Improving the reporting of randomised trials: CONSORT Statement and beyond

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“The whole of medicine depends on the transparent reporting of clinical trials”

Drummond Rennie, *JAMA* 2001

- **“This leads one to consider if it is possible, in planning a trial, in reporting the results, or in assessing the published reports of trials, to apply criteria which must be satisfied if the analysis is to be entirely acceptable….**
- **“A basic principle can be set up that … it is at least as important to describe the techniques employed and the conditions in which the experiment was conducted, as to give the detailed statistical analysis of results.”**
- **“If cases are allotted to a control group or to a treatment group … what method of random selection is used?”**

[Daniels M. Scientific appraisement of new drugs in tuberculosis. *Am Rev Tuberc* 1950;61:751-6.]

5. Preparation of Report

The object of the report must be to set out the aims of the investigation, the conditions under which it was conducted, the results, and the conclusions that may be drawn from them. It must state how the patients were selected. The composition of the groups treated must be given in sufficient detail to allow assessment of their comparability; data will be required on the age-composition, the stage and location of the disease, the presence of other lesions, the treatment previously given, the bacteriological confirmation of diagnosis. A description of the procedures of the trial is indispensable; failure on this point leaves one in considerable doubt concerning the validity of some published work. Departures from the agreed procedures must be listed and explained, as for instance reasons for exclusion of cases initially admitted to the trial. Treatments given in addition to those under study must be described and taken into account in the analysis.

Daniels M. Clinical evaluation of chemotherapy in tuberculosis. *Br Med Bull* 1951;7:320-6.

“… editors could greatly improve the reporting of clinical trials by providing authors with a list of items that they expected to be strictly reported.”

[DerSimonian R et al, *NEJM* 1982]

CONSORT 1996

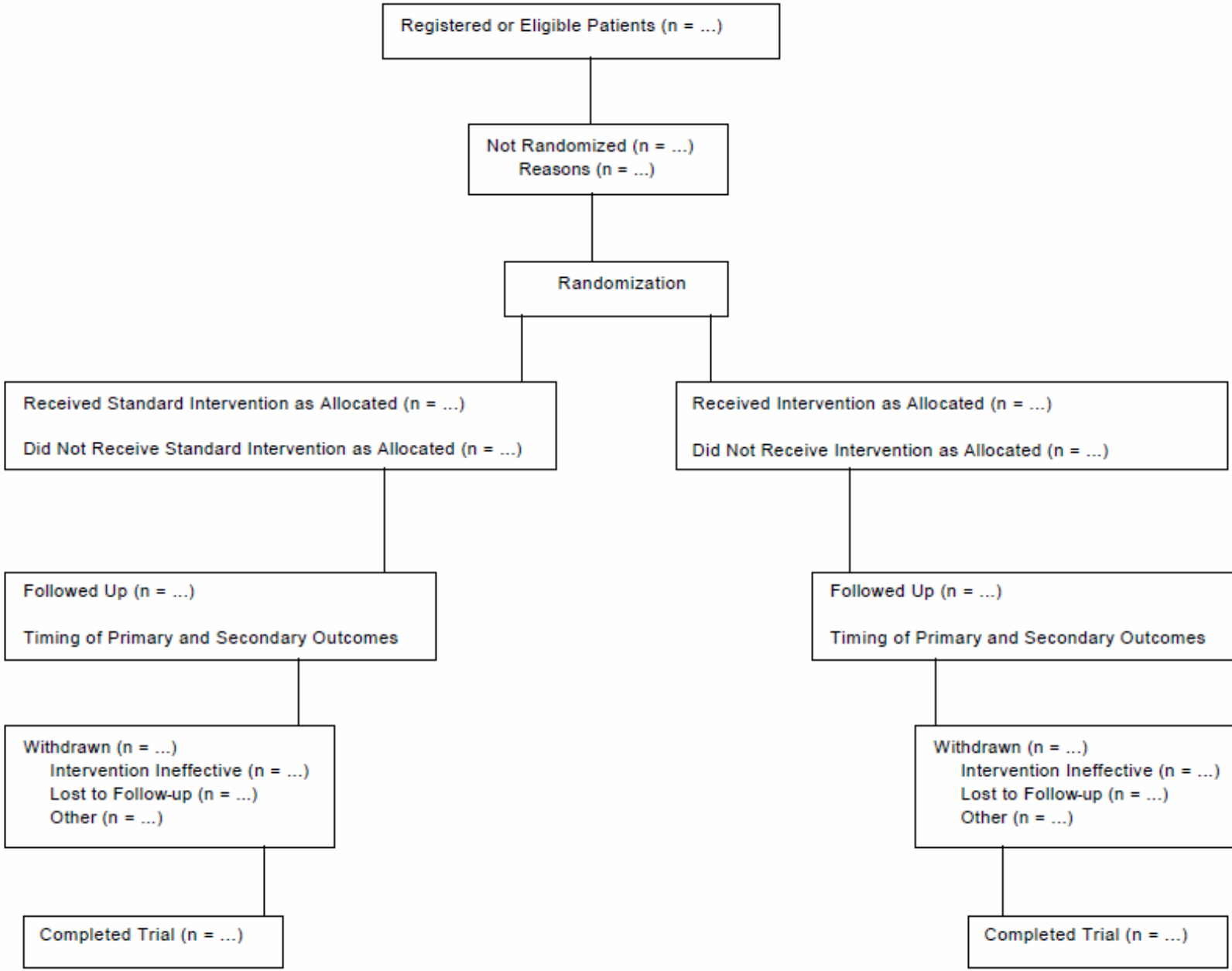
Special Communication

Improving the Quality of Reporting of Randomized Controlled Trials

The CONSORT Statement

Colin Begg, PhD; Mildred Cho, PhD; Susan Eastwood, ELS(D); Richard Horton, MB; David Moher, MSc; Ingram Olkin, PhD; Roy Pitkin, MD; Drummond Rennie, MD; Kenneth F. Schulz, PhD; David Simel, MD; Donna F. Stroup, PhD

Heading	Subheading	Descriptor	Was it Reported?
Title		Identify the study as a randomized trial.[7]	
Abstract		Use a structured format.[8,9]	
Introduction		State prospectively defined hypothesis, clinical objectives, and planned subgroup or covariate analyses[10]	
Methods	Protocol	Describe Planned study population, together with inclusion/exclusion criteria. Planned interventions and their timing. Primary and secondary outcome measure(s) and the minimum important difference(s), and indicate how the target sample size was projected.[2,11] Rationale and methods for statistical analyses, detailing main comparative analyses and whether they were completed on an intention-to-treat basis.[12,13] Prospectively defined stopping rules (if warranted)[14]	
	Assignment	Describe Unit of randomization (eg, individual, cluster, geographic).[15] Method used to generate the allocation schedule.[16] Method of allocation concealment and timing of assignment.[17] Method to separate the generator from the executor of assignment.[17,18]	
	Masking (Blinding)	Describe mechanism (eg, capsules, tablets); similarity of treatment characteristics (eg, appearance, taste); allocation schedule control (location of code during trial and when broken); and evidence for successful blinding among participants, person doing intervention, outcome assessors, and data analysts.[19,20]	
Results	Participant Flow and Follow-up	Provide a trial profile (Figure) summarizing participant flow, numbers and timing of randomization assignment, interventions, and measurements for each randomized group .[3,21]	
	Analysis	State estimated effect of intervention on primary and secondary outcome measures, including a point estimate and measure of precision (confidence interval).[22,23] State results in absolute numbers when feasible (eg, 10/20, not 50%). Present summer ,y data and appropriate descriptive and inferential statistics in sufficient detail to permit alternative analyses and replication .[24] Describe prognostic variables by treatment group and any attempt to adjust for them.[25] Describe protocol deviations from the study as planned, together with the reasons.	
Comment		State specific interpretation of study findings, including sources of bias and imprecision (internal validity) and discussion of external validity, including appropriate quantitative measures when possible. State general interpretation of the data in light of the totality of the available evidence.	


Registered or Eligible Patients (n = ...)
Not Randomized (n = ...)
Reasons (n = ...)
Randomization
Received Standard Intervention as Allocated (n = ...)
Did Not Receive Standard Intervention as Allocated (n = ...)
Received Intervention as Allocated (n = ...)
Did Not Receive Intervention as Allocated (n = ...)
Followed Up (n = ...)
Timing of Primary and Secondary Outcomes
Followed Up (n = ...)
Timing of Primary and Secondary Outcomes
Withdrawn (n = ...)
Intervention Ineffective (n = ...)
Lost to Follow-up (n = ...)
Other (n = ...)
Withdrawn (n = ...)
Intervention Ineffective (n = ...)
Lost to Follow-up (n = ...)
Other (n = ...)
Completed Trial (n = ...)
Completed Trial (n = ...)

2001 Revision of CONSORT

- **Major revision begun in 2000 – published in 2001**

- **Checklist – major revision**
- **Also small changes to flow diagram**

- **Short paper ("The CONSORT Statement")**
  - published in 3 journals

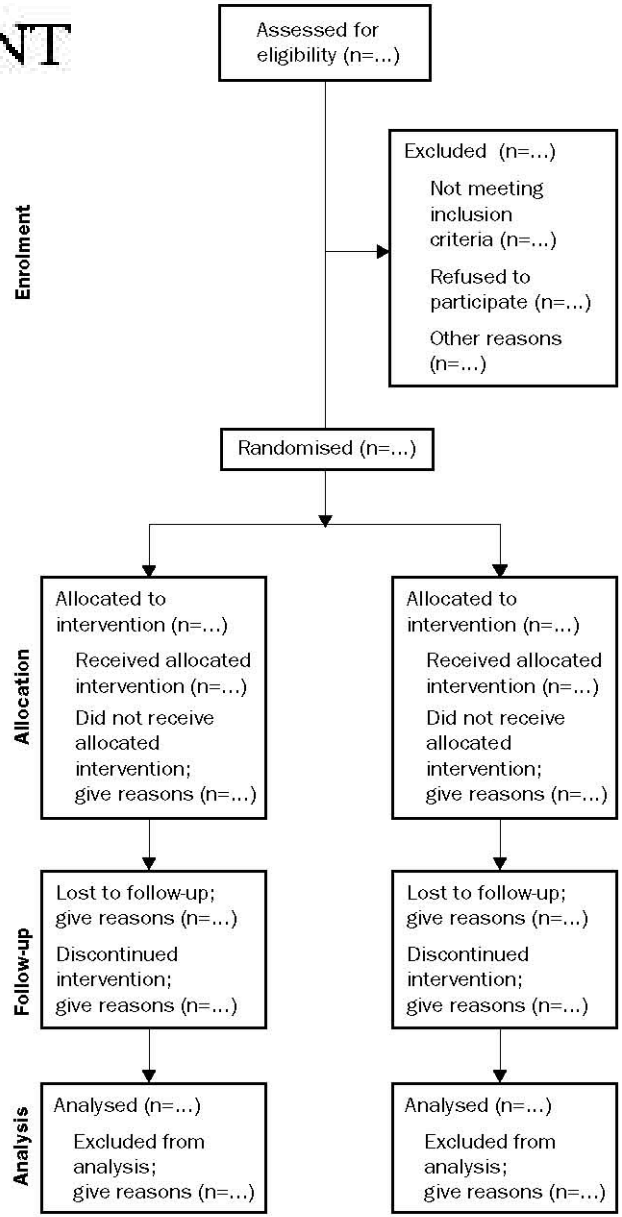
- **Explanatory paper (E&E)**

CONSORT STATEMENT

	Item number	Descriptor	Reported on page number
Title and abstract	1	How participants were allocated to interventions (eg, "random allocation", "randomised", or "randomly assigned").	
Introduction			
Background	2	Scientified background and explanation of rationale.	
Methods			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (eg, multiple observations, training of assessors, &c).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomisation			
Sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (eg, blocking, stratification).	
Allocation concealment	9	Method used to implement the random allocation sequence (eg, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were aware of group assignment. If not, how the success of masking was assessed.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses, such as subgroup analyses and adjusted analyses.	
Results			
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group, report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention to treat". State the results in absolute numbers when feasible (eg, 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (eg, 95% CI).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory.	
Adverse events	19	All important adverse events or side-effects in each intervention group.	
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalisability	21	Generalisability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

Checklist of items to include when reporting a randomised trial

CONSORT STATEMENT



Flow diagram of the progress through the phases of a randomised trial

Rationale for checklist items

- Necessary to evaluate the study
- Evidence-based, whenever possible
- Minimum set of essential items

The “explanation and elaboration” manuscript

- **To enhance the use and dissemination of CONSORT**
- **For each checklist item: examples of good reporting and explanation, with relevant empirical evidence**

Ann Intern Med. 2001;134:663-694.

The Revised CONSORT Statement for Reporting Randomized Trials: Explanation and Elaboration

Douglas G. Altman, DSc; Kenneth F. Schulz, PhD; David Moher, MSc; Matthias Egger, MD; Frank Davidoff, MD; Diana Elbourne, PhD; Peter C. Gøtzsche, MD; and Thomas Lang, MA, for the CONSORT Group

CONSORT Extensions to other trials designs

- **Modifications to and possibly additions to the checklist items**
  - Possibly also modification of the flow diagram.
- **Extensions were planned for 6 trial designs**
  - cluster randomised trials
  - non-inferiority and equivalence trials
  - multi-arm parallel group trials
  - crossover trials
  - factorial trials
  - within-person randomised trials
- **Also in development**
  - N-of-1 trials

Better Reporting of Harms in Randomized Trials: An Extension of the CONSORT Statement

John P.A. Ioannidis, MD; Stephen J.W. Evans, MSc; Peter C. Gøtzsche, MD, DrMedSci; Robert T. O'Neill, PhD; Douglas G. Altman, DSc; Kenneth Schulz, PhD; and David Moher, PhD, for the CONSORT Group*

In response to overwhelming evidence and the consequences of poor-quality reporting of randomized, controlled trials (RCTs), many medical journals and editorial groups have now endorsed the CONSORT (*Con*solidated *S*tandards *o*f *R*eporting *T*rials) statement, a 22-item checklist and flow diagram. Because CONSORT primarily aimed at improving the quality of reporting of efficacy, only 1 checklist item specifically addressed the reporting of safety.

Considerable evidence suggests that reporting of harms-related data from RCTs also needs improvement. Members of the CONSORT Group, including journal editors and scientists, met in Montebello, Quebec, Canada, in May 2003 to address this problem. The result is the following document: the standard CONSORT checklist with 10 new recommendations about reporting harms-related issues, accompanying explanation, and examples to highlight specific aspects of proper reporting.

We hope that this document, in conjunction with other CONSORT-related materials (www.consort-statement.org), will help authors improve their reporting of harms-related data from RCTs. Better reporting will help readers critically appraise and interpret trial results. Journals can support this goal by revising Instructions to Authors so that they refer authors to this document.

Ann Intern Med. 2004;141:781-788. www.annals.org

For author affiliations, see end of text.

For definitions of terms, see Glossary.

*For a list of members of the CONSORT Group, see Appendix 1, available at www.annals.org.

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."**
- **"Authors and editors should ensure that reporting of AEs in HAART trials follows the CONSORT guidelines for reporting on harms in randomized trials."**

Implementations of CONSORT

- **Acupuncture (STRICTA)**
- **Herbal medicines**
- **Pragmatic trials**
- **Non-pharmacological treatments**

OPEN ACCESS Freely available online

PLoS MEDICINE

CONSORT for Reporting Randomized Controlled Trials in Journal and Conference Abstracts: Explanation and Elaboration

Sally Hopewell[1,2*], Mike Clarke[1,3], David Moher[4,5], Elizabeth Wager[6], Philippa Middleton[7], Douglas G. Altman[2], Kenneth F. Schulz[8], and the CONSORT Group

2010 Revision of CONSORT

- Meeting in January 2007
- Revised checklist
- Short paper (published in 9 journals)
- Revised (and expanded) explanatory paper (E&E)

RESEARCH METHODS & REPORTING

CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials

Kenneth F Schulz,[1] Douglas G Altman,[2] David Moher,[3] for the CONSORT Group

Major changes in 2010

- **Added 3 new items**
  - Registration, Protocol, Funding
- **Added several sub-items**
  - e.g. any important changes to methods after trial commencement, with a discussion of reasons
- **Made some items more specific**
  - e.g. allocation concealment mechanism, blinding
- **We simplified and clarified the wording throughout**

- NB Changes are documented in paper

Blinding in CONSORT 2010

- **We added the specification of how blinding was done and, if relevant, a description of the similarity of interventions and procedures**
- **We eliminated text on "how the success of blinding (masking) was assessed"**
  - lack of empirical evidence supporting the practice
  - theoretical concerns about the validity of such assessment

Evolution of the CONSORT Statement

Outcomes

- **CONSORT 1996**
  - "Primary and secondary outcome measure(s) ..."
- **CONSORT 2001**
  - "Clearly defined primary and secondary outcome measures ..."
- **CONSORT 2010**
  - "Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed"

Evolution of the CONSORT Statement

Interventions

- **CONSORT 1996**
  - "Planned interventions and their timing"
- **CONSORT 2001**
  - "Precise details of the interventions intended for each group and how and when they were actually administered"
- **CONSORT 2010**
  - "The interventions for each group with sufficient details to allow replication, including how and when they were actually administered"

What do we need to know about treatment allocation?

- **Was the allocation sequence generated in an appropriately unpredictable way, e.g. by randomization ["Sequence generation"]**
  - How was the sequence determined?

- **Was the act of allocating a treatment to a patient done without any knowledge of what treatment they will get? ["Allocation concealment"]**
  - What was the mechanism of allocation?

Description of randomization in RCTs

So important that CONSORT checklist has 3-4 items:

Item 8a. Method used to generate the random allocation sequence

Item 8b. Type of randomisation; details of any restriction (such as blocking and block size)

Item 9. Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned

Item 10. Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions

Good (clear) reporting

Sequence generation:

- "Independent pharmacists dispensed either active or placebo inhalers according to a computer generated randomization list."
- … The randomization code was developed using a computer random number generator to select random permuted blocks. The block lengths were 4, 8, and 10 varied randomly …"

Clear reporting but poor methodology

“Randomization was alternated every 10 patients, such that the first 10 patients were assigned to early atropine and the next 10 to the regular protocol, etc. To avoid possible bias, the last 10 were also assigned to early atropine.”

[Lessick et al, *Eur J Echocardiography* 2000;1:257-62]

Clear reporting?

“Patients were assigned to either the intervention or control group, by selection of a card from a pile of equal numbers of cards for each group.”

[*Lancet* 2002; 360: 1455–61.]

- **“Randomization was alternated every 10 patients, such that the first 10 patients were assigned to early atropine and the next 10 to the regular protocol, etc. To avoid possible bias, the last 10 were also assigned to early atropine.”**

Concealed allocation?

- **“Randomization was carried out by having prepared in advance a small box with 50 identically sized pieces of paper folded so that they could not be read. 25 had A and 25 had B written on them. The box was shaken and one of the pieces of paper was removed from the box blindly.”**

[Coan et al (1980) cited by van Tulder et al. Spine 1999.]

"They were randomised by selecting from random numbers held in sealed envelopes"

"Randomisation was performed in advance with a random number table by a hospital pharmacist not involved in the study, and treatment allocations were sealed in opaque envelopes. Investigators were blind to these allocations."

"My question is: Are we making an impact?"

Comparing trial publications with protocols – sample size and analysis

- **Unacknowledged discrepancies between protocols and publications**
  - **sample size calculations (18/34 trials),**
  - **methods of handling protocol deviations (19/43)**
  - **missing data (39/49),**
  - **primary outcome analyses (25/42)**
  - **subgroup analyses (25/25)**
  - **adjusted analyses (23/28)**

- **Interim analyses were described in 13 protocols but mentioned in only five corresponding publications**

[Chan et al, *BMJ* 2008]

Viewpoint

Lancet 1999; 353: 490-3

How can medical journals help prevent poor medical research? Some opportunities presented by electronic publishing

Iain Chalmers, Douglas G Altman

"Electronic publication of a protocol could be simply the first element in a sequence of "threaded" electronic publications, which continues with reports of the resulting research (published in sufficient detail to meet some of the criticisms of less detailed reports published in print journals), followed by deposition of the complete data set."

Sharing data is not a new idea

- **“Experience has shown the advantage of occasionally rediscussing statistical conclusions, by starting from the same documents as their author. I have begun to think that no one ought to publish biometric results, without lodging a well-arranged … copy of his data in some place where it should be accessible, under reasonable restrictions, to those who desire to verify his work.”**

Galton F. *Biometrika* 1901

- **“…the data of almost any laboratory worker, if he conscientiously describes his technique and material, have considerable value for an indefinite period.”**

Dunn HL. *Physiol Rev* 1929

Annals of Internal Medicine | ACADEMIA AND CLINIC

Reproducible Research: Moving toward Research the Public Can Really Trust

Christine Laine, MD, MPH; Steven N. Goodman, MD, PhD, MHS; Michael E. Griswold, PhD; and Harold C. Sox, MD

A community of scientists arrives at the truth by independently verifying new observations. In this time-honored process, journals serve 2 principal functions: evaluative and editorial. In their evaluative function, they winnow out research that is unlikely to stand up to independent verification; this task is accomplished by peer review. In their editorial function, they try to ensure transparent (by which we mean clear, complete, and unambiguous) and objective descriptions of the research. Both the evaluative and editorial functions go largely unnoticed by the public—the former only draws public attention when a journal publishes fraudulent research. However, both play a critical role in the progress of science. This paper is about both functions. We describe the evaluative processes we use and announce a new policy to help the scientific community evaluate, and build upon, the research findings that we publish.

Ann Intern Med. 2007;146:450-453. www.annals.org
For author affiliations, see end of text.

www.consort-statement.org