Why we need high-quality reporting of clinical trials

Doug Altman

The EQUATOR Network

Centre for Statistics in Medicine, Oxford, UK

Research and publication

- **Medical research should advance scientific knowledge and – directly or indirectly – lead to improvements in treatment or prevention of disease**

- **If research is not published it might as well not have been done**
  - Implications for *access* to research

- **A research report is the only tangible evidence that the study was done**

The impact of a research article

- **Scientific manuscripts should present sufficient data so that the reader can fully evaluate the information and reach his or her own conclusions about results**
  - to assess reliability and relevance
- **Readers need a clear understanding of exactly what was done**
  - Clinicians
    - To learn how to treat their patients better
  - Researchers
    - To judge the truth of the findings (impact on own research)
    - To help plan a similar study
    - To include the study in a systematic review (meta-analysis)

What should be reported?

Methods

- **All key aspects of how the study was done**
  - "Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results."

    [International Committee of Medical Journal Editors]
- **Same principle should apply to all aspects of methodology**

Results

- **Main findings (corresponding to pre-specified plan)**

What do we mean by poor reporting?

Mainly

- **Key information is missing, incomplete or ambiguous**
  - Methods
  - Findings

Also

- **Selective reporting**
- **Misleading interpretation**
- **etc**

Evidence of poor reporting

- **There is considerable evidence that many published articles omit vital information**
  - Many reviews of published research articles, especially randomised trials

- **We cannot tell exactly how the research was done**

Reports of RCTs indexed on PubMed

519 Randomised trials published in Dec 2000

Failure to report key aspects of trial conduct:

	Dec 2000 (N=519)	Dec 2006 (N=616)
Defined primary outcome(s)	45%	53%
Sample size calculation	27%	45%
Method of random sequence generation	21%	34%
Method of allocation concealment	18%	25%
Whether blinded	40%	41%

[Chan & Altman, *Lancet* 2005; Hopewell et al, *BMJ* 2010]

Modest improvement between 2000 and 2006

Review of 158 reports of RCTs in surgery published in 2004

Reporting of details of the intended intervention

- **Surgical procedure** **87 %**
- **Pre-operative care** **15 %**
- **Anaesthesia** **35 %**
- **Post-operative care** **49 %**

Surgeons

- **Selection criteria for surgeon** **41 %**
- **Number of surgeons involved** **32 %**

[Jacquier et al. *Ann Surg* 2006]

Reporting of adverse events in RCTs of HAART: systematic review.

[Chowers et al. *J Antimicrob Chemother* 2009]

- **Only 16/49 trials reported AEs with no pre-selection**
- **67% reported only some AEs**
  - e.g. the most frequent, if P<0.05, or 'selected' AEs
- **"These facts obstruct our ability to choose HAART based on currently published data."**

ELSEVIER

Journal of Clinical Epidemiology ■ (2010) ■

Journal of Clinical Epidemiology

REVIEW ARTICLE

Reviews assessing the quality or the reporting of randomized controlled trials are increasing over time but raised questions about how quality is assessed

Agnes Dechartres[a,b,c,d,*], Pierre Charles[b], Sally Hopewell[a,e], Philippe Ravaud[b,c,d], Douglas G. Altman[a]

- **177 reviews published 1987-2007, 58% after 2002**
  - 131 (74%) quality of RCTs
  - 44 (25%) quality of reporting
  - 2 (1%) assessed both
- **74 different items and 26 different scales used**
- **Allocation sequence generation and concealment were reported in 41% and 40%, respectively**

Selective reporting

[Dwan *et al, PLoS ONE* 2008]

- **Reviewed 16 cohort studies that assessed *study publication bias* and *outcome reporting bias* in randomised controlled trials**
- **Strong evidence that studies reporting positive or significant results were more likely to be published and outcomes that were statistically significant were more likely to be fully reported**
- **Frequent discrepancies between publications and original trial protocols**
  - 40–62% of studies had at least one primary outcome changed, newly introduced or omitted

Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials

Sylvain Mathieu, MD
Isabelle Boutron, MD, PhD
David Moher, PhD
Douglas G. Altman, DSc
Philippe Ravaud, MD, PhD

Context As of 2005, the International Committee of Medical Journal Editors required investigators to register their trials prior to participant enrollment as a precondition for publishing the trial's findings in member journals.

Objective To assess the proportion of registered trials with results recently published in journals with high impact factors; to compare the primary outcomes specified in trial registries with those reported in the published articles; and to determine whether primary outcome reporting bias favored significant outcomes

323 randomised trials
- 46% adequately registered
- 28% not registered
- 14% registered after the completion of the study
- 11% registered with no/unclear description of primary outcome

147 adequately registered trials
- 31% had evidence of discrepancies between the outcomes registered and the outcomes published.
- When it could be assessed, statistically significant results were favoured in 83% (19 of 23)

nity has embraced this policy, as seen by a marked increase in trial registration

sequent publication indicated that selective outcome reporting is prevalent.

Impact of poor reporting

- **Cumulative published evidence is misleading**
- **Adverse effects on**
  - Other researchers
  - Clinicians
  - Patients
- **"Failures in the system of reporting clinical trials findings can result in harm to patients"** [Glass 1994]

Poor reporting is a serious problem for systematic reviews and clinical guidelines

- **"The biggest problem was the quality of reporting, which did not allow us to judge the important methodological items ..."**

- **"Data reporting was poor. 15 trials met the inclusion criteria for this review but only 4 could be included as data were impossible to use in the other 11."**

(Cochrane Library, accessed on 18 Sept 07)

Whose fault is poor reporting?

- **Poor reporting indicates a collective failure of authors, peer reviewers, and editors**

  … on a massive scale

- **Researchers (authors) may not know what information to include in a report of research**

- **Editors may not know what information should be included**

What help can be given to authors?

What help can be given to editors?

Why is clear and transparent reporting important?

- **"If reporting is inadequate—namely, information is missing, incomplete, or ambiguous—assumptions have to be made, and, as a result, important findings could be missed and not acted upon.**
- **Alternatively, false outcomes might be identified and used in practice."**

[Needleman et al , *J Dent Res* 2008]

What should be reported?

"Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results."

[International Committee of Medical Journal Editors]

- **A similar principle should extend to all study aspects**
  - Selection of participants, Interventions, Outcomes etc
- **The goal should be transparency**
  - Should not mislead
  - Should allow replication (in principle)
  - Data should be able to be incorporated in a later meta-analysis

The CONSORT Statement for reporting RCTs

[Schulz *et al, BMJ* 2010]

- **Minimum set of essential items necessary to evaluate the study**
- **25 items that should be reported in a paper**
  - Based on empirical evidence where possible
- **Also a flow diagram describing patient progress through the trial**
- **Long explanatory paper (E&E)**
- **Several subsequent extensions**

www.consort-statement.org

What does the poor quality of published studies tell us about peer review?

- **Peer review is difficult and only partly successful**
- **Reviewers (and editorial staff) are unable to eliminate errors in methodology and interpretation**
- **Readers should not assume that papers published in peer reviewed journals are scientifically sound**
  - But, many readers (including other researchers) DO assume that papers published in peer reviewed journals are scientifically sound

⇒ **Important that misleading papers are identified**

⇒ **Good reporting is critical**

EQUATOR: Enhancing the QUAlity and Transparency Of health Research

- **EQUATOR grew out of the work of CONSORT and other guidelines groups**
- **Guidelines are available but not widely supported by medical journals or adhered to by researchers**
  - Their potential impact is blunted
  - They need to be actively promoted
- **EQUATOR Network**
  - Editors of general and specialty journals, researchers, guideline developers, medical writers

"Better reporting, better reviewing, better editing"

equator network

equator network

Good reporting is not an optional extra: it is an essential component of doing good research

www.consort-statement.org
www.strobe-statement.org
www.equator-network.org

Taxonomy of poor reporting

- **Non-reporting (or delayed reporting) of entire studies**
  (even when some results have been presented in public)
- **Selective reporting of only some patient outcomes or analyses**
- **Inconsistencies between sources**
  - e.g. publication vs protocol or register
- **Incomplete reporting: data cannot be included in meta-analysis**
- **Omission of crucial aspects of research methods**
- **Selective reporting of multiple alternative analyses**
- **Misinterpretation of findings (spin)**
  - e.g. post hoc change of focus; misleading abstract