Ninth International Congress on Peer Review and Scientific Publication

Drummond Rennie Inaugural Lecture

Bias, Spin, and Problems With Transparency of Research

Isabelle Boutron

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Cochrane France

Université Paris Cité

Instituts thématiques Inserm Institut national de la santé et de la recherche médicale

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

- The whole of medicine depends on the transparent reporting of clinical trials

(JAMA 2001)

Trial Registration

A Great Idea Switches From Ignored to Irresistible

Drummond Rennie, MD

IN A RECENT ARTICLE IN *JAMA* ON THE REGISTRATION OF clinical trials,[1] Dickersin and I pointed out that, 30 years after the idea of registering trials had been proposed, 18 years after registration of trials at inception had been shown to eliminate publication bias, and despite the pres-

the results would be treated as trade secre
made public?

RECENT DEVELOPMENTS

On June 2, 2004, Eliot Spitzer, the attor
State of New York, sued GlaxoSmithKli
of th

CONSORT
TRANSPARENT REPORTING of TRIALS

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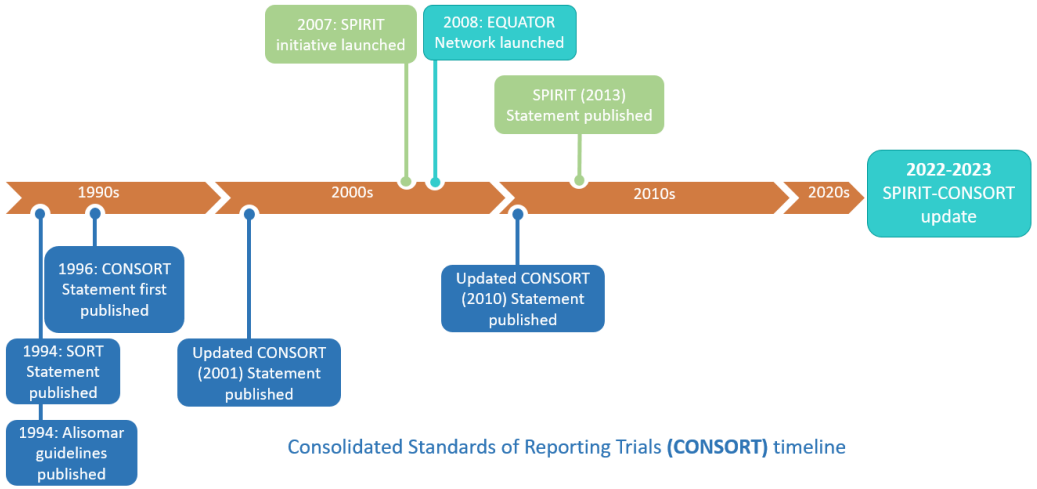
SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

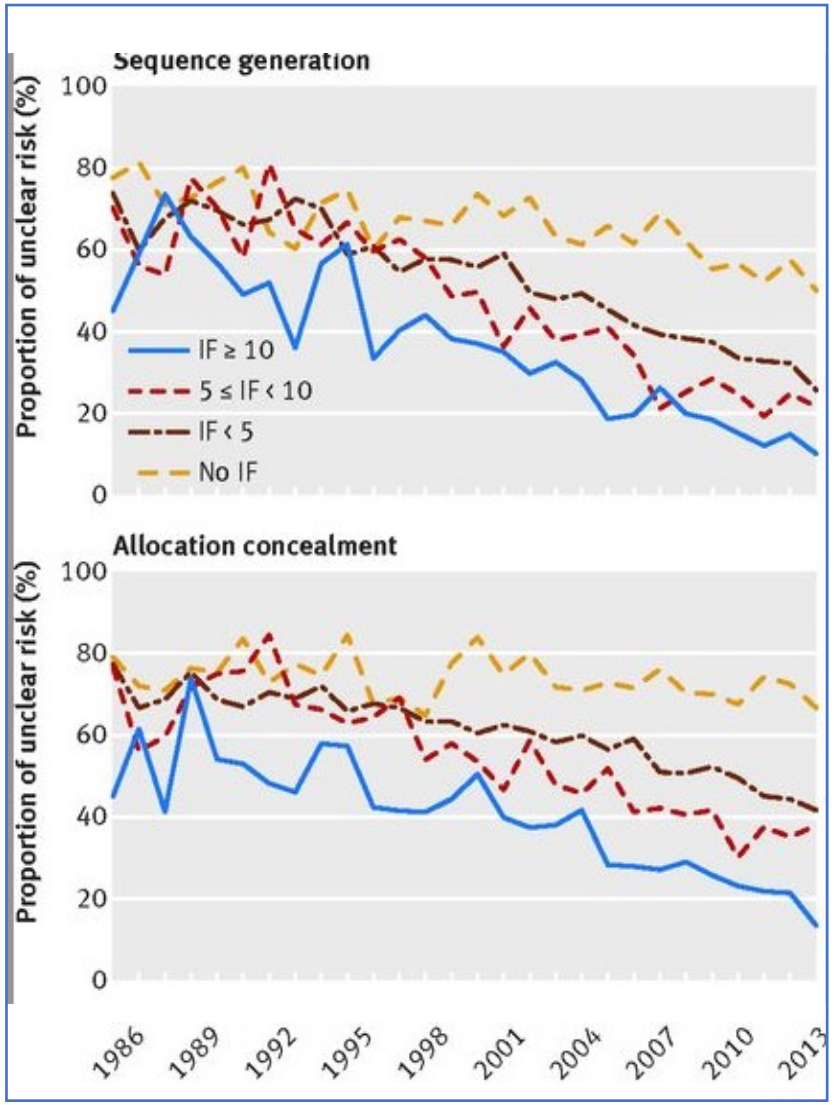
Standard Protocol Items: Recommendations for Interventional Trials **(SPIRIT)** timeline

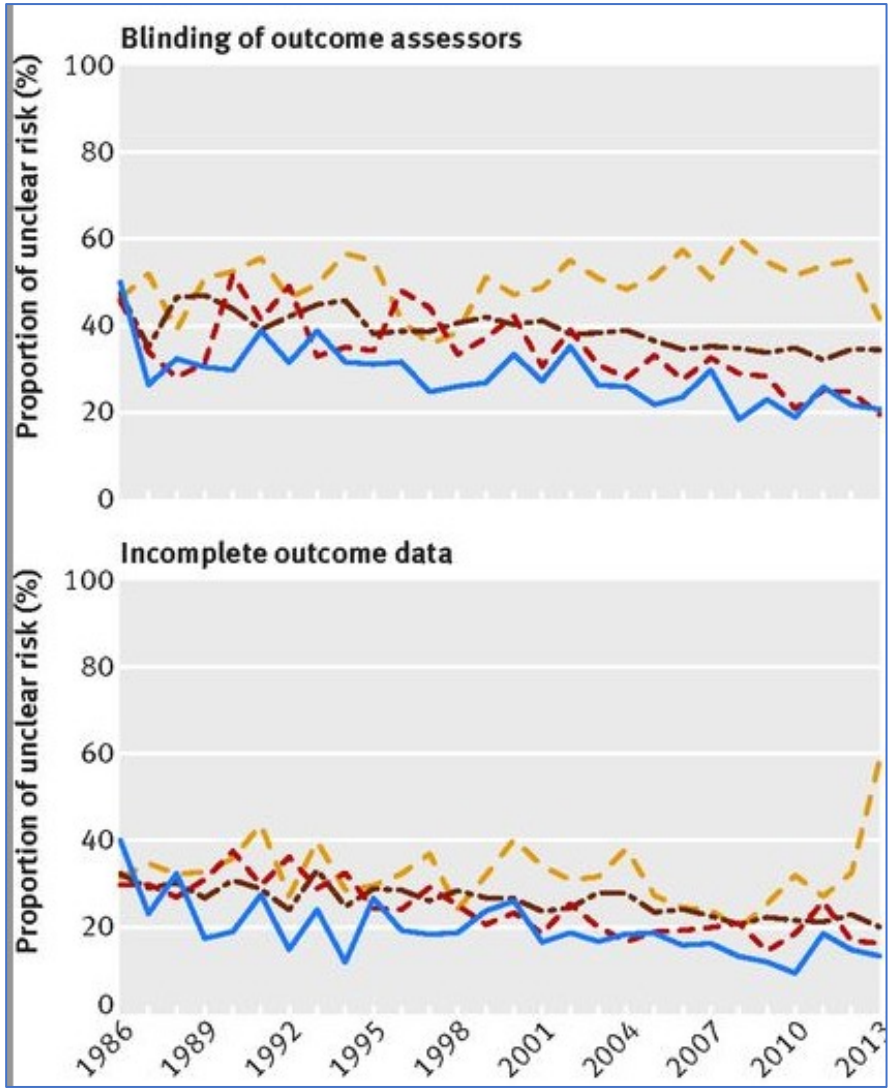


Consolidated Standards of Reporting Trials **(CONSORT)** timeline

Rennie JAMA 2004
Hopewell S, Boutron I, Chan AW, Collins GS, de Beyer JA, Hróbjartsson A, Hansen Nejstgaard C, Østengaard L, Schulz KF, Tunn R, Moher D Nature Med in press

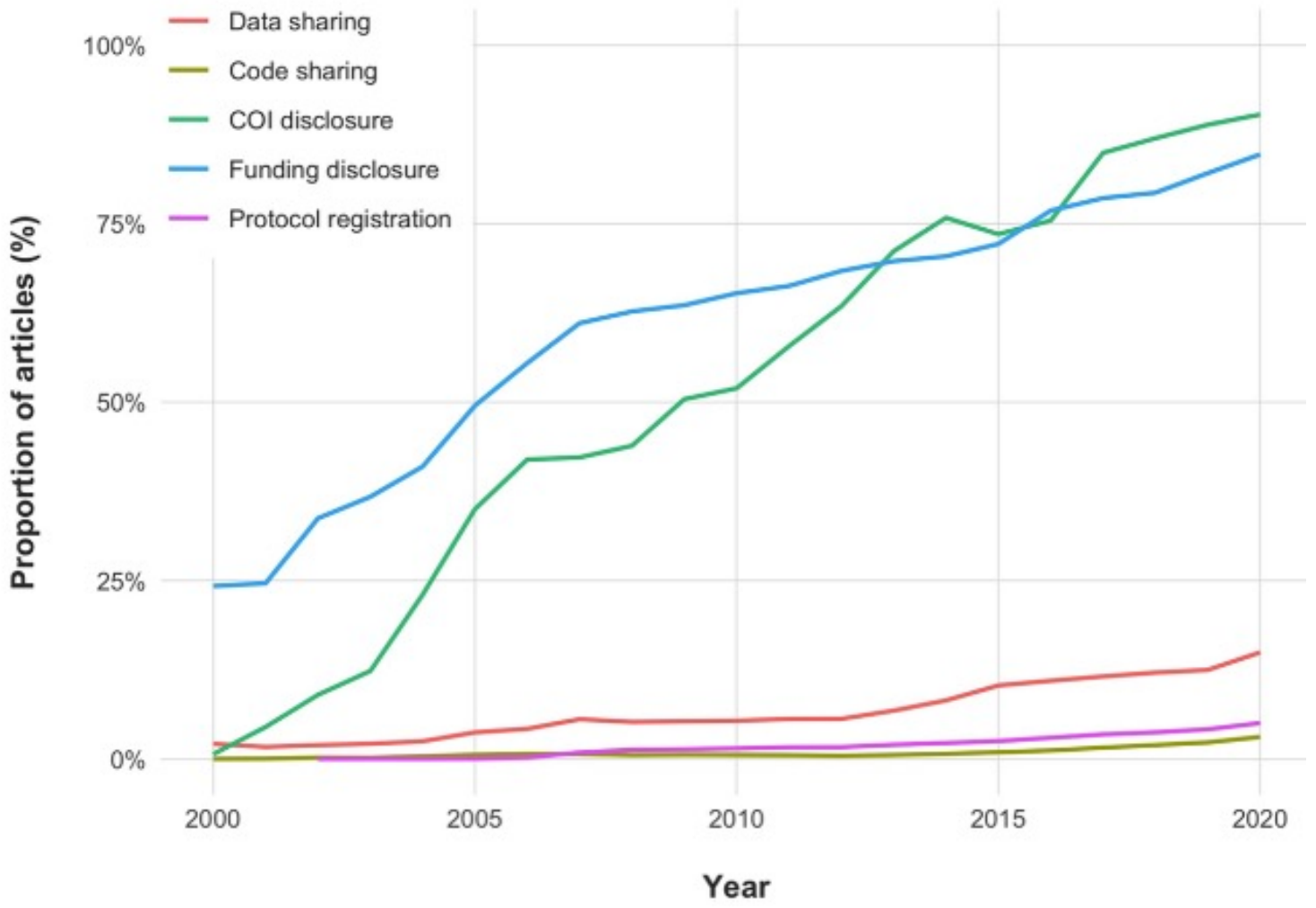
Evolution of poor reporting over time in 20 920 randomized controlled trials included in Cochrane reviews





Dechartres A, Trinquart L, Atal I, Moher D, Dickersin K, Boutron I, Perrodeau E, Altman DG, Ravaud P. BMJ. 2017

Indicators of transparency across the entire open biomedical literature on PMC

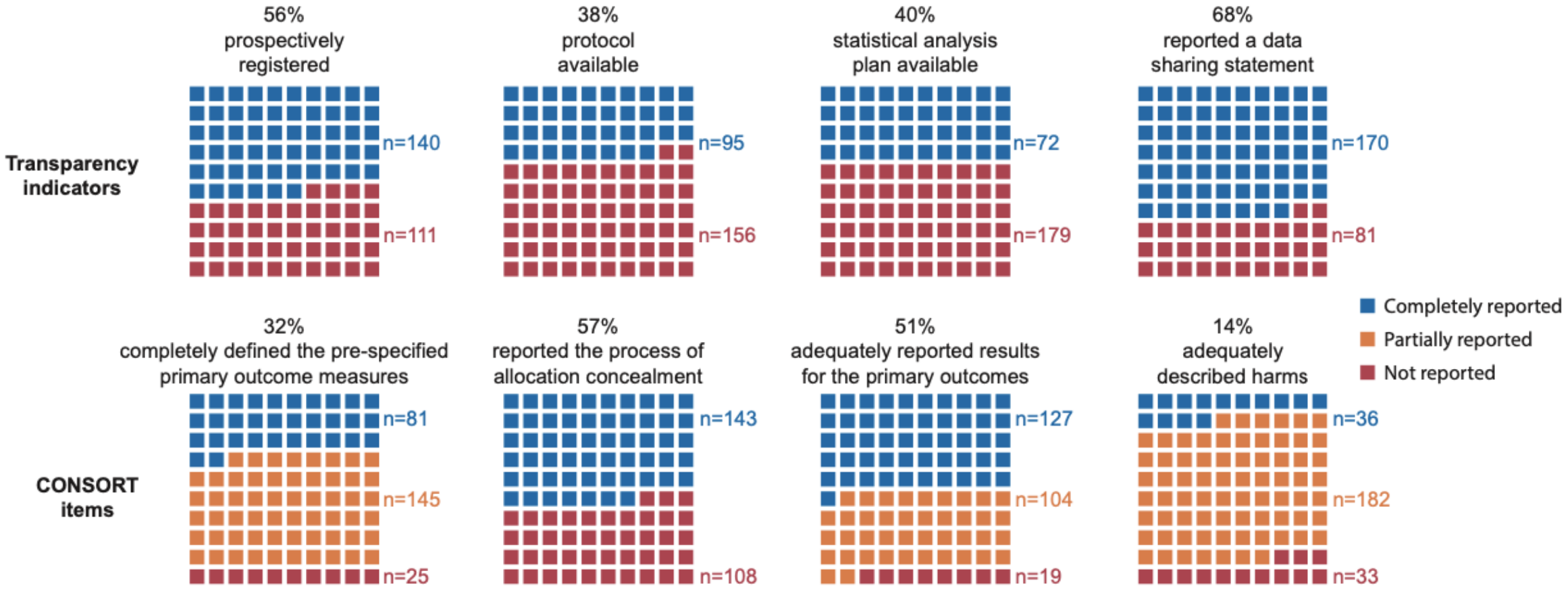


2.75 million articles on PubMed Central (PMC).

Serghiou S, Contopoulos-Ioannidis DG, Boyack KW, Riedel N, Wallach JD, et al. PLOS Biology 2021

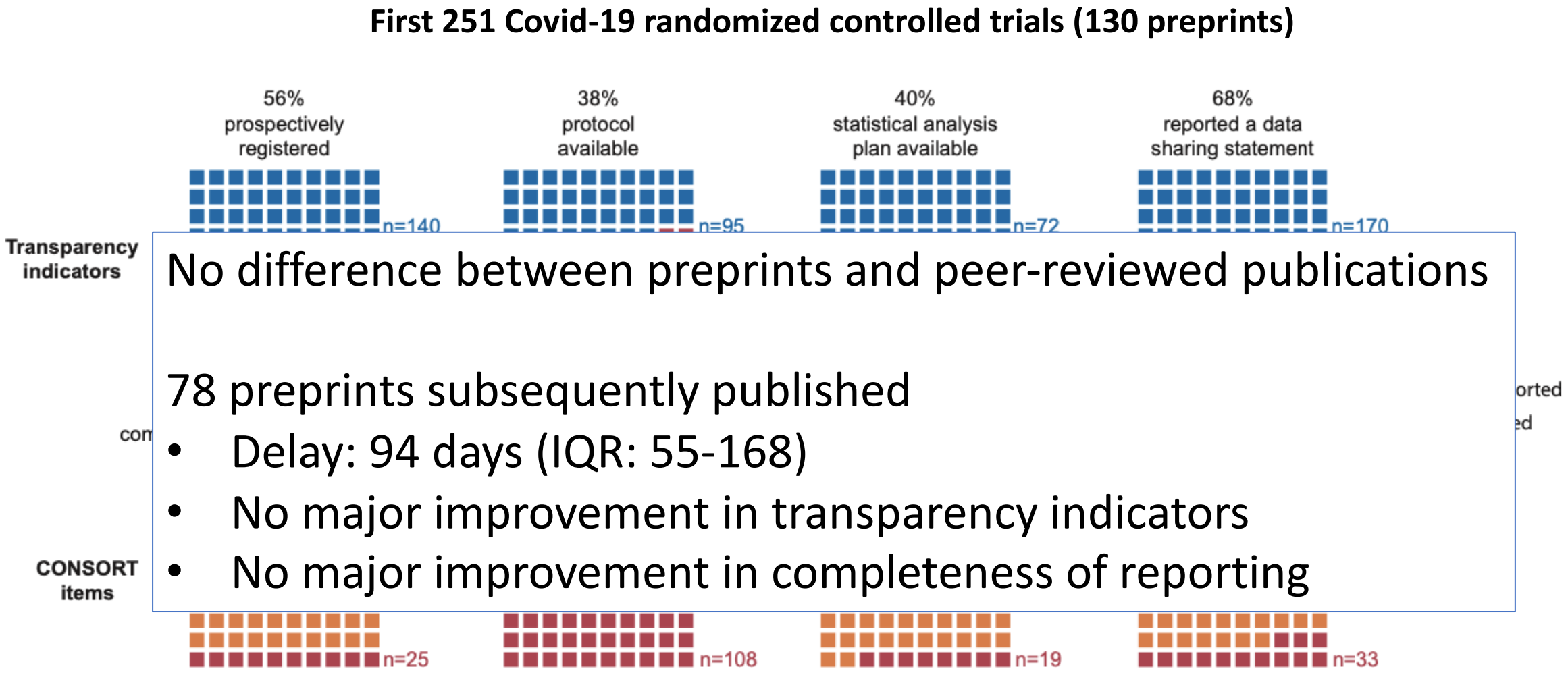
Incomplete reporting

First 251 Covid-19 randomized controlled trials (130 preprints)



Kapp P, Esmail L, Ghosn L, Ravaud P, Boutron I BMC Med accepted / peer-review congress

Incomplete reporting



Kapp P, Esmail L, Ghosn L, Ravaud P, Boutron I BMC Med accepted / peer-review congress

Impact of the peer review process on completeness of reporting

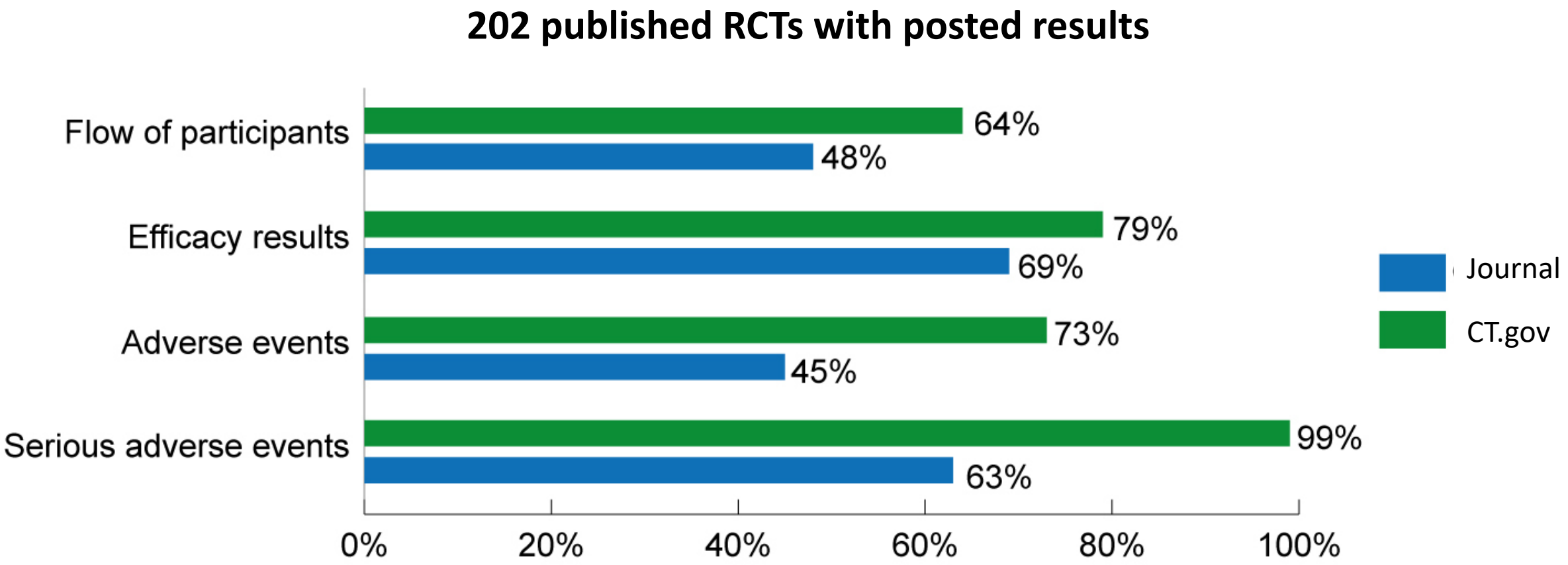
- 93 RCTs published
- First submission / Peer-reviewers' comments/ Published article

A median of **11%** (range 1-60%) **words deleted** and **20% added** (range 2-88%).

Adequate reporting	Submitted	Published
Sequence generation	47%	59%
Allocation concealment	34%	44%
Blinding	33%	45%
Primary outcome	51%	51%
Results for the primary outcome	35%	35%

Hopewell S, Collins GS, Boutron I, Yu LM, Cook J, Shanyinde M, Wharton R, Shamseer L, Altman DG. BMJ. 2014

Other sources of information: Results posted on clinical trials registries



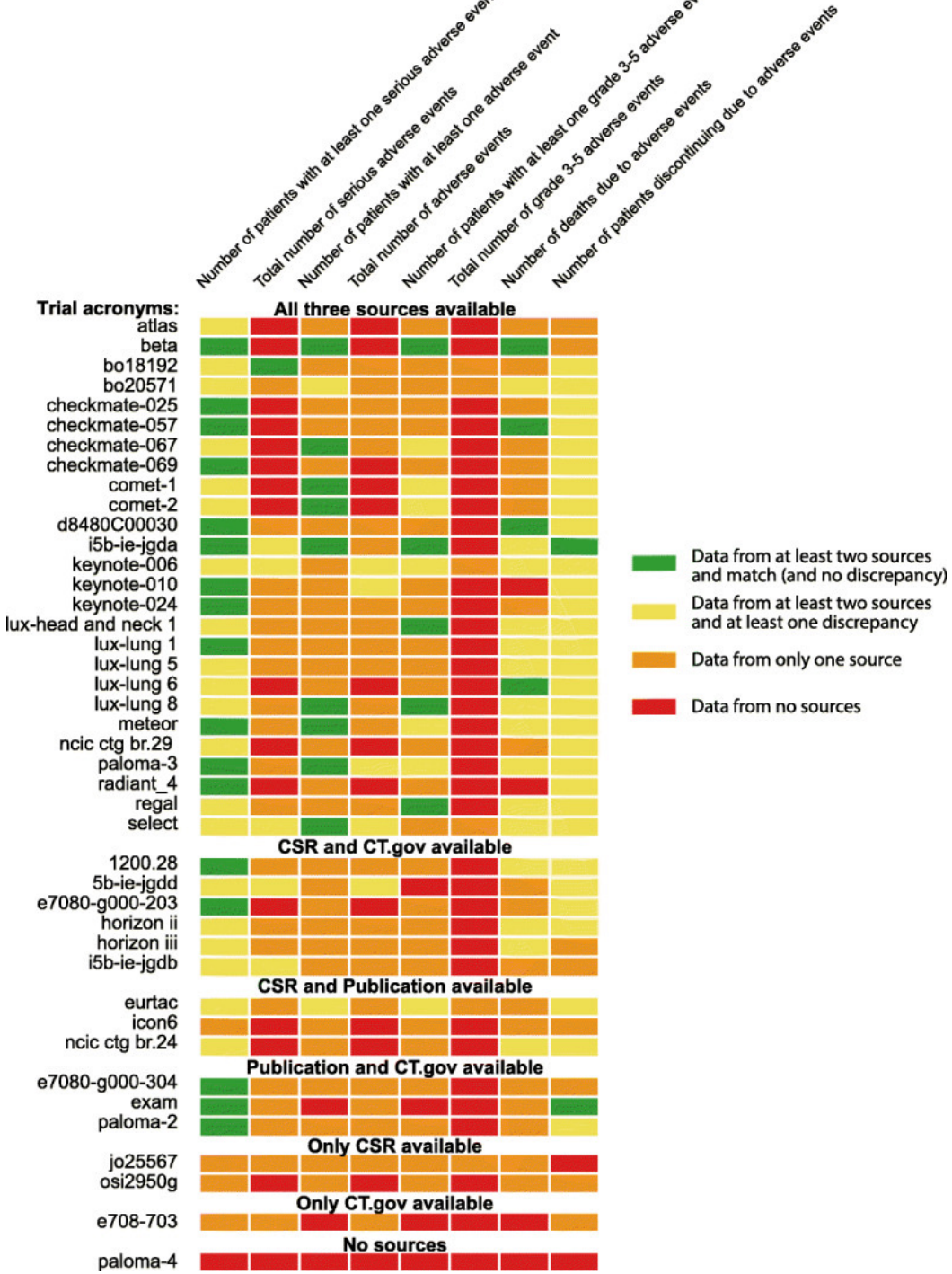
Riveros C, Dechartres A, Perrodeau E, Haneef R, Boutron I, Ravaud P, Plos Med, 2013

Other sources of information: Clinical study reports (CSR)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

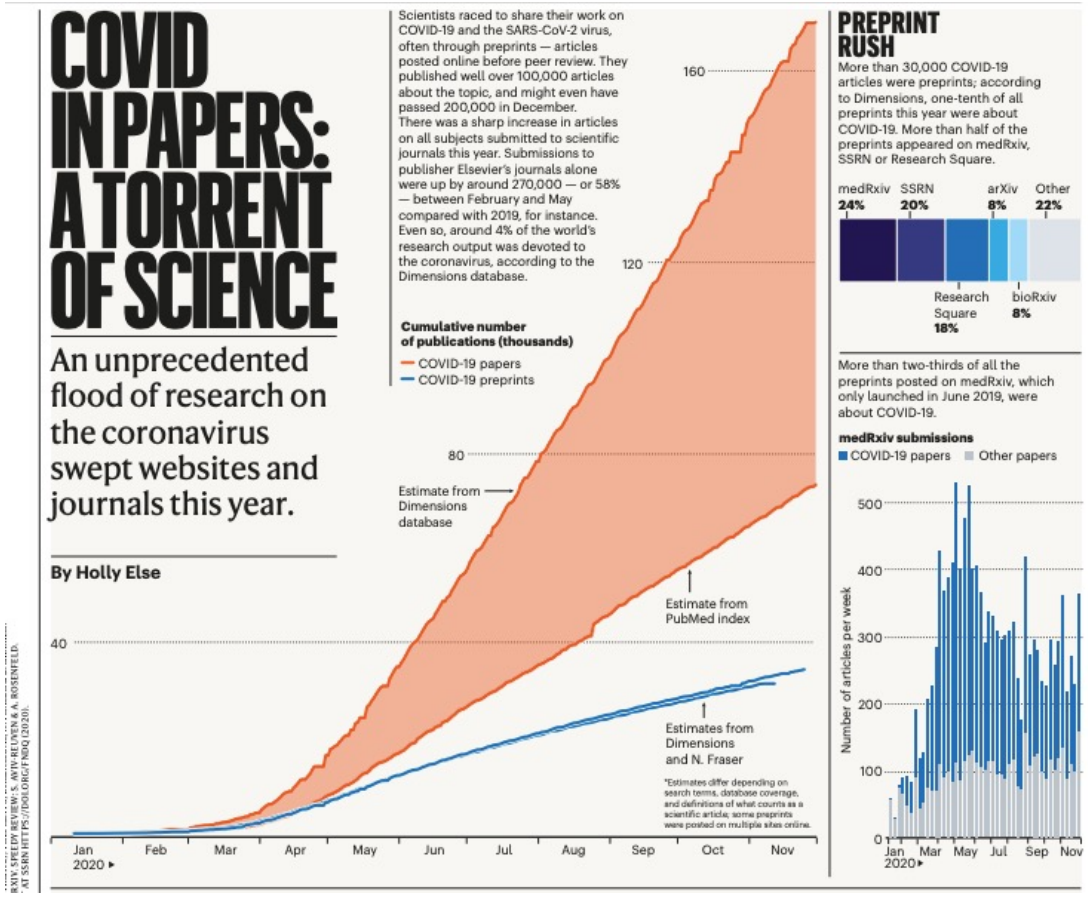
Clinical data publication

- 42 trials (2015-18)
- Harms reporting was more complete in CSRs than other sources.
- Marked discrepancies in harms data between sources



Paludan-Müller AS, Créquit P, Boutron I. BMC Med. 2021

Living sources of information: Preprints



COVID IN PAPERS: A TORRENT OF SCIENCE

An unprecedented flood of research on the coronavirus swept websites and journals this year.

By Holly Else

Scientists raced to share their work on COVID-19 and the SARS-CoV-2 virus, often through preprints — articles posted online before peer review. They published well over 100,000 articles about the topic, and might even have passed 200,000 in December. There was a sharp increase in articles on all subjects submitted to scientific journals this year. Submissions to publisher Elsevier's journals alone were up by around 270,000 — or 58% — between February and May compared with 2019, for instance. Even so, around 4% of the world's research output was devoted to the coronavirus, according to the Dimensions database.

Cumulative number of publications (thousands)
COVID-19 papers
COVID-19 preprints

Estimate from Dimensions database
Estimate from PubMed index
Estimates from Dimensions and N. Fraser
*Estimates differ depending on search terms, database coverage, and definitions of what counts as a scientific article; some preprints were posted on multiple sites online.

Jan 2020 Feb Mar Apr May Jun Jul Aug Sep Oct Nov

PREPRINT RUSH

More than 30,000 COVID-19 articles were preprints; according to Dimensions, one-tenth of all preprints this year were about COVID-19. More than half of the preprints appeared on medRxiv, SSRN or Research Square.

medRxiv 24% SSRN 20% Research Square 18% arXiv 8% bioRxiv 8% Other 22%

More than two-thirds of all the preprints posted on medRxiv, which only launched in June 2019, were about COVID-19.

medRxiv submissions
COVID-19 papers Other papers
Number of articles per week
Jan 2020 Mar May Jul Sep Nov

Oikonomidi et al. BMC Medicine (2020) 18:402
https://doi.org/10.1186/s12916-020-01880-8

BMC Medicine

RESEARCH ARTICLE Open Access

Changes in evidence for studies assessing interventions for COVID-19 reported in preprints: meta-research study

Theodora Oikonomidi[1,2,3*], Isabelle Boutron[1,2,3], Olivier Pierre[1,2,3], Guillaume Cabanac[4], Philippe Ravaud[1,2,3,5] and the COVID-19 NMA Consortium

139 studies reported in multiple sources (several preprint versions; journal article)

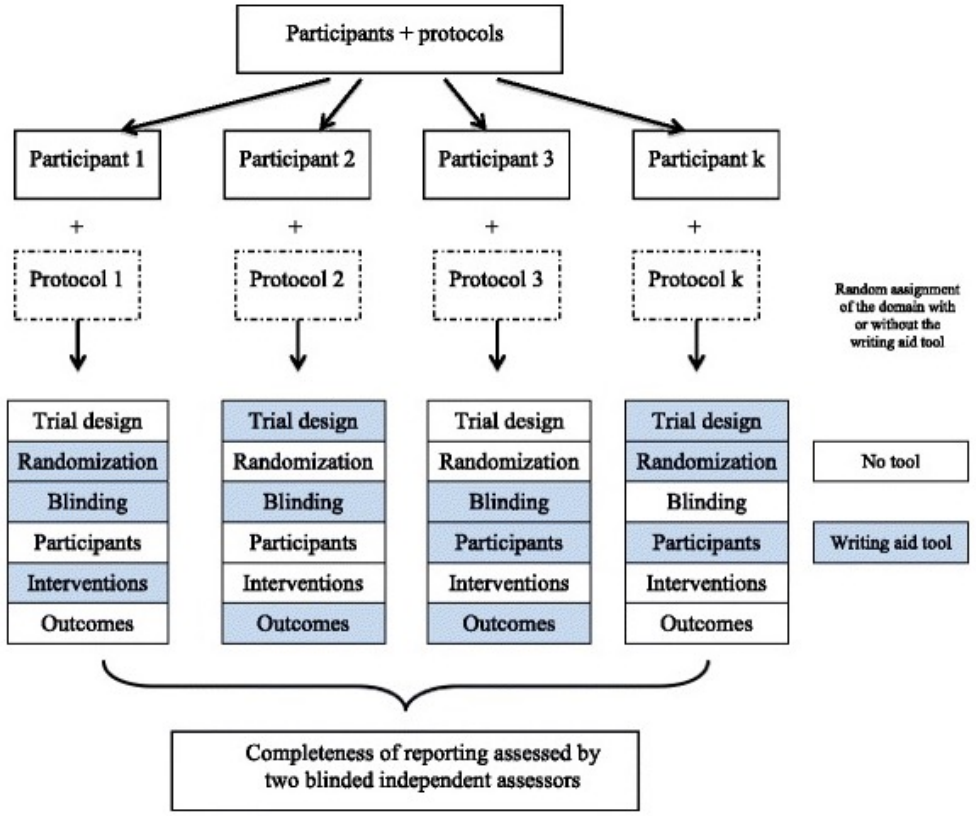
- Evidence is not stable between and within evidence sources
- 45% there was a change in at least one evidence component (results; conclusion)

Oikonomidi T, Boutron I, Pierre O, Cabanac G, Ravaud P; COVID-19 NMA Consortium. BMC Med 2020

COBWEB Consort-based WEB tool an online writing aid tool for writing a randomized trial report

Report, edit, share, and export your trial manuscript in line with the CONSORT statement and its subsequent extensions.

"Split-manuscript randomized controlled trial "



Completeness of reporting (0-10)
writing aid tool vs none

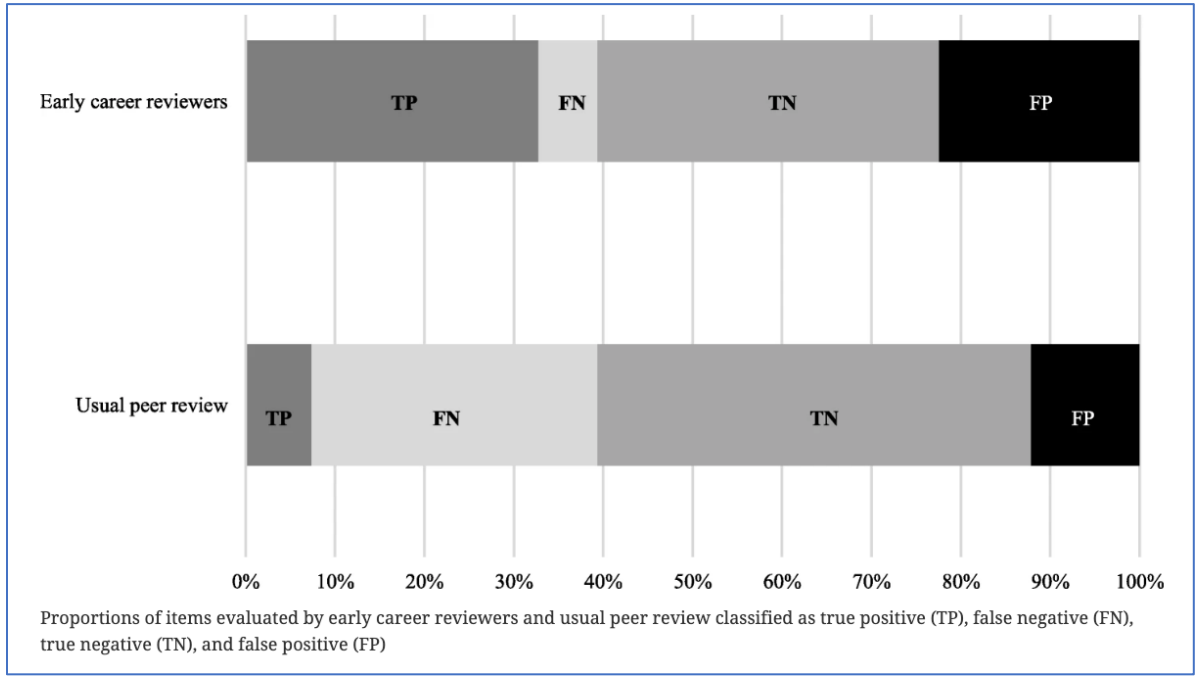
Mean Difference = 2.1 [1.5;2.7]

https://cobweb.clinicalepidemio.fr/

Barnes C, Boutron I, Giraudeau B, Porcher R, Altman DG, Ravaud P BMC Med 2015

COBPeer A Consort-Based Peer-Review Tool

Accuracy of early career researchers using CobPeer



Proportions of items evaluated by early career reviewers and usual peer review classified as true positive (TP), false negative (FN), true negative (TN), and false positive (FP)

120 manuscripts

- Usual peer-review process
- Early career researchers using CobPeer

TP: true positive
FN: false negative
TN: true negative
FP: false positive

	Early carer researchers using Cobpeer	Usual peer-review process	P-value
Sensitivity	83.6 [79.7–87.0]	19.0 [15.4–23.1]	< 0.001
Specificity	62.9 [59.1–66.6]	79.9 [76.6–82.9]	< 0.001

Chauvin A, Ravaud P, Moher D, Schriger D, Hopewell S, Shanahan D, Alam S, Baron G, Regnaux JP, Crequit P, Martinez V, Riveros C, Le Cleach L, Recchioni A, Altman DG, Boutron I. BMC Med 2019

Bias in reporting: Selective reporting of outcomes


RESEARCH Open Access

Assessment of transparency and selective reporting of interventional trials studying colorectal cancer

Anna Pellat[1,2*], Isabelle Boutron[2,3] and Philippe Ravaud[2,3]

BMC Cancer

- 101 RCTs of colorectal cancer (2018-22)
  - **49%** trials were retrospectively registered
  - **23%** trials had primary outcome(s) switching
  - Impact of the switch could be assessed for **16 trials**
    - 6 (38%) favored statistically significant results

Pellat A, Boutron I, Ravaud P. BMC Cancer. 2022

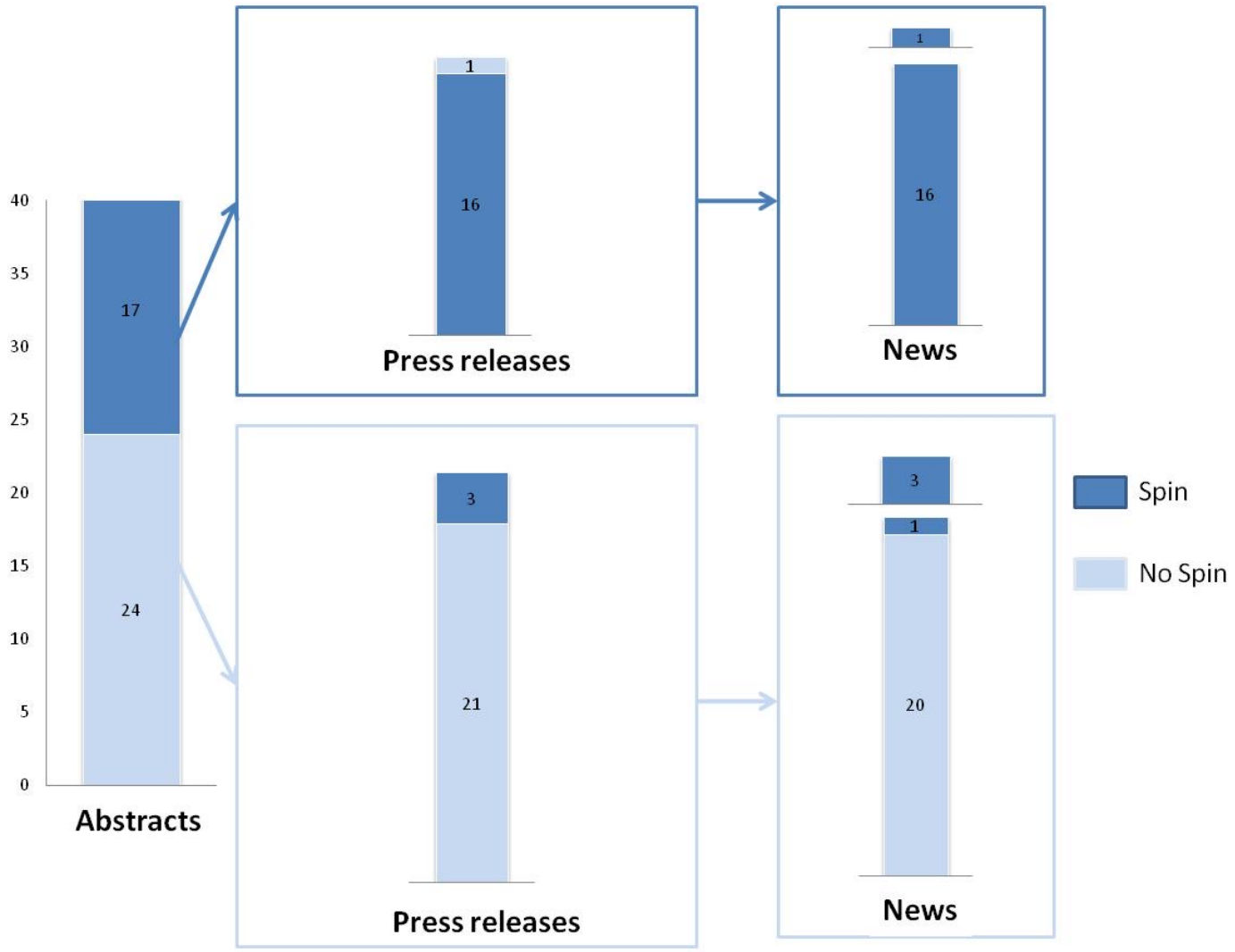
Distorted reporting: Spin practices

- Spin = specific intentional or unintentional reporting that fails to faithfully reflect the findings and could affect the impression the results produce in readers

- Prevalence of spin
  - 44% to 86%

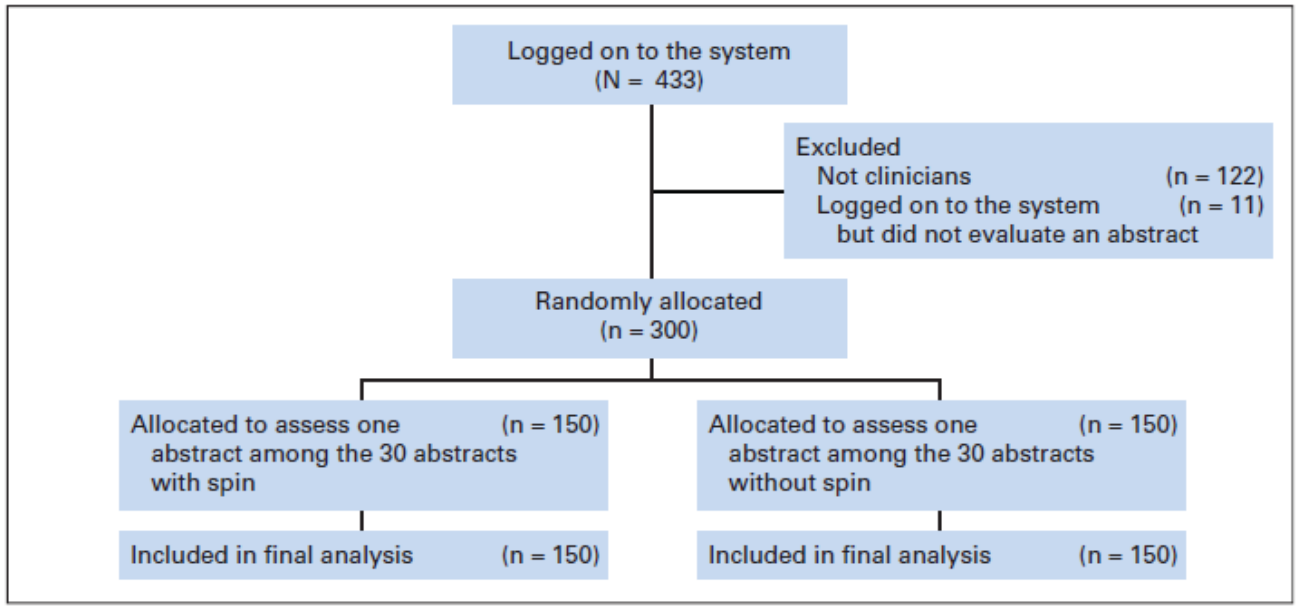
Boutron I, Ravaud P. Proc Natl Acad Sci U S A. 2018
Chiu K, Grundi Q, Bero L Plos Biology 2017

Spin disseminates from the publication to the press release and the news



Yavchitz A, Boutron I, Bafeta A, Marroun I, Charles P, Mantz J, Ravaud P. PLoS Med. 2012

Spin impacts readers' interpretation



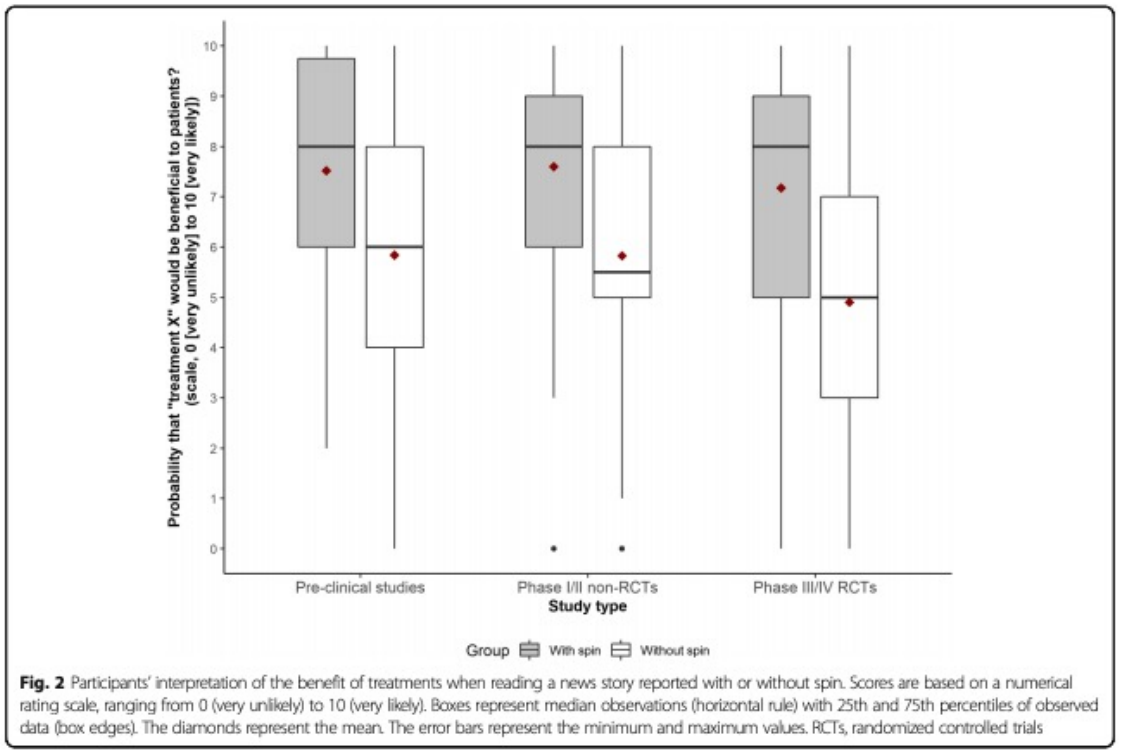


Fig. 2 Participants' interpretation of the benefit of treatments when reading a news story reported with or without spin. Scores are based on a numerical rating scale, ranging from 0 (very unlikely) to 10 (very likely). Boxes represent median observations (horizontal rule) with 25th and 75th percentiles of observed data (box edges). The diamonds represent the mean. The error bars represent the minimum and maximum values. RCTs, randomized controlled trials

Based on this abstract, do you think treatment A would be beneficial to patients?

Scale, 0 [very unlikely] to 10 [very likely)

Mean difference = 0.71 (95% CI, 0.07-1.35); P .03

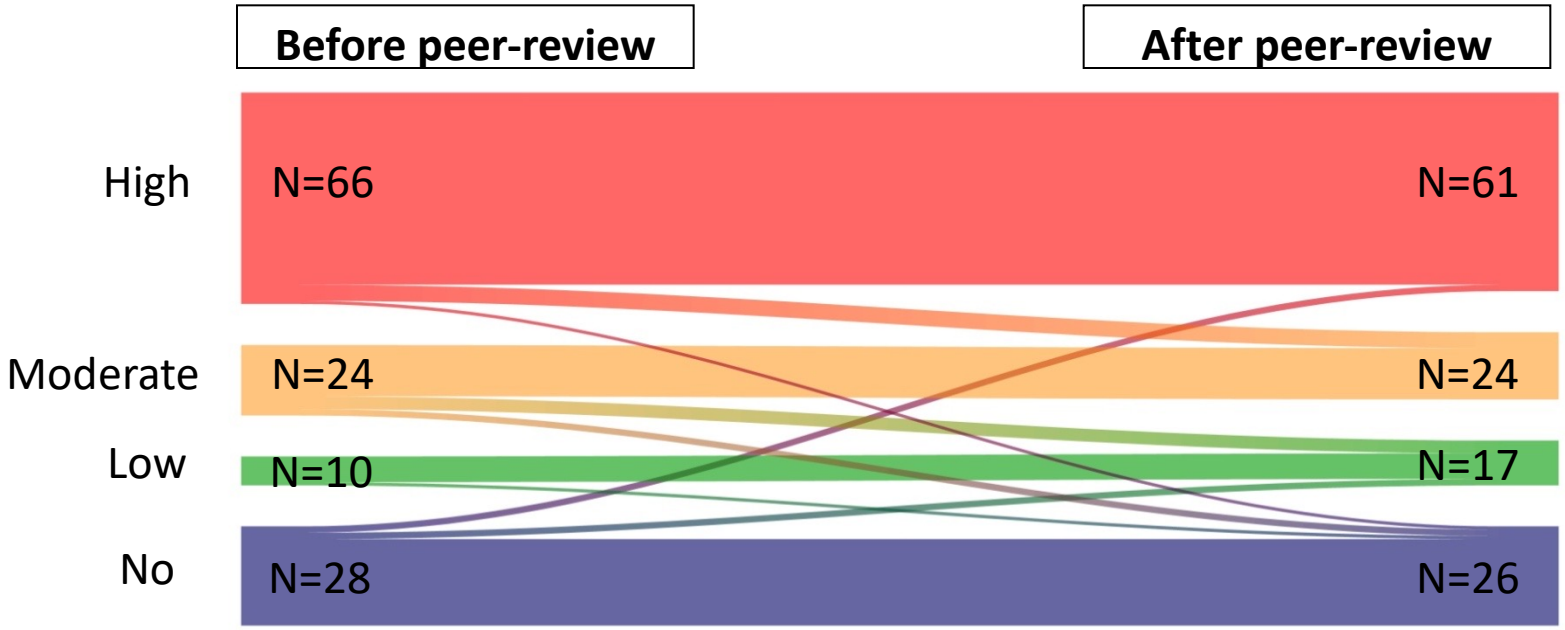
"What do you think is the probability that 'treatment X' would be beneficial to patients?" (scale, 0 [very unlikely] to 10 [very likely])

Boutron I, Altman DG, Hopewell S, Vera-Badillo F, Tannock I, Ravaud P. J Clin Oncol. 2014

Boutron I, Haneef R, Yavchitz A, Baron G, Novack J, Oransky I, Schwitzer G, Ravaud P. BMC Med. 2019

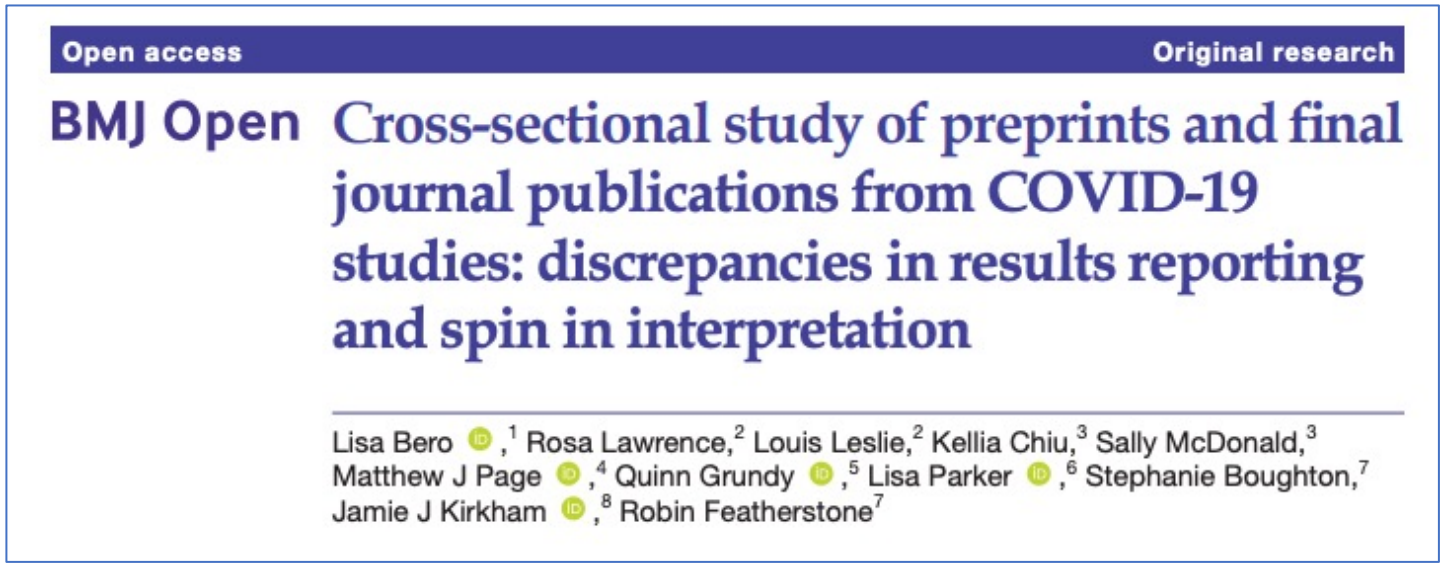
Can peer reviewers reduce spin?

Non-randomized studies assessing a therapeutic intervention published in open access journals (n=128).



76% of peer reviewers failed to identify spin in abstract conclusions

Lazarus C, Haneef R, Ravaud P, Hopewell S, Altman DG, Boutron I. Clin Epidemiol. 2016

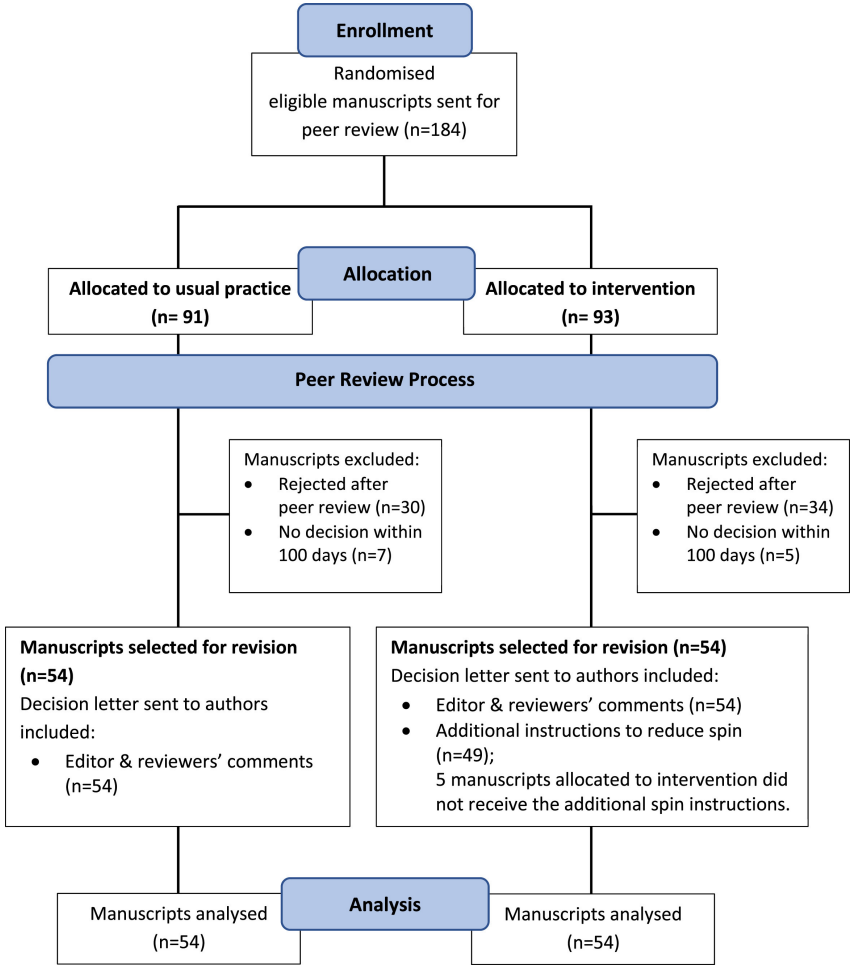


67 interventional and observational studies of COVID-19

- Spin was removed between the preprint and journal publication in **7%**
- Spin was added in **1%**

Bero L, Lawrence R, Leslie L, Chiu K, McDonald S, Page MJ, Grundy Q, Parker L, Boughton S, Kirkham JJ, Featherstone R. BMJ Open 2021

A randomized trial of an editorial intervention to reduce spin in the abstract's conclusion showed no significant effect



Intervention: email with short instructions to reduce spin

Instructions for authors to reduce spin

With your revision, please carefully check and confirm that your abstract conclusion:

- Focuses on the primary aim and primary outcome(s) of your study (e.g., avoids selective reporting or focusing on the subgroup, secondary, or exploratory analysis)
- Includes only information supported by evidence and in accordance with the results of your study (e.g., avoids claims of significant effect with nonstatistically significant outcomes)
- Avoids any interpretation that is not consistent with your study design or the results (e.g., avoids causal claims in studies with nonrandomized designs, or inappropriate extrapolation of results to different populations or outcomes than investigated in your study)
- Avoids recommendations for practice not justified by study findings (e.g., calls for action that have not been evaluated)

Abstract conclusion with spin

- Intervention: 57%
- Comparator: 63%
- RD = 6% (-24% to 13%)

Ghannad M, Yang B, Leeflang M, Aldcroft A, Bossuyt PM, Schroter S, Boutron I. J Clin Epidemiol. 2021

Rethinking scholarly communication

Format of scholarly communication

- Large freedom given to the authors
- Multiple sources of information for the same study fragmented, not always accessible
- One off publication difficult to amend or correct if needed
- No attempt to overcome cognitive bias in results interpretation

Peer-review process

- Unrealistic expectations (number of tasks and limited number of experts involved)
- One size fits all: same process whatever the study impact
- Crowdsourcing
- AI-assisted peer-review

Make peer review scientific

Thirty years on from the first congress on peer review, **Drummond Rennie** reflects on the improvements brought about by research into the process — and calls for more.

COMMENT

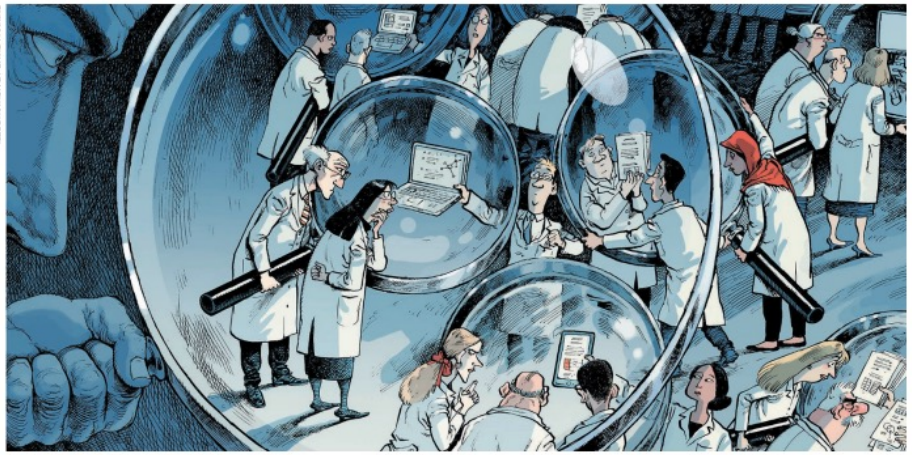


ILLUSTRATION BY DAVID PARKINS

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But it is a humar
involved brings pre
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identifies high-quality
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ting gross fraud. More recently,
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now makes such disclosures compulsory. Its develop evidence-based lists of items to be to eventual publication. There seems to be

URE | 31

"it (peer-review) is a human system. Everybody involved brings prejudices, misunderstandings and gaps in knowledge, so no one should be surprised that peer review is often biased and inefficient."