Can we trust medical research literature?

Poor reporting and its consequences

Iveta Simera
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Disclosure

- Deputy Director, UK EQUATOR Centre
- EQUATOR is funded by grants from the UK NIHR, MRC, CSO, and PAHO
- My salary is fully paid from the EQUATOR programme grants
- No paid consultation for industry
- Workshops & seminars for journals

- Co-editor in Chief, Research Integrity and Peer Review (published by BiomedCentral)
• Still a key vehicle for communicating research findings

• Scientific manuscripts should present sufficient data so that the reader can
  - Fully evaluate the information
  - Reach his or her own conclusions about methods and results (their reliability and relevance)
How well are users’ needs satisfied?

- Focus on reliability and usability
The systematic review process

- Should be based on a protocol

- Key steps:
  - Formulation of a clear question
  - Eligibility criteria for studies
  - Search for potentially relevant studies
  - Selection of studies into the review
  - Extraction of data
  - Assessment of methodological quality of included studies (risk of bias)
  - Synthesis of findings (possibly using meta-analysis)
  - Presentation of data and results
  - Interpretation and drawing conclusions
Search for relevant studies

- Is all research published?
- Non-publication of research is very common
  - Failure to publish a report of a completed study (even if presented at a conference)
  - Large number of studies investigating publication bias

*BMJ 2013:*
585 large RCTs
Registered on Clinicaltrials.gov
Completed before 2009

Search in Nov 2012:
171 (29%) unpublished
(almost 300k participants)
- 138 (78%) no results available on clintrials.gov
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SERIOUS problem: Non-publication of research
Selection of studies

- Eligibility criteria – population, intervention, etc.

- Hoffmann et al, BMJ 2013;347:f3755
  - 133 RCT of NPI published in 2009 in 6 gen med j
  - Only 53/137 (39%) interventions were adequately described
Selection of studies

- Eligibility criteria – population, intervention, etc.

**SERIOUS problem:** Poor description of interventions

- Hoffmann et al, BMJ 2013;347:f3755
- 133 RCT of NPI published in 2009 in 6 gen med j
- Only 53/137 (39%) interventions were adequately described
Assessing risk of bias

A critical element of a systematic review

- Risk of bias results from suboptimal methods
- Methods need to be reported well to allow assessment of risk of bias

![Risk of bias assessment table](image-url)
A critical element of a systematic review is assessing risk of bias. This involves:

- Risk of bias results from suboptimal methods.
- Methods need to be reported well to allow assessment of risk of bias.

SERIOUS problem:

Unclear description of methods.
• 443 screened articles (included 29 in the review)
  – “Approximately 29 % of screened articles were excluded because they did not have means and standard deviations of diet in each group at baseline and post-intervention available” approx. 150 papers
Poor reporting of adverse effects

78 SR of RCTs of gastroenterology interventions 2008-2012:
- 26 (33%) did not refer to harms of the intervention anywhere in the article
- AE data presented in result section frequently misrepresented in the discussion:
  - Results: “adverse events were not well reported”
  - Discussion: “adverse events are minimal and the risk benefit ration is good”
Poor reporting of adverse effects

SERIOUS problem:

Poor reporting of data
Reporting deficiencies – a big problem for systematic reviews

- Formulation of a clear question
- Eligibility criteria for studies
- **Search** for potentially relevant studies
- **Selection** of studies into the review
- **Extraction of data**
- Assessment of methodological quality of included studies (**risk of bias**)
- **Synthesis** of findings (possibly using meta-analysis)
- Presentation of data and results
- Interpretation and drawing conclusions
Deficiencies in research literature

- Non-reporting (or delayed reporting) of whole studies
- Incomplete reporting
- Selective reporting
- Misleading reporting

All of these are very common!
**Exercise prescription: a case for standardised reporting**

Susan Carolyn Slade, Jennifer Lyn Keating

**ABSTRACT**

**Background**: Structured, regular exercise is recommended to improve health outcomes. Exercise takes many forms and varies in type, intensity, duration and frequency. The authors used the example of exercise for chronic health conditions to examine how these programmes are described and summarised in systematic reviews.

**Methods**: Two independent reviewers conducted a review of exercise reporting practices using the exercise effects for chronic conditions as the primary material. Inclusion criteria: systematic reviews summarised the effects of exercise programmes for chronic health conditions. Exclusion criteria: review, non-human studies, reports of exercise effects for chronic conditions.

**Results**: Only 16 of 41 RCTs published after 2000 examined the effects of exercise programmes for chronic health conditions. Only 6 of these RCTs reported exercise outcomes in a standardised manner. The remaining 10 RCTs reported exercise outcomes using a variety of measures.

**Conclusion**: Exercise is beneficial for people with cystic fibrosis, chronic obstructive pulmonary disease, intermittent claudication, knee osteoarthritis and low back pain.

Exercise is a non-specific term. It includes activities that vary in type, frequency, intensity, mode and environmental requirements. It may be conceptualised as a series of specific movements to train or develop the body with routine practice or as any kind of physical training to promote physical health. Exercise can vary with respect to the type of muscle contraction, load, speed and range of movement, number of repetitions and sets, order of exercises and rest times. It is used to improve these cells or organs, the selection of an intervention.

**An appeal to medical journal editors: the need for a full description of laboratory methods and specimen handling in clinical study reports**


**Adequacy of Published Oncology Randomized Controlled Trials to Provide Therapeutic Details Needed for Clinical Application**

Jennifer M. Duff, Helen Leather, Edmund O. Waldman, Kourtney D. LaPlant, Thomas J. George Jr.

Manuscript received July 9, 2009; revised March 15, 2010; accepted March 16, 2010.

Correspondence to: Thomas J. George Jr, MD, FACP, Division of Hematology-Oncology, Department of Medicine, University of Florida, PO Box 102270, Gainesville, FL 32610-2270; e-mail: tjohoran@ucf.edu.

Background: Randomized controlled trials (RCTs) improve clinical care through evidence-based practice, but specific details of therapeutic administration are not always available. The Adequate Description (AD) criteria were developed to assess the reporting methodology in RCTs to ensure that readers have access to the treatment elements necessary for replication of the trial design. We assessed the reporting methodology in RCTs published in the New England Journal of Medicine (NEJM), Journal of Clinical Oncology (JCO), Journal of the National Cancer Institute (JNCI), and the Journal of Clinical Oncology (JCOC) in 2005 and 2006.

Methods: Ten essential elements of RCT reporting were identified and included in the AD criteria. These elements included the maximum number of cycles, indications, treatment administration, patient characteristics, follow-up, and adverse events.

Results: Of the 103 RCTs, 77% did not substantially report all 10 elements. The most common missing elements were (1) indications (83%), (2) patient characteristics (82%), and (3) adverse events (80%).

Discussion: These findings suggest that RCTs published in these journals do not provide adequate therapeutic details.

**Publication Bias in Antipsychotic Trials: A Systematic Review of Efficacy Comparing the Published Literature with the Food and Drug Administration Database**

Lee Shapley

Received 5 February 2009; returned 3 April 2009; revised 20 April 2009

Objective: Our objectives were to systematically assess the quality of (AERs) in publications of trials of highly active antiretroviral therapy (HAART) and to examine whether reporting quality affects the effect estimates reported for treatment outcomes.

**Methods**: We searched the PubMed, Cochrane library and EMBASE databases. We included all published randomized controlled trials of HAART.

**Results**: Forty-nine trials, including 19,982 patients, published between 1996 and 2007, were included in the analysis. There was no evidence of publication bias in the 10 trials included in the analysis. The extracted effect sizes were heterogeneous, which is consistent with the wide range of effect sizes reported in the literature.

**Conclusion**: The results of this systematic review suggest that publication bias may not be a significant factor in the reporting of treatment outcomes in randomized controlled trials of HAART.

**Electronic search strategies to identify reports of cluster randomized trials in MEDLINE: low precision will improve with adherence to reporting standards**

Monica Taljaard, Jessie McGowan, Jeremy M Grimshaw, Jamie C Brehaut, Andrew McRae, Martin P Eccles, Alan Donner

Objective: To identify reports of cluster randomized trials (CRTs) in MEDLINE.

**Methods**: We searched MEDLINE for reports of CRTs using a combination of keywords and controlled vocabulary. We also searched for reports of CRTs using a combination of keywords and controlled vocabulary.

**Results**: We identified 18 reports of CRTs in MEDLINE. The precision of the search was low, with many false positives and a high rate of false negatives. The precision of the search improved when adherence to reporting standards was achieved.

**Conclusion**: Electronic search strategies to identify reports of CRTs in MEDLINE are not yet robust. However, with adherence to reporting standards, the precision of these searches will improve.
Fixing medical research literature

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<th>Non-reporting (or delayed reporting) of whole studies:</th>
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<td>- Often studies with ‘disappointing’ results</td>
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<th>Incomplete reporting:</th>
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<tr>
<td>- Omission of crucial aspects of research methods (study participants, interventions, randomization in trials, etc.)</td>
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<td>- Incomplete results: data cannot be included in meta-analysis</td>
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<td>- Inadequate reporting of harms</td>
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<th>Selective reporting:</th>
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<tr>
<td>- Outcomes</td>
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<td>- Analyses (e.g. subgroups, alternative analyses)</td>
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<th>Misleading reporting:</th>
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<td>- Misinterpretation of study findings “spin” (e.g. presenting study in more positive way; discrepancies between abstract and full text, etc.)</td>
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<td>- Misrepresentation of study design (e.g. study claiming it is an RCT when it is not)</td>
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<td>- Unacknowledged discrepancies between sources of information (publication conflicts with study protocol or information in the trial register)</td>
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No single (or simple) solution
Possible solutions