Reducing waste and increasing the value of biomedical research

Clinical Epidemiology Program, Centre for Practice Changing Research, Ottawa Hospital Research Institute; School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Canada

31st May 2016

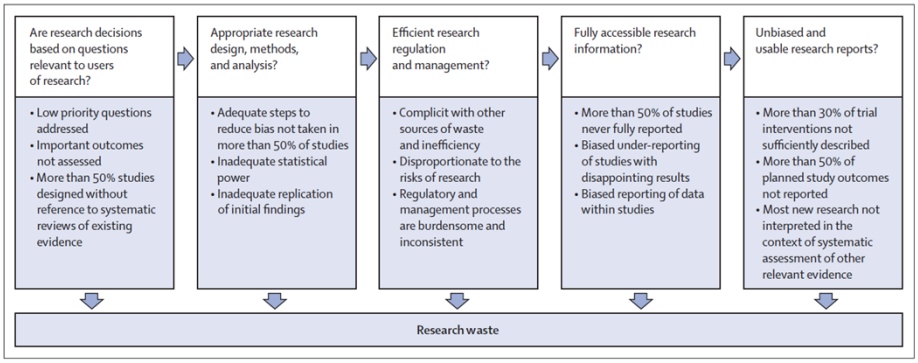
Disclosures

- Co editor-in-chief *Systematic Reviews*
- Member of editorial board of several journals
- Advisory member International Congress on Peer Review and Biomedical Publication
- Member of PLoS ONE's Human Research Advisory Committee
- University of Ottawa Medical Journal Faculty Advisory Board member
- Member of the EQUATOR Network's executive group
- Member of the REWARD alliance team
- Received funding for journalology (publication science) research from the Cochrane Collaboration; BioMed Central, Elsevier; and Garfield Foundation

Outline of my presentation

- Quality of reported clinical and preclinical research
- Efforts to improve the quality of published research
  - The REWARD alliance
  - Publications officer
  - Core competencies for editors, peer reviewers and authors

The research continuum



Context

- Massive publications-industrial complex
- About 6,000 publishers
- About 30,000 journals
- Produces about 3 millions manuscripts, annually, of which 50% are published

The published record

- It's tarnished ☹☹☹☹☹
- There is considerable avoidable waste in the biomedical industrial complex

Authors cannot adequately describe basic essential information for readers

- 10 essential elements about intervention
  - e.g., drug name, dose, route....
- examined 262 reports of randomized trials from most prominent oncology journals
- overall, only 11% of articles reported all 10 essential items

Duff JM et al. JNCI 2010 102:702-705

Delivering the best care to patients

- "Thoughtful consideration of reporting trial-related procedures that could assist with turning "best evidence" to "best Practice" would be worthwhile"
- "Careful and consistent reporting would help to promote safe and effective clinical application of oncology therapeutics ..."

Dancey JNCI 2010; 102:670-671

http://compare-trials.org/

67	9	301	357
TRIALS CHECKED TO DATE	TRIALS WERE PERFECT	OUTCOMES NOT REPORTED	NEW OUTCOMES SILENTLY ADDED

)n average, each trial reported just 62.0% of its specified outcomes. And on average, each trial ilently added 5.3 new outcomes.

58	6	31	16
LETTERS SENT	LETTERS PUBLISHED	LETTERS UNPUBLISHED AFTER 4 WEEKS	LETTERS REJECTED BY EDITOR

RESEARCH ARTICLE SUMMARY

PSYCHOLOGY

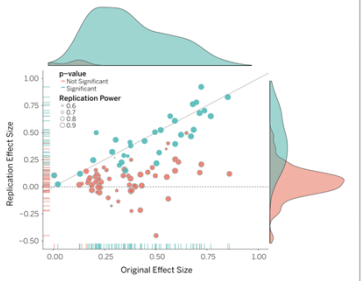
Estimating the reproducibility of psychological science

Open Science Collaboration*

INTRODUCTION: Reproducibility is a defining feature of science, but the extent to which it characterizes current research is unknown. Scientific claims should not gain credence because of the status or authority of their originator but by the replicability of their supporting evidence. Even research of exemplary quality may have irreproducible empirical findings because of random or systematic error.

RATIONALE: There is concern about the rate and predictors of reproducibility, but limited evidence. Potentially problematic practices include selective reporting, selective analysis, and insufficient specification of the conditions necessary or sufficient to obtain the results. Direct replication is the attempt to recreate the conditions believed sufficient for obtaining a previously observed finding and is the means of establishing reproducibility of a finding with new data. We conducted a large-scale, collaborative effort to obtain an initial estimate of the reproducibility of psychological science.

RESULTS: We conducted replications of 100 experimental and correlational studies published in three psychology journals using high-powered designs and original materials when available. There is no single standard for evaluating replication success. Here, we evaluated reproducibility using significance and *P* values, effect sizes, subjective assessments of replication teams, and meta-analysis of effect sizes. The mean effect size (r) of the replication effects (M_r = 0.197, SD = 0.257) was half the magnitude of the mean effect size of the original effects (M_r = 0.403, SD = 0.188), representing a



Replication

NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring[1,2]. As leaders of the US National Institutes of Health (NIH), we share this concern and here explore some of the significant interventions that we are planning.

Science has long been regarded as 'self-correcting', given that it is founded on the replication of earlier work. Over the long term, that principle remains true. In the shorter term, however, the checks and balances that once ensured scientific fidelity have been hobbled. This has compromised the ability of today's researchers to reproduce others' findings.

Let's be clear: with rare exceptions, we have no evidence to suggest that irreproducibility is caused by scientific misconduct. In 2011, the Office of Research Integrity of the US Department of Health and Human Services pursued only 12 such cases[3]. Even if this represents only a fraction of the actual problem, fraudulent papers are vastly ing agencies to establish or enforce policies that insist on data access.

PRECLINICAL PROBLEMS

Reproducibility is potentially a problem in all scientific disciplines. However, human clinical trials seem to be less at risk because they are already governed by various regulations that stipulate rigorous design and independent oversight — including randomization, blinding, power estimates, pre-registration of outcome measures in standardized, public databases such as ClinicalTrials.gov and oversight by institutional review boards and data safety monitoring boards. Furthermore, the clinical trials community has taken important steps towards adopting standard reporting elements[7].

Preclinical research, especially work that uses animal models[4], seems to be the area that is currently most susceptible to reproducibility issues. Many of these failures have simple and practical explanations: different animal strains, different lab environments or subtle changes in protocol. Some irreproducible reports are probably the result of coincidental findings that happen to reach statistical significance, coupled with publication bias.

Incomplete Reporting

Macleod et al., 2015

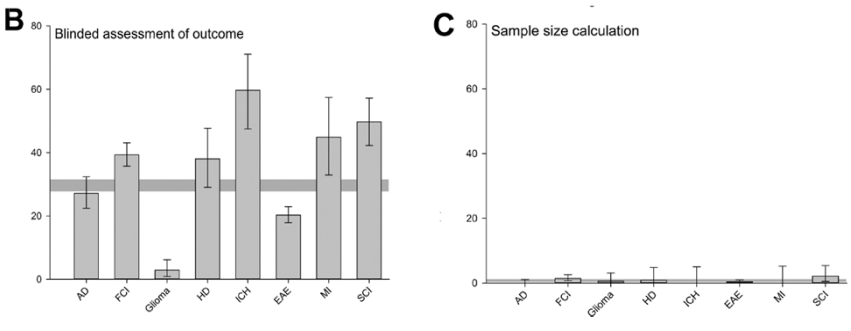


Fig 2. Prevalence of reporting of (A) randomisation, (B) blinded assessment of outcome, (C) sample size calculations, and (D) conflict of interest reporting in 2,671 publications describing the efficacy of interventions in animal models of Alzheimer's disease (AD, *n* = 324 publications), focal cerebral ischaemia (FCI, 704), glioma (175), Huntington's disease (HD, 113), intracerebral haemorrhage (ICH, 72), experimental autoimmune encephalomyelitis (EAE, 1029), myocardial infarction (MI, 69), and spinal cord injury (SCI, 185) identified in the context of systematic reviews. Vertical error bars represent the 95% confidence intervals, and the horizontal grey bar represents the 95% confidence interval of the overall estimate (S2 Data).

OPEN ACCESS Freely available online PLoS BIOLOGY

Publication Bias in Reports of Animal Stroke Studies Leads to Major Overstatement of Efficacy

Emily S. Sena[1,2,3], H. Bart van der Worp[4], Philip M. W. Bath[5], David W. Howells[2,3], Malcolm R. Macleod[1,6]*

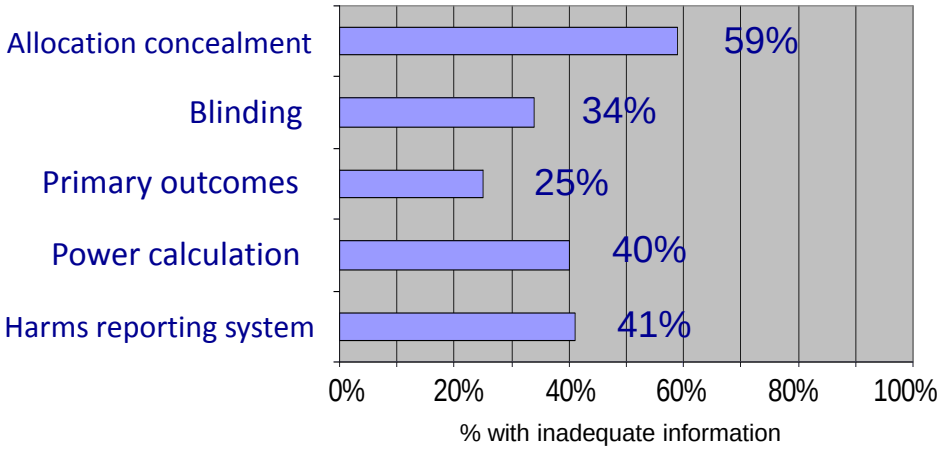
1 Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, United Kingdom, 2 National Stroke Research Institute, Austin Health, University of Melbourne, Melbourne, Victoria, Australia, 3 Department of Medicine, Austin Health, University of Melbourne, Melbourne, Victoria, Australia, 4 Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands, 5 Stroke Trials Unit, University of Nottingham, Nottingham, England, United Kingdom, 6 Department of Neurology, NHS Forth Valley, Stirling, Scotland, United Kingdom

Abstract

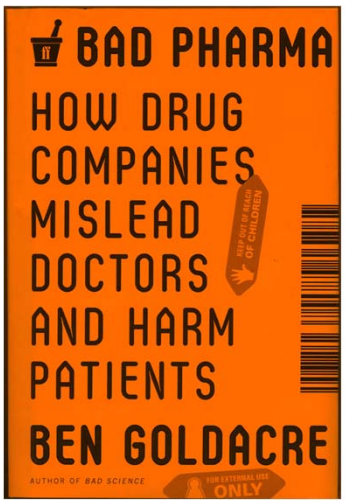
The consolidation of scientific knowledge proceeds through the interpretation and then distillation of data presented in research reports, first in review articles and then in textbooks and undergraduate courses, until truths become accepted as such both amongst "experts" and in the public understanding. Where data are collected but remain unpublished, they cannot contribute to this distillation of knowledge. If these unpublished data differ substantially from published work, conclusions may not reflect adequately the underlying biological effects being described. The existence and any impact of such "publication bias" in the laboratory sciences have not been described. Using the CAMARADES (Collaborative Approach to Meta-analysis and Review of Animal Data in Experimental Studies) database we identified 16 systematic reviews of interventions tested in animal studies of acute ischaemic stroke involving 525 unique publications. Only ten publications (2%) reported no significant effects on infarct volume and only six (1.2%) did not report at least one significant finding. Egger regression and trim-and-fill analysis suggested that publication bias was highly prevalent (present in the literature for 16 and ten interventions, respectively) in animal studies modelling stroke. Trim-and-fill analysis suggested that publication bias might account for around one-third of the efficacy reported in systematic reviews, with reported efficacy falling from 31.3% to 23.8% after adjustment for publication bias. We estimate that a further 214 experiments (in addition to the 1,359 identified through rigorous systematic review; non publication rate 14%) have been conducted but not reported. It is probable that publication bias has an important impact in other animal disease models, and more broadly in the life sciences.

Of 525 unique publications involving 1,359 experiments: 31% overestimate efficacy; 16% experiments remain unpublished; 2% of publications reported no significant treatment effects

Protocols lack important information



Mhaskar R et al, J Clin Epid 2012; Chan AW et al, BMJ 2008, JAMA 2004; Scharf O, J Clin Oncol 2006; Pildal J, BMJ 2005; Hróbjartsson A et al, J Clin Epid 2009



ALL HAVE PASSED PEER REVIEW AND EDITORIAL APPROVAL

Expenditures on biomedical research

Clinical Review & Education

Special Communication | SCIENTIFIC DISCOVERY AND THE FUTURE OF MEDICINE

The Anatomy of Medical Research
US and International Comparisons

Hamilton Moses III, MD; David H. M. Matheson, JD, MBA; Sarah Cairns-Smith, PhD; Benjamin P. George, MD, MPH; Chasa Piltsch, MPhil; E. Ray Dorsey, MD, MBA

IMPORTANCE Medical research is a prerequisite of clinical advances, while health service research supports improved delivery, access, and cost. Few previous analyses have compared the United States with other developed countries.

OBJECTIVES To quantify total public and private investment and personnel (economic inputs) and to evaluate resulting patents, publications, drug and device approvals, and value created (economic outputs).

EVIDENCE REVIEW Publicly available data from 1994 to 2012 were compiled showing trends in US and international research funding, productivity, and disease burden by source and industry type. Patents and publications (1981-2011) were evaluated using citation rates and impact factors.

FINDINGS (1) Reduced science investment: Total US funding increased 6% per year (1994-2004), but rate of growth declined to 0.8% per year (2004-2012), reaching $417 billion (4.5%) of total health care expenditures. Private sources increased from 46% (1994) to 58% (2012). Industry reduced early-stage research, favoring medical devices, bioengineered drugs, and late-stage clinical trials, particularly for cancer and rare diseases. National Institutes of Health allocations correlate imperfectly with disease burden, with cancer and HIV/AIDS receiving disproportionate support. (2) Underfunding of service innovation: Health services research receives $5.0 billion (0.3% of total health care expenditures) or only 1/20th of science funding. Private insurers ranked last (0.04% of revenue) and health systems 19th (0.1% of revenue) among 22 industries in their investment in innovation. An increment of $8 billion to $15 billion yearly would occur if service firms were to reach median research and development funding. (3) Globalization: US government research funding declined from 57% (2004) to 50% (2012) of the global total, as did that of US companies (50% to 41%), with the total US (public plus private) share of global research funding declining from 57% to 44%. Asia, particularly China, tripled investment from $2.6 billion (2004) to $9.7 billion (2012) preferentially for education and personnel. The US share of life science patents declined from 57% (1981) to 51% (2011), as did those considered most valuable, from 73% (1981) to 59% (2011).

CONCLUSIONS AND RELEVANCE New investment is required if the clinical value of past scientific discoveries and opportunities to improve care are to be fully realized. Sources could include repatriation of foreign capital, new innovation bonds, administrative savings, patent pools, and public-private risk-sharing collaborations. Given international trends, the United States will relinquish its historical international lead in the next decade unless such measures are undertaken.

Editorials pages 143 and 145

Supplemental content at jama.com

Author Affiliations: The Alerion Institute and Alerion Advisors LLC, North Garden, Virginia (Moses); Johns Hopkins School of Medicine, Baltimore, Maryland (Matheson); Boston Consulting Group, Boston, Massachusetts (Matheson, Cairns-Smith, Piltsch); University of Rochester School of Medicine, Rochester, New York (George, Dorsey); Stanford University School of Medicine, Stanford, California (Piltsch).

Corresponding Author: Hamilton Moses III, MD, Alerion, PO Box 150, North Garden, VA 22959 (hm@alerion.us).

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Industry Breakout - Life Sciences

Mon, 12/09/2013 - 6:10am

by R&D Magazine/Battelle

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Summary

As represented in this Forecast, the life science industry includes biopharmaceuticals, medical instruments and devices, animal/agricultural bioscience and commercial research and testing. However, the industry's R&D spending is driven primarily by the mass and research intensity of the biopharmaceutical sector, which accounts for nearly 85% of all expenditures.

The life science industry's research activities in the United States continue to lead the world, but it is an area that also remains in significant transition. Not only is life science—led by the biopharmaceutical sector—the leading U.S. industry in terms of volume of research, U.S. life science R&D accounts for 46% of the global total—one of the highest shares in any industry.

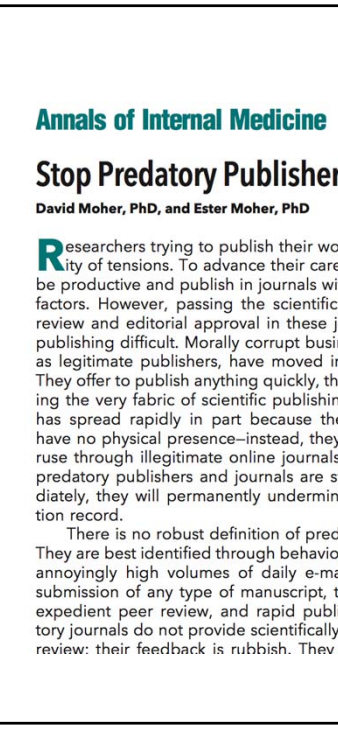
Still, pressures persist to improve on productivity, product pipelines and ROI in consideration of expiring patents, cost pressures and the rising complexity of innovation in drug development. While primarily affecting the biopharmaceutical sector, the medical device sector is not immune to some of these trends. A new factor complicating the R&D environment for the life science industry is the set of changes in the U.S. healthcare landscape mandated by the Affordable Care Act. While it is hard to predict exactly how this new law will affect life science R&D, these transitions and uncertainties suggest that while the U.S. remains a global leader life science R&D, it is vulnerable, especially as European competitors and new, emerging Asian competitors target life science research for growth.

For the U.S. life science industry, we project a small rebound over 2013 levels (up 2.2%) to R&D spending of about $93 billion in 2014, with the growth coming primarily from smaller biopharmaceutical innovators and medical device manufacturers.

The global expansion of the life science industry has slowed over the last few years, but the industry is forecast to have a stronger recovery (up 3.1%) to more than $201 billion in 2014.

Regulatory Context Influences U.S. R&D Outlook

The U.S. life science industry emerged from the combined challenges of the recession and patent expirations with fresh strategies for R&D. Traditional pharmaceutical companies, while still massive and investing significant resources in R&D, continue to struggle with reduced product pipelines and productivity from discovery through development. As these firms rationalize drug development activities, R&D spending often declines and programs are sometimes reduced and refocused. Smaller



Annals of Internal Medicine

IDEAS AND OPINIONS

Stop Predatory Publishers Now: Act Collaboratively

David Moher, PhD, and Ester Moher, PhD

Researchers trying to publish their work face a duality of tensions. To advance their careers, they must be productive and publish in journals with high impact factors. However, passing the scientific rigor of peer review and editorial approval in these journals makes publishing difficult. Morally corrupt businesses, posing as legitimate publishers, have moved into this space. They offer to publish anything quickly, thus circumventing the very fabric of scientific publishing. This cancer has spread rapidly in part because these publishers have no physical presence—instead, they conduct their ruse through illegitimate online journals. Unless these predatory publishers and journals are stopped immediately, they will permanently undermine the publication record.

There is no robust definition of predatory journals. They are best identified through behavior and practice: annoyingly high volumes of daily e-mails requesting submission of any type of manuscript, the promise of expedient peer review, and rapid publication. Predatory journals do not provide scientifically rigorous peer review; their feedback is rubbish. They also have dis-

Prospective authors need to be aware of the hazards of predatory journals and take the time to more fully assess the merits of submitting any manuscript to them. A previous assessment of these invitations (2) found that they can all be deleted; the Web sites can be added to personal and institutional e-mail filters and thus be blocked. Further, requests for submission should be viewed with caution. It is rare for a legitimate journal to send blanket requests for manuscript submission. An exception would be a personalized correspondence from a senior editor encouraging submission of a specific editorial, commentary, review, or research report.

Why have legitimate publishers not done more to combat their predatory counterparts? This is in stark contrast to their progressive collaborative action to create the CrossRef products (www.crossref.org). Similarly, editorial groups seem silent and have not proposed any plan to stop predatory journals. Yet, they used their bully pulpit to demand clinical trial registration, which similarly posed a threat to the quality of reported health research (3).

SEARCH

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Previous Congresses

Sixth International Congress on Peer Review and Biomedical Publication
The Sixth International Congress on Peer Review and Biomedical Publication was held September 10-12, 2009, in Vancouver, BC, Canada. As with the previous Congresses, our aim was to improve the quality and credibility of biomedical peer review and publication and to help advance the efficiency, effectiveness, and equitability of the dissemination of biomedical information throughout the world. Four hundred twenty-four participants from 32 countries attended the Congress.

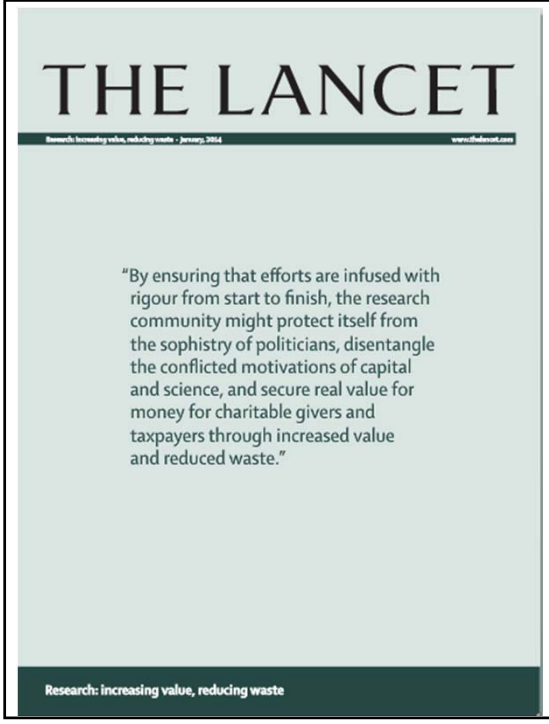
Previous Peer Review Congress Programs and Abstracts
Sixth Congress held September 2009 in Vancouver
Fifth Congress held September 2005 in Chicago
Fourth Congress held September 2001 in Barcelona
Third Congress held September 1997 in Prague

***JAMA* Peer Review Theme Issues**
Containing abstracts and articles from the Fourth, Third, and Second Peer Review Congresses.

June 5, 2002 Issue
July 15, 1998 Issue
July 13, 1994 Issue

Photos courtesy of Ted Grudzinski

The EQUATOR Network



"Our belief is that research funders, scientific societies, school and university teachers, professional medical associations, and scientific publishers (and their editors) can use this Series as an opportunity to examine more forensically why they are doing what they do...and whether they are getting the most value for the time and money invested in science."

Lancet series (2014) increasing value, reducing waste

- 7 articles
- 42 authors
- > 50 journal pages
- Several hundred references citing problems (and evidence) in the entire research process
  - From questions asked to how research is reported
- Clinical and preclinical research

Increasing value, reducing waste

- Series has 17 recommendations
- Targeted:
  - funders, government, journals, academic institutions, regulators, and researchers

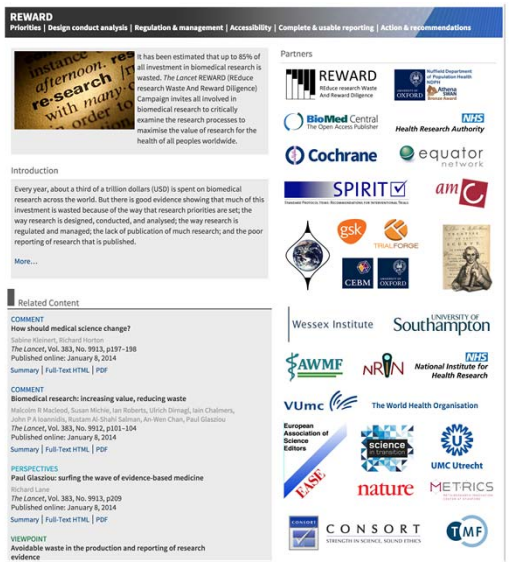
Recommendations and monitoring

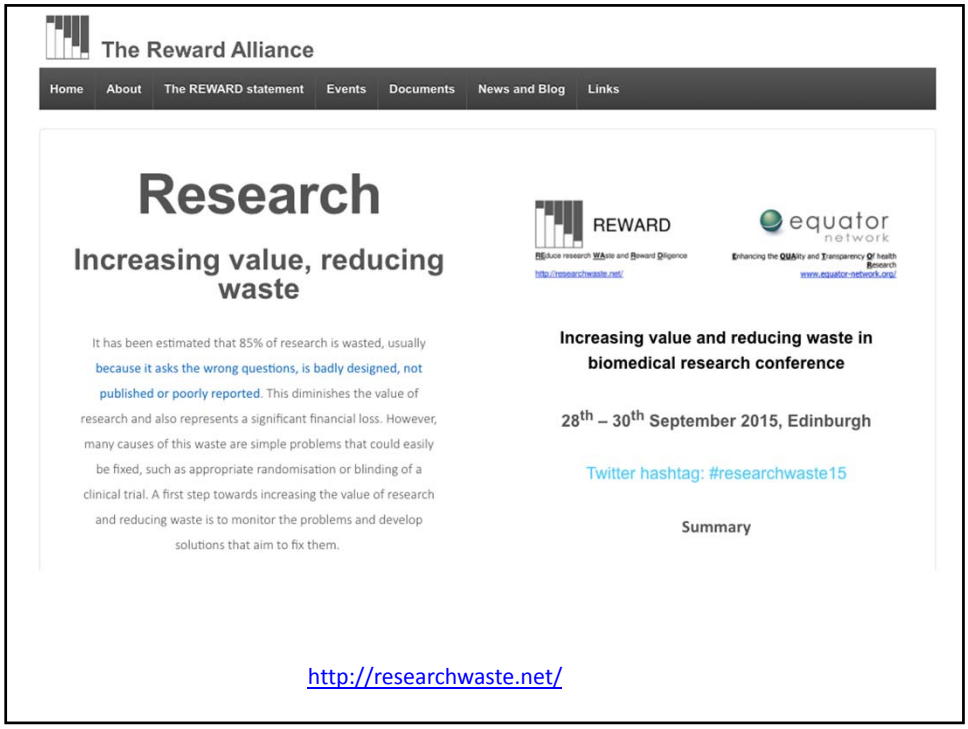
- Recommendation (3)
  - institutions and funders should adopt performance metrics that recognise full dissemination of research and reuse of original datasets by external researchers
- Monitor
  - assessment of the proportion of institutional and funding-agency policies that explicitly reward dissemination of study protocols, reports, and participant-level data
- Groups affected
  - HIRO, Altmetric, U15, CIHR, other national/regional funders

Recommendations and monitoring

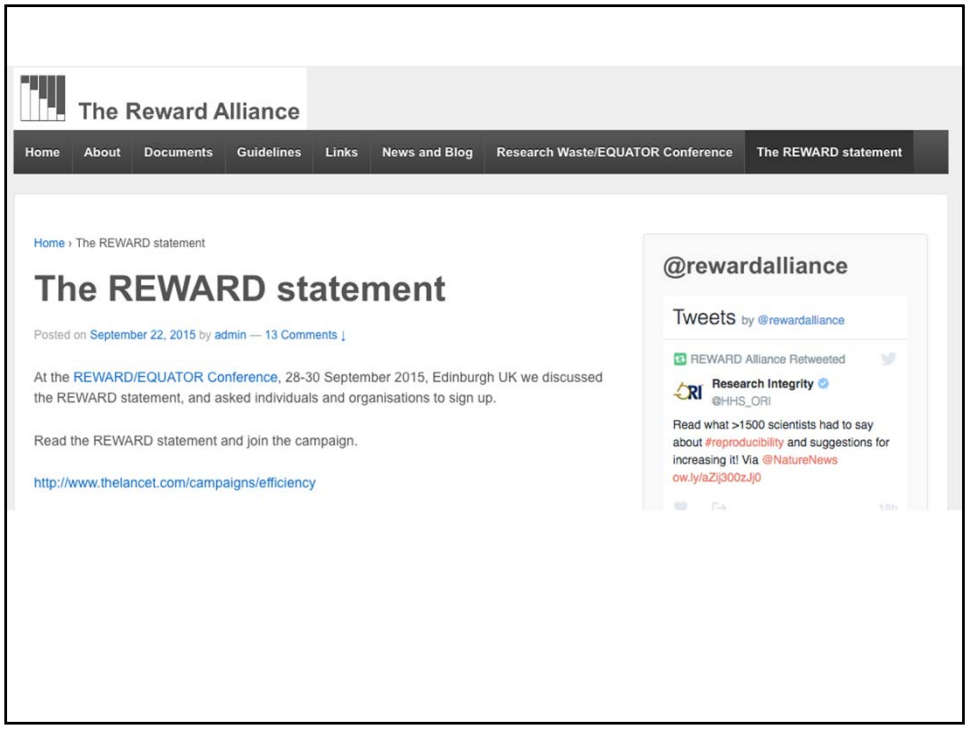
- Recommendation (5)
  - Make publicly available the full protocols, analysis plans or sequence of analytical choices, and raw data for all designed and undertaken biomedical research
- Monitoring
  - Proportion of reported studies with publicly available (ideally preregistered) protocol and analysis plans, and proportion with raw data and analytical algorithms publicly available within 6 months after publication of a study report
- Groups affected
  - HIRO, PROSPERO, PRISMA-P, SPIRIT, clinicaltrials.gov, ISRCTN, WHO platform

http://www.thelancet.com/campaigns/efficiency





http://researchwaste.net/



"WE RECOGNISE THAT, WHILE WE STRIVE FOR EXCELLENCE IN RESEARCH, THERE IS MUCH THAT NEEDS TO BE DONE TO REDUCE WASTE AND INCREASE THE VALUE OF OUR CONTRIBUTIONS. WE MAXIMISE OUR RESEARCH POTENTIAL WHEN:

- **WE SET THE RIGHT RESEARCH PRIORITIES;**
- **WE USE ROBUST RESEARCH DESIGN, CONDUCT AND ANALYSIS;**
- **REGULATION AND MANAGEMENT ARE PROPORTIONATE TO RISKS;**
- **ALL INFORMATION ON RESEARCH METHODS AND FINDINGS ARE ACCESSIBLE;**
- **REPORTS OF RESEARCH ARE COMPLETE AND USABLE.**

WE BELIEVE WE HAVE A RESPONSIBILITY NOT JUST TO SEEK TO ADVANCE KNOWLEDGE, BUT ALSO TO ADVANCE THE PRACTICE OF RESEARCH ITSELF. THIS WILL CONTRIBUTE TO IMPROVEMENT IN THE HEALTH AND LIVES OF ALL PEOPLES, EVERYWHERE. AS FUNDERS, REGULATORS, COMMERCIAL ORGANISATIONS, PUBLISHERS, EDITORS, RESEARCHERS, RESEARCH USERS AND OTHERS – WE COMMIT TO PLAYING OUR PART IN INCREASING VALUE AND REDUCING WASTE IN RESEARCH."

RESEARCH

Avoidable waste of research related to inadequate methods in clinical trials

Youri Yordanov,[1, 2] Agnes Dechartres,[1, 3, 4] Raphaël Porcher,[1, 3, 4] Isabelle Boutron,[1, 3, 4, 5] Douglas G Altman,[6] Philippe Ravaud[1, 3, 4, 5, 7]

[1]Centre de Recherche Epidémiologie et Statistique, INSERM U1153, Paris, France
[2]Service des Urgences, Hôpital Saint-Antoine, Assistance Publique-Hôpitaux de Paris, Paris, France
[3]Centre d'Epidémiologie Clinique, Hôpital Hôtel-Dieu, Assistance Publique-Hôpitaux de Paris, Paris, France
[4]Faculté de Médecine, Université Paris Descartes, Sorbonne Paris Cité, Paris, France
[5]French Cochrane Centre, Paris, France

ABSTRACT

OBJECTIVE
To assess the waste of research related to inadequate methods in trials included in Cochrane reviews and to examine to what extent this waste could be avoided. A secondary objective was to perform a simulation study to re-estimate this avoidable waste if all trials were adequately reported.

DESIGN
Methodological review and simulation study.

DATA SOURCES
Trials included in the meta-analysis of the primary outcome of Cochrane reviews published between April 2012 and March 2013.

high risk; in these, we identified 25 types of methodological problem. Adjustments were possible in 136 trials (96%). Easy adjustments with no or minor cost could be applied in 71 trials (50%), resulting in 17 trials (12%) changing to low risk for all domains. So the avoidable waste represented 12% (95% CI 7% to 18%) of trials with at least one domain at high risk. After correcting for incomplete reporting, avoidable waste due to inadequate methods was estimated at 42% (95% CI 36% to 49%).

CONCLUSIONS
An important burden of wasted research is related to inadequate methods. This waste could be partly avoided by simple and inexpensive adjustments.

Barnes *et al. BMC Medicine* (2015) 13:221
DOI 10.1186/s12916-015-0460-y

BMC Medicine

RESEARCH ARTICLE Open Access

Impact of an online writing aid tool for writing a randomized trial report: the COBWEB (Consort-based WEB tool) randomized controlled trial

Caroline Barnes[2,3], Isabelle Boutron[1,2,3*], Bruno Giraudeau[3,4], Raphael Porcher[1,2,3], Douglas G Altman[5] and Philippe Ravaud[1,2,3,6]

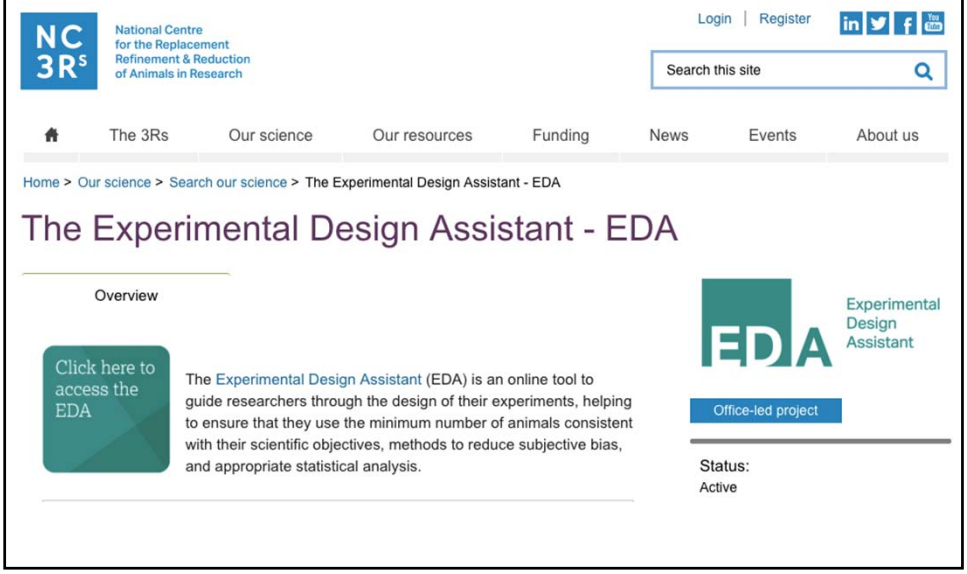
Abstract

Background: Incomplete reporting is a frequent waste in research. Our aim was to evaluate the impact of a writing aid tool (WAT) based on the CONSORT statement and its extension for non-pharmacologic treatments on the completeness of reporting of randomized controlled trials (RCTs).

Methods: We performed a 'split-manuscript' RCT with blinded outcome assessment. Participants were masters and doctoral students in public health. They were asked to write, over a 4-hour period, the methods section of a manuscript based on a real RCT protocol, with a different protocol provided to each participant. Methods sections were divided into six different domains: 'trial design', 'randomization', 'blinding', 'participants', 'interventions', and 'outcomes'. Participants had to draft all six domains with access to the WAT for a random three of six domains. The random sequence was computer-generated and concealed. For each domain, the WAT comprised reminders of the corresponding CONSORT item(s), bullet points detailing all the key elements to be reported, and examples of good reporting. The control intervention consisted of no reminders. The primary outcome was the mean global score for completeness of reporting (scale 0–10) for all domains written with or without the WAT.

Results: Forty-one participants wrote 41 different manuscripts of RCT methods sections, corresponding to 246

Experimental design assistant: https://eda.nc3rs.org.uk/



MiRoRMethods in Research on Research

MiRoR

Joint doctoral training programme, dedicated to **Methods in Research on Research** in the field of clinical research (http://miror-ejd.eu)

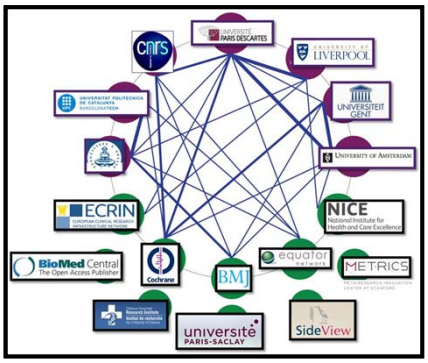
Goal

To train **15 PhD students** to become the future generation of high-level scientists to develop innovative methods of Research on Research

Funding

Marie Skłodowska-Curie Actions -Innovative Training Networks (ITN) - European Joint doctorate (EJD)

7 European Universities and 10 International Partners



MiRoR Methods in Research on Research

Who's listening to the Lancet's series?

Moher D, et al. Lancet 2016 Apr 9;387(10027):1573-86

Do we need an observatory to monitor change over time?

Review

Increasing value and reducing waste in biomedical research: who's listening?

David Moher, Paul Glasziou, Iain Chalmers, Mona Nasser, Patrick M M Bossuyt, Daniël A Korevaar, Ian D Graham, Philippe Ravaud, Isabelle Boutron

The biomedical research complex has been estimated to consume almost a quarter of a trillion US dollars every year. Unfortunately, evidence suggests that a high proportion of this sum is avoidably wasted. In 2014, *The Lancet* published a series of five reviews showing how dividends from the investment in research might be increased from the relevance and priorities of the questions being asked, to how the research is designed, conducted, and reported. 17 recommendations were addressed to five main stakeholders—funders, regulators, journals, academic institutions, and researchers. This Review provides some initial observations on the possible effects of the Series, which seems to have provoked several important discussions and is on the agendas of several key players. Some examples of individual initiatives show ways to reduce waste and increase value in biomedical research. This momentum will probably move strongly across stakeholder groups, if collaborative relationships evolve between key players; further important work is needed to increase research value. A forthcoming meeting in Edinburgh, UK, will provide an initial forum within which to foster the collaboration needed.

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Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada (D Moher PhD, Prof I D Graham PhD); **School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, ON, Ottawa, Canada** (D Moher, Prof I D Graham); **Centre for**

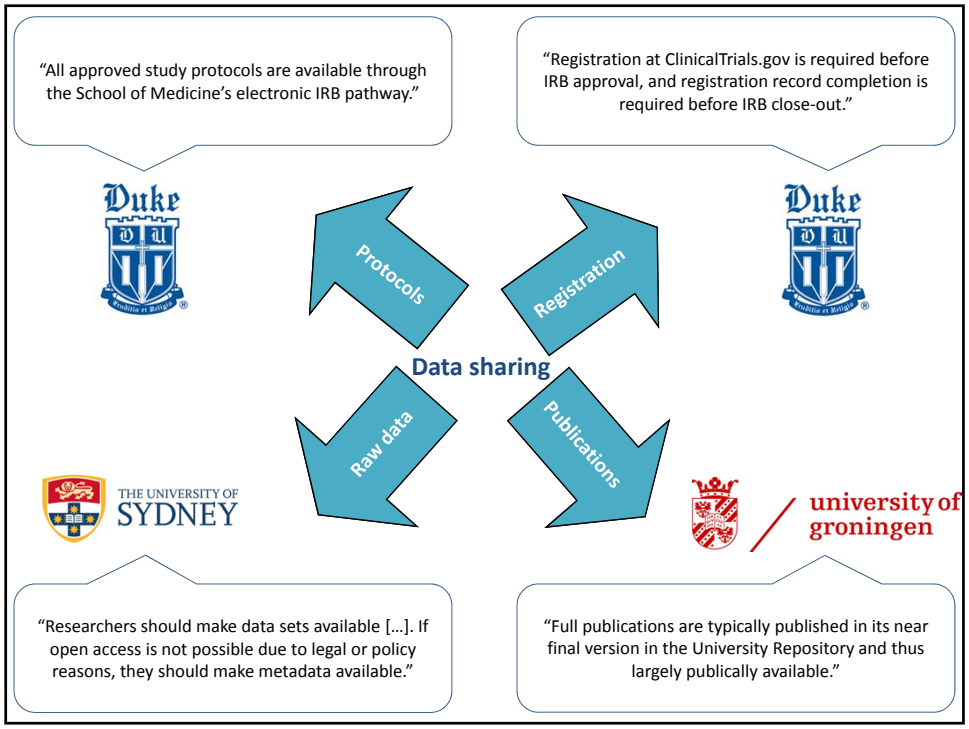
"… to have provoked several important discussions and is on the agendas of several key players. Some examples of individual initiatives show ways to reduce waste and increase value in biomedical research"

Initial overview assessment of series

- Academic institutions
  - top 100 universities from the *Times Higher Education* World University Rankings 2013-2014
- Funders
  - searched the websites of six major funders and examined documents such as instructions to funding applicants.
- Journals
  - 119 core clinical journals included in Medline's Abridged Index Medicus
  - Interviewed editors-in-chief; editorial editor
- Researchers
  - list of influential researchers (Boyack et al. Eur J Clin Invest. 2013 Dec;43(12):1339-65).

Methods and Results

- Academic institutions
- Deans and directors of research of the medical schools of the top 100 universities from the *Times Higher Education* World University Rankings 2013-2014 were invited to participate in a five-question email survey
- 26% response rate

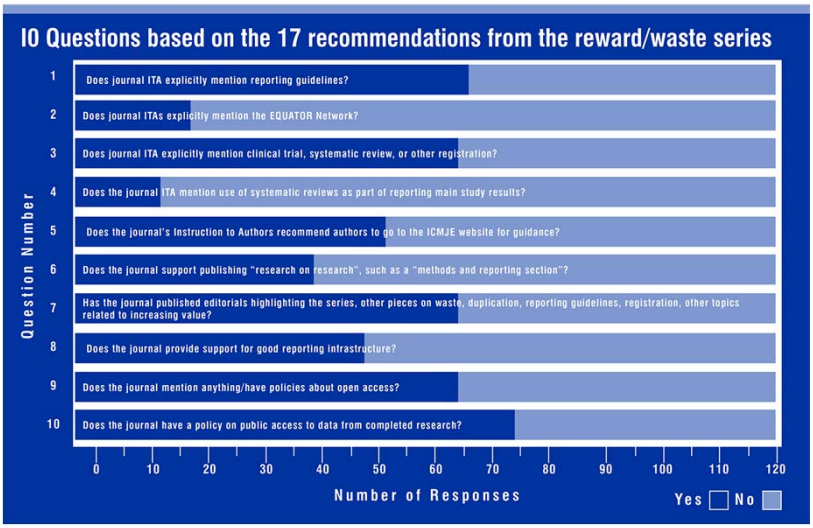


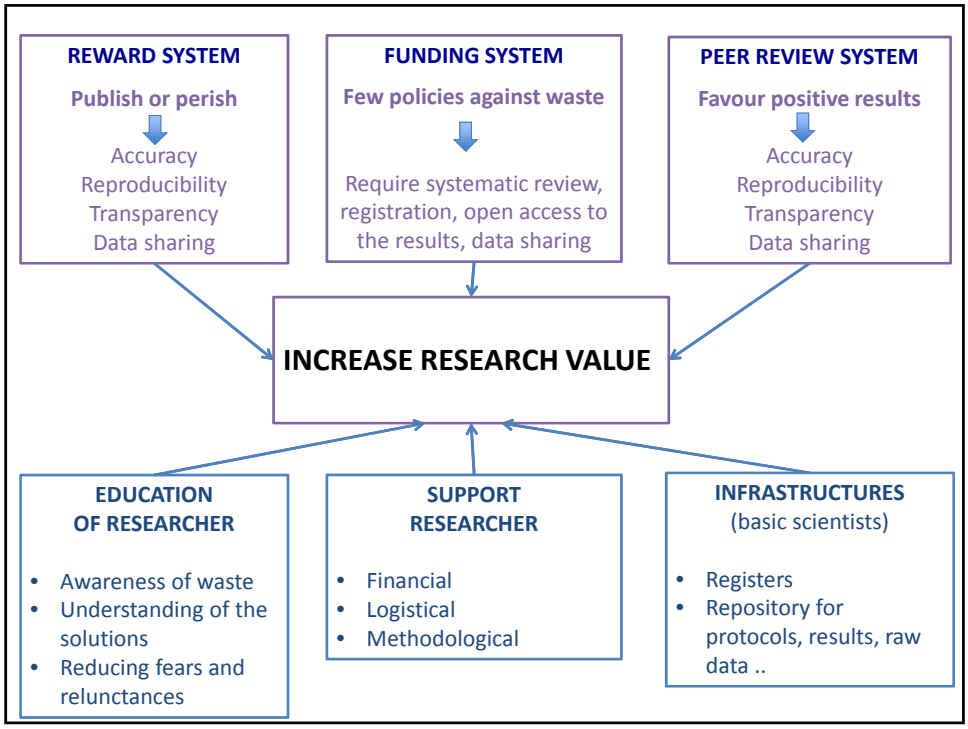
Results, examined 6 research funders

	Public /patient involved in decision?	Use SR to inform decision	Require prior registration of research	Public access to protocol of research
NIHR (England)	Strong	For any studies	For clinical trial and other studies	Yes – for HTA programme
MRC (UK)	Limited / Selective	For clinical trials	For clinical trials	No
NHMRC (Australia)	Limited / Selective	No	For clinical trials	No
NIH (USA)	Moderate	No	For clinical trials	No
CIHR (Canada)	Limited / Selective	No	For clinical trials	No
DFG (Germany)	Limited / Selective	For clinical trials	For clinical trials	No

THE JOURNALS' STORY

Examined core clinical journals included in Medline's Abridged Index Medicus.





Researchers (Authors)

- Most researchers agreed that the series was important to increase research value
- However, basic scientists and clinical researchers had notably different perceptions of the concept of waste in research
  - eg, "[…] to state that 85% of research funding is wasted is an insult to current research efforts"; "There is no […] waste in pure, basic science
  - "In basic science, there is a great need for flexibility to modify the protocol in response to the latest finding. Too rigorous control on the planning of experiments would simply kill the last nerve in basic research"; "Research is not a car factory"

Example, journals

- A 2012 survey of journals' instructions to peer reviewers shows that reference to or recommendations to use reporting guidelines during peer review was rare (19 of 116 journals assessed; 16%).
  - Positive incremental change could be observing at least a 10% improvement in guidance to peer reviewers in the 116 journals initially surveyed.

Hirst A, Altman DG. PLoS One. 2012;7(4):e35621.

http://compare-trials.org/

67	9	301	357
TRIALS CHECKED TO DATE	TRIALS WERE PERFECT	OUTCOMES NOT REPORTED	NEW OUTCOMES SILENTLY ADDED

)n average, each trial reported just 62.0% of its specified outcomes. And on average, each trial ilently added 5.3 new outcomes.

58	6	31	16
LETTERS SENT	LETTERS PUBLISHED	LETTERS UNPUBLISHED AFTER 4 WEEKS	LETTERS REJECTED BY EDITOR

5th World Conference on Research Integrity

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ESSAY

Four Proposals to Help Improve the Medical Research Literature

David Moher[1]*, Douglas G. Altman[2]

1 Clinical Epidemiology Program, Ottawa Hospital Research Institute; School of Epidemiology, Public Health and Preventive Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada, **2** Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

* dmoher@ohri.ca

Summary Points

- The evidence base underpinning clinical practice is deeply flawed.
- There must be better value gained from resources invested in medical research.
- We make four proposals: (1) introducing publications officers; (2) developing core competencies for editors and peer reviewers, around which (3) training can be tailored; and (4) training authors to write articles fit for purpose.
- All of these ideas need to be piloted and evaluated, and implemented if proven effective.
- We suggest dedicated funding for initiatives aimed at understanding and improving the way that research is conducted and published.
- Academic institutions, funders, publishers, and others should support and implement effective processes to improve the reliability of the medical research literature.

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Citation: Moher D, Altman DG (2015) Four Proposals to Help Improve the Medical Research Literature. PLoS Med 12(9): e1001864. doi:10.1371/journal.pmed.1001864

Published: September 22, 2015

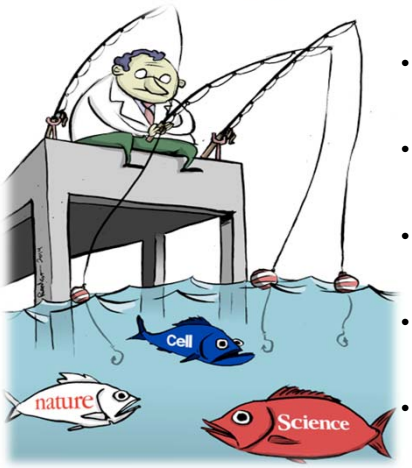
- Publications officer
- Core competencies for editors and peer reviewers
- Training authors

Introducing the Publications Officer

- Why hire a Publications Officer?
  - Responsibilities of authorship, metrics, research integrity, publication ethics, and publishing landscape are (apparently) learned on the job.
  - No formal training on how to write manuscripts exists within the vast majority of universities and research institutions
  - Mountains of evidence that reporting quality of research is very poor in both clinical and pre-clinical research.

Publications Officer Remit

- Provide support at the back end of research



- Educate personnel on publication models, including the variety of open access formats
- Promote and facilitate the use of reporting guidelines
- Assist researchers with other aspects of the journal submission process
- Facilitate regular rounds presentations to educate on topics related to journalology
- Meet one-on-one to discuss publication topics

Further emphasis on research in context

The Lancet asked authors in July, 2005, to present their clinical trials within the context of previous research findings and to explain how their findings affect the summary of evidence.[1] 5 years later, Michael Clarke and colleagues[2] assessed how five major general medical journals (*Annals of Internal Medicine, BMJ, JAMA, The Lancet,* and *The New England Journal of Medicine*) had implemented a CONSORT requirement[3] requesting authors to take into account the totality of evidence when reporting trial data. The answer was that progress has been painfully slow or

www.thelancet.com Vol 384 December 20/27, 2014

"Editors will use this information at the first assessment stage"

Comment

ıt. As a response, in 2010, we introduced a more earch in context panel, required for all research rt from systematic reviews and meta-analyses, ussion section with the headings: Systematic ł Interpretation.[4] In reality, these panels are ded at a late stage in the peer-review process ntly inadequate with the Interpretation section ating the research findings.

ıry, 2014, Iain Chalmers, John Ioannidis, Shahi Salman, An-Wen Chan, and Paul Glasziou nark *Lancet* Series on *Research: increasing value, ıste*,[5–9] which grew out of an earlier Viewpoint[10] ghted how a substantial proportion of research sted and that this waste is eminently avoidable. authors made wide-reaching recommendations

Panel: **Research in context**

Evidence before this study
This section should include a description of all the evidence that the authors considered before undertaking this study. Authors should state: the sources (databases, journal or book reference lists, etc) searched; the criteria used to include or exclude studies (including the exact start and end dates of the search), which should not be limited to English language publications; the search terms used; the quality (risk of bias) of that evidence; and the pooled estimate derived from meta-analysis of the evidence, if appropriate.

Added value of this study
Authors should describe here how their findings add value to the existing evidence (including an updated meta-analysis, if appropriate).

Implications of all the available evidence
Authors should state the implications for practice or policy and future research of their study combined with existing evidence.

Kleinert S, Benham L, Collingridge D, Summerskill W, Horton R. Further emphasis on research in context. Lancet 2014; 384: 2176–77.

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Archives of Physical Medicine and Rehabilitation
journal homepage: www.archives-pmr.org
Archives of Physical Medicine and Rehabilitation 2014;95:415-7

EDITORIAL

Elevating the Quality of Disability and Rehabilitation Research: Mandatory Use of the Reporting Guidelines

With the remarkable growth of disability- and rehabilitation-related research in the last decade, it is imperative that we support the highest quality research possible. With cuts in research funding, rehabilitation research is now under a microscope like never before, and it is critical that we put our best foot forward.

To ensure the quality of the disability and rehabilitation research that is published, the 28 rehabilitation journals simultaneously publishing this editorial (see acknowledgments) have agreed to take a more aggressive stance on the use of reporting guidelines.* Research reports must contain sufficient information to allow readers to understand how a study was designed and conducted, including variable definitions, instruments and other measures, and analytical techniques.[1] For review articles, systematic or narrative, readers should be informed of the rationale and details behind the literature search strategy. Too often articles fail to include their standard for inclusion and their criteria for evaluating quality of the studies.[2] As noted by Doug Altman, co-originator of the Consolidated Standards of Reporting Trials (CONSORT) statement and head of the Centre for Statistics in Medicine at Oxford University: "Good reporting is not an optional extra; it is an essential component of good research…we all share this obligation and responsibility."[3]

What are Reporting Guidelines?

Reporting guidelines are documents that assist authors in reporting research methods and findings. They are typically presented as checklists or flow diagrams that lay out the core reporting criteria required to give a clear account of a study's methods and results. The intent is not just that authors complete a specific reporting checklist but that they ensure that their articles contain key elements. Reporting guidelines should not be seen as an administrative burden; rather, they are a template by which an author can construct their articles more completely.

Reporting guidelines have been developed for almost every study design. More information on the design, use, and array of reporting guidelines can be found on the website for the Enhancing the Quality and Transparency of Health Research (EQUATOR) network,[4] an important organization that promotes improvements in the accuracy and comprehensiveness of reporting. Examples include the following:

(1) CONSORT for randomized controlled trials (www.consort-statement.org);
(2) Strengthening the Reporting of Observational studies in Epidemiology (STROBE) for observational studies (http://strobe-statement.org/);
(3) Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for systematic reviews and meta-analyses (www.prisma-statement.org/);
(4) Standards for the Reporting of Diagnostic accuracy studies (STARD) for studies of diagnostic accuracy (www.stard-statement.org/); and
(5) Case Reports (CARE) for case reports (www.care-statement.org/).

There is accumulating evidence that the use of reporting guidelines improves the quality of research. Turner et al[5] established that the use of the CONSORT statement improved the completeness of reporting in randomized controlled trials. Diagnostic accuracy studies appeared to show improvement in reporting standards when the STARD guidelines were applied.[6] Early evidence also suggests that inclusion of reporting standards during peer review raises manuscript quality.[7] The International Committee of Medical Journal Editors now encourages all journals to monitor reporting standards and collect associated reporting guideline checklists in the process.[8] Furthermore, the National Library of Medicine also now actively promotes the use of reporting guidelines.[9]

How will Reporting Guidelines be Integrated Into Manuscript Flow?

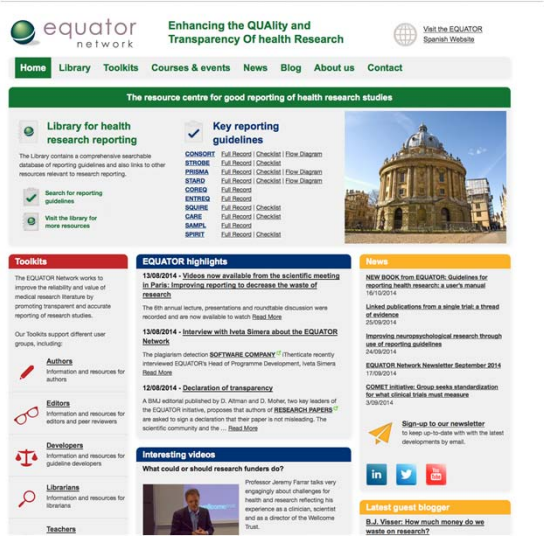
By January 1, 2015, all of the journals publishing this editorial will have worked through implementation and the mandatory use of guidelines and checklists will be firmly in place. Because each journal has its unique system for managing submissions, there may be several ways that these reporting requirements will be integrated into the manuscript flow. Some journals will make adherence to reporting criteria and associated checklists mandatory for all submissions. Other journals may require them only when the article is closer to acceptance for publication. In any case, the onus will be on the author not only to ensure the inclusion of the appropriate reporting criteria but also to document evidence of inclusion through the use of the reporting guideline checklists. Authors should consult the Instructions for Authors of participating journals for more information.

An audio podcast accompanies this article.
Listen at www.archives-pmr.org.

* Physical Therapy, the Journal of Orthopaedic & Sports Physical Therapy, the Journal of Physiotherapy, and the European Journal of Physical and Rehabilitation Medicine have already successfully required reporting guidelines, one for as many as 10 years.

http://dx.doi.org/10.1016/j.apmr.2013.12.010

How to use reporting guidelines optimally



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Low technology solutions to writing research

RESEARCH ARTICLE Open Access

Impact of an online writing aid tool for writing a randomized trial report: the COBWEB (Consort-based WEB tool) randomized controlled trial

Caroline Barnes[2,3], Isabelle Boutron[1,2,3*], Bruno Giraudeau[3,4], Raphael Porcher[1,2,3], Douglas G Altman[5] and Philippe Ravaud[1,2,3,6]

Abstract

Background: Incomplete reporting is a frequent waste in research. Our aim was to evaluate the impact of a writing aid tool (WAT) based on the CONSORT statement and its extension for non-pharmacologic treatments on the completeness of reporting of randomized controlled trials (RCTs).

Methods: We performed a 'split-manuscript' RCT with blinded outcome assessment. Participants were masters and doctoral students in public health. They were asked to write, over a 4-hour period, the methods section of a manuscript based on a real RCT protocol, with a different protocol provided to each participant. Methods sections were divided into six different domains: 'trial design', 'randomization', 'blinding', 'participants', 'interventions', and 'outcomes'. Participants had to draft all six domains with access to the WAT for a random three of six domains. The random sequence was computer-generated and concealed. For each domain, the WAT comprised reminders of the corresponding CONSORT item(s), bullet points detailing all the key elements to be reported, and examples of good reporting. The control intervention consisted of no reminders. The primary outcome was the mean global score for completeness of reporting (scale 0–10) for all domains written with or without the WAT.

Results: Forty-one participants wrote 41 different manuscripts of RCT methods sections, corresponding to 246

Avoid submissions to predatory journals

'Predatory' open access: a longitudinal study of article volumes and market characteristics

Cenyu Shen* and Bo-Christer Björk

Abstract

Background: A negative consequence of the rapid growth of scholarly open access publishing funded by article processing charges is the emergence of publishers and journals with highly questionable marketing and peer review practices. These so-called predatory publishers are causing unfounded negative publicity for open access publishing in general. Reports about this branch of e-business have so far mainly concentrated on exposing lacking peer review and scandals involving publishers and journals. There is a lack of comprehensive studies about several aspects of this phenomenon, including extent and regional distribution.

Methods: After an initial scan of all predatory publishers and journals included in the so-called Beall's list, a sample of 613 journals was constructed using a stratified sampling method from the total of over 11,000 journals identified. Information about the subject field, country of publisher, article processing charge and article volumes published between 2010 and 2014 were manually collected from the journal websites. For a subset of journals, individual articles were sampled in order to study the country affiliation of authors and the publication delays.

Results: Over the studied period, predatory journals have rapidly increased their publication volumes from 53,000 in 2010 to an estimated 420,000 articles in 2014, published by around 8,000 active journals. Early on, publishers with more than 100 journals dominated the market, but since 2012 publishers in the 10–99 journal size category have captured the largest market share. The regional distribution of both the publisher's country and authorship is highly

How to prepare articles for data sharing

- Coming very soon to a journal near you
- Developing guidance and policy

thebmj

BMJ 2014;349:g6870 doi: 10.1136/bmj.g6870 (Published 9 December 2014) Page 1 of 15

RESEARCH

Discontinuation and non-publication of surgical randomised controlled trials: observational study

OPEN ACCESS

Stephen J Chapman *academic foundation trainee*[1], Bryony Shelton *medical student*[2], Humza Mahmood *medical student*[3], J Edward Fitzgerald *general surgery registrar*[4], Ewen M Harrison *senior lecturer in general surgery*[5], Aneel Bhangu *clinical lecturer in colorectal surgery*[3]

OPEN ACCESS Freely available online PLOS BIOLOGY

Publication Bias in Reports of Animal Stroke Studies Leads to Major Overstatement of Efficacy

Emily S. Sena[1,2,3], H. Bart van der Worp[4], Philip M. W. Bath[5], David W. Howells[2,3], Malcolm R. Macleod[1,4]*

Abstract

The consolidation of scientific knowledge proceeds through the interpretation and then distillation of data presented in research reports, first in review articles and then in textbooks and undergraduate courses, until truths become accepted as such both amongst "experts" and in the public understanding. Where data are collected but remain unpublished, they cannot contribute to this distillation of knowledge. If these unpublished data differ substantially from published work, conclusions may not reflect adequately the underlying biological effects being described. The existence and any impact of such "publication bias" in the laboratory sciences have not been described. Using the CAMARADES (Collaborative Approach to Meta-analysis and Review of Animal Data in Experimental Studies) database we identified 16 systematic reviews of interventions tested in animal studies of acute ischaemic stroke involving 525 unique publications. Only ten publications (2%) reported no significant effects on infarct volume and only six (1.2%) did not report at least one significant finding. Egger regression and trim-and-fill analysis suggested that publication bias was highly prevalent (present in the literature for 16 and ten interventions, respectively) in animal studies modelling stroke. Trim-and-fill analysis suggested that publication bias might account for around one-third of the efficacy reported in systematic reviews, with reported efficacy falling from 31.3% to 23.8% after adjustment for publication bias. We estimate that a further 214 experiments (in addition to the 1,359 identified through rigorous systematic review; non publication rate 14%) have been conducted but not reported. It is probable that publication bias has an important impact in other animal disease models, and more broadly in the life sciences.

- Developing guidance for greater use of institutional open access repositories

Core competency training for editors

- All is not well with biomedical journal editors
- Do scientific editors know what they are doing?
  - What is published has been approved by editors
  - COMPARE project
    - Parasites
    - Changing primary outcomes without attribution
    - Little institutional history of CONSORT endorsement
    - Little understanding of CONSORT
  - WAME listserv
  - A trial result

Core competency training for peer reviewers

- Peer review is very expensive
  - More than $3 billions dollars, annually
  - Spend more than 15 millions hours, annually
- Almost all peer reviewers complete peer review without any formal training and not certified
- Not the optimal way to instil confidence in readers, provide value for money to funders, or ensure patients can trust the research record
- Develop a comprehensive program to identify core competencies
- Tailor training to the core competencies

Training authors

- Promote formal training in writing as part of university training
  - Writing
  - Train authors to use reporting guidelines
  - Declaration of Transparency
  - Research integrity

HOW BEST TO REWARD BIOMEDICAL RESEARCHERS

Thank you☺