

Publication and reporting bias: a long history towards open science

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Open Science European Conference Paris, France February 4, 2022















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



NOVUM ORGANUM. plena imparitatis,tamen affingit Parallela, & Correspondentia, & Relativa quæ, non funt. Hinc Commenta illa, In caleflibus omnia moveri per circulos perfectos, lincis fpiralibus & draconibus (nifi nomine tenus) prorsus rejectis. Hinc elementum Ignis cum Orbe suo introductum est ad constituendum quaternionem cum reliquis tribus, quæ fubijciuntur fenfui. Etiam Elementis (quæ vocant) imponitur ad placitum decupla proportio exceffus, in raritate ad invicem.& huiufmodi fomnia. Neque vanitas ista tantum valet in dogmatibus, yerum etiam in Notionibus fimplici-XLVI. Ntellectus humanus in iis quæ semel

placuerunt, (aur quia recepta funt & credita, aut quia delectant,) alia etiam omnia trahit ad fuffragationem, & confenfum cum illis : Et licet maior fit inftantiarum vis & copia, quæ occurrunt in contrarium; tamen cas aut non obfervat, aut contemnit, aut diftinguendo fummovet & reiicit, non fine magno & perniciofo præiudicio, quo prioribus illis Syllepfibus authoritas maneat inviolata. Itaque recte refpondit ille, qui, cum fufpenfa tabula in templo ci monftraretur corum ; qui vota folverant, quod

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

- 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."



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

Placebo or selective

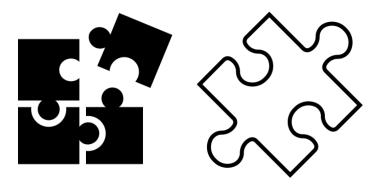
- Unscientific: altered evidence on the benefit and harms of reboxetine
- Unethical: breached participant trust
- Uninformative: constituted research waste

		Placebo or selective	2				
	Reboxetine (n/N)	serotonin reuptake inhibitor (n/N)	Odds ratio (95% CI)		Odds ratio (95% Cl)	Ratio of odds ratios; published:unpublished	
Reboxetine v placebo						(95% CI)	
Remission							
Published (1)	60/126	34/128			2.51 (1.49 to 4.25)		
Unpublished (6)	395/938	379/930	-		1.06 (0.88 to 1.28)	2.37 (1.36 to 4.13)	115
Total (7)	455/1064	413/1058	-		1.17 (0.91 to 1.51)		
Response							
Published (1)	70/126	43/128			2.47 (1.49 to 4.11)		
Unpublished (6)	469/938	439/930			1.12 (0.93 to 1.35)	2.21 (1.28 to 3.79)	99
Total (7)	539/1064	482/1058	•		1.24 (0.98 to 1.56)		
Patients with adverse	events						
Published (2)	108/154	91/156			2.67 (0.52 to 13.79))	
Unpublished (6)	839/979	713/959		_	2.15 (1.66 to 2.80)	1.24 (0.24 to 6.53)	25
Total (8)	947/1133	804/1115			2.14 (1.59 to 2.88)		
Withdrawal owing to a	adverse event	ts					
Published (2)	15/154	16/156	_		0.95 (0.45 to 1.99)		
Unpublished (6)	122/979	48/959	_		2.61 (1.79 to 3.80)	0.36 (0.16 to 0.84)	-57
Total (8)	137/1133	64/1115			2.21 (1.45 to 3.37)		
		0.20	0.33 0.50 1 2	3 5			
For remissio	n/response		Control Re better	boxetine better			
For patients owing to adv		vents and withdrawals	Control Re worse	boxetine worse	Ey	ding 2010	_

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

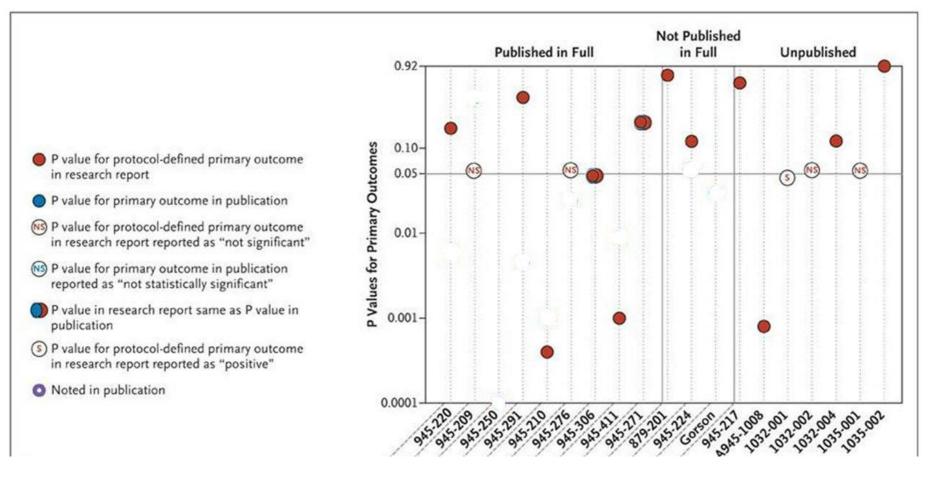


Outcome reporting bias in industry-sponsored trials of gabapentin for off-label use

- 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

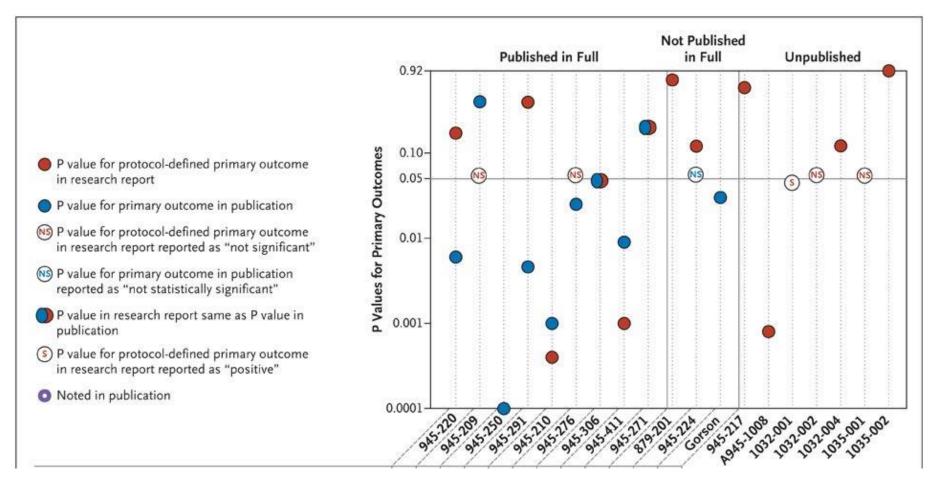


Published evidence did not match that in clinical study reports





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

1997			2007 FDAAA		2009 ct.gov		2013 <i>BMJ</i> requires		
FDAMA	2005		expands		adds		anonymized		
calls for	ICMJE requires		ct.gov to include		Adverse Event		participant level data		
public registry	registration of trials		results		module		availability		
	2000	2006		2008		2011		2016	
	ct.gov launched	WHO		ct.gov		EMA		Final	
		establishes ICTRP		releases results		rule		Rule and	
		ICTRP		database				NIH	
	nd Drug Administration Modernization Act							Policy	
WHO: World He	rials.gov ional Committee of Medical Journal Editors ealth Organization ional Clinical Trials Registry Platform								

FDAAA: FDA Amendments Act

EMA: European Medicines Agency

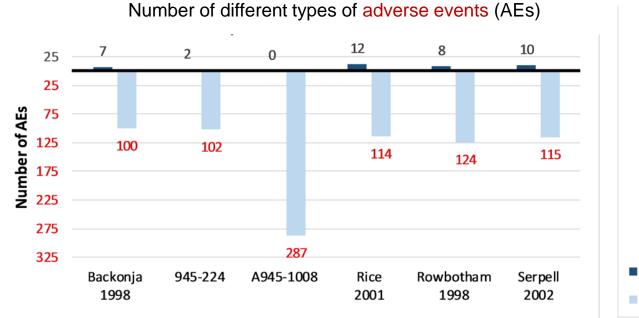
BMJ: British Medical Journal

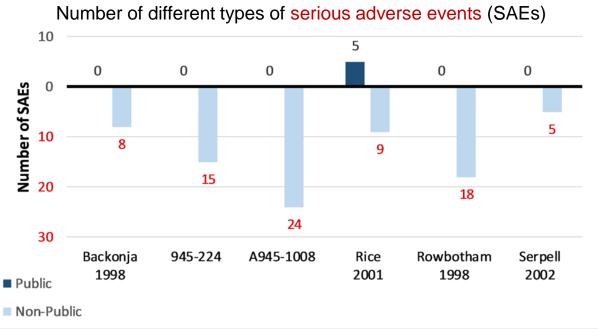
NIH: National Institutes of Health



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.







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





Sharing Clinical Trial Data

OF THE NATIONAL ACADEMIES

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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