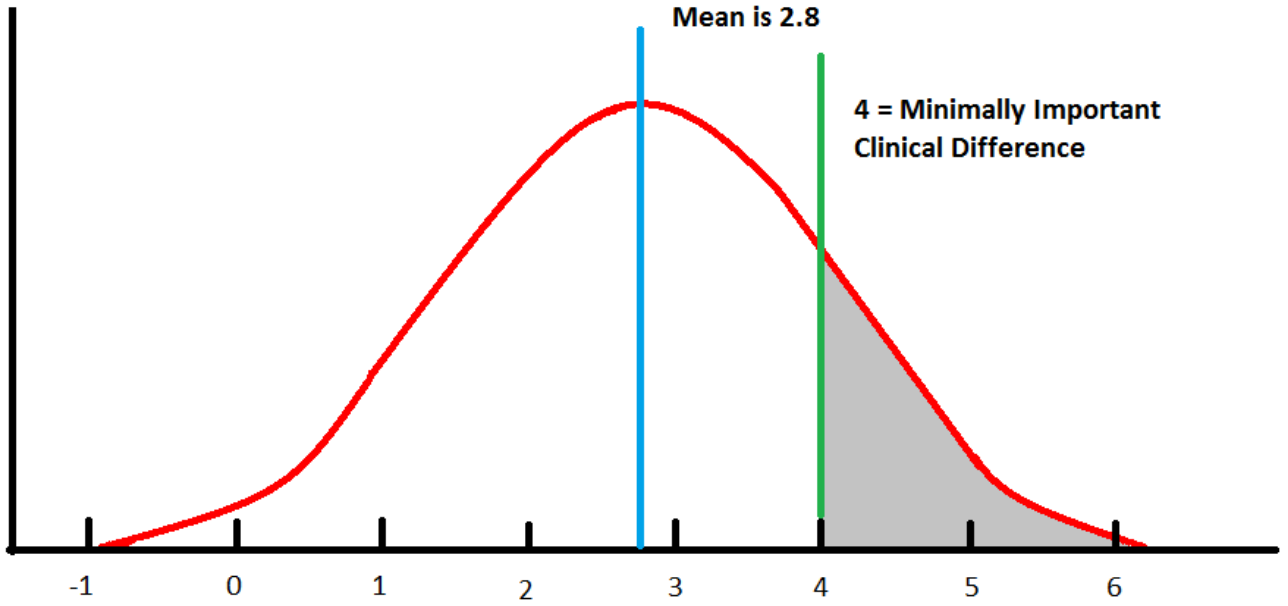
Example: Donepezil for Dementia

ADAS-Cog score change at the bottom.

Means vs How Many Get Better

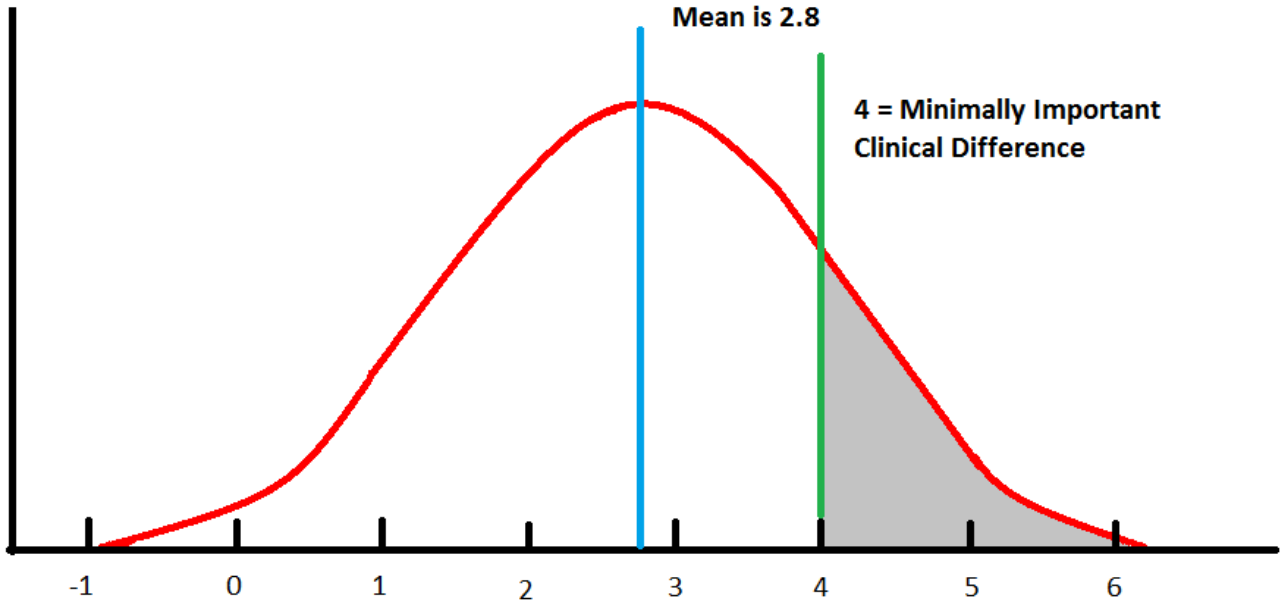
Example: Donepezil for Dementia

ADAS-Cog score change at the bottom.

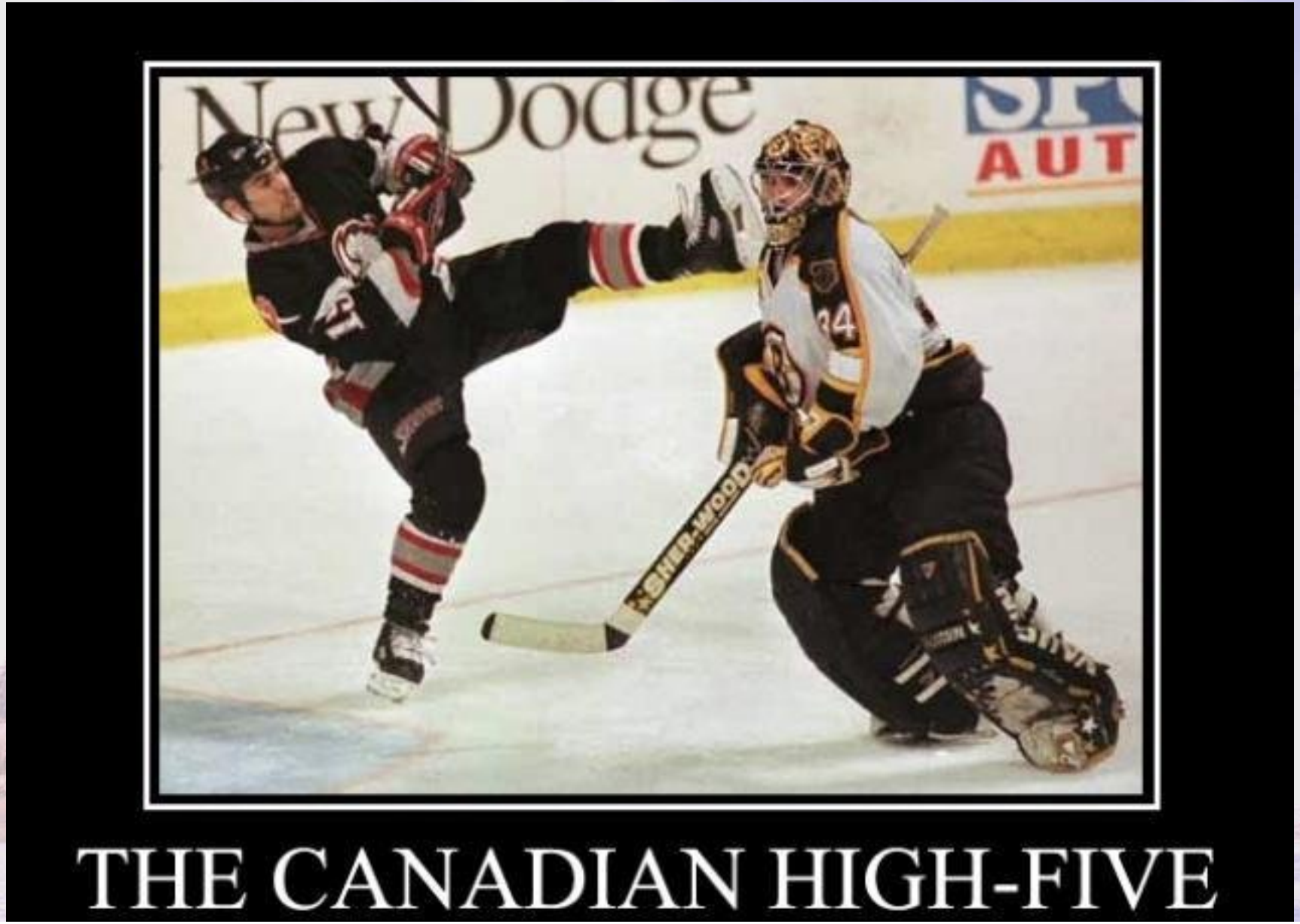


Means vs How Many Get Better

So the average patient is NOT noticeably better
BUT, in 1 in 10 (NNT 10) are.



Almost There,…

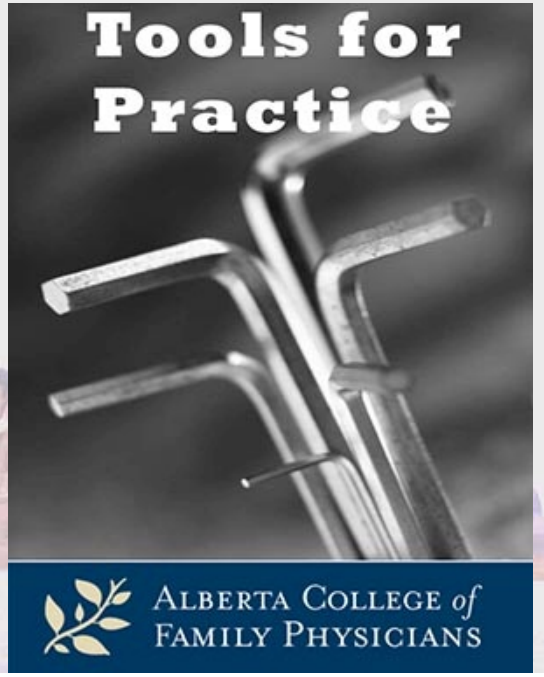


Seven Things We've Learned

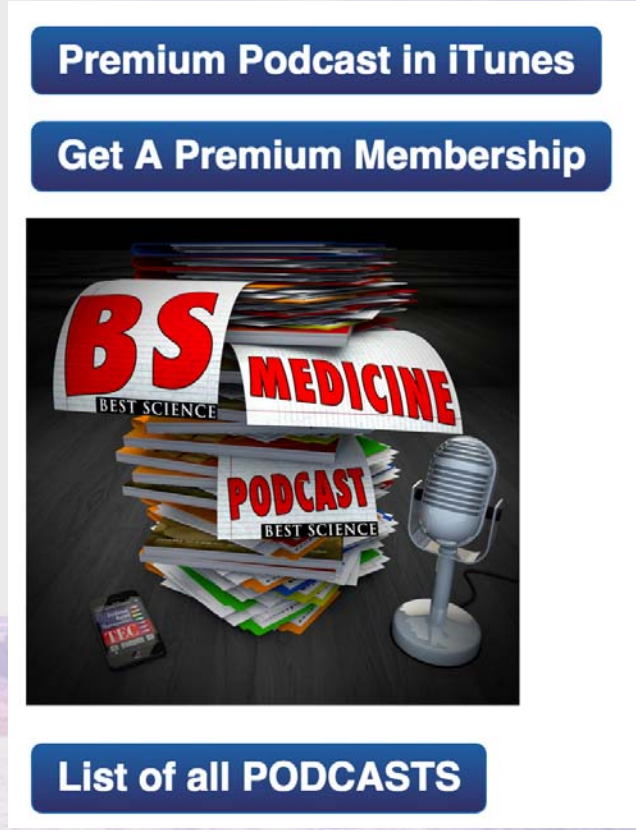
1. Patient Oriented Evidence that Matters
2. Ask "Does it work" NOT "How it works"
3. Association is NOT causation
4. Relative Risk is useless without baseline risk
5. Meta-Analysis can be mystery meat.
6. Statistics does not trump common sense
7. When thinking about symptom scales: How many people are better & by how much

Tools for Practice (www.acfp.ca)
Best Science Medicine

- Sign up to receive (free!)
  - subscribetfp@acfp.ca
- Suggest topics
- Become a peer reviewer



- Therapeutics Education Collaboration (TEC) or BS Medicine Podcast.



STOP