London Health Sciences Centre

St JOSEPH'S HEALTH CARE LONDON

WHAT PROPORTION OF EVIDENCE IS VALID & RELEVANT?

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MEDICI
Medical Evidence
Decision Integrity
Clinical Impact

OBJECTIVES

What proportion of evidence published is valid and relevant to practice

Does p-hacking and publication bias occur?

What proportion is 'wasted'?

..in anesthesia, perioperative medicine, and critical care

"If you torture the data long enough, it will confess."

Ronald Coase

Professor Emeritus of Economics
University of Chicago Law School

"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

1) Shoot 2) Draw Target

Needle in the Haystack Evidence

- **$ Billions are spent annually on research and publication**
- **~15 years to get research into policy and practice**
- **<50% receive recommended care**
- **30% of patients receive care is not needed or that was potentially harmful**

Research Waste +

Evidence Reversals

Disaster for EBHC!

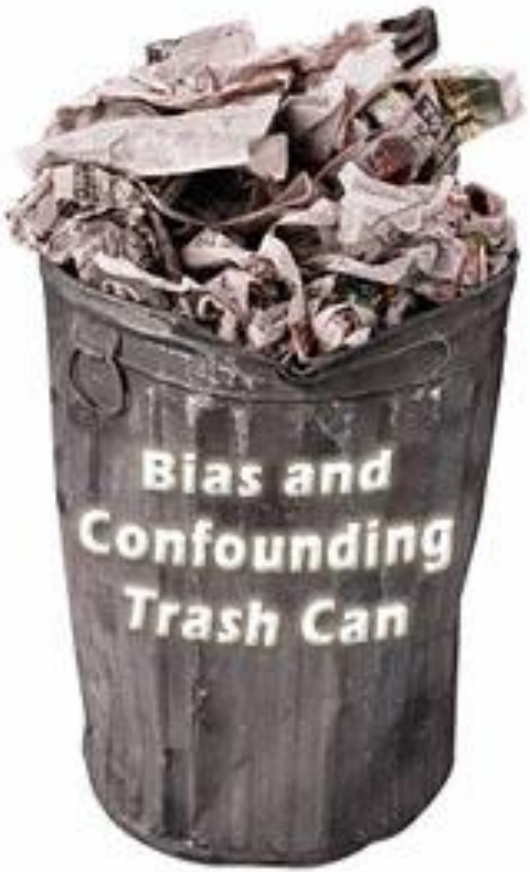
Not all ‘evidence’ is equal

Evidence…in Context

Key Questions	Published Evidence	Contextualized Evidence
Can it work	…in the ideal setting?	…here?
Does it work	…in real world settings?	...here?
Is it worth it	…for whom?	...here?

How much evidence in medicine is valid AND relevant? (Glasziou 2006)

- 120+ journals scanned
  - 60,000 articles
- Is it **valid**? (<5%)
  - Intervention: RCT
  - Prognosis: inception cohort
- Is it **relevant?**
  - < 0.5% selected
- **Valid + Clinically Important?**
  - **<<2% of the literature**



Glasziou P. Evid Based Med 2006;11:101.
Haynes B. Evid Based Med 2005;10:35.
Ebell. J Am Board Fam Pract 1999;12:225-235.
www.evidence-basedmedicine.com

Glasziou EBM 2007

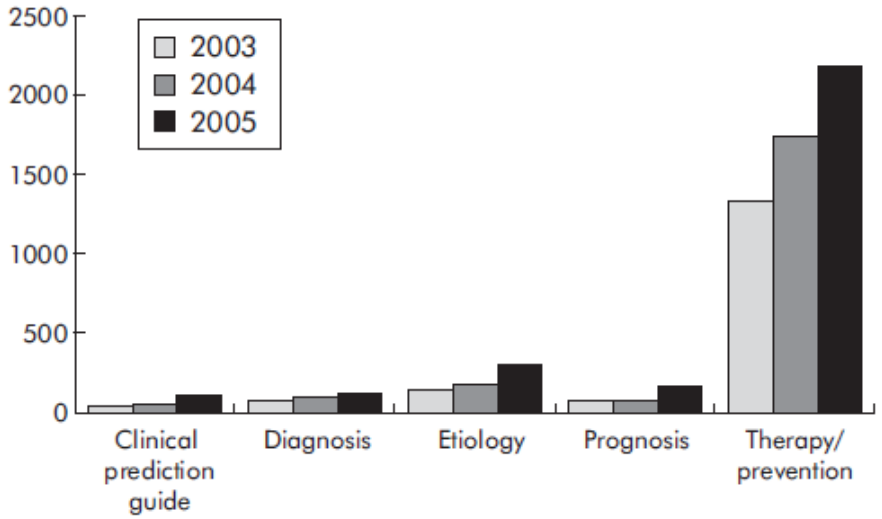
EBM notebook

The EBM journal selection process: how to find the 1 in 400 valid and highly relevant new research articles

I am sometimes asked why we have so many articles in the "Therapeutics" section of the Journal compared with the other sections. The answer largely lies in the material we have to work with. It is helpful to understand how we process articles from original journals to abstract. So here is a brief description:

Step 1. We scan around 135 primary journals to check whether original research articles pass our basic validity criteria (see "Purpose and procedure" for details of these criteria). However, only around 5% (1 in 20) of the 50 000 published articles pass these criteria.[1]

Step 2. Articles that pass the basic validity criteria are then sent out to several practising clinicians for rating (from a database of around 2900). This is now done through a website where the raters can read the paper and rate it separately for relevance and newsworthiness, and also write



Number of articles from 135 journals which passed the validity criteria and were sent out for clinician rating, shown by category and year

Methods

- **Journals:** Medline search of all journals related to Anaesthesia, Anesthesia, Pain, Analgesia, Perioperative Medicine, Sedation, Critical Care
- **For Studies of <u>Interventions</u>, criteria for Valid + Relevant:**
  - Randomized trial
  - Reporting on clinically relevant outcomes

Key Results (1)

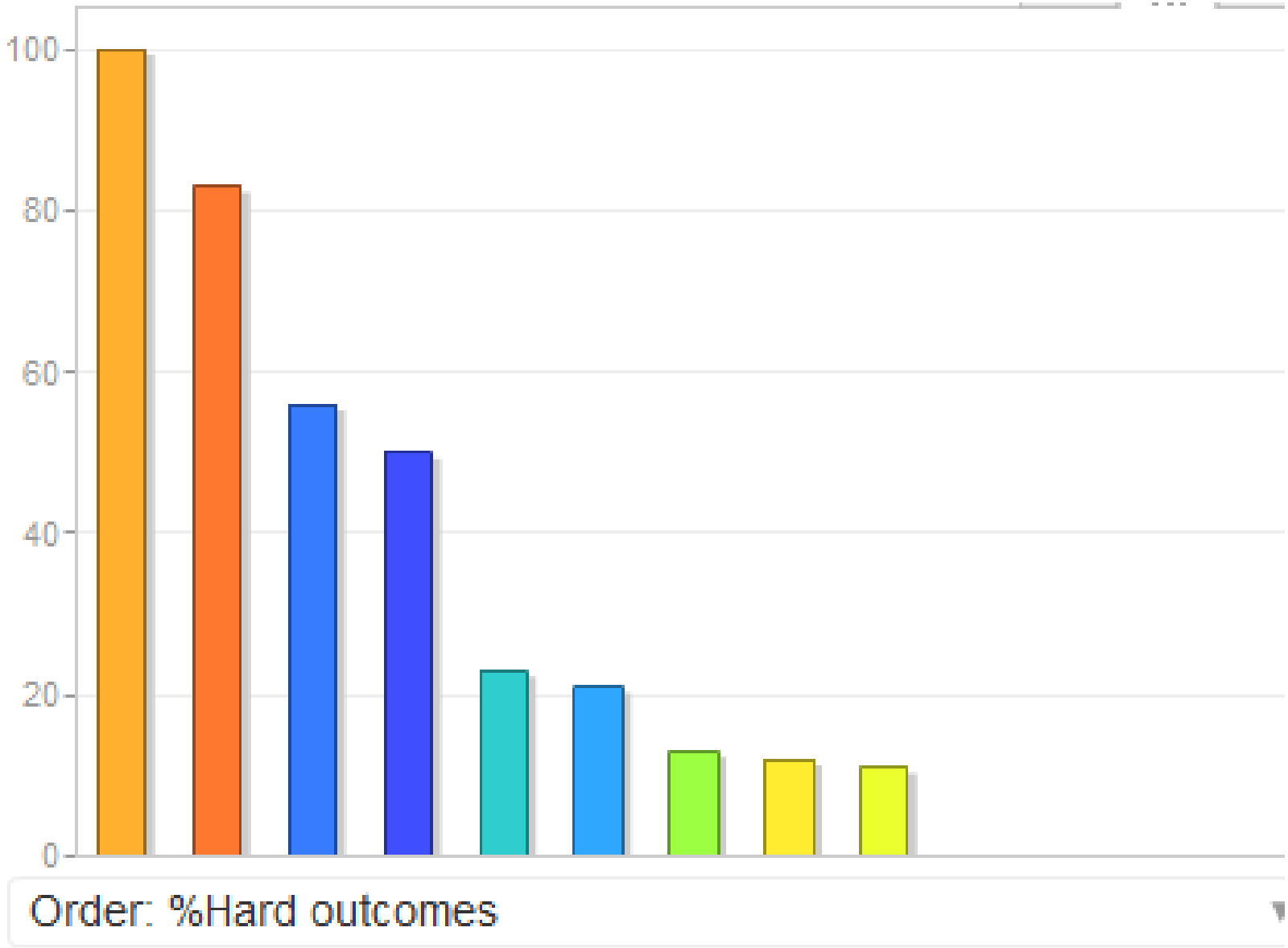
- **Number of Articles:** 39,019
- **Number of clinical trials:** 16,178
- **Number of RCTs:** **11,868**

- **Median No. of Patients/RCT:** **40 [20 to 120]**

Key Results (2)

- **Clinically relevant outcomes:** 39%
- **Valid and Relevant Studies:** 28%
- **“Positive” Conclusion for 1* Outcome:** 74%

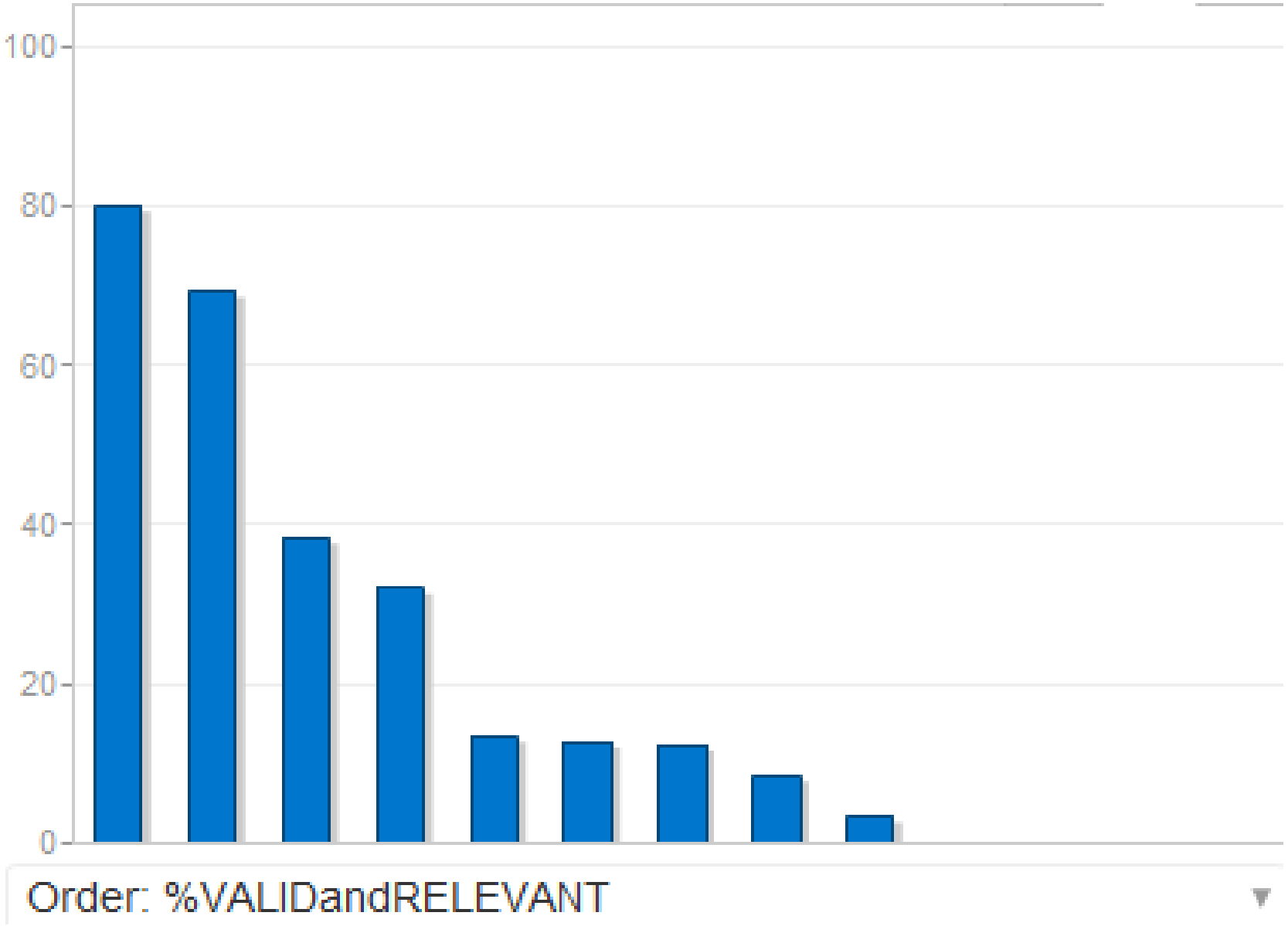
Clinically Relevant Outcomes Reported: Mean 39% (0 to 100%)



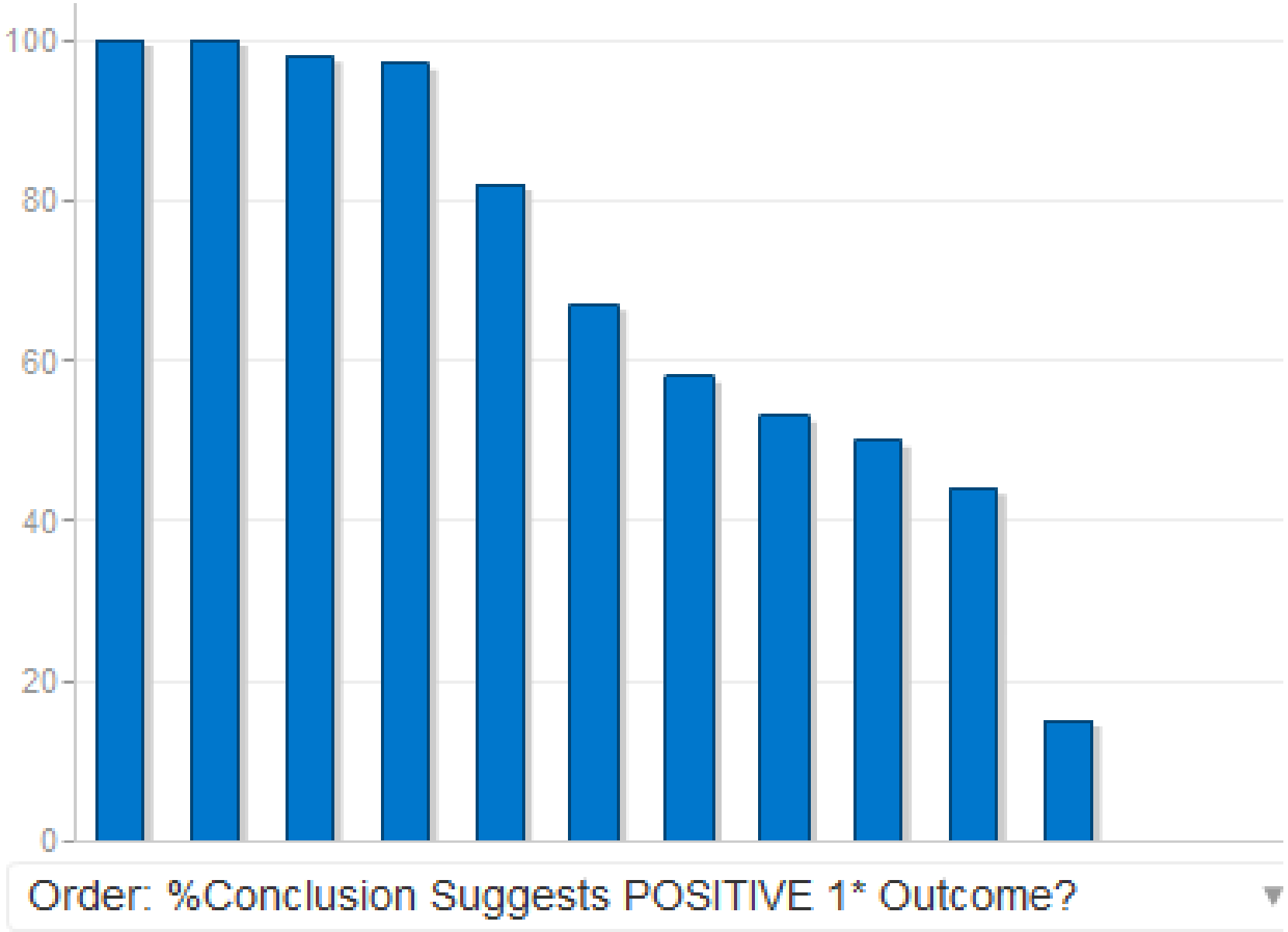
Common Surrogate Outcomes

- MAP, CVP, HR
- TnI, TnT, CRP
- Tidal volume, minute ventilation
- Oxygenation
- Hgb or RBC units
- Opioid Use, Anesthetic Doses Used
- Perfusion, Blood Flow
- Quality of view
- Speed of intubation
- “faster” everything….

Valid and Relevant Study: Mean 28% (0 to 80%)



“Positive” Primary Outcome: Mean 74% (0 to 100%)



Then | Now


High
Impact
Factor
Low
Impact
Factor

https://docs.google.com/spreadsheets/d/1Ng9YVL8kK72SszZj3qf4Oozg-oyjyxTl1m0diYa3nUo/pubchart?oid=173864532&format=interactive

Key Lessons Learned

Surrogate Outcome Idolatry

Most outcomes were surrogates, and this has not improved over time

False Discovery Rate & P-Hacking

P-value is a blunt arbiter!

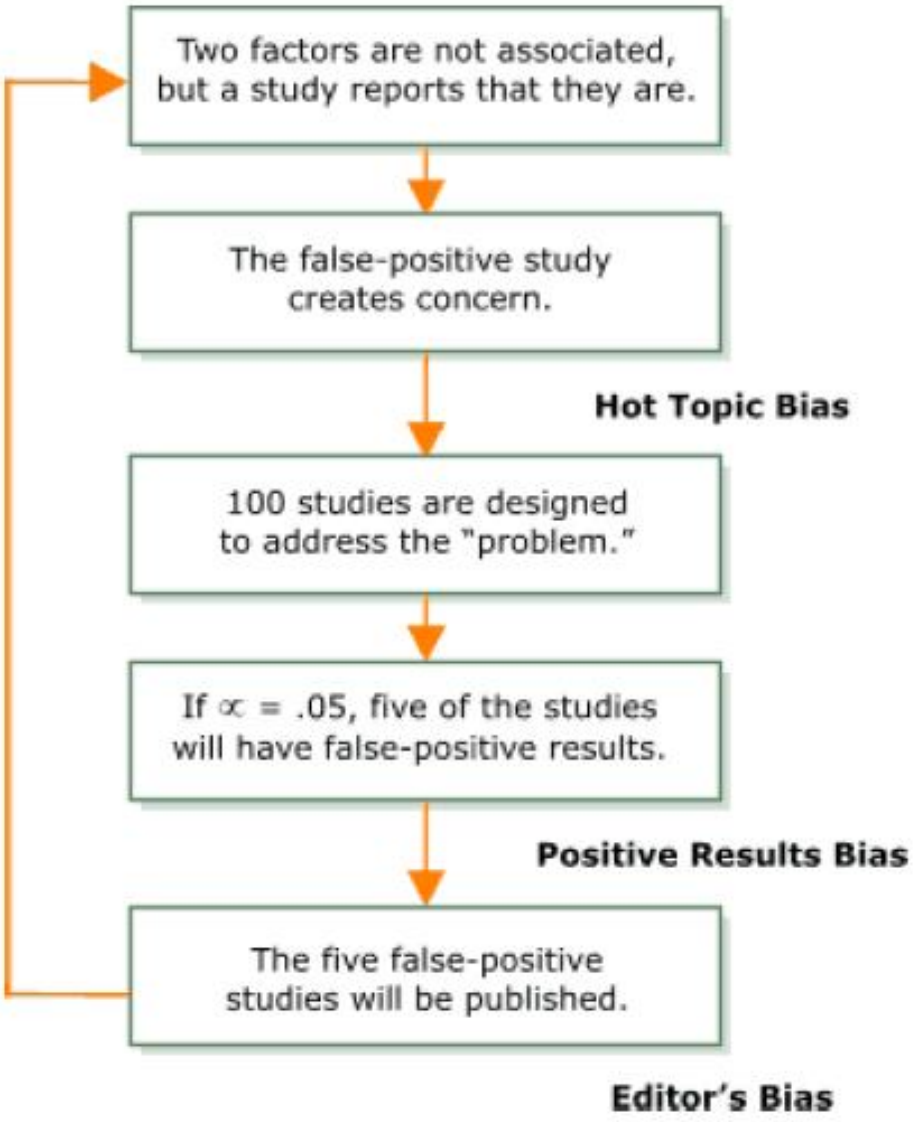
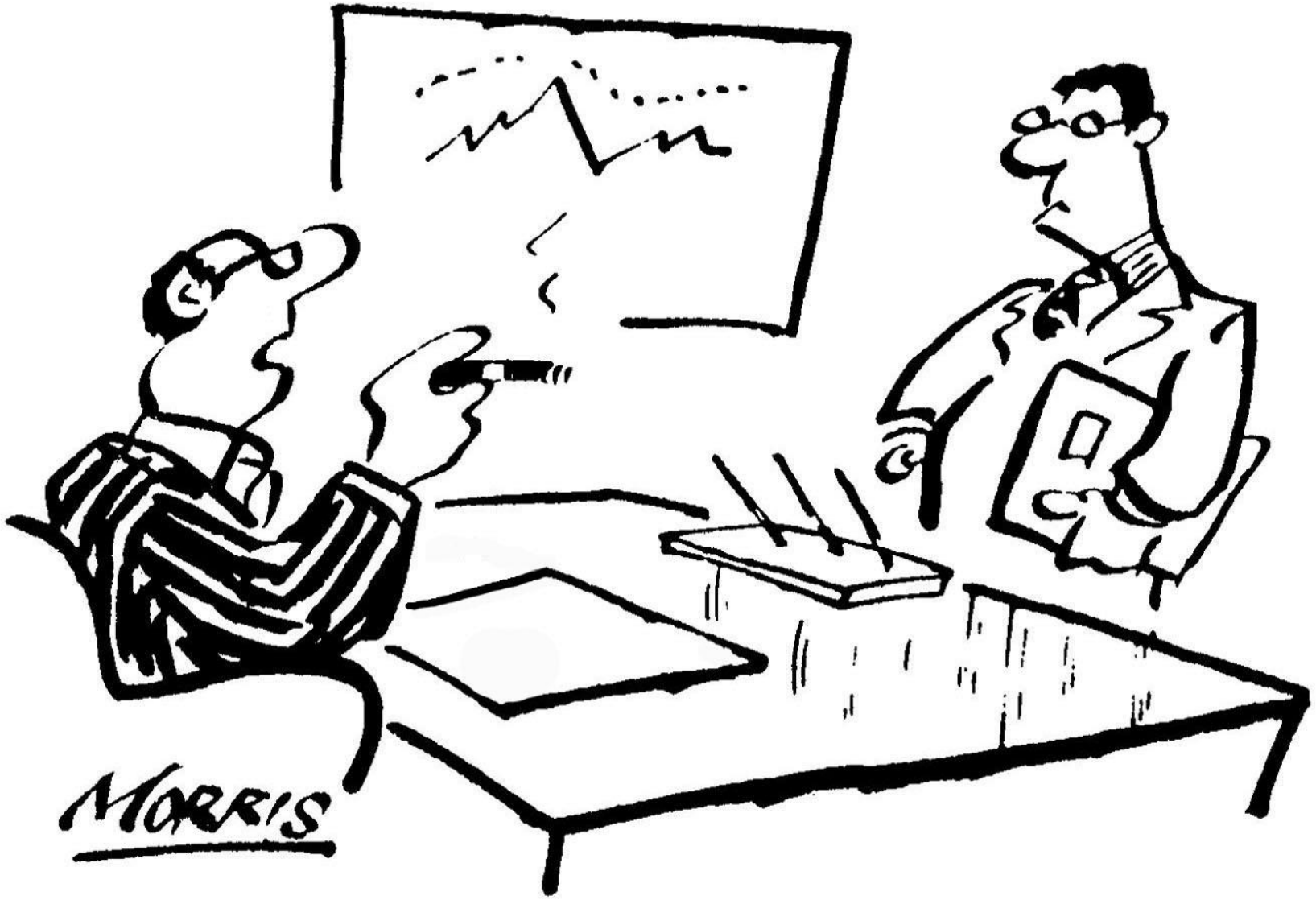


Figure. The false-positive research cycle.

Choi, et al. Public Health Res Pract Policy 2005


SHOOT
FIRST
AND THEN
DRAW
THE TARGET



"That's what I want to say. See if you can find some statistics to prove it."

Publication Bias

Accessible reporting

Proportion of funded/completed research that is reported

50%

Waste in Research

Significant "Leakage" from Bench to Bedside

Conclusions

- **In ~12,000 published RCTs, less than 30% are valid and relevant**

AND

- **The verity of these is in question due to p-hacking and publication bias**
  - **75% reported a positive primary outcome**
  - **< 50% published**

- **Too much (low-value) research and publication**
- **Needle in the haystack evidence**
- **Evidence synthesis contributes to over-inflated estimates**