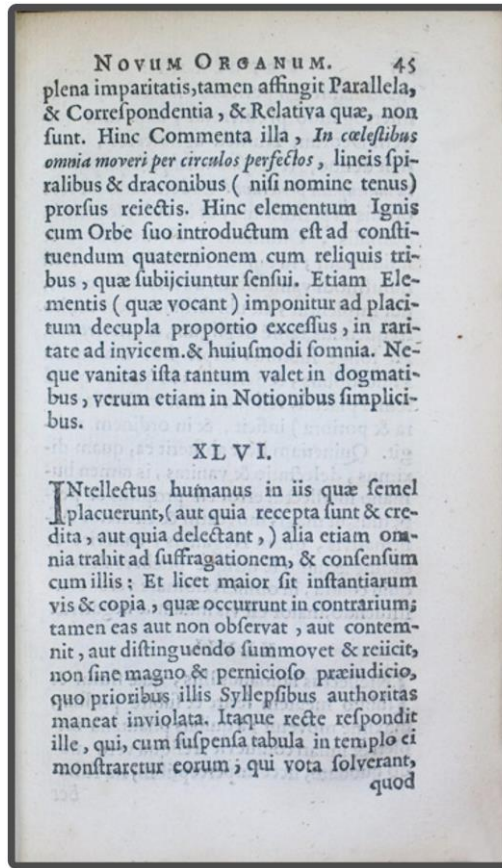
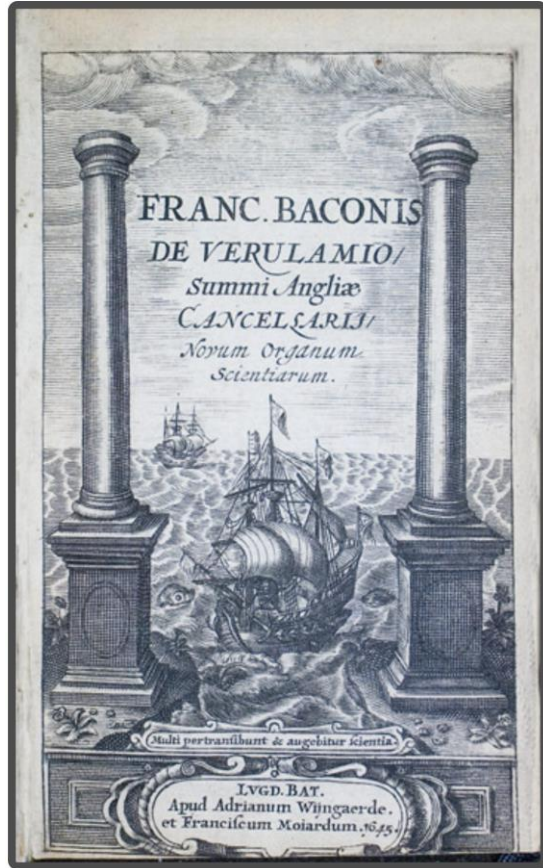


Publication and reporting bias: a long history towards open science

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Selective reporting of findings from scientific research is a long-known phenomenon



- In the 17th century, **Francis Bacon** noted that *“The human intellect ...is more moved by affirmatives than by negatives.”*
- **Robert Boyle**, the chemist, lamented the common tendency among scientists *not to publish their results until they had a “system” worked out, with the result that “many excellent notions or experiments are, by sober and modest men, suppressed.”*

<https://www.jameslindlibrary.org/research-topics/biases/reporting-bias/>

Selective reporting of findings from scientific research is a long-known phenomenon

“A negative result may be dull but often it is no less important than the positive; and in view of that importance it must, surely, be established by adequate publication of the evidence.”

- Austin Bradford Hill 1956

“A positive result is exciting and interesting and gets published quickly. A negative result, or one which is inconsistent with current opinion, is either unexciting or attributed to some error and is not published. So that at first in the case of a new therapy there is a clustering toward positive results with fewer negative results being published. Then some brave or naïve or nonconformist soul, like the little child who said that the emperor had no clothes, comes up with a negative result which he dares to publish. That starts the pendulum swinging in the other direction, and now negative results become popular and important.”

- Seymour Kety 1959

Types of reporting biases

Reporting bias arises when the dissemination of research is influenced by the nature and direction of findings.

- Not reporting studies at all (also known as non-publication bias)
- Reporting studies in part
- Reporting in a manner that is difficult for others to access
- Reporting without transparency (duplicate publication, spin)



“Sweep it under the carpet at CEPT University,” by Vaishal Dalal (Photo Credit: Wikipedia Commons)

Not reporting studies (non-publication bias)

RESEARCH ARTICLE

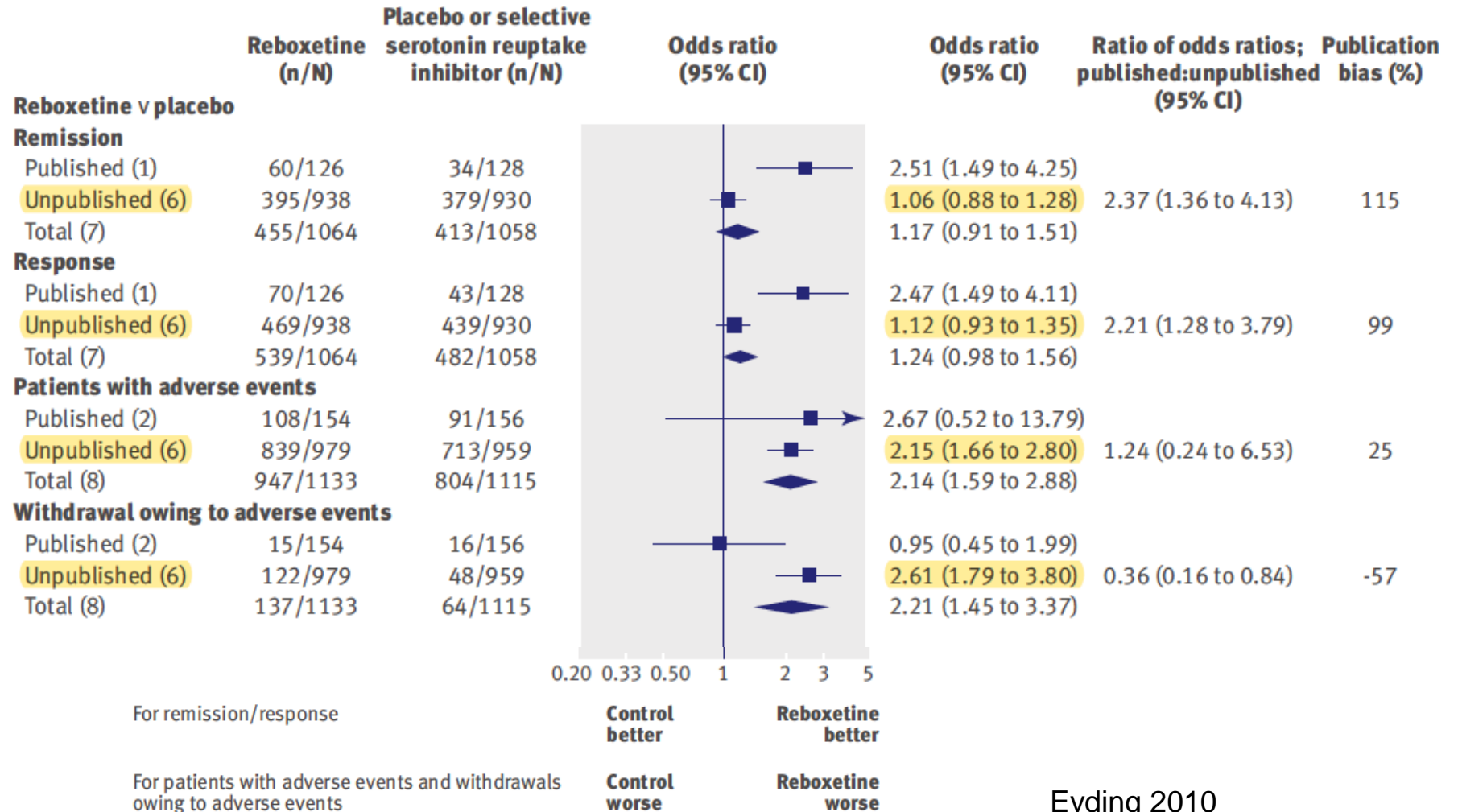
Extent of Non-Publication in Cohorts of Studies Approved by Research Ethics Committees or Included in Trial Registries

Christine Schmucker¹, Lisa K. Schell¹, Susan Portalupi¹, Patrick Oeller¹, Laura Cabrera¹, Dirk Bassler³, Guido Schwarzer², Roberta W. Scherer⁵, Gerd Antes¹, Erik von Elm⁴, Joerg J. Meerpohl^{1*} on behalf of the OPEN consortium¹

- Analysis of inception cohorts of studies approved by research ethics committees or included in trial registries
- Between **45%-60%** of randomized trials were published
- Nearly **3 times** more likely to be published if results were statistically significant

Not reporting trials - consequences

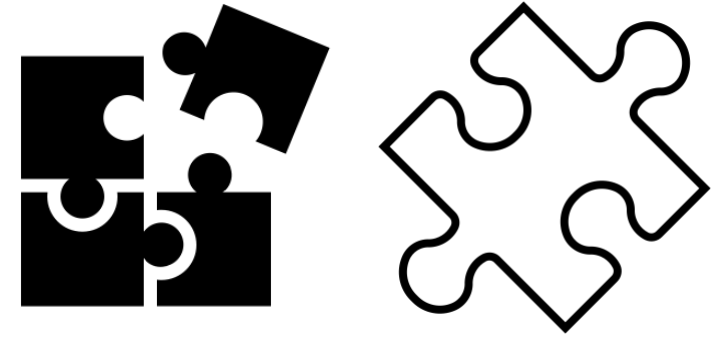
- **Unscientific:** altered evidence on the benefit and harms of reboxetine
- **Unethical:** breached participant trust
- **Uninformative:** constituted research waste



Reporting trials in part

Outcome reporting bias manifests in different forms when reporting of the outcomes is influenced by the nature and direction of findings:

- Not reporting pre-specified outcomes
- Reporting primary outcome as secondary outcome (and vice versa)
- Introducing new outcomes
- Reporting outcomes such that they are differentially accessible

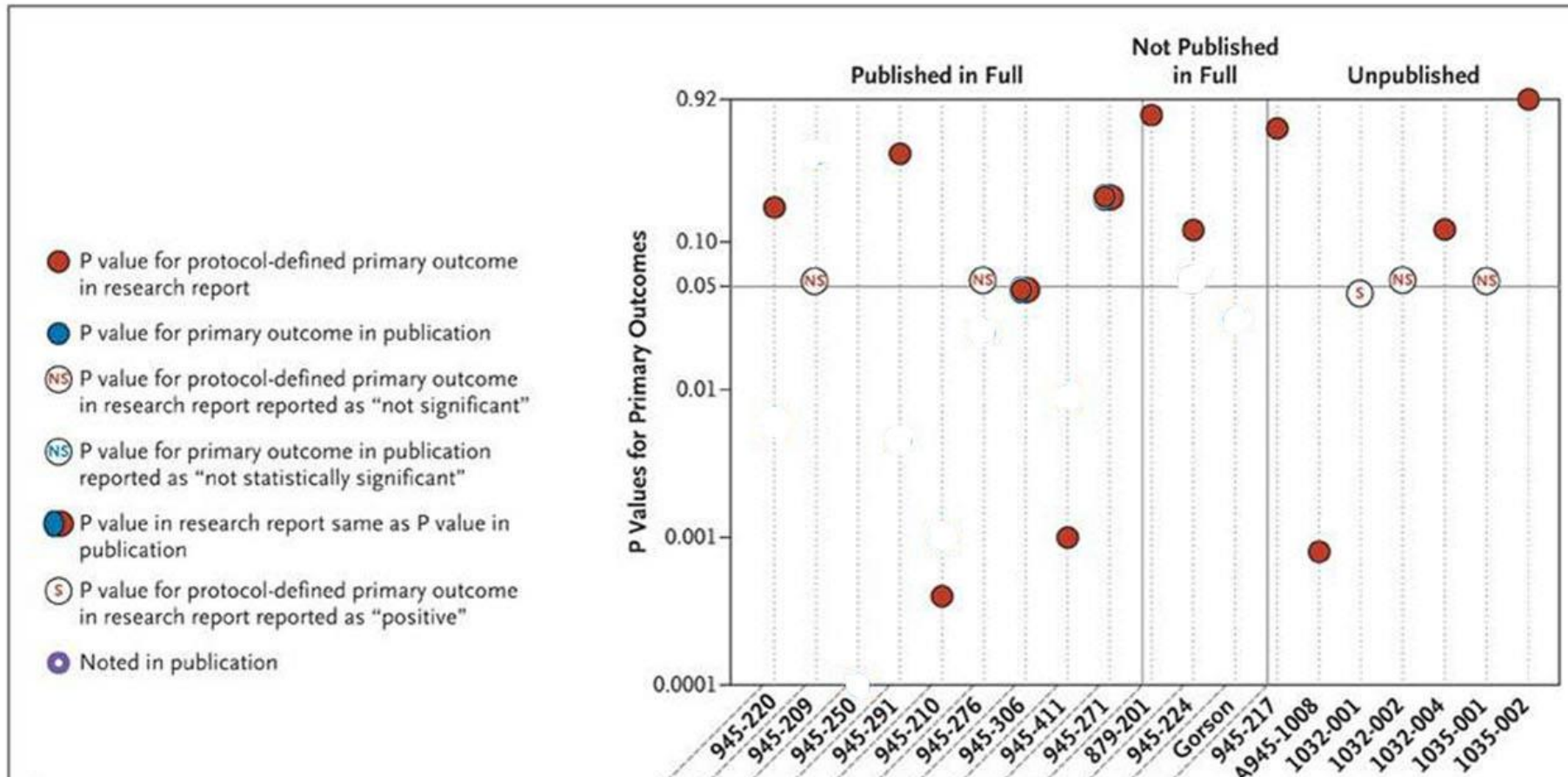


No cherry picking

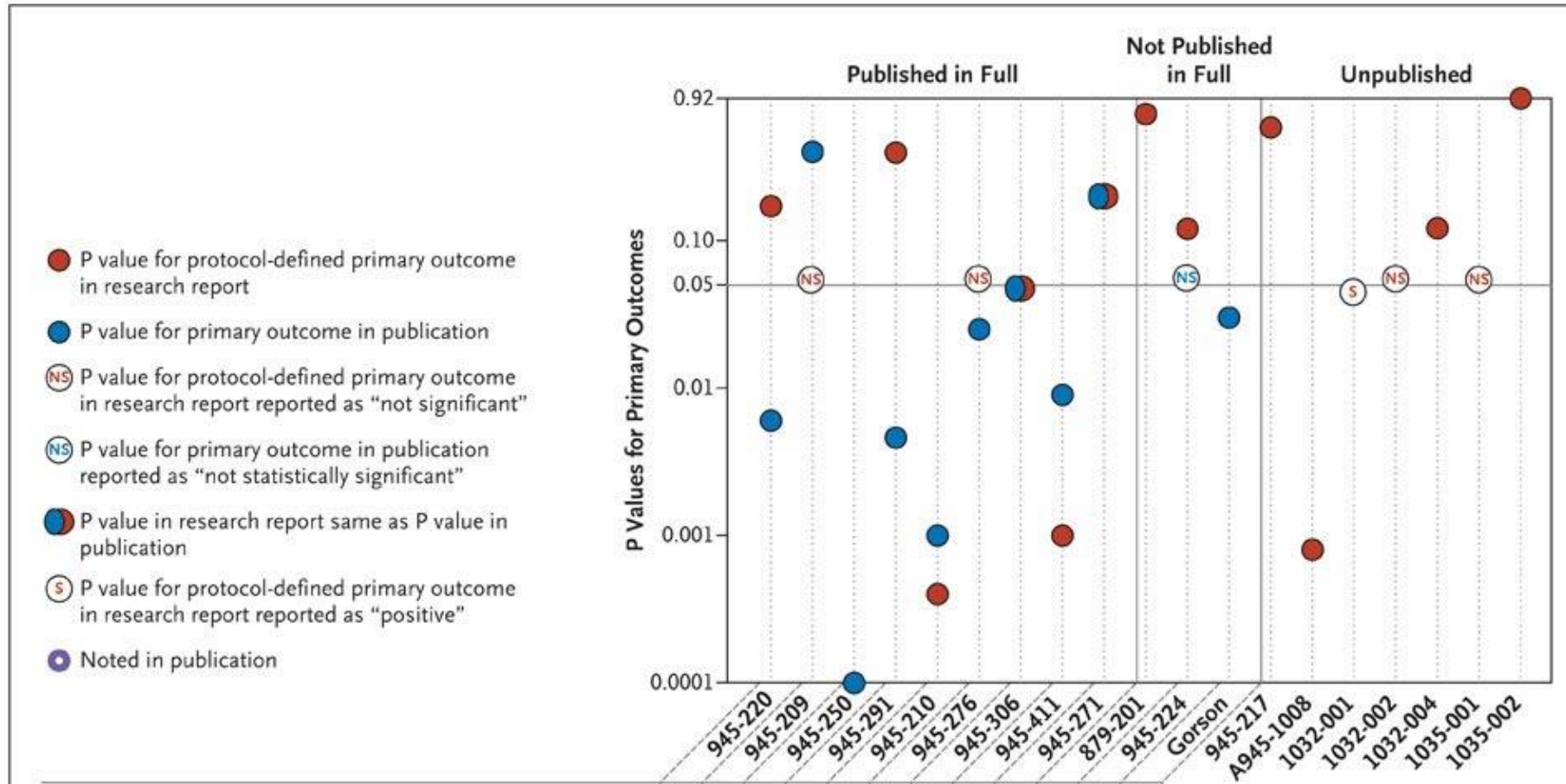
Outcome reporting bias in industry-sponsored trials of gabapentin for off-label use

- Comparison of protocol to publication for statement of “primary” outcome
- 21 primary outcomes ‘pre-specified’ in the protocol
 - 11 reported with no changes
 - 10 not reported or reported as secondary outcomes
 - 17 new primary outcomes added (some were secondary outcomes in protocol)
- 28 primary outcomes in ‘main’ publication

Published evidence did not match that in clinical study reports



P values for protocol-defined primary outcome in clinical study report and in main publication



Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias — An Updated Review

Kerry Dwan*, Carrol Gamble, Paula R. Williamson, Jamie J. Kirkham, for the Reporting Bias Group[†]

Department of Biostatistics, University of Liverpool, Liverpool, England

- Statistically significant outcomes were more likely to be reported in full
 - Efficacy outcomes: **2.2-2.7 times** greater odds
 - Harm outcomes: **4.7 times** greater odds
- **40–62%** of studies had at least one primary outcome changed, newly introduced, or omitted, when trial publications were compared with protocols

Reporting in a manner that is difficult for others to access



Cochrane Database of Systematic Reviews

Full publication of results initially presented in abstracts (Review)

Scherer RW, Meerpohl JJ, Pfeifer N, Schmucker C, Schwarzer G, von Elm E

- A systematic review of 425 studies (307,028 abstracts) discovered that only **37.3%** were subsequently published in full (**59.8%** for randomized trials)
- “Significant” results were **1.31** times more likely to published in full
- “Positive” results, defined as a result favoring the experimental treatment, were **1.17** times more likely to be published in full

Who contributes to biased reporting of clinical trials?

- Researchers failed to submit trial results for publication was the primary reason for unpublished clinical trials (“not interested in the results” and “lack of time”)
- Researchers’ perception that positive results are favored by editors (outcome reporting bias), and unawareness of the seriousness of under-reporting



Researchers



Peer reviewers

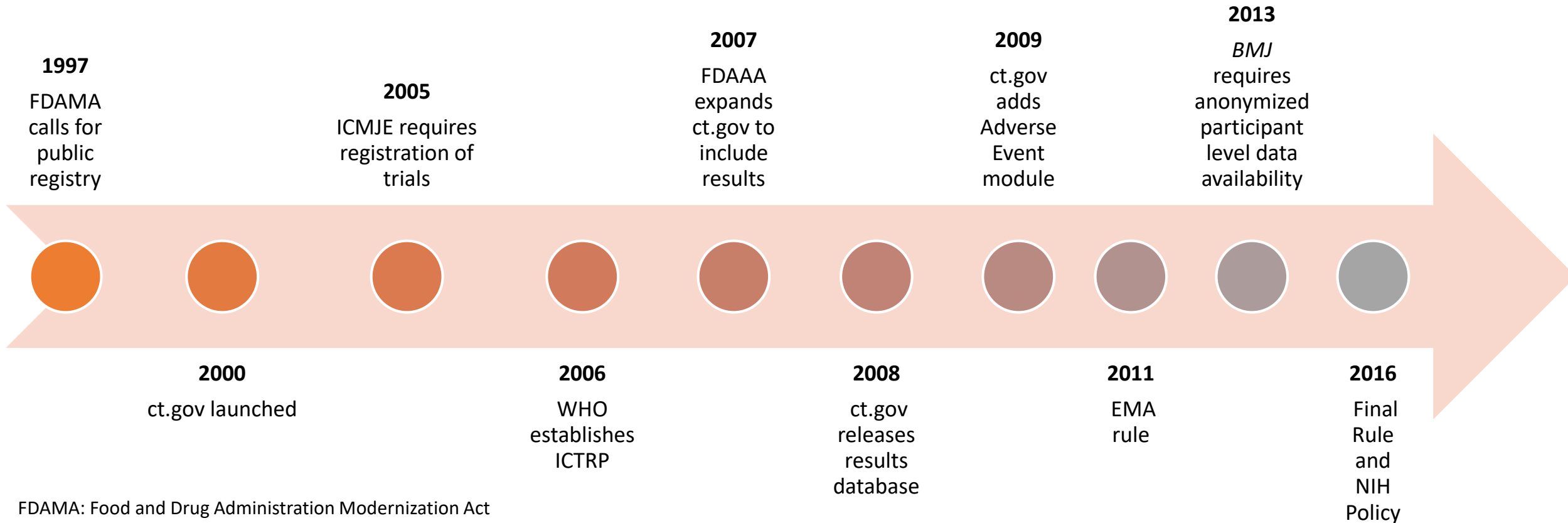


Editors

Addressing reporting biases

- Trial registration and results database
 - Data sharing
 - Access to study documents
 - Reporting guidelines
 - Core outcome sets
-

A timeline of trial registration seminal events

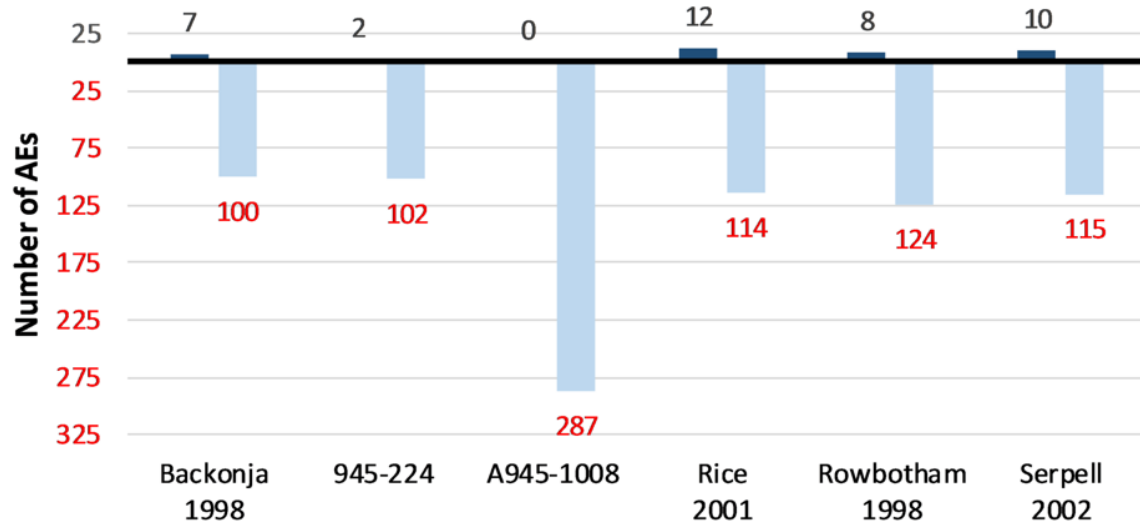


FDAMA: Food and Drug Administration Modernization Act
 ct.gov: ClinicalTrials.gov
 ICMJE: International Committee of Medical Journal Editors
 WHO: World Health Organization
 ICTRP: International Clinical Trials Registry Platform
 FDAAA: FDA Amendments Act
 EMA: European Medicines Agency
 BMJ: British Medical Journal
 NIH: National Institutes of Health

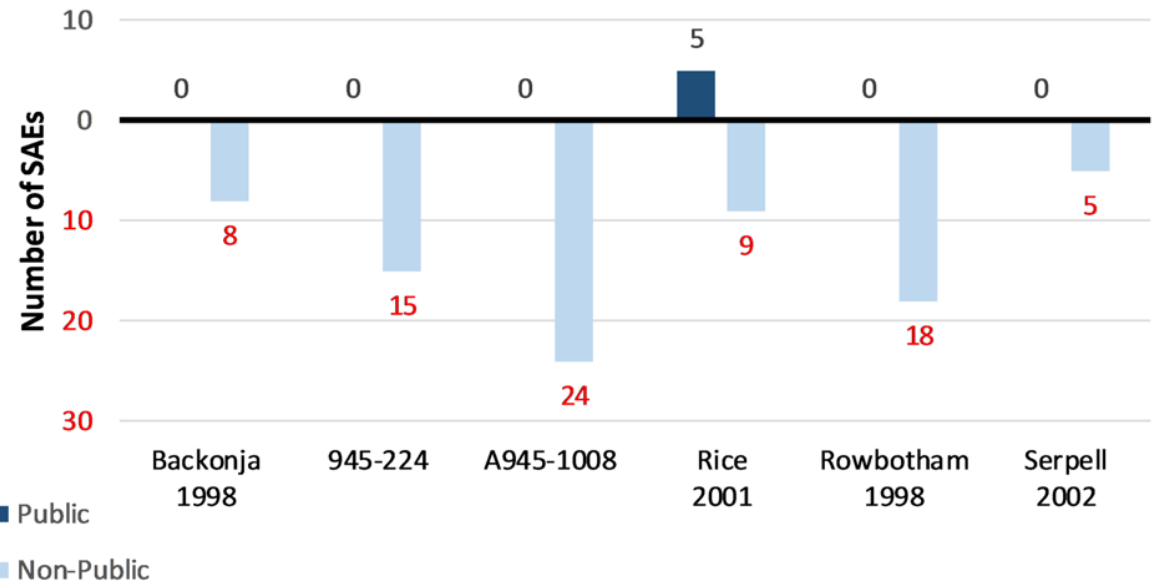
Access to study documents

Public access to **protocols** (including statistical analysis plan) and **clinical study reports** is essential for preserving the societal value of clinical trials.

Number of different types of **adverse events** (AEs)



Number of different types of **serious adverse events** (SAEs)



Why share your research data?

The move towards clinical trial data sharing is part of a wider movement towards open science:

- Increase scientific value
- Moral obligations
- Funders' mandate
- Journals' requirement



Conclusions

- Reporting of biomedical research is biased when it is influenced by the nature and direction of their findings.
- Reporting biases can take many forms.
- Reporting biases typically result in spurious exaggeration of beneficial effects and suppression of harmful effects of interventions.
- Clinical trial registration, access to protocols and statistical analysis plans, guidelines for transparent and complete reporting, adoption of core outcome sets, and data sharing are critical to prevent reporting biases.

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