

RESEARCH

Many reports of randomised trials still don't begin or end with a systematic review of the relevant evidence

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ABSTRACT

Background: Existing evidence should provide ethical, scientific and environmental justification for new randomised trials and users of the findings of these trials need to see them in the context of similar trials. Since 1997, audits have been done of reports of randomised trials in *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet*, and *New England Journal of Medicine* to see if results are placed in context in the Discussion section of the report and, since 2005, to see if systematic reviews are used in the Introduction section.

Methods: We handsearched each May 2012 issue of these five journals to identify reports of randomised trials. Introduction and Discussion sections were categorised on the basis of their use of systematic reviews.

Results: Thirty-five reports of randomised trials were included. Considering the Introduction sections: 5 were said to be the first trial, 1 used an updated systematic review in the design, 13 discussed previous systematic reviews, 10 mentioned other trials, and 6 didn't mention other trials or claim to be the first. Considering the Discussion sections: 2 were said to be the first trial, 2 contained a systematic review integrating the new trial, 11 mentioned a systematic review, and 20 made no apparent systematic attempt to place findings in full context. There was variability across the journals, with reports in the *Lancet* making notably more use of systematic reviews.

Conclusions: Many trials still do not use systematic reviews in their design and reporting.

BACKGROUND

The scientific, ethical and environmental justification for any new study should be a systematic review of the relevant research that already exists. This avoids waste that would come from seeking to answer a question with the new study that had been answered reliably by earlier studies, and should help to ensure that the new study is designed in a way that learns from successes and failures of the past.¹ When the study's findings are reported, these should be presented to readers within an updated systematic review of similar studies, to avoid undue emphasis solely on the results of the new study, to maximise the value of past studies (including the one being reported for the first time), and to provide the reader with a summary of all the relevant evidence.² In the Explanation and Elaboration document for the most recent CONSORT statement in 2010, the authors "recommend that, at a minimum, the discussion should be as systematic as possible and be based on a comprehensive search, rather than being limited to studies that support the results of the current trial."³ Unfortunately, despite some progress towards achieving these goals, the healthcare literature still includes many reports of randomised trials that do not meet these standards. This study, which updates earlier audits, was conducted in 2012 to provide up-to-date data for a series of papers highlighting problems in, and suggesting solutions for, waste in research.

The earlier audits were conducted in May 1997⁴, 2001⁵, 2005⁶, and 2009.⁷ Those audits assessed a total of 106

reports of randomised trials from *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet* and the *New England Journal of Medicine*. The findings of the new trial were integrated into a systematic review in three (3%) of these (all published in the *Lancet*), and 22 (21%) cited a previous systematic review but did not integrate the findings of the trial. Considering the other 81 reports, 12 (11%) appeared to be the first trial and, hence, the totality of the evidence for the purpose of this audit. However, even though the reports of the other 69 (65%) trials included citations to trials, they did not provide information to suggest that these citations arose from a systematic attempt to set the results of the new trial in context.⁷ Therefore, across a dozen years of these high profile journals, most reports of randomised trials had failed to provide the reader with sufficient information to assess the contribution of the new trial to the totality of the evidence base, and, as a consequence, failed to provide the reliable and robust evidence needed to help people make well-informed decisions and choices about the healthcare interventions that had been evaluated. However, alongside the publication of our 2009 audit in the *Lancet*,⁷ an editorial by Clark and Horton outlined a new policy for that journal in which authors of all research studies, not just randomised trials, would be asked to include an updated systematic review in their Discussion section.⁸ This led to the inclusion of a box in research reports in the *Lancet* that allows authors to describe a systematic review which integrates their findings.

The inclusion of a systematic review in the Introduction section of the report of a randomised trial provides an indication that the new trial had been designed and conducted with due consideration to existing research. This aspect of our research began in a limited way in 2005 and was extended in 2009. Of the 47 reports of trials published in the five journals in May of those two years, 16 (34%) mentioned a systematic review in their Introduction.⁷ Recent work by Jones et al. has found that 37 of 48 randomised trials funded by the UK's National Institute for Health Research Health Technology Assessment (NIHR HTA) programme in 2006-2008, referenced a systematic review in the application, with 20 of these using information from the systematic review in the design or planning of the new trial.⁹

METHODS

We repeated the audit in May 2012. As in each of the previous studies, we focused on how well the Discussion section of each report placed the results of the new trial in the context of other relevant research. As in the 2009 audit, we also investigated whether the reports included information about systematic reviews or other trials in their Introduction section.

We continued with our earlier definition of "trial," which is based on the definition of randomised and quasi-randomised trials used by The Cochrane Collaboration: "the individuals (or other units) followed in the trial were assigned prospectively to one of two (or more) alternative forms of health care using random allocation or some quasi-random method of allocation (such as alternation, date of birth, or case record number)."⁷ Eligible reports were those published as a full article or paper which was principally concerned with providing findings for the outcomes studied in the trial and was published in one of the five target journals during May 2012.

Both authors handsearched the relevant issues of the journals independently to identify eligible reports. The Introduction and Discussion sections of each eligible report were then assessed independently by both authors to decide whether an updated systematic review was included, or whether reference was made to a systematic review of direct relevance to the comparison of interventions assessed in the trial. We discussed our findings and reached agreement on all coding.

FINDINGS

We identified 35 reports of randomised trials across the five journals. The findings for the Introduction and Discussion sections are shown in Tables 1 and 2, along with data from previous audits. We found one eligible report in *Annals of Internal Medicine*, three in *BMJ*, seven in *JAMA*, nine in *Lancet* and 15 in *New England Journal of Medicine*.

Considering the Introduction sections, 5 (14%) of the 35 reports claimed to be the first trial at the time the study was

	2009 N=29	2012 N=35
First trial addressing the question	5	5
Contained an updated systematic review which was used to design the new trial	1	1
Discussed a previous systematic review in the topic area for the trial	10	13
Contains references to other randomised trials	4	10
Does not contain references to other randomised trials, and does not claim to be the first trial	9	6

Table 1. Classification of Introduction sections in reports of randomised published in May 2009 and May 2012 in *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet*, and *New England Journal of Medicine*

initiated. The use of an updated systematic review to design the trial was referred to the Introduction section of one (3%) report, and 13 (37%) discussed previous systematic reviews. Ten (29%) reports mentioned others trials in their Introduction and 6 (17%) did not mention other trials or claim to be the first.

Turning to the Discussion sections, 2 (6%) of the 35 trials said that they were the only trial of the topic. Two (6%) reports contained a systematic review integrating the new trial^{10, 11} and 11 (31%) mentioned a systematic review. Twenty (57%) made no apparent systematic attempt to place findings in full context.

A particularly noticeable difference to earlier years is that the proportion of reports of randomised trials in the *Lancet*, which either integrated the results of the new trial into a systematic review or mentioned a systematic review in their Discussion, now stands at 86% (6 of 7) of reports of randomised trials that did not claim to be the only trial, with one of these integrating the findings of the new trial into a systematic review. (Two reports of trials in the *Lancet* claimed to be the only trial in the Discussion section.) In contrast, nine (60%) of 15 reports of randomised trials in the *New England Journal of Medicine* in May 2012 appeared to make no systematic attempt to place the findings of the new trial in the context of reports of other, similar studies.

DISCUSSION

Considering all five of these general medical journals together, there appears to be relatively little evidence of progress in regard to the integration of the findings of new trials into an updated systematic review. Furthermore, the proportion of trials referring to systematic reviews in their Discussion section (with or without integration of the new trial's findings) appears not to be increasing. Excluding trials that appeared to be the only trial in the

	1997 N=26	2001 N=33	2005 N=18	2009 N=29	2012 N=35
First trial addressing the question	1	3	3	5	2
Contained an updated systematic review integrating the new results	2	0	0	1	2
Discussed a previous systematic review in the topic area of the new trial but did not attempt to integrate their results	4	3	5	10	11
No apparent systematic attempt to set the results in the context of other trials	19	27	10	13	20

Table 2. Classification of Discussion sections in reports of randomised published in May 1997, May 2001, May 2005, May 2009 and May 2012 in *Annals of Internal Medicine, BMJ, JAMA, Lancet, and New England Journal of Medicine*

topic area, the proportion was 24% of reports in 1997, 10% in 2001, 33% in 2005, 46% in 2009 and 39% in 2012. This is despite the fact that there are now more than 5000 full Cochrane Reviews in the *Cochrane Database of Systematic Reviews*¹² and several thousand more systematic reviews are published each year in other places.^{13, 14} However, there is considerable heterogeneity across the five journals in this sample, which will be explored further in a future report of the 2013 audit.

In summary, this latest update of the “islands” project shows that many randomised trials still do not place their findings in the context of an up-to-date systematic review of other relevant evidence, and that only one of the five high profile medical journals we studied, the *Lancet*, is achieving this for most of the trial reports that it publishes. However, that journal’s introduction of a dedicated box to research articles for an outline of the findings of a relevant systematic review and the recent publication of an extension to the PRISMA Statement covering the reporting of systematic reviews in abstracts¹⁵ show that it is possible to report key elements from a systematic review within the confines of an article for which the main focus is the new randomised trial. This, coupled with the increasing uptake of the CONSORT reporting guidelines,¹⁶ will hopefully lead to benefits for the users of reports of randomised trials.

REFERENCES

- Clarke M. Doing new research? Don’t forget the old. Nobody should do a trial without reviewing what is known. *PLoS Med*. 2004 1(2):100-02.
- Chalmers I, Altman DG. How can medical journals help prevent poor medical research? Some opportunities presented by electronic publishing. *Lancet*. 1999 Feb 6;353(9151):490-3.
- Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010 Mar 23;340:c869.
- Clarke M, Chalmers I. Discussion sections in reports of controlled trials published in general medical journals: islands in search of continents? *JAMA*. 1998 Jul 15;280(3):280-2.
- Clarke M, Alderson P, Chalmers I. Discussion sections in reports of controlled trials published in general medical journals. *JAMA*. 2002 Jun 5;287(21):2799-801.
- Clarke M, Hopewell S, Chalmers I. Reports of clinical trials should begin and end with up-to-date systematic reviews of other relevant evidence: a status report. *J R Soc Med*. 2007 Apr;100(4):187-90.
- Clarke M, Hopewell S, Chalmers I. Clinical trials should begin and end with systematic reviews of relevant evidence: 12 years and waiting. *Lancet*. 2010 Jul 3;376(9734):20-1.
- Clark S, Horton R. Putting research into context – revisited. *Lancet*. 2010 Jul 3;376(9734):10-11.
- Jones AP, Conroy E, Williamson PR, Clarke M, Gamble C. The use of systematic reviews in the planning, design and conduct of randomised trials: a retrospective cohort of NIHR HTA funded trials. *BMC Med Res Methodol*. 2013 Mar 25;13:50.
- Merry SN, Stasiak K, Shepherd M, Frampton C, Fleming T, Lucassen MFG. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ*. 2012 Apr 18;344:e2598.
- Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet*. 2012 May 19;379(9829):1887-92.
- Clarke M, Li Y. Editorial for Issue 2 2012. *Journal of Evidence Based Medicine*. *J Evid Based Med*. 2010;5:47.
- Moher D, Tetzlaff J, Tricco AC, Sampson M, Altman DG. Epidemiology and reporting characteristics of systematic reviews. *PLoS Med*. 2007 Mar 27;4(3):e78.
- Bastian H, Glasziou P, Chalmers I. Seventy-five trials and eleven systematic reviews a day: how will we ever keep up? *PLoS Med*. 2010 Sep 21;7(9):e1000326.

15. Beller EM, Glasziou PP, Altman DG, Hopewell S, Bastian H, Chalmers I, et al. PRISMA for abstracts: reporting systematic reviews in journal and conference abstracts. *PLoS Med.* 2013 10(4):e1001419.
 16. Turner L, Shamseer L, Altman DG, Weeks L, Peters J, Kober T, et al. Consolidated standards of reporting trials (CONSORT) and the completeness of reporting of randomised controlled trials (RCTs) published in medical journals. *Cochrane Database Syst Rev.* 2012 Nov 14;11:MR000030.
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