

Agenda

- Evidence
- Components of meta-analysis
- Pseudoscience, critical thinking
- Open office hours

- Presentations start NEXT WEDS!!
- 10-15 mins: background, data source, a couple of figures you made
 - **DO:** show that you've put some effort into your project; try to have a narrative
 - **DON'T:** show groundbreaking research that will solve all major societal issues
- Sign-up sheet goes live 8p tonight

Meta-Analysis

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true.

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a p -value less than 0.05. Research is not most appropriately represented and summarized by p -values, but, unfortunately, there is a widespread notion that medical research articles

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R + 1)$. The probability of a study finding a true relationship reflects the power $1 - \beta$ (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate, α . Assuming that c relationships are being probed in the field, the expected values of the 2×2 table are given in Table 1. After a research finding has been claimed based on

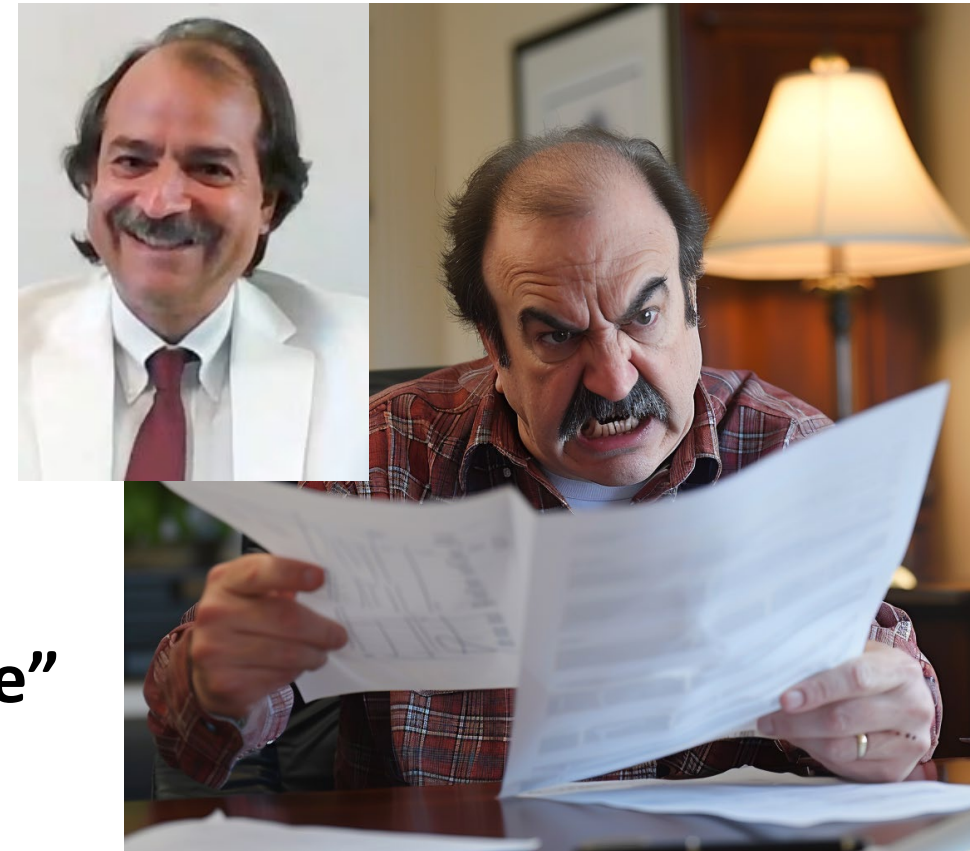
It can be proven that most claimed research findings are false.

Ioannidis' complaints

Claims most studies suffer from problems regarding:

- Sample size
- Size of the effect
- Confirmation bias
- Flexibility bias
- Conflicts of interest
- Scientific hotness/popularity

“What matters is the totality of the evidence”



Humans are NOT to blame for global warming, says Greenpeace co-founder, as he insists there is 'no scientific proof' climate change is manmade

- Patrick Moore has poured cold water on manmade global warming theories
- The Canadian said that
- He said that there's 'no
- Moore was a member of

There is no scientific proof of man-made global warming and a hotter earth would be 'beneficial for humans and the majority of other species', according to a founding member of environmental campaign group Greenpeace.

By [TED THORNHILL](#)
PUBLISHED: 08:12 EDT, 27 Feb

The assertion was made by Canadian ecologist Patrick Moore, a member of Greenpeace from 1971 to 1986, to U.S senators on Tuesday.

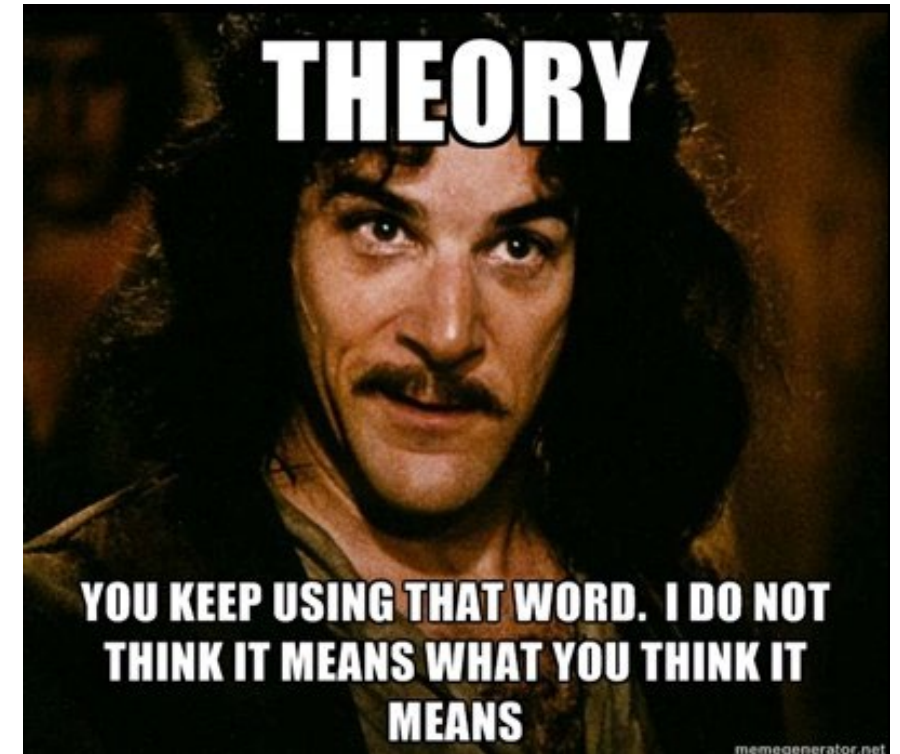
He told The Senate Environment and Public Works Committee: 'There is no scientific proof that human emissions of carbon dioxide (CO₂) are the dominant cause of the minor warming of the Earth's atmosphere over the past 100 years. If there were such a proof it would be written down for all to see. No actual proof, as it is understood in science, exists.'

Science is about *testing* hypotheses, not *proving*

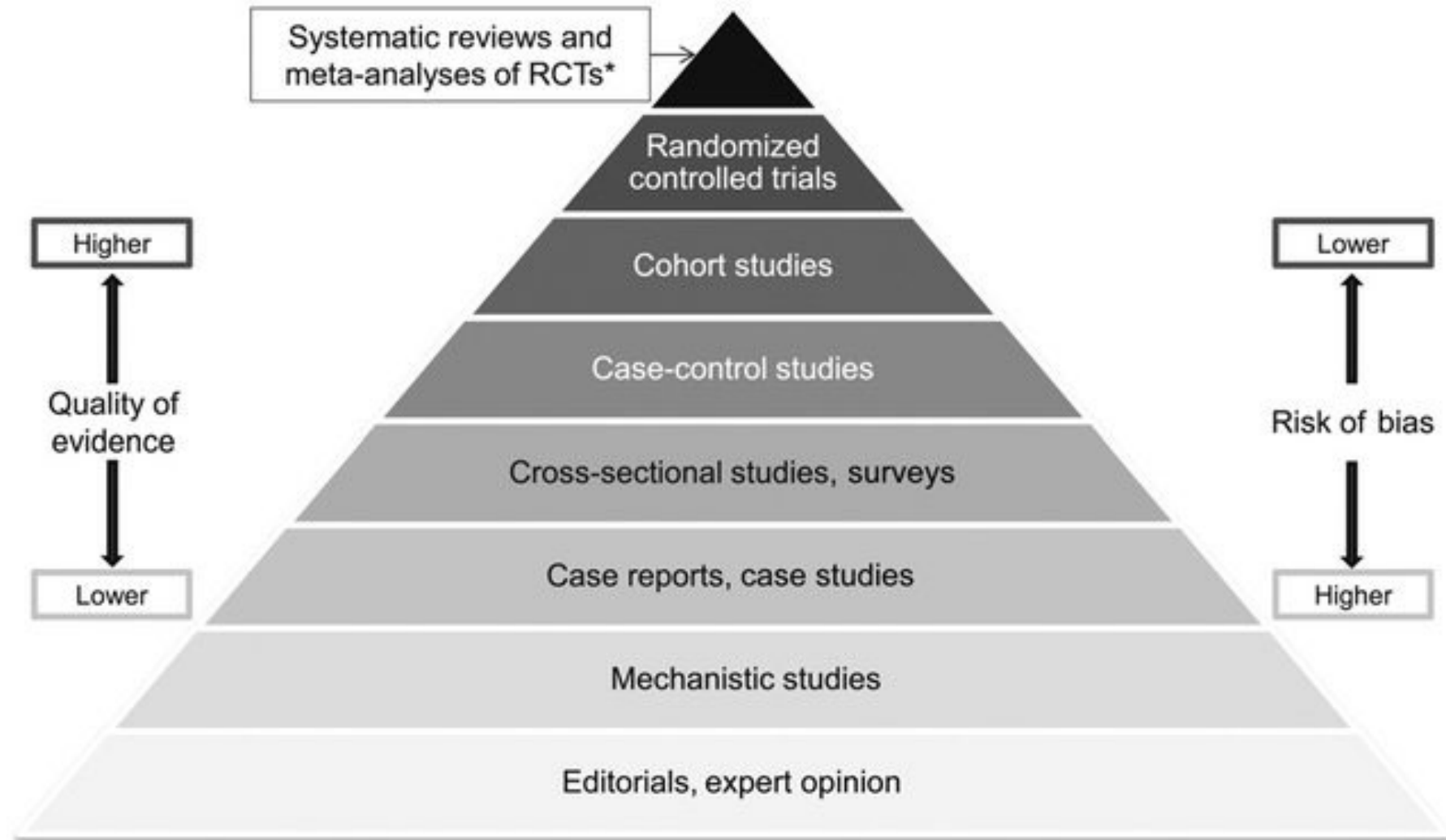
- Proof
 - Just obliterate this word from your vocabulary
- Theory
 - Supported by many tested hypotheses
 - Is falsifiable
 - “Climate change is just a theory”
- Hypothesis
 - A baby theory
 - Is falsifiable
 - Evidence supports a hypothesis and rejects an alternative; evidence points in a direction
 - “Climate change is caused by humans”
- Data
 - Facts, measurements, only become evidence in context of a hypothesis and alternative hypotheses

Something is **falsifiable** *only if* it is **quantifiable**

[One of Jacob's favorite TED talks](#)

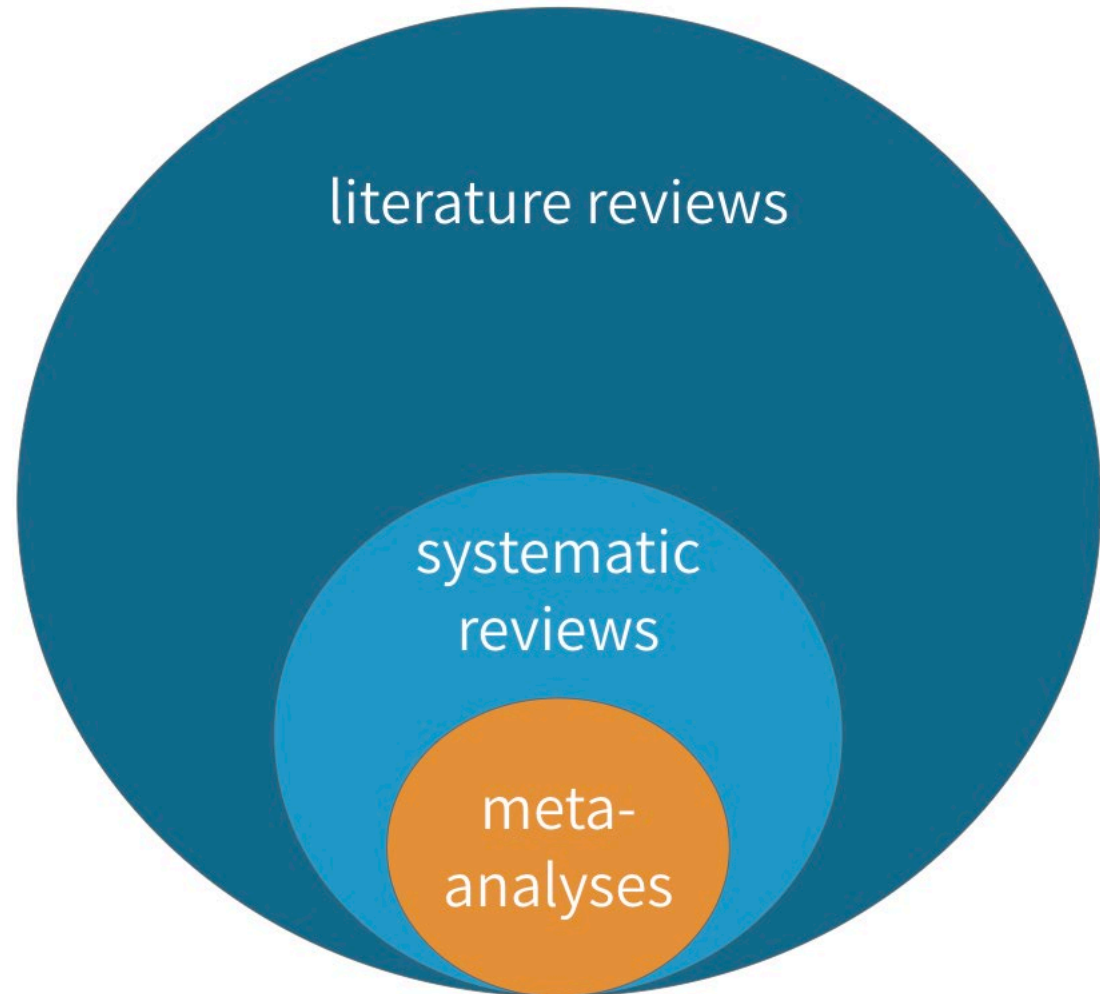


Pyramid of Evidence



Anecdotes, Daily Mail, TikTok videos etc. (hearsay, tabloids, social media)

Meta-analysis vs. Systematic reviews



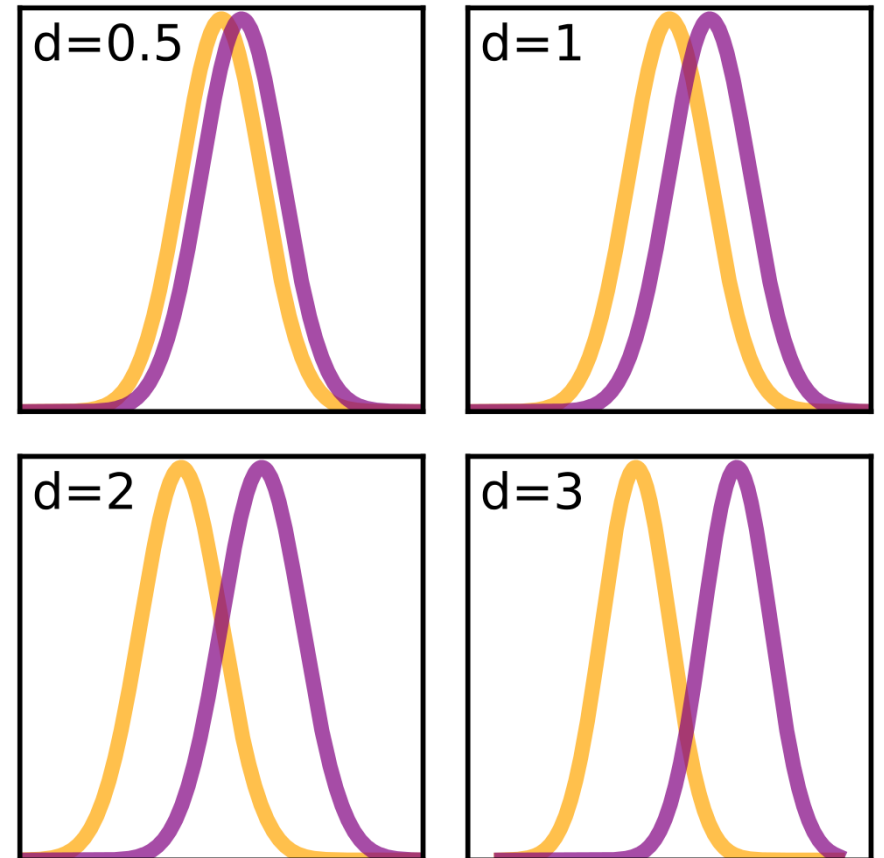
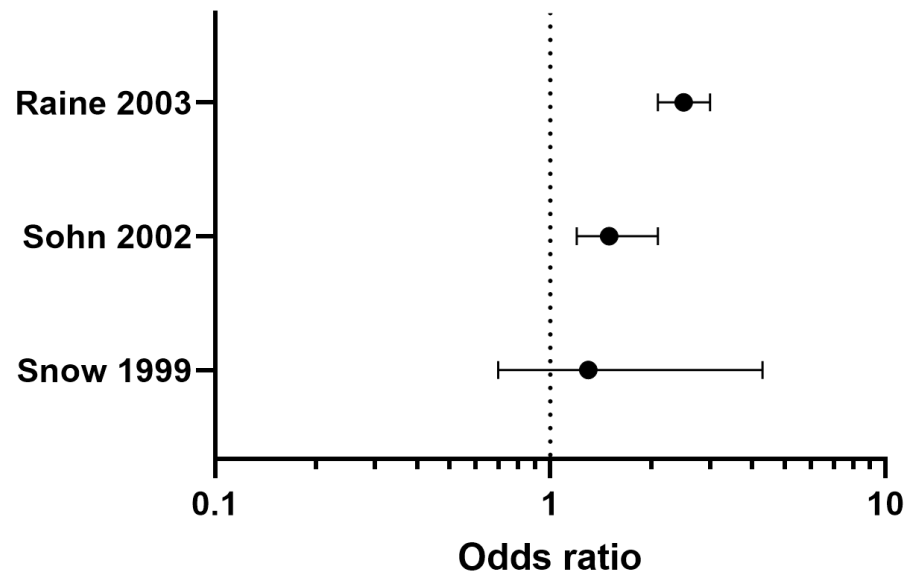
- Purpose is to answer specific research question
- Meta-analysis is **quantitative**, statistical analysis of combined results from multiple studies

Inclusion criteria, bias assessment

- Literature search is conducted systematically, criteria determined *before* search
- Criteria (See [Cochrane Handbook for Systematic Reviews](#)):
 - Type of studies (e.g. experimental, observational?)
 - Type of participants (e.g. how is the condition defined?)
 - Type of intervention (e.g. what are experimental and control conditions?)
 - Type of outcome (e.g. are outcomes discrete or continuous?)
- Bias: 'Low', 'High', 'Some concerns' (See [Cochrane Handbook](#))
 - Sampling bias, measurement bias, missing data, etc.
 - None of this is news, but know that there are formal methods

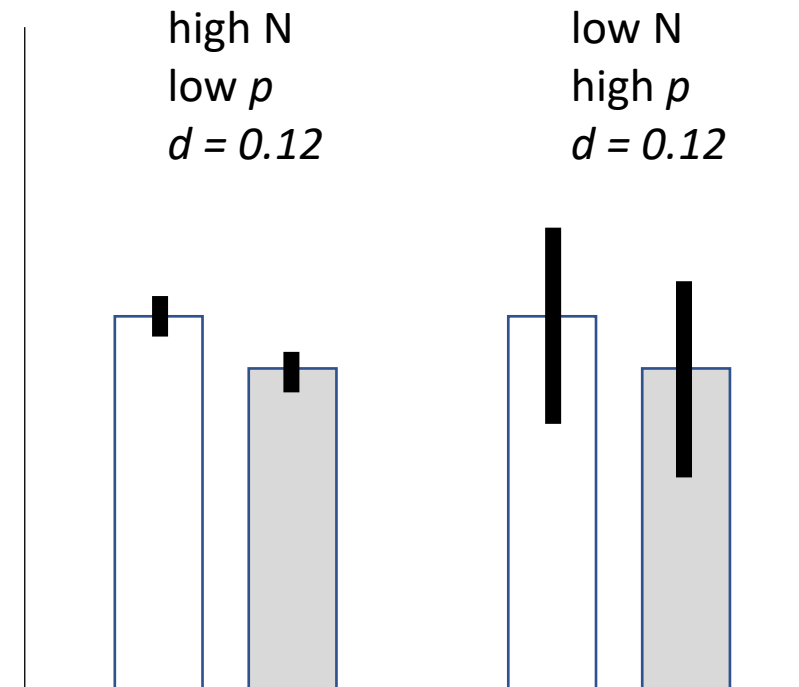
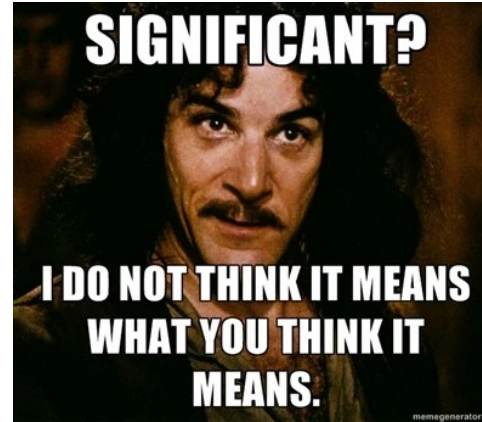
Effect sizes

- Correlation family, e.g. Pearson's r
- Difference family, e.g. Cohen's d
- Categorical family, e.g. odds ratios



Effect sizes

- Why not p -values?
- Statistical significance
 - p -value makes a statistical statement about whether a result of one study is due to sampling
 - Scales with N
- Clinical significance
 - Effect size captures magnitude of a difference
 - An effect may be “statistically significant” but meaningless in real life



Power

- How much N do you need, IF an effect exists?
- Need some preliminary data to compute (means and variance)
- “One limitation is the small sample size” translates “This study is under-powered”

Anticipated Means

Group 1 [?](#) ±

Group 2 [?](#)

▼

Enrollment ratio [?](#)

Type I/II Error Rate

Alpha [?](#)

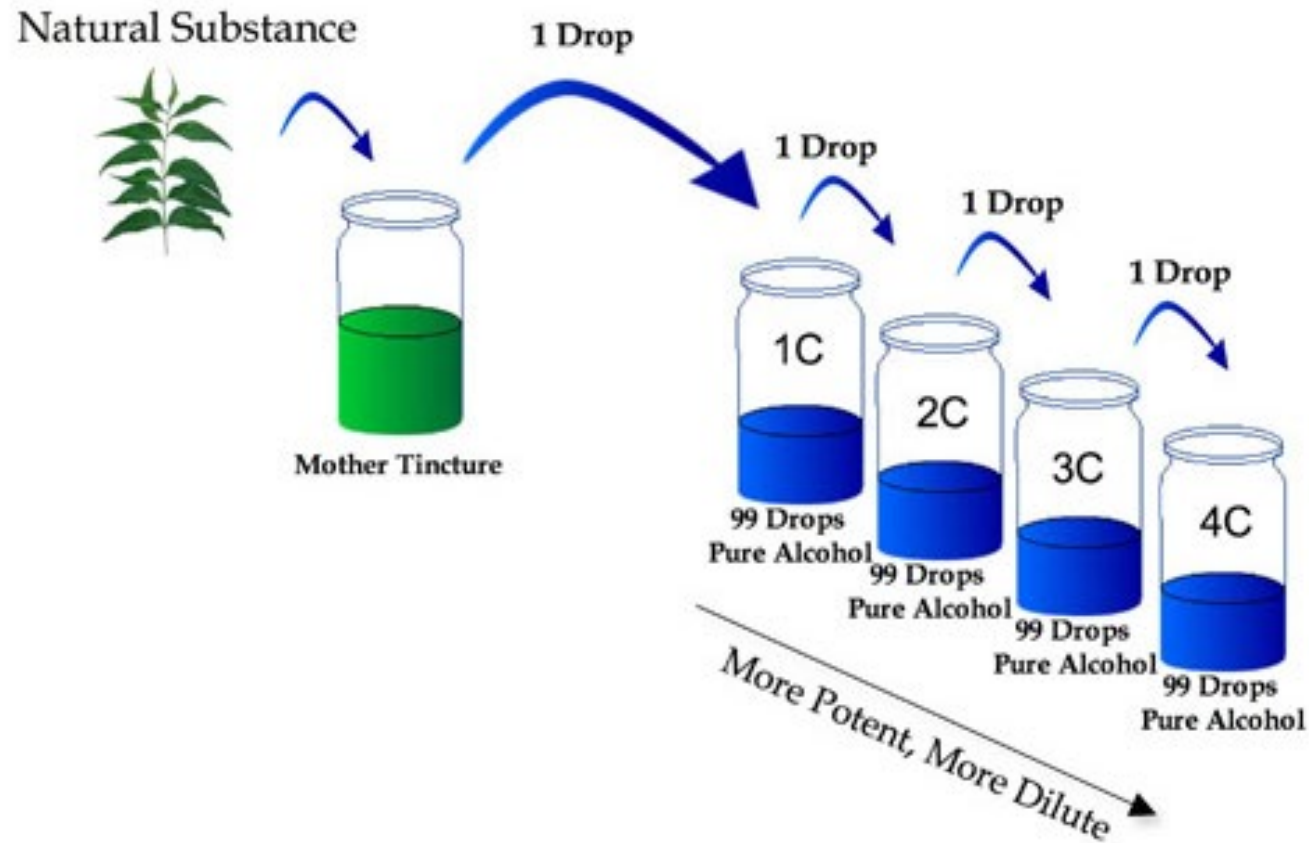
Power [?](#)

80%

Sample Size	
Group 1	4
Group 2	4
Total	8

Homeopathy

How Remedies are Made - Potentizing



Each vial is shaken vigorously after each dilution is made.

RESEARCH

Open Access

Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis

Robert T Mathie^{1*}, Suzanne M Lloyd², Lynn A Legg³, Jürgen Clausen⁴, Sian Moss⁵, Jonathan RT Davidson⁶ and Ian Ford²

Abstract

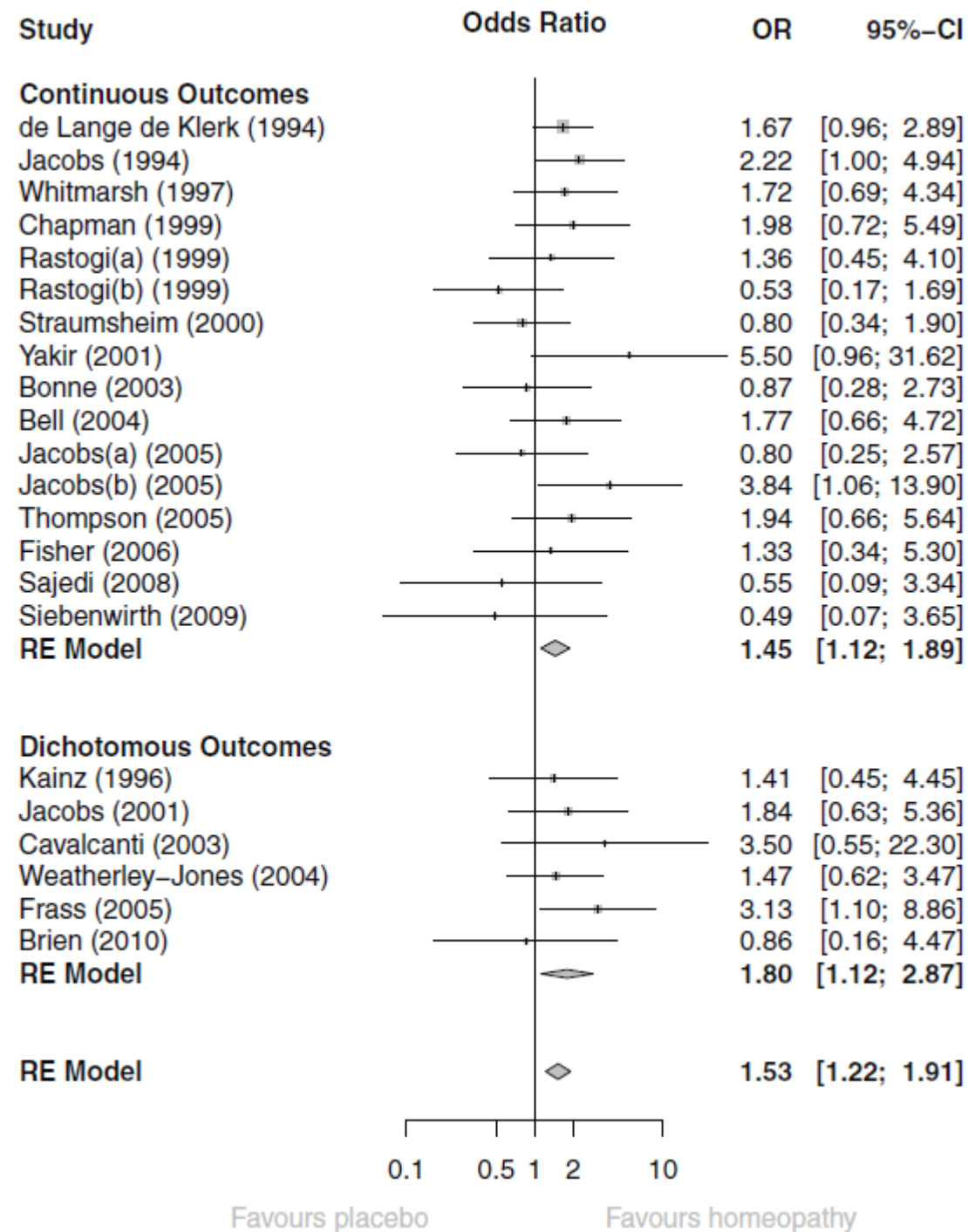
Background: A rigorous and focused systematic review and meta-analysis of randomised controlled trials (RCTs) of individualised homeopathic treatment has not previously been undertaken. We tested the hypothesis that the outcome of an individualised homeopathic treatment approach using homeopathic medicines is distinguishable from that of placebos.

Methods: The review's methods, including literature search strategy, data extraction, assessment of risk of bias and statistical analysis, were strictly protocol-based. Judgment in seven assessment domains enabled a trial's risk of bias to be designated as low, unclear or high. A trial was judged to comprise 'reliable evidence' if its risk of bias was low or was unclear in one specified domain. 'Effect size' was reported as odds ratio (OR), with arithmetic transformation for continuous data carried out as required; OR > 1 signified an effect favouring homeopathy.

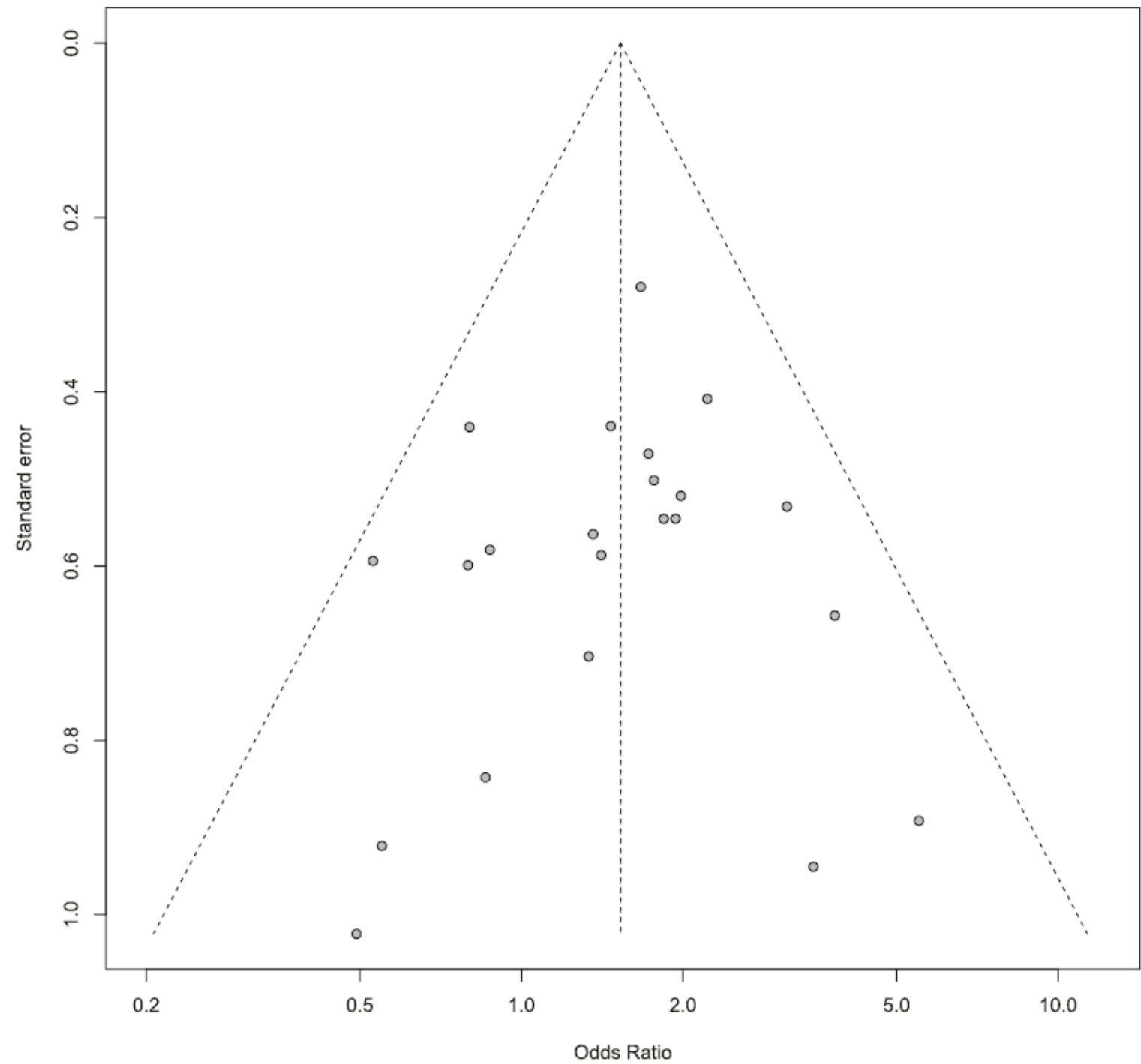
Table 3 Risk-of-bias assessments for trials: (a) included in meta-analysis and (b) not included in meta-analysis

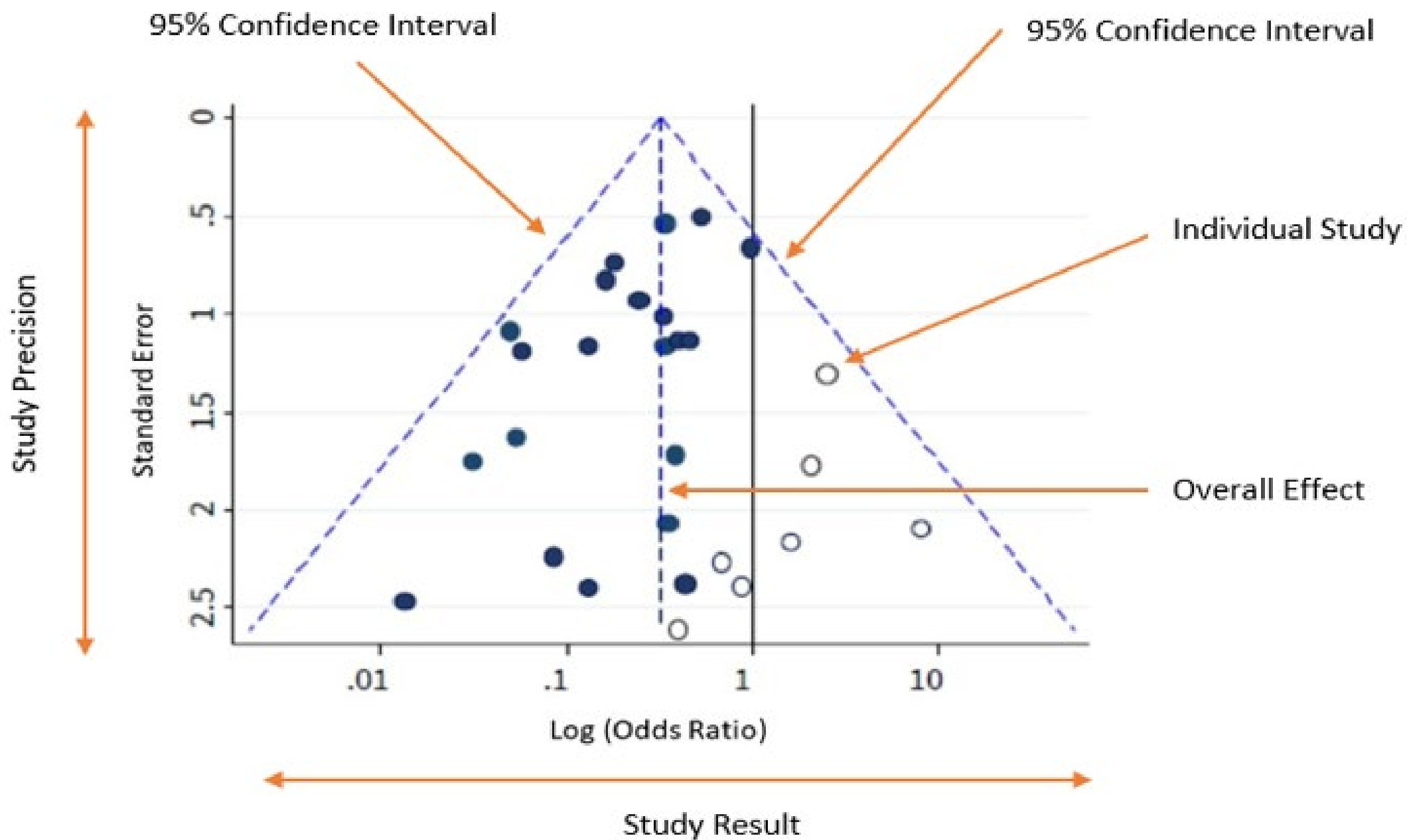
#	First author	Year	Risk-of-bias domain							Risk of bias	Risk-of-bias rating
			I	II	IIIa	IIIb	IV	V ^a	VI		
(a): Included in meta-analysis											
A11	de Lange de Klerk	1994	U	U	U	U	Y	Y	Y	Uncertain	B4
A19	Jacobs	1994	Y	Y	Y	Y	U	Y	Y	Uncertain ^b	B1
A25	Kainz	1996	U	U	U	U	U	Y	U	Uncertain	B6
A10	Chapman	1999	Y	U	Y	Y	Y	Y	Y	Uncertain	B1
A35	Straumsheim	2000	U	U	Y	Y	Y	Y	Y	Uncertain	B2
A20	Jacobs	2001	Y	Y	Y	Y	U	Y	Y	Uncertain ^b	B1
A41	Yakir	2001	U	U	Y	Y	U	Y	Y	Uncertain	B3
A06	Bonne	2003	U	U	Y	Y	Y	Y	U	Uncertain	B3
A05	Bell	2004	Y	Y	Y	Y	Y	Y	U	Uncertain ^b	B1
A14	Frass	2005	Y	U	Y	U	Y	Y	Y	Uncertain	B2
A23	Jacobs	2005a	Y	U	Y	Y	Y	Y	Y	Uncertain	B1
A36	Thompson	2005	Y	U	Y	Y	Y	Y	Y	Uncertain	B1
A40	Whitmarsh	1997	U	U	Y	U	Y	U	N	High	C1.4
A31	Rastogi (a)	1999	U	U	U	U	N	N	U	High	C2.5
A31	Rastogi (b)	1999	U	U	U	U	N	N	U	High	C2.5
A09	Cavalcanti	2003	U	U	Y	Y	N	Y	U	High	C1.3
A38	Weatherley-Jones	2004	Y	U	Y	Y	N	Y	Y	High	C1.1
A22	Jacobs	2005b	Y	Y	Y	Y	N	Y	Y	High	C1.0
A13	Fisher	2006	Y	U	Y	Y	N	Y	U	High	C1.2
A32	Sajedi	2008	U	U	U	U	N	Y	Y	High	C1.4
A33	Siebenwirth	2009	U	Y	Y	Y	N	Y	N	High	C2.1
A07	Brien	2011	Y	Y	Y	Y	N	Y	Y	High	C1.0

Forest plot



Funnel plot





Conclusions

- There was a small, statistically significant, treatment effect of individualised homeopathic treatment that was robust to sensitivity analysis based on 'reliable evidence'.
- Findings are consistent with sub-group data available in a previous 'global' systematic review of homeopathy RCTs.
- The overall quality of the evidence was low or unclear, preventing decisive conclusions.
- New RCT research of high quality on individualised homeopathy is required to enhance

the totality of reliable evidence and thus enable clearer interpretation and a more informed scientific debate.

How did this get published?

the conclusions are far too positive. the most important finding of the review is clearly that no sound evidence of efficacy was found. this has to be expressed more clearly in the 1st sentence of the conclusion.

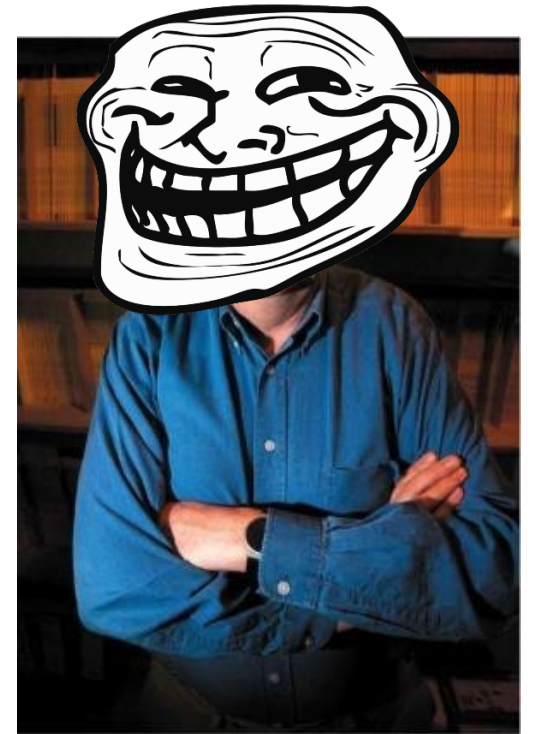
conflicts of interest: does employment by the HOMEOPATHIC RESEARCH INSTITUTE constitute a conflict?

Level of interest

Please indicate how interesting you found the manuscript:

An exceptional article that should be press released to journalists

[You can read the authors' responses here](#)



[Edzard Ernst, modern hero](#)

Evidence-based vs. Science-based thinking

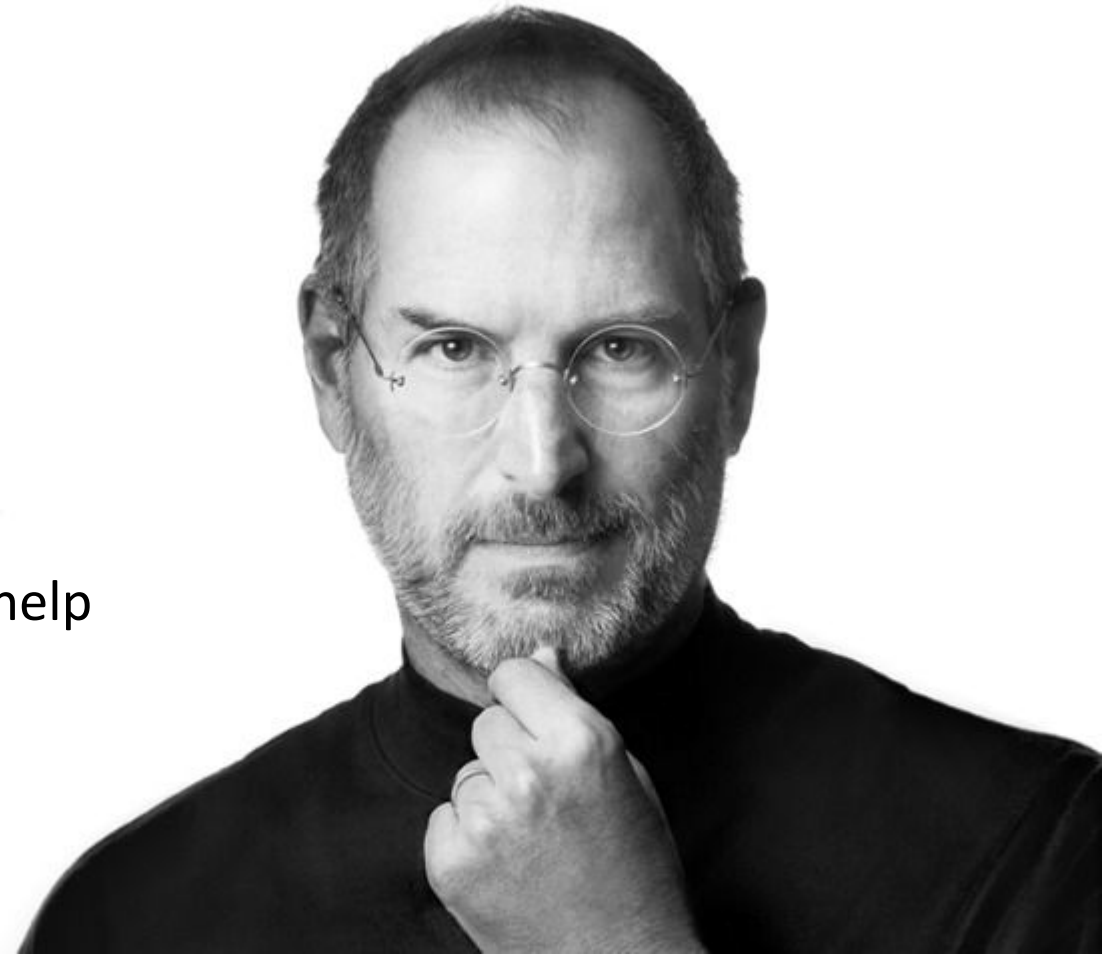
- Are all research questions valid?

Remember Bayes:

- **Evidence-based thinking** weighs likelihood of a hypothesis given data
- **Science-based thinking** adds prior plausibility of a hypothesis
- **Power:** What's the likelihood Homeopathy works?
- **Science-based:** What's the likelihood Homeopathy works, given we know it's bullshit?
- [Science-Based Medicine blog](#)
- Jacob's favorite podcast: [Skeptic's Guide to the Universe](#)

Critical thinking – the stakes are high

- Steve Jobs changed the world with tech
- Diagnosed with pancreatic cancer in 2003
- Sought “alternative treatment” for 9 months
 - Aggressive vegan diet, acupuncture, psychics
- Died from pancreatic tumor complications in 2011
- The world lost a great mind; pseudoscience didn't help
- [More reading](#)



Lab Wrap-up

4 things you need to **rock the world** as a data scientist:

- Data
- Code
- Critical thinking
- Communicating with others

Jacob's opinionated list of *super-powers*:

- Thinking slowly
 - Debugging
-
- Regular Expressions
 - Logical Indexing
 - Visualization



Thank you for being awesome students & humans

