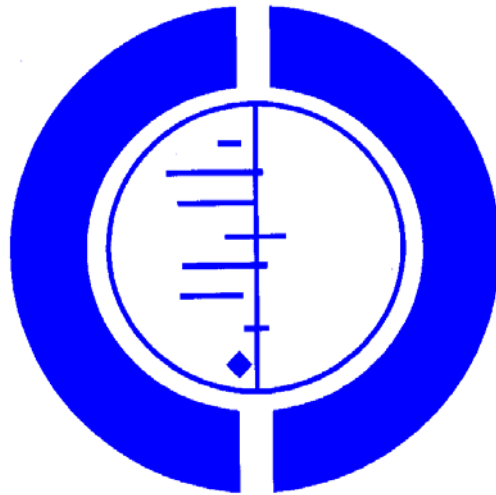


The Cochrane Collaboration Methods Groups Newsletter

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PURPOSE OF THE NEWSLETTER

One of the primary roles of Methods Groups is to offer advice and support to other Cochrane entities. The main aims of this Newsletter are, therefore, to share information among Methods Groups and to inform others within The Cochrane Collaboration about their work. The target audience is primarily members of The Cochrane Collaboration Methods Groups but also includes other members of the Collaboration and people outside the Collaboration with an interest in methodological aspects of healthcare research.

The Newsletter is published once a year and this is the twelfth edition. Archive copies of the Newsletters are available from The Cochrane Collaboration website at: www.cochrane.org/newslett/index.htm. Each issue contains relevant news from The Cochrane Collaboration, reports of recent methodological research (both within and outside the Collaboration), as well as recurrent topics such as details of forthcoming meetings, updates from individual Methods Groups and details of new Cochrane methodology reviews.

The opinions expressed in the Newsletter do not necessarily reflect the opinion of the editors, The Cochrane Collaboration, or anyone other than the authors of the individual articles. Contact details for all the Methods Groups and other contributors to the Newsletter, a guide to more information about The Cochrane Collaboration and details of Cochrane websites and Cochrane Centres can be found at the end of the Newsletter.

This Newsletter has been produced by the UK Cochrane Centre with resources from the National Institute for Health Research in the UK. The Newsletter is distributed to members of Methods Groups and all Cochrane entities. If you would like to suggest topics for future issues or to receive additional copies, please contact the UK Cochrane Centre.

ABOUT THIS ISSUE

This year's Newsletter continues to focus on some of the challenging issues facing the methodology of Cochrane and other types of systematic reviews. March 2008 saw the launch of RevMan 5 and the new *Cochrane Handbook for Systematic Reviews of Interventions*. We include a series of articles about RevMan 5 and the new Handbook, along with articles about the introduction of Summary of Findings and Risk of Bias tables in Cochrane reviews, the introduction of diagnostic test accuracy reviews and overviews of reviews - which will now be possible using the new RevMan 5 software.

As with previous years, this issue includes structured abstracts and commentaries on topical methodological issues. These include: a study examining how authors of systematic reviews that include randomized trials that are stopped early for benefit, address this in their reviews; a study investigating barriers to participation in randomized trials; and a further study examining selective reporting in prognostic studies.

As ever, we are very grateful to the many people who have contributed to this Newsletter. We should welcome additional volunteers to help with the preparation of structured abstracts and commentaries for reports of methodology research. Suggestions for future themes or content of the Newsletter would be most appreciated.



ARTICLES

RevMan 5: Is rolling ...

Monica Kjeldstrøm

Between the beginning of December 2007 and the end of February 2008, five Cochrane Review Groups (CRGs) and some of their authors used RevMan 5 for processing amended and new protocols and reviews. At the submission deadline for Issue 2, 2008 of *The Cochrane Library*, these pilot CRGs submitted a total of 23 methodology reviews in the new RevMan 5 format (10 protocols and 13 reviews), and 99 intervention reviews (27 protocols and 72 reviews). In total, there were 22 new protocols and seven new reviews: the remaining reviews were *amended* reviews (reviews revised with minor changes).

At the end of the RevMan 5 Pilot, all five pilot CRGs were supportive of proceeding with rolling out RevMan 5 to the other CRGs and their authors. Wiley-Blackwell also reported that the submission from the five pilot CRGs had been successful and all the RevMan 5 reviews were published in Issue 2, 2008 of *The Cochrane Library*.

RevMan 5 was released Collaboration-wide on 14 March 2008 and, by the end of April 2008, the RevMan team had recorded more than 3000 individual downloads of the software. Over the next several months, until the middle of November 2008, the editorial bases of CRGs, in close collaboration with their author teams, will move existing reviews to the new RevMan 5 format. At the same time, the CRGs will also be supporting the creation of new reviews that can take full advantage of the new features, such as Risk of Bias tables and Summary of Findings tables. From Issue 4, 2008 of *The Cochrane Library*, Wiley-Blackwell will be ready to publish diagnostic test accuracy reviews



and overviews of reviews, two new review types supported by RevMan 5. Find out more about RevMan 5 at www.cochrane.net/RevMan.

RevMan 5: New Cochrane Handbook for Systematic Reviews of Interventions

Sally Green and Julian Higgins

The *Cochrane Handbook for Systematic Reviews of Interventions* (the Handbook) has undergone a substantial update, and Version 5 of the Handbook is now available online at www.cochrane-handbook.org and in RevMan 5. In addition, for the first time, the Handbook will soon be available as a printed volume, published by Wiley-Blackwell. We are anticipating release of this at the Colloquium in Freiburg.

Version 5 of the Handbook describes the new methods available in RevMan 5, as well as containing extensive guidance on all aspects of Cochrane review methodology. It has a new structure, with 22 chapters divided into three parts.

Part 1, relevant to all reviews, introduces Cochrane reviews, covering their planning and preparation, and their maintenance and updating, and ends with a guide to the contents of a Cochrane protocol and review.

Part 2, relevant to all reviews, provides general methodological guidance on preparing reviews, covering question development, eligibility criteria, searching, collecting data, within-study bias (including completion of the Risk of Bias table), analysing data, reporting bias, presenting and interpreting results (including Summary of Findings tables).

Part 3 addresses special topics that will be relevant to some, but not all, reviews, including particular considerations in addressing adverse effects, meta-analysis with non-standard study designs and using individual participant data. This part has new chapters on incorporating economic evaluations, non-randomized studies, qualitative research, patient-reported outcomes in reviews, prospective meta-analysis, reviews in health promotion and public health, and the new review type of overviews of reviews.

The revised Handbook for intervention reviews does not cover Cochrane diagnostic test accuracy reviews; methods for these are described in a separate Handbook.

Some areas of new, extended or substantively changed advice, such as the Risk of Bias tool and Summary of Findings tables, are highlighted in the following articles.

The new Handbook has been developed as a collaborative effort of the Cochrane Collaboration's Methods Groups and members of the Handbook Advisory Group, and incorporates feedback and advice from Cochrane Review

Groups and review authors. We are grateful to all for their contributions.

RevMan 5: Summary of Findings tables

Holger Schünemann, Andy Oxman, Gordon Guyatt, Nancy Santesso and Jan Brozek

With the release of RevMan 5 and the new *Cochrane Handbook for Systematic Reviews of Interventions*, review authors are encouraged to include a Summary of Findings table in their review. A Summary of Findings table is an optional, although strongly recommended, means of presenting findings for the most important outcomes, whether or not evidence for outcomes is available from research studies (i.e. the summary for an outcome may be "no research evidence available"). A Summary of Findings table includes, where appropriate: typical absolute risks for people receiving experimental and control interventions; estimates of relative effect (e.g. risk ratio or odds ratio); a depiction of the quality of the body of evidence; comments; and footnotes. The assessment of the quality of the body of evidence should follow the GRADE framework, which combines considerations of Risk of Bias, directness, heterogeneity, precision and publication bias.

The *Cochrane Handbook for Systematic Reviews of Interventions* (www.cochrane-handbook.org) includes a full specification and discussion of Summary of Findings tables in Chapter 11 (Section 11.5) 'Presenting results and Summary of Findings tables'; and an overview of the GRADE system in Chapter 12 (Section 12.2) 'Interpreting results and drawing conclusions'.

We strongly encourage authors to use the GRADEpro software available for download at www.cochrane.net/grade to create Summary of Findings tables. The software imports information needed to prepare the table from a RevMan file; leads authors through the development of a Summary of Findings table, including judgements about the quality of evidence; provides context sensitive help; and produces a formatted table that can be imported into RevMan.

The format of Summary of Findings tables produced using GRADEpro has been developed over several years through wide consultation, user testing and evaluation. It is designed to support the optimal presentation of the key findings of reviews.

The current version of GRADEpro is usable with the Windows operating system only.



RevMan 5: Risk of Bias tool

Sally Hopewell and Julian Higgins

The extent to which a Cochrane review can draw valid conclusions about the effects of an intervention depends on whether the data and results from the included studies are themselves valid. In particular, a meta-analysis of invalid studies may produce misleading results. An assessment of the validity of the included studies is, therefore, an essential component of a Cochrane review and should influence the analysis, interpretation, and conclusions of the review.

RevMan 5 and the new Version 5.0.0 of the *Cochrane Handbook for Systematic Reviews of Interventions* contain a new approach for assessing the risk of bias in studies included in Cochrane reviews. It is a two-part tool, addressing six specific domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and 'other issues'. A Risk of Bias table should be prepared to present the results from this tool for each included study. The first part of the tool involves describing what was reported to have happened in the study. The second part of the tool involves assigning a judgement relating to the risk of bias for that entry. This is achieved by answering a pre-specified question about the adequacy of the study in relation to the entry, such that a judgement of 'Yes' indicates low risk of bias, 'No' indicates high risk of bias, and 'Unclear' indicates unclear or unknown risk of bias.

The domains included in the new Risk of Bias tool, with details of what is required in a Risk of Bias table, include:

- **Sequence generation:** describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
- **Allocation concealment:** describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.
- **Blinding of participants, personnel and outcomes:** describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.
- **Incomplete outcome data:** describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.

- **Selective outcome reporting:** state how the possibility of selective outcome reporting was examined by the review authors, and what was found.

- **Other sources of bias:** state any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.

The new tool specifically addresses risk of bias rather than quality. Furthermore, some sources of bias, such as blinding and incomplete outcome data, may differ for different outcomes, so authors are encouraged to assess them separately for different outcomes. Ambiguous terms such as 'double-blind' and 'intention-to-treat' are discouraged in favour of specific descriptions, e.g. *who* was blinded, and *which participants* were included in the analysis (and why). Detailed criteria for these judgements are included in Chapter 8, 'Assessing risk of bias in included studies', of the new Handbook (www.cochrane-handbook.org).

RevMan 5: Diagnostic test accuracy reviews

Mariska Leeflang

RevMan 5 enables the development of Cochrane reviews of diagnostic test accuracy (DTA). Diagnostic test accuracy is the ability of a test to differentiate between participants with and without a particular target condition or disease. Typical outcome measures are sensitivity (the true positive proportion) and specificity (the true negative proportion). As the methods and reporting of these reviews differ markedly from intervention reviews, it was a lot of work for the IMS team to make RevMan 5 suitable for diagnostic test accuracy reviews and they did a great job!

The differences between intervention and DTA reviews start with the title of the DTA review and continue into its text, where specific headings are needed. Also, the 'Characteristics of Included Studies' involve different items. The diagnostic counterpart of the Risk of Bias table is the methodological quality table. The relationship between certain design features and biased results is not (yet) established and may differ for sensitivity and specificity outcomes. These are the main reasons why there is no Risk of Bias table for DTA reviews, but a methodological quality table instead.

The most important new features can be found in the data and analysis section. Data tables result in two coupled forest plots, one for sensitivity and one for specificity. There is no summary pooled estimate (the 'diamond') at the bottom of the forest plots. The results are also depicted in a ROC plot. The analyses need to be done outside RevMan, but the parameters for these analyses can be entered into RevMan and can subsequently be used to draw summary ROC curves or point estimates with a 95% confidence ellipse.



If you would like more information about Cochrane DTA reviews, please visit the DTA website at <http://srdata.cochrane.org/en/index.html>.

RevMan 5: Overviews of reviews

Lorne Becker

With the growth of *The Cochrane Library*, there are now many situations in which different interventions for a given clinical condition or health problem are assessed in two or more Cochrane intervention reviews. As an example, seven different Cochrane reviews address the possible interventions for a child who wets the bed. While the various Cochrane reviews usually refer to one another, it can be difficult for a decision maker (such as a clinician, policy maker, or informed consumer) to get the ‘big picture’ of what is contained in *The Cochrane Library* about the decision they face. Cochrane overviews (previously called ‘Umbrella reviews’) are designed to address this gap.

Each overview will focus on a specific clinical decision and will serve as a ‘friendly front end’ to *The Cochrane Library*, allowing the reader a quick summary (and an exhaustive list) of Cochrane intervention reviews relevant to that decision and of their findings. In the absence of a relevant Cochrane intervention review, Cochrane overviews may additionally include systematic reviews published elsewhere.

Overviews have a similar structure to intervention reviews, but include reviews rather than individual studies as their primary unit of focus and analyses. An ‘overviews of reviews’ table, designed to reflect the Summary of Findings tables in Cochrane intervention reviews, is used to summarize and compare findings from the intervention reviews included in the overview. With the release of RevMan 5, it is now possible to publish Cochrane overviews as part of the *Cochrane Database of Systematic Reviews*, but several have already appeared as ‘Umbrella reviews’ in *Evidence-Based Child Health: A Cochrane Review Journal*.

This new type of Cochrane review raises a number of methodological challenges, some of which have already been addressed in presentations at recent Cochrane Colloquia. The Cochrane working group that developed overviews included members of several Methods Groups (Statistical, Adverse Effects, and Prognosis) and we look forward to continued input from Methods Groups as overviews are produced and published.

Towards better reporting of health research: update on the EQUATOR Network development

Iveta Simera and Doug Altman

The EQUATOR Network (Enhancing the QUALity and Transparency Of health Research) is an international initiative that aims to improve the reliability of scientific publications by promoting transparent and accurate reporting of health research through the efficient use of robust reporting guidelines.

Last year we described the project’s initial phase. Since then, EQUATOR has made considerable progress. We have focused on a few strategic goals – identifying potential partners, collaborators and user groups; securing sustainable funding; collating resources and creating an EQUATOR website; and establishing our presence in the world of health research publishing.

EQUATOR aims to increase the use of reporting guidelines. The EQUATOR website and training courses are the primary tools for achieving this goal. Our website (www.equator-network.org/) is becoming a known resource of available reporting guidance. This initial simple site is being gradually developed to provide a comprehensive digital library for health research reporting, guidance for the development of robust reporting guidelines, tools to facilitate their use, educational materials and EQUATOR training courses.

Groups that would especially benefit from learning more about the importance of high quality of research reporting and use of reporting guidelines are researchers (authors and readers of research articles), journal editors, peer reviewers, and research funders. The first phase of the EQUATOR training programme development will focus on journal editors and peer reviewers. They play an important role in safeguarding the high quality of research publications. This group is also relatively easy to reach with potentially a good ratio of costs invested in the training programme development and benefits derived from its implementation. The first three training workshops were piloted this year; they were all attached to important meetings, which raised the awareness of good reporting and the EQUATOR Network considerably (International Society for Medical Publication Professionals, Philadelphia, April 2008; Council of Science Editors’ Annual Meeting, Vancouver, May 2008; and EQUATOR Network Launch Meeting, London, June 2008).

The EQUATOR Network is steadily growing. Over 200 people have already registered through our website to become part of this initiative. We want to encourage mutual collaboration and harvest the expertise of this group through an online discussion forum and through participation in the EQUATOR voluntary committees advising on the development of different activities (e.g. website, training, research projects, etc.).

The EQUATOR Network is still in its ‘infant’ stage; it needs good ‘parenting’ and abundance of good advice, commitment and contributions. We would like to hear from individuals and organizations who are willing to contribute to our effort towards more reliable health research literature.



The EQUATOR Network Steering Group: Doug Altman, Director, Centre for Statistics in Medicine, Oxford, UK. John Hoey, Program Director, Community Medicine, Queen's University, Kingston, Canada. David Moher, Director, Chalmers Research Group, Ottawa, Canada. Kenneth Schulz, Vice President, Quantitative Sciences, Family Health International, Chapel Hill, USA. Contact: Iveta Simera, EQUATOR Network Project Manager, iveta.simera@csm.ox.ac.uk.

We should like to thank the National Health Service National Library for Health and National Institute for Health Research, UK for providing funding for the EQUATOR project.



PUBLISHED METHODOLOGICAL RESEARCH - structured abstracts and commentaries

Systematic reviewers neglect bias that results from trials stopped early for benefit

Bassler D, Ferreira-Gonzalez I, Briel M, Cook DJ, Devereaux PJ, Heels-Ansell D, Kirpalani H, Meade MO, Montori VM, Rozenberg A, Schünemann HJ, Guyatt GH. *Journal of Clinical Epidemiology* 2007; 60:869-873.

STRUCTURED ABSTRACT

Background: As randomized trials accrue patients and measure outcomes, interim results sometimes suggest large treatment effects that appear unlikely to be due to chance. Consequently, the investigators may conclude that one treatment is superior to the other and stop the trial before reaching the target sample size.

Objective: To examine how authors of systematic reviews that include randomized trials that are stopped early for benefit (truncated randomized trials) address the potential for overestimation of treatment effects and to determine the impact of the truncated randomized trials on pooled results.

Design: *The Cochrane Library* and MEDLINE were searched and systematic reviews that included at least one truncated randomized trial were evaluated. Approaches that authors used to address potential overestimates of treatment effect by including truncated randomized trials were documented. The impact of truncated randomized trials in meta-analyses of the outcomes that led to their early termination were assessed.

Main results: Of 96 systematic reviews that included at least one truncated randomized trial, 44 (46%) included more than one truncated randomized trial, 68 (71%) did not mention truncation at all, and two (2%) documented early stopping for benefit as a criterion for methodological quality. Of 47 meta-analyses in which authors reported, or it was possible to calculate, the contribution of the truncated randomized trials to the pooled results, the truncated randomized trials contributed more than 40% of the weight in 16/47 (34%).

Conclusion: Most systematic reviews and meta-analyses including truncated randomized trials fail to consider the possible overestimates of effect that may result from early stopping for benefit. Safeguards are recommended to address this possibility.

COMMENTARY

Prepared by Jayne Tierney

Benefits that are seen early in randomized controlled trials can occur by chance¹, and are often implausibly large.² Stopping randomized trials early on the basis of such results can exaggerate treatment effects, which may be exacerbated further, if one or more of these 'truncated' trials are subsequently included in a meta-analysis. This is a likely scenario, because randomized trials stopped early for benefit are often published in high impact journals and achieve a high profile.²

The authors of this paper³ systematically identified 96 systematic reviews that incorporated at least one trial that had stopped early for benefit. The majority of these reviews included a meta-analysis of the outcome used as the basis for stopping the trial, either as the primary or secondary analysis, and used a fixed-effect model. Where it could be calculated, the weight contributed by the truncated randomized trials was greater than 40% in about a third of the primary and half of the secondary analyses. Despite these findings, the potential impact of the truncated randomized trials on the results of these systematic reviews was rarely mentioned, and only two reviews formally assessed this using sensitivity analyses.

The study highlights that randomized trials that stop early for benefit are commonly included in systematic reviews, but are rarely accounted for. The authors acknowledge that they may have failed to identify some truncated randomized trials, because they are not always clearly reported as such, and so the problem may well be underestimated. They recommend that authors of systematic reviews report randomized trials that have stopped early, and take them into account in explorations of heterogeneity. Unfortunately, this can only be achieved if the rules or reasons for stopping trials early are regularly provided in trial reports.

Simulation studies have suggested that when the true effect of a treatment is small, randomized trials that have stopped early will inflate estimates of effect and increase heterogeneity (artificially) in meta-analysis.⁴ If using a



fixed-effect model in this scenario, smaller trials, which are also likely to be those that stopped early, will contribute less weight to the meta-analysis and so bias in the estimation of effect is likely to be small.⁴ However, a random-effects model would place more emphasis on small trials that stopped early, with potentially greater bias in the meta-analysis estimate.⁴ Thus, there is a need to investigate how randomized trials that stopped early for benefit might influence the results of a cohort of real systematic reviews, ideally ones showing variation in the magnitude of the treatment effect, and spanning a number of healthcare areas.

In the meantime, where possible, authors of systematic reviews should report randomized trials that stopped early, and carry out sensitivity analyses to examine how estimates of effect and heterogeneity are influenced by these trials. If it is not clear whether included trials have stopped early, standard methods of assessing small study effects may help identify these, other small study biases or both.⁵ Users of systematic reviews should be aware that randomized trials that have stopped early for benefit are another potential source of bias in meta-analysis.

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Impact of adjustment for quality on results of meta-analyses of diagnostic accuracy

Leeftang M, Reitsma J, Scholten R, Rutjes A, Di Nisio M, Deeks J, Bossuyt P. *Clinical Chemistry* 2007; 53:164-172.

STRUCTURED ABSTRACT

Background: Healthcare professionals seeking the best information about diagnostic tests increasingly turn to systematic reviews of test accuracy studies, yet a review's summary estimate can be biased if the studies in the review are flawed. An evaluation of the quality of the original studies, therefore, is an essential component of any systematic review.

Objective: To examine whether and to what extent different strategies of defining and incorporating quality of included studies affect the results of meta-analyses of diagnostic accuracy.

Design: The methodological quality of 487 diagnostic accuracy studies in 30 systematic reviews were assessed using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) checklist. Three different statistical approaches to incorporate the quality assessment results into meta-analyses were applied: (a) The 'restrict' strategy applied to meta-analysis of high quality studies only. Studies were regarded as 'high quality' when they fulfilled all quality criteria. (b) The 'adjust all' strategy involved multivariable adjustment for all individual quality items by including all these items in a single multivariable model, irrespective of the strength of the association between these items and the diagnostic odds ratio (DOR). (c) The 'selective adjustment' strategy consisted of multivariable adjustment for only those quality items that were significantly associated with the DOR in a univariable analysis. Magnitudes of DOR, widths of their confidence intervals and changes in a hypothetical clinical decision were compared between the three strategies.

Main results: Applying an evidence-based definition of quality (items 5, 6, 10, and 11 of the QUADAS checklist) identified 72 (15%) of the 487 original studies as of high quality. This small number was partly due to poor reporting of quality items. None of the strategies for accounting for differences in quality led systematically to accuracy estimates that were less optimistic than ignoring quality in meta-analyses. Limiting the review to high-quality studies considerably reduced the number of studies in all reviews, with wider confidence intervals as a result. In 18 reviews, the quality adjustment would have resulted in a different decision about the usefulness of the test.

Conclusions: Although reporting the results of quality assessment of individual studies is necessary in systematic reviews, reader wariness is warranted regarding claims that differences in methodological quality have been accounted for. Obstacles for adjusting for quality in meta-analyses are poor reporting of design features and patient characteristics and the relatively low number of studies in most diagnostic reviews.

COMMENTARY

Prepared by Penny Whiting



This article looks at different strategies for incorporating quality into diagnostic test accuracy reviews. Quality assessment is an essential component of any systematic review, but there is debate regarding the best method for incorporating the results of the quality assessment. Although a number of previous studies¹⁻⁶ have investigated the quality of test accuracy studies, very few studies have looked at how quality should be incorporated into the review.

This study was generally well conducted, although it does suffer from some minor limitations. The Moses-Littenberg Summary Receiver Operating Characteristic model with the diagnostic odds ratio (DOR) as the primary outcome measure was used for the analysis. However, as the authors acknowledge, quality may affect estimates of sensitivity and specificity while leaving the DOR unchanged. A more robust analysis would have used the bivariate model to investigate the effects of quality on estimates of both sensitivity and specificity.

Two sets of quality items were used to incorporate quality based on subgroups of three and four items included in the QUADAS tool. A problem with using a definition of quality based on a limited number of items is that although these may be the most important quality items for one particular topic, for other topics other items may be of greater importance. A related problem is judging studies to be of 'high quality'. The results of this study suggest that a generalised approach where all studies that fulfil certain criteria are considered to be of high quality is not appropriate for test accuracy studies. This is similar to the finding that quality scores should not be used in diagnostic test accuracy reviews as different methods of weighting individual items from the same quality assessment tool produces different quality scores and differing conclusions on the effects of quality.⁴

Incorporation of the results of the quality assessment into systematic reviews should therefore involve investigation of the association of individual quality items with estimates of diagnostic accuracy. The quality assessment should be tailored to the review topic and items thought to be of particular importance to this topic should be pre-specified and investigated as individual co-variables in the analysis.

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A systematic review highlights threats to validity in studies of barriers to cancer trial participation

Fayter D, McDavid C, Eastwood A. *Journal of Clinical Epidemiology* 2007; 60:990-1001.

STRUCTURED ABSTRACT

Background: Recruitment to trials of cancer treatments continues to present a challenge and may limit the statistical power of the trial to detect a treatment effect. Additionally, the external validity of the trial will be threatened because the sample may be less representative of the population in which the treatment might be used. At worst the trial may not recruit sufficient numbers of participants to proceed. Low participation rates may thus delay the potential introduction of new treatments and more detailed evaluation of existing ones.

Objective: To investigate the barriers, modifiers, and benefits involved in participating in randomized controlled trials of cancer therapies as perceived by healthcare providers and patients.

Design: A systematic review of the literature was conducted to identify published and unpublished studies in any language using electronic databases searched from 1996 to 2004, contact with experts, and searching reference lists. All study designs were acceptable provided relevant data were reported. Two reviewers were involved in the selection of studies, data extraction, and quality assessment processes. Studies were combined in a narrative synthesis.

Main results: Fifty-six studies met the inclusion criteria and represented the perspective of the patient or the healthcare provider or both. Although a range of barriers to trial participation were identified, a number of threats to the internal and external validity of the included studies limited interpretation of the evidence.

Conclusions: The limitations within the evidence base do not permit a clear interpretation of the barriers, moderators, and benefits involved in participation in cancer trials. It is recommended that trialists prospectively identify the issues relevant to a particular trial using the current research as a



starting point. Checklists are reported to help guide this process.

COMMENTARY

Prepared by Shaun Treweek

Randomized trials are widely considered the best way to evaluate the effect of healthcare interventions but recruiting participants can be a challenge. Estimates vary as to what proportion of trials fail to recruit to target and on time but around half is probably conservative. Some trials are sunk by poor recruitment and all trialists fear the deceptively harmless-sounding Lasagna's Law, where eligible participants suddenly vanish as soon as a trial starts.

Given this, high quality reviews, such as that by Fayter and colleagues on participation in cancer trials, are to be welcomed. The review is not one of interventions, rather the reviewers were interested in the barriers, modifiers and benefits involved in participating in cancer trials as perceived by health professionals and patients.

The review had two main findings. Firstly, the quality of the literature on this topic is often poor, with selection bias, small samples, untested survey instruments and problematic data collection being common. This, along with poor reporting, meant that it was difficult to say whether the identified predictors of trial participation were really predictors, or just features of the study designed to identify them. The second finding is that these weaknesses make it impossible to state with confidence that X, Y and Z are, and always are, barriers to trial participation. There are candidates: time constraints, resource issues and the importance of the research question being three. But at present we must content ourselves with checklists of issues worth considering.

Disappointing perhaps. How much more satisfying it would be to be able to say that we know what the barriers to participating in cancer (and other) trials are. However, if trialists start to use the checklists given in this review when planning their trials, it seems reasonable to believe that many recruitment problems will be avoided, or at least reduced. If these same trialists then report how they identified and addressed barriers to participation perhaps authors of reviews will one day be able to present X, Y and Z to a waiting world.

Randomized trials with concurrent economic evaluations reported unrepresentatively large clinical effect sizes

Gilbody S, Bower P, Sutton AJ. *Journal of Clinical Epidemiology* 2007; 60:781-786.

STRUCTURED ABSTRACT

Background: There is an increasing interest in both clinical effectiveness and cost-effectiveness when examining the

role of new and innovative healthcare interventions. The quality of any economic evaluation will only be as good as the clinical effectiveness data on which it is based. There is a danger that the decision to publish trial-based economic studies is in some way influenced by the results of either the clinical evaluation or the economic evaluation potentially making interventions seem more attractive or cost-effective than they really are.

Objective: To examine whether randomized economic evaluations report clinical effectiveness estimates that are unrepresentative of the totality of the research literature.

Design: From 36 studies (12,294 patients) of enhanced care for depression, the pooled clinical effect sizes in studies with a concurrent economic evaluation were compared to those in studies that did not publish a concurrent economic evaluation, using meta-regression.

Main results: The pooled clinical effect size of studies publishing an economic evaluation was almost twice as large as that of studies that did not publish an economic evaluation (pooled standardized mean difference [SMD] in randomized trials with an economic evaluation = 0.34; 95% CI = 0.23-0.46; pooled SMD in randomized trials without an economic evaluation = 0.17; 95% CI = 0.10-0.25). This difference was statistically significant (SMD between group difference = -0.17; 95% CI: -0.31 to -0.02; P = 0.02).

Conclusions: Publication of an economic evaluation of enhanced care for depression was associated with a larger clinical effect size. Cost-effectiveness estimates should be interpreted with caution, and the representativeness of the clinical data on which they are based should always be considered. Further research is needed to explore this observed association and potential bias in other areas.

COMMENTARY

Prepared by Ian Shemilt

Healthcare decision makers often need to consider not only whether an intervention works but also whether its adoption will lead to a more efficient use of resources. Optimal decisions therefore require 'best evidence' on both effectiveness and cost-effectiveness.

Full economic evaluation involves the comparative analysis of alternative courses of action in terms of both costs (resource use) and consequences (beneficial and adverse effects)¹. As the authors of this study highlight, the quality of any full health economic evaluation is in part predicated on the reliability of the clinical effectiveness data on which it is based. Economic evaluations based on unreliable estimates of intervention effects are likely to generate unreliable estimates of intervention cost-effectiveness.

The study finds that clinical effect sizes in randomized trials of enhanced care for depression that published an economic evaluation are systematically larger than those in randomized trials that did not publish an economic



evaluation. This finding is plausibly attributed to presence of publication bias in favour of studies that cast enhanced care as comparatively attractive in terms of cost-effectiveness. The study is an important contribution to a growing body of methodological research literature on publication bias in economic evaluation² and complements recent work on sources and quality of evidence used in the development of economic decision models in health technology assessments.^{3,4}

This finding has two practical implications for authors of Cochrane reviews aiming to include coverage of evidence obtained from published and unpublished health economic evaluations. First, when assessing the quality of a full economic evaluation, the critical appraisal process should include consideration of all sources of potential bias that may apply to the effectiveness study (or studies) on which the economic evaluation is based. Second, the direction and magnitude of clinical effect sizes observed in included full economic evaluations (and possibly a pooled effect size from several economic evaluations) should, wherever possible, be set in the context of pooled effect sizes obtained using a meta-analysis of included effectiveness studies. This will allow authors of reviews to comment on whether the extant health economics literature is based on reliable evidence of intervention effects. Further guidance on these issues is published in a new chapter on 'Incorporating economics evidence' in the new *Cochrane Handbook for Systematic Reviews of Interventions*.²

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Systematic reviews of test accuracy should search a range of databases to identify primary studies

Whiting P, Westwood M, Burke M, Sterne J, Glanville J.
Journal of Clinical Epidemiology 2008; 61:357-364.

STRUCTURED ABSTRACT

Background: Extensive literature searches that aim to identify as many relevant studies as possible are key components of a systematic review. Failure to identify and include relevant studies in a diagnostic test accuracy systematic review may lead to biased estimates of accuracy and reduced precision.

Objective: To estimate the yield from searching a range of bibliographic databases and additional sources to identify diagnostic test accuracy studies for systematic reviews.

Design: An empirical study was conducted to assess eight diagnostic test accuracy systematic reviews and their database searches: MEDLINE, EMBASE, BIOSIS, Science Citation Index, LILACS, Pascal and CENTRAL. Studies included in each systematic review were used as the 'gold standard' against which yield was estimated. For each database, studies were classified in each gold standard set as being (1) included in the database and identified by searches, (2) included and not identified by searches, and (3) not included in the database. To assess the value of searching databases beyond MEDLINE, the numbers and proportions of studies in the gold standard sets were calculated for those (1) not identified by searching MEDLINE; (2) not included in any of the databases searched and (3) not identified by the searches of any of the databases searched for the reviews. For each review the number of records retrieved by the searches of each database was recorded to calculate the 'NNR' - the number of titles and abstracts that have to be read to identify one relevant study. Review authors were also contacted to determine how studies not found in any of the databases searched were identified to provide an indication of the value of searching additional sources such as grey literature, handsearching, reference checking, or contacting subject experts or test manufacturers.

Main results: No search identified all studies in any gold standard set. EMBASE, Science Citation Index, and BIOSIS contained studies that were not in MEDLINE. The highest proportion of records in the gold standard study set were included in and retrieved by searching MEDLINE. A slightly smaller proportion of studies in the gold standard sets were included in EMBASE and sensitivity remained high. Even though significant proportions of the gold standard study sets were included in Science Citation Index, BIOSIS and Pascal, the searches of these databases often performed with low sensitivity. Over 20% of studies in the gold standard sets were not identified by searching MEDLINE. Six studies in LILACS were not in any other



database. The majority (80%) of database searches used in individual reviews produced NNR values less than 200. Eight gold standard studies were not included in any of the databases, and a further 22 were not identified by the electronic search strategies.

Conclusions: Systematic reviews of diagnostic test accuracy studies should search a range of databases. Even searches designed to be very sensitive, that do not use study design filters, can fail to identify relevant studies. Other supplementary methods for locating studies such as reference checking of relevant studies should be used.

COMMENTARY

Prepared by Anne Eisinga

Most research into the retrieval of test accuracy studies has focused on developing and evaluating methodological search filters of diagnostic terms, a process that is impeded by inadequate and inconsistent reporting, the absence of appropriate indexing terms in some databases, and inconsistent indexing in databases where terms are available. The use of these filters can lead to the omission of a considerable number of relevant studies¹⁻⁴. This new study examines eight systematic reviews, for which extensive, well-documented searches (not limited by filters) had been carried out at the Centre for Reviews and Dissemination, University of York. It is a timely, informative and well-conducted study, providing useful insight into which sources are likely to be worth searching to retrieve studies of diagnostic test accuracy for inclusion in systematic reviews. It is the first such study. The only other related research⁵ compares five specialist review databases for locating systematic reviews of diagnostic studies. Both studies have been used to inform the forthcoming 'Searching for studies' chapter of the *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*.

Whiting et al used a relative recall gold standard⁶ to assess the yield from searching a range of bibliographic databases and other sources. Further research is needed to assess the potential yield of test accuracy studies in biomedical and subject-specific databases not examined in this study, such as CINAHL, PsycINFO etc.

The study found that authors of systematic reviews of test accuracy who search a single database, such as MEDLINE, are very likely to miss relevant studies. MEDLINE, EMBASE, BIOSIS and Science Citation Index each provided additional studies for the reviews included in this study. Little or no additional yield was derived from searching Pascal or CENTRAL. Although searching LILACS did not identify many relevant studies overall, those identified were often not in any of the other databases but the number needed to be read (NNR) to find one relevant study was the highest of all the databases.

Thirty studies (6%) included in the eight systematic reviews were not identified by searches of these databases. The most

effective additional method for finding them was by checking the bibliographies of studies found for the reviews.

The additional yield from grey literature databases was very limited for the reviews examined by this study. However, the authors rightly point out that searching such sources may be of value if unpublished studies are likely to report results that differ consistently from the published literature. We do not know if this is the case at the moment, because the importance of publication bias in systematic reviews of test accuracy is unknown.

This retrospective study reveals that even searches designed to be very sensitive (using a range of subject headings, free text terms, synonyms, truncation and not including a diagnostic filter) fail to identify some relevant studies that are in the databases that were searched.

The authors pinpoint the key area for future research: to compare the proportion of a consistently derived gold standard set of studies identified by searches that used a diagnostic filter with the proportion of studies identified by searches that did not use such a filter in order to address the important question of whether a filter reduces the number of relevant studies identified or simply limits the number of irrelevant titles and abstracts to be checked.

Other factors than the effectiveness of searching can also affect the completeness of the set of studies included in systematic reviews. Whiting et al were not able to assess the quality of screening by the review authors – where very large numbers of studies retrieved by database searches must be screened, agreement between review authors may be reduced and the probability of missing relevant articles may be higher. Further research on methods to reduce the number of records to be screened without excluding relevant studies is needed; the potential to develop new, more effective filters remains. The authors will undertake textual analysis of the gold standard sets from this study in further research, using the methods they and others developed, which were recently used to revise the Cochrane Highly Sensitive Search Strategy for identifying reports of randomized trials in MEDLINE⁷. Progress should also come with further uptake of the STARD guidelines⁸ for reporting diagnostic test accuracy studies. This should facilitate better use of existing indexing terms and, together with encouraging database producers to introduce specific terms for diagnostic accuracy studies, should enhance the potential for development of more efficient search filters.

Authors of forthcoming Cochrane systematic reviews of diagnostic test accuracy will document their search strategies and yield, which should also provide evidence on which sources are worth searching for studies of diagnostic test accuracy.

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Almost all articles on cancer prognostic markers report statistically significant results

Kyzas PA, Denaxa-Kyza D, Ioannidis JP. *European Journal of Cancer* 2007; 43:2559-2579.

STRUCTURED ABSTRACT

Background: Cancer prognosis has been a field of intensive research for many years. Besides traditional clinical markers, basic and translational research have generated

hundreds of candidate markers for prediction of outcomes in cancer patients.

Objective: To understand and examine the extent of the pursuit for statistically significant results in the prognostic literature of cancer, by selective reporting of specific analyses and outcomes favouring results that pass the threshold of nominal statistical significance.

Design: Three hundred and forty articles included in prognostic marker meta-analyses were evaluated (Database 1) and 1575 articles on cancer prognostic markers were published in 2005 (Database 2). Each article was examined to see whether the abstract reported any statistically significant prognostic effect for any marker and any outcome ('positive' articles). 'Negative' articles were further examined for statements made by the investigators to overcome the absence of prognostic statistical significance. Articles from Database 1 were also examined to understand how the relative risks were included in the respective meta-analyses.

Main results: 'Positive' prognostic articles comprised 90.6% and 95.8% in Databases 1 and 2 respectively. Most of the 'negative' prognostic articles claimed significance for other analyses, expanded on non-significant trends or offered apologies that were occasionally remote from the original study aims. Only five articles in Database 1 (1.5%) and 21 in Database 2 (1.3%) were fully 'negative' for all presented results in the abstract and without efforts to expand on non-significant trends or to defend the importance of the marker with other arguments. Of the statistically non-significant relative risks in the meta-analyses, 25% had been presented as statistically significant in the primary papers using different analyses compared to the respective meta-analyses.

Conclusions: Almost all articles on cancer prognostic marker studies highlight some statistically significant results. Under strong reporting bias, statistical significance loses its discriminating ability for the importance of prognostic markers.

COMMENTARY

Prepared by Richard Riley

Reporting biases in the included studies are a major threat to the credibility of meta-analysis. Studies may be unpublished if their results are not statistically significant, whilst published studies often neglect or partially report non-significant results. Such biases cause meta-analysis to overestimate the true effect of interest, and are well documented for randomized trials. For less rigorous study designs, such as observational studies, the fear is that reporting biases are even worse. Kyzas et al. demonstrate why, in the field of prognosis, such fears are justified. They reviewed 1915 articles on cancer prognostic markers, and found that 94.9% reported a statistically significant prognostic result in the abstract. Of the remaining 98 articles, only 26 were fully 'negative' in that they did not



elaborate on non-significant trends or provide other (non-prognostic) significant results. Thus totally 'negative' articles represented less than 1.5% of the prognostic literature assessed, dramatically highlighting a bias towards reporting 'positive' results.

Such evidence reinforces why an assessment of reporting bias is a crucial part of Cochrane reviews. It should also motivate us to help improve new research, in order to facilitate evidence-based reviews in the long term. For example, Cochrane reviews are clearly assisted by reporting guidelines such as the CONSORT Statement for randomized trials and the STARD guidelines for diagnostic accuracy studies. In this context, the newly registered Cochrane Prognosis Methods Group (see page 27) aims to facilitate higher quality primary prognosis research, working towards evidence-based prognosis reviews in the future.¹ Members are actively involved in methodological work and in developing research standards, exemplified by the REMARK guidelines for reporting prognostic marker studies,² which Kyzas et al. note as a step forward. Prognostic researchers and other Methods Groups are encouraged to support this initiative, in order to help collectively to alleviate problems akin to those commendably highlighted by Kyzas et al.

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Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration

Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M, STROBE Initiative. *PLoS Medicine* 4: e297.

STRUCTURED ABSTRACT

Background: Much medical research is observational. The reporting of observational studies is often of insufficient quality. Poor reporting hampers the assessment of the strengths and weaknesses of a study and the generalisability of its results.

Objective: To develop recommendations to improve the quality of reporting of observational studies resulting in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.

Design: A two-day workshop in September 2004 was convened with methodologists, researchers, and journal editors to draft a checklist of items. This list was subsequently revised during several meetings of the co-ordinating group and in e-mail discussions with the larger group of STROBE contributors, taking into account empirical evidence and methodological considerations. The workshop and the subsequent iterative process of consultation and revision resulted in the STROBE Statement.

Main results: The STROBE Statement is a checklist of 22 items relating to the title, abstract, introduction, methods results and discussion sections of articles. Eighteen items are common to cohort studies, case-control studies and cross-sectional studies and four are specific to each of three study designs. The STROBE Statement provides guidance to authors about how to improve the reporting of observational studies and facilitates critical appraisal and interpretation of studies by review authors, journal editors and readers. The explanatory and elaboration document is intended to enhance the use, understanding, and dissemination of the STROBE Statement. The meaning and rationale for each checklist item are presented. For each item, one or several published examples and, where possible, references to relevant empirical studies and methodological literature are provided. Examples of useful flow diagrams are also included. The STROBE Statement, this explanatory document, and the associated website (www.strobe-statement.org/) should be helpful resources to improve reporting of observational research.

Conclusions: The STROBE Statement aims to provide helpful recommendations for reporting observational studies in epidemiology. Good reporting reveals the strengths and weaknesses of a study and facilitates sound interpretation and application of study results. The STROBE Statement may also aid in planning observational studies, and guide peer reviewers and editors in their evaluation of manuscripts.

COMMENTARY

Prepared by Barney Reeves

The STROBE Statement is the most recent statement to recommend a checklist of items that authors should address when reporting research.^{1,2} Similar statements, which reviewers may be more familiar with such as CONSORT and STARD, have now been brought together through the EQUATOR Network³ (www.equator-network.org/index.aspx?o=1032) (see page 6). One STROBE publication summarizes the items on the checklist¹ and the other explains and elaborates the 22 items included.² The latter includes helpful examples of good reporting practice and the authors define carefully what they mean by commonly used epidemiological terms, also pointing out that terms are often used incorrectly or imprecisely. Researchers who want to implement STROBE should read these details with the care with which they have been written.



STROBE aims to improve reporting of observational studies, to make reporting more ‘transparent’. So, like CONSORT, STROBE is not directly about the quality of the research. However, better reporting should facilitate critical appraisal by both users and review authors, by ensuring that information about important features of a study are reported. The scope of STROBE is analytical observational epidemiology but, early on, consensus participants chose to focus on the three most commonly used designs, namely cohort, case-control and cross-sectional studies. The authors make it clear that the scope of STROBE includes observational studies of the benefits and harms of medical interventions.¹ Therefore, my comments are about how STROBE may help authors of reviews of observational studies of medical interventions with key challenges: (a) identifying the design used by researchers, and assessing (b) the likelihood of reporting bias and (c) the susceptibility of reported effect estimates to confounding.

(a) Item 1 requires authors to “indicate the study’s design in the title or the abstract.” Unfortunately, observational studies have disparate designs and there is no consensus about their labels; consider, for example, use of the terms ‘trial’ and ‘cohort study’. This item should lead to improved *declarations* of study design but may not address the ability of review authors to determine the eligibility of a study from its title and abstract. Item 4 requires key elements of study design to be described and compliance with this item should help review authors to complete a checklist of what researchers did.⁴

(b) Item 3 requires authors to “state specific objectives, including any pre-specified hypotheses,” and item 7 requires authors to “clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers.” The requirement for a protocol is one of the most important features of a randomized trial to protect against reporting bias, although randomized trials remain at risk.⁵ Therefore, in reports of observational studies, distinguishing aspects of a study that were pre-specified and those that were not, should hold for outcomes (and, ideally, other study details), as well as hypotheses, to avoid open season with respect to reporting bias. STROBE does not appear to do this explicitly. Similarly, the STROBE authors acknowledge the problems of informal/multiple looks at observational data but do not explicitly require authors to identify analyses that were pre-specified or to describe the history behind the particular ‘look’ that is reported. (Pre-specification may be intended by qualification of item 7: “define all *variables considered for and included in the analysis, including all outcomes, ...*”). This point is very important in the specific context of *reviewing* observational studies since there is a real danger that reporting biases can cause collective observational evidence to mislead rather than inform.

(c) Item 7 applies to reporting definitions for confounding factors as well as outcomes. In addition, items 11 and 12 require detailed explanation of “how quantitative variables were handled in analyses” and “statistical methods, including those used to control for confounding”. These

items should help reviewers to understand how researchers measured confounders and controlled for them, and how these features varied across studies.

Like other recommendations to improve the reporting of research, STROBE prompts authors about things they should report – and even provides examples of the kinds of phrases required. Obviously, researchers need to report honestly as well as transparently. Checking honesty is likely to be more difficult with observational studies than randomized trials if definitions cannot be checked against a detailed protocol. I recall a discussion with colleagues some years ago about helping review authors to ‘smell a rat’ when appraising OSMI; I have a nagging worry that STROBE may help the rats to disguise their smells. Peer-reviewer, and review author, beware! “All that glitters is not gold ...gilded tombs do worms enfold”.

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CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration

Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, Schulz KF, CONSORT Group. *PLoS Medicine* 2008; 5:e20.

STRUCTURED ABSTRACT



Background: Clear, transparent, and sufficiently detailed abstracts of conferences and journal articles related to randomized controlled trials are important because readers often base their assessment of a trial solely on information in the abstract.

Objective: To extend the CONSORT (Consolidated Standards of Reporting Trials) Statement to develop a minimum list of essential items, which authors should consider when reporting the results of an RCT in any journal or conference abstract.

Design: A list of items from existing quality assessment tools and empirical evidence was generated. A three-round, modified-Delphi process was used to select items. In all, 109 participants were invited to participate in an electronic survey; the response rate was 61%. Survey results were presented at a meeting of the CONSORT Group in Montebello, Canada, in January 2007, involving 26 participants, including clinical trialists, statisticians, epidemiologists, and biomedical editors. Checklist items were discussed for eligibility for inclusion in the final checklist. The checklist was then revised to ensure that it reflected discussions held during and subsequent to the meeting.

Main results: CONSORT for Abstracts recommends that abstracts relating to randomized trials have a structured format. Items should include details of trial objectives; trial design (e.g. method of allocation, blinding/masking); trial participants (i.e. description, numbers randomized, and number analyzed); interventions intended for each randomized group and their impact on primary efficacy outcomes and harms; trial conclusions; trial registration name and number; and source of funding. It is recommended that the checklist be used in conjunction with its explanatory document, which includes examples of good reporting, rationale, and evidence, when available, for the inclusion of each item.

Conclusions: CONSORT for Abstracts aims to improve reporting of abstracts of randomized trials published in journal articles and conference proceedings. It will help authors of abstracts of these trials provide the detail and clarity needed by readers wishing to assess a trial's validity and the applicability of its results.

COMMENTARY

Prepared by Antje Timmer

Often, information from abstracts is the only information readers get about studies. Reasons differ – readers may lack the time, journal access or language skills to read a full paper. Or, in the case of conference abstracts, the abstract may even be the only report available on a certain study. Whatever the reason, it seems of high importance that the information in the abstract is correct and sufficiently detailed to assess the validity of a study.

CONSORT for Abstracts provides a guideline for informative and concise reporting of randomized controlled clinical trials in journal and conference abstracts. The checklist is available from the CONSORT webpage (www.consort-statement.org). Items for this list were selected using Delphi rounds based on existing quality assessment tools. Following this procedure, information on title, author, contact details, funding and trial registration number were deemed necessary, as were details on the methods (participants' eligibility criteria and setting, interventions, primary outcome, randomization and blinding) and results (numbers randomized, numbers analyzed, recruitment, outcome (results for each group, effect size, precision) and harms). Generally, a structured format is recommended but CONSORT for Abstracts does not give any formal instructions on headings or word count.

The detailed explanatory paper was published in *PLoS Medicine*, presenting information on the item selection procedure. This paper is particularly helpful for authors of abstracts, as all items are introduced using easy to follow examples for illustration. The introduction of CONSORT for Abstracts is also accompanied by a comment in the *Lancet*.¹

It is hoped that CONSORT for Abstracts will be a success similar to CONSORT, with many journals adopting this guideline. It will also be a huge benefit for Cochrane review authors. We will still have to retrieve full articles for quality assessment and data extraction. However, screening for eligible studies will, it is hoped, be greatly facilitated: CONSORT for Abstracts should help to separate the wheat from the chaff.

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EMPIRICAL STUDIES WITHIN THE COLLABORATION

This section aims to highlight some of the current methodological research being carried out within The Cochrane Collaboration. To register ongoing methodological research within The Cochrane Collaboration please contact shopewell@cochrane.co.uk.



Systematic reviews of adverse effects: framework for a structured approach

Yoon K Loke, Deirdre Price, Andrew Herxheimer for the Cochrane Adverse Effects Methods Group

Title: Systematic reviews of adverse effects: framework for a structured approach.

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Background: As every healthcare intervention carries some risk of harm, clinical decision making needs to be supported by a systematic assessment of the balance of benefit to harm. A systematic review that considers only the favourable outcomes of an intervention, without also assessing the adverse effects, can mislead by introducing a bias favouring the intervention. Much of the current guidance on systematic reviews is directed towards the evaluation of effectiveness; but this differs in important ways from the methods used in assessing the safety and tolerability of an intervention.

Objective: To discuss why, how and when to include adverse effects in systematic reviews.

Location: University of East Anglia, UK.

Methods: The discussion paper, which presupposes a basic knowledge of systematic review methodology, was developed by consensus among experienced review authors, members of what was then the Adverse Effects Subgroup of The Cochrane Collaboration, and supplemented by a consultation of content experts in review methodology, as well as those working in drug safety.

Summary of main results: A logical framework for making decisions in reviews that incorporate adverse effects is provided. Situations where a comprehensive investigation of adverse effects is warranted and suggested strategies to identify practicable and clinically useful outcomes are explored. The advantages and disadvantages of including observational and experimental study designs are reviewed. The consequences of including separate studies for intended and unintended effects are explained. Detailed advice is given on designing electronic searches for studies with adverse effects data. Authors of reviews considering adverse effects are given general guidance on the assessment of study bias, data collection, analysis, presentation and interpretation of harms in a systematic review.

Conclusions: Readers need to recognize how strategic choices made in the review process determine what harms are found and how findings may affect clinical decisions. Researchers undertaking a systematic review incorporating adverse effect data should understand the rationale for the

suggested methods and be able to implement them in their review.

Reference:

Loke YK, Price D, Herxheimer A, Cochrane Adverse Effects Methods Group. Systematic reviews of adverse effects: framework for a structured approach. *BMC Medical Research Methodology* 2007; 7:32.

Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials

Julie Pildal, Asbjørn Hróbjartsson, Karsten Juhl Jørgensen, J Hilden, Doug Altman and Peter Gøtzsche

Title: Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials.

Contact: Julie Pildal, The Nordic Cochrane Centre, Rigshospitalet, 3343 Blegdamsvej 9, DK-2100 Copenhagen, Denmark. E-mail: jp@cochrane.dk.

Background: Randomized trials which did not report adequate allocation concealment have been shown to overestimate the benefit of experimental interventions. Without concealment the person in charge of enrolment might channel participants with a better prognosis into his or her preferred treatment, for instance by influencing whether a participant enters the trial at all. The blinding of key people in the trial, sometimes referred to as double-blinding can, however, be inconsistently interpreted.

Objective: To estimate the number of conclusions based on statistically significant results in meta-analyses that would no longer be supported if only trials with reported adequate allocation concealment were included.

Location: The Nordic Cochrane Centre, Denmark.

Methods: A random sample of 38 reviews from Issue 2, 2003 of *The Cochrane Library* and 32 other reviews from PubMed accessed in 2002 were included in the sample. Eligible reviews presented a binary effect estimate from a meta-analysis of randomized trials as the first statistically significant result that supported a conclusion in favour of one of the interventions.

Summary of main results: Thirty-four of the 70 meta-analyses contained a mixture of trials with unclear or inadequate concealment as well as trials with adequate allocation concealment. Four meta-analyses only contained trials with adequate concealment, and 32, only trials with unclear or inadequate concealment. When only trials with adequate concealment were included, 48 of 70 conclusions (69%; 95% CI: 56-79%) lost support. The loss of support mainly reflected loss of power (the total number of participants was reduced by 49%) but also a shift in the point estimate towards a less beneficial effect.



Conclusions: Two-thirds of conclusions in favour of one of the interventions were no longer supported if only trials with adequate allocation concealment were included.

Reference:

Pildal J, Hróbjartsson A, Jørgensen KJ, Hilden J, Altman DG, Gøtzsche PC. Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials. *International Journal of Epidemiology* 2007; 36:847-857.

Reports of clinical trials should begin and end with up-to-date systematic reviews of other relevant evidence

Mike Clarke, Sally Hopewell and Iain Chalmers

Title: Reports of clinical trials should begin and end with up-to-date systematic reviews of other relevant evidence: a status report.

Contact: Mike Clarke, UK Cochrane Centre, National Institute for Health Research, Summertown Pavilion, Middle Way, Oxford, OX2 7LG, UK. E-mail: mclarke@cochrane.co.uk.

Background: Scientific and ethical justification for new clinical trials requires them to have been designed in the light of scientifically defensible assessments of relevant previous research. Reliable interpretation of the results of new clinical trials entails setting them in the context of updates of the reviews upon which they were deemed scientifically and ethically justifiable. Previous research has shown that most reports of randomized trials published in five general medical journals in May 1997 and May 2001 failed to set their results in the context of the findings from similar research.

Objective: To investigate the extent to which the introduction and discussion sections of randomized trials published in five leading medical journals in May 2005 incorporate information about systematic reviews.

Location: UK Cochrane Centre, Oxford, United Kingdom.

Methods: A report was eligible for inclusion as a 'trial' if it met the following three criteria: Firstly, it was published during May 2005 as a full report or paper (that is, not in the editorial, news, research letters, short reports or correspondence sections of the journals), in the *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet* or *New England Journal of Medicine*. Secondly, on the basis of information in the report, "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)" – that is, randomized and quasi-randomized trials, as defined by The Cochrane Collaboration. Finally, the report was principally concerned with the outcomes studied in the trial.

Summary of main results: Eighteen reports of randomized trials were identified. The introduction sections referred to systematic reviews in five (27%) of these reports. None of the discussion sections of the 15 reports of trials, that were not the first published trials to address the question studied, placed the results of the new trial in the context of an updated systematic review of other research. Although reference was made to relevant systematic reviews in five of these 15 reports, there was no integration (quantitative or qualitative) of the results of the new trials in an update of these reviews. In the remaining ten reports there was no evidence that any systematic attempt had been made to set the new results in the context of previous trials.

Conclusions: There is no evidence of progress between 1997 and 2005 in the proportion of reports of trials published in general medical journals which discussed new results within the context of up-to-date systematic reviews of relevant evidence from other controlled trials. Although the proportion of trials referring to systematic reviews in discussion sections has increased, the majority of reports continued to fail even to do this. Similarly, most researchers appear not to have considered a systematic review when designing their trial. Researchers and journal editors do a disservice to the interests of the public and others involved in healthcare decision making by acquiescing in this situation.

Reference:

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. *Journal of the Royal Society of Medicine* 2007; 100:187-190.

Usefulness of systematic review search strategies in finding child health systematic reviews in MEDLINE

Nicole Boluyt, Lisa Tjosvold, Carol Lefebvre, Terry P Klassen and Martin Offringa

Title: Usefulness of systematic review search strategies in finding child health systematic reviews in MEDLINE.

Contact: Nicole Boluyt, Center for Pediatric Clinical Epidemiology, Room H3-145, Emma Children's Hospital, Academic Medical Centre, PO Box 22700, Amsterdam, the Netherlands. Email: n.boluyt@amc.uva.nl.

Background: Several search strategies for locating systematic reviews in MEDLINE have been developed and validated; however, the performance of these filters has never been evaluated in the totality of all articles included in MEDLINE, nor have they been tested for sensitivity and precision in finding child health systematic reviews.

Objective: To determine the sensitivity and precision of existing search strategies for retrieving child health systematic reviews in MEDLINE using PubMed.



Location: Center for Pediatric Clinical Epidemiology, Amsterdam, the Netherlands.

Methods: Articles reporting on the development and validation of systematic review search filters in MEDLINE were identified by searching MEDLINE from January 1995 to January 2006 with the following MeSH terms: *MEDLINE*, *Information Storage and Retrieval/methods*, and *Review, Literature*. In addition, reference lists of relevant articles were reviewed and content experts were contacted to find additional studies. To improve precision, the systematic review filters were combined with a sensitive filter developed by the Cochrane Child Health Field to retrieve only studies in children.

Summary of main results: Nine search filters were identified. The sensitivity of the systematic review filters combined with the child filter ranged from 68% to 96%; sensitivity of the child filter alone was 98%. The number of records retrieved in PubMed (limited to January 1990 to January 2006) by the systematic review filters combined with the child filter ranged from 7861 to 618,053. Precision for the combined filters ranged from 2% to 52%. Poor reporting of specific systematic review criteria, in both titles and abstracts in 25% of the records screened, meant that it was unclear whether the article concerned a systematic review according to the definition used in this review.

Conclusions: The high numbers of records yielded by sensitive search strategies and low precision threaten the use of systematic reviews for clinical decision making and guideline development. The reporting of specific systematic review criteria in titles and abstracts was poor, and reporting recommendations given by Quality of Reporting of Meta-analyses (QUOROM) should be used more strictly. To make identification using MEDLINE easier, there is an urgent need to set minimal criteria that any review should fulfil for it to be indexed as a systematic review.

Reference:

Boluyt N, Tjosvold L, Lefebvre C, Klassen TP, Offringa M. Usefulness of systematic review search strategies in finding child health systematic reviews in MEDLINE. *Archives of Pediatric and Adolescent Medicine* 2008; 162:111-116.

Ghost authorship in industry-initiated randomised trials

Peter C Gøtzsche, Asbjørn Hróbjartsson, Helle Krogh Johansen, Mette T Haahr, Douglas G Altman and An-Wen Chan

Title: Ghost authorship in industry-initiated randomised trials.

Contact: Peter C Gøtzsche, Nordic Cochrane Centre, Rigshospitalet, Dept 7112, Blegdamsvej 9, Copenhagen, DK-2100, Denmark. Email: pcg@cochrane.de.

Background: Ghost authorship, the failure to name, as an author, an individual who has made substantial contributions to an article, may result in lack of accountability. The prevalence and nature of ghost authorship in industry-initiated randomized trials is not known.

Objective: To examine the prevalence and nature of ghost authorship in a cohort of industry-initiated randomized trials by comparing the trial protocols with subsequent publications.

Location: Nordic Cochrane Centre, Denmark.

Methods: All published industry-initiated randomized trials approved in 1994–1995 by the Scientific Ethical Committees for Copenhagen and Frederiksberg in Denmark, were compared with their corresponding trial protocol. Ghost authorship was defined as present if individuals who wrote the trial protocol, performed the statistical analyses, or wrote the manuscript, were not listed as authors of the publication, or as members of a study group or writing committee, or in an acknowledgment.

Summary of main results: Forty-four industry-initiated trials were identified. There were no reports of any trial protocol or publication that stated explicitly that the clinical study report or manuscript was to be written by the clinical investigators, and none of the protocols stated that clinical investigators were to be involved with data analysis. There was evidence of ghost authorship for 33 trials (75%; 95% CI 60%-87%). The prevalence of ghost authorship was increased to 91% (40 of 44 articles; 95% CI 78%-98%) when including cases where a person qualifying for authorship was acknowledged rather than appearing as an author. In 31 trials, the ghost authors identified were statisticians. It is likely that some ghost authors were overlooked as there was limited information to identify the possible omission of other individuals, who would have qualified as authors.

Conclusions: Ghost authorship in industry-initiated trials was very common. Its prevalence could be considerably reduced, and transparency improved, if existing guidelines were followed, and if protocols were publicly available.

Reference:

Gøtzsche PC; Hróbjartsson A; Johansen HK; Haahr MT; Altman DG, Chan A-W. Ghost authorship in industry-initiated randomised trials. *PLoS Medicine* 2007; 4:e19.





Thomas C Chalmers M.D. Award - 2007

The Thomas C Chalmers M.D. prize is awarded annually for the best oral or poster presentation at the Cochrane Colloquium. In 2007, in São Paulo, Brazil, it was jointly awarded to Jan Friedrich, Neill Adhikari, Arne Ohlsson and Joseph Beyene for their study entitled, 'Ratio of means as an alternative to mean differences for analyzing continuous outcome variables in meta-analysis: a simulation study' and to Nikolaos Patsopoulos, John Ioannidis and Evangelos Evangelou for their study entitled, 'Uncertainty of heterogeneity in meta-analysis'.

Ratio of means as an alternative to mean differences for analyzing continuous outcome variables in meta-analysis

Jan O Friedrich, Neill KJ Adhikari, Arne Ohlsson and Joseph Beyene

Title: Ratio of means as an alternative to mean differences for analyzing continuous outcome variables in meta-analysis: a simulation study.

Contact: Jan O. Friedrich, St. Michael's Hospital, University of Toronto, Bond Street, Toronto, Ontario M5B 1W8, Canada. Email: j.friedrich@utoronto.ca.

Background: In meta-analysis of continuous outcomes, the most commonly used effect measure is the difference in means, either directly [mean difference (MD)] or divided by the pooled standard deviation [standardized mean difference (SMD)]. We recently used a new method to meta-analyse continuous outcomes by calculating a ratio of mean values (RoM) instead of a difference for each study. We estimated the variance of this ratio using the Delta method and used inverse variance weighting to pool ratios. Both SMD and RoM but not MD allow pooling of studies with outcomes expressed in different units and comparisons of effect sizes across different interventions. Interpretation of SMD requires knowledge of the pooled standard deviation (SD), a quantity generally unknown to clinicians. In contrast, this information is not required when using RoM to estimate the expected treatment effect for a particular patient.

Objective: To test the hypothesis that MD, SMD and RoM exhibit comparable performance characteristics using simulation.

Location: University of Toronto, Canada.

Methods: Parameter values used to simulate data sets (SAS version 8.2) were chosen to be representative of those commonly encountered in meta-analyses of continuous outcomes: effect sizes (0.2, 0.5, or 0.8 pooled SD units to represent small, medium, and large effect sizes), SD (10%, 40%, or 70% of the mean value to reflect a narrow, medium

and broad distribution), number of trials (5, 10, or 30), number of control and experimental participants per trial group (10 or 100), and heterogeneity ($I^2=0$ or 50% to 95%). The simulations used equal standard deviations for the control and experimental groups and were repeated 10,000 times for each scenario.

Summary of main results: Whereas the MD method was relatively free of bias (<1.5%) for all scenarios, the SMD method exhibited negative bias (around 5%) in the scenarios with few patients ($n=10$), as described previously. The RoM method was free of bias (<1.5%) except for some scenarios with a broad distribution and medium to large effect sizes. There was a negative bias ranging from 1.6% to 3.8% for such scenarios with 10 patients per trial group and 10 or 30 trials, and a positive bias of around 2% for such scenarios with 100 patients per trial group, five trials and significant heterogeneity ($I^2>90\%$). The proportion of the scenarios for which the 95% confidence interval contained the true effect size (i.e. coverage) was identical for all scenarios with minimal bias. The coverage was as expected (i.e. close to 95%) for the scenarios with no heterogeneity, but decreased when heterogeneity was introduced. RoM scenarios with 30 trials and negative bias exceeding 1.5% (discussed above) demonstrated lower coverage than MD (89% to 92% vs. 94%). Coverage of RoM was also slightly lower than MD (90% to 92% vs. 92% to 94%) with broad distribution, medium to large effect sizes, 100 patients per trial group, 10 or 30 trials, and significant heterogeneity. The proportion of the scenarios that yield significant treatment effects (i.e. statistical power) was identical for all scenarios with minimal bias. Scenarios with negative bias demonstrated decreased statistical power. Compared to the MD method, simulated heterogeneity estimates for the SMD and RoM methods were lower in the scenarios in which they exhibited bias. This is because the bias decreased the weighting of extreme values. In the scenarios exhibiting minimal bias, heterogeneity was similar among methods.

Conclusions: Simulation suggests that the performance characteristics (bias, coverage, statistical power) of the RoM method compares favourably to the traditionally used MD and SMD methods. Similar to binary outcome analysis, this straightforward method provides researchers with the option of using a ratio method, which may be more interpretable by clinicians.

Reference: Friedrich J, Adhikari N, Ohlsson A, Beyene J. Ratio of means as an alternative to mean differences for analyzing continuous outcome variables in a meta-analysis: a simulation study. *XV Cochrane Colloquium*; 2007 Oct 23-27; São Paulo, Brazil:97.

Uncertainty of heterogeneity in meta-analysis

Nikolaos A Patsopoulos, John PA Ioannidis and Evangelos Evangelou



Title: Uncertainty of heterogeneity in meta-analysis.

Contact: Nikolaos A Patsopoulos, Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina 45110, Greece. E-mail: npatsop@cc.uoi.gr.

Background: An important aim of systematic reviews and meta-analysis is to understand the extent to which different studies on the same or different topics give similar or dissimilar results. While the reasons for clinical, methodological, and biologic heterogeneity may be topic-specific and need a multifaceted approach for their evaluation each time, statistical examination of heterogeneity may be possible to perform with the same methods in all meta-analyses. Inferences about the clinical importance and generalizability of the results are often considerably affected by the presence or absence of statistical heterogeneity and its extent.

Objective: To evaluate empirically the extent of uncertainty in I^2 estimates.

Location: University of Ioannina School of Medicine, Greece.

Methods: We considered meta-analyses in the *Cochrane Database of Systematic Reviews* (Issue 4, 2005) with four or more synthesized studies and binary outcomes. Eventually, we analysed 1,011 eligible meta-analyses. The second data set was a previously described database of 50 meta-analyses of gene-disease associations that had found a nominally statistically significant effect ($p < 0.05$) for proposed genetic risk factors. For each meta-analysis we calculated I^2 and respective 95% confidence intervals. Finally, we evaluated 11 systematic reviews that included randomized trials and that were published in the *BMJ* between 1 July 2005 and 1 January 2006.

Summary of main results: The median (IQR) number of studies was seven (5-11) and 20 (13-26), respectively and the median (IQR) total sample size was 1112 (512-2691) and 4660 (2823-8761), respectively for Cochrane and genetic meta-analyses. The median (IQR) I^2 was 21.1% (0% to 49.7%) and 37.6% (4.6% to 59.5%), respectively, in the two databases. Of the meta-analyses where the I^2 is $\leq 25\%$ (little heterogeneity), 83% (448/539) in the Cochrane and 73% (16/22) of the genetic risk factor meta-analyses have upper 95% confidence intervals that cross into the range of large heterogeneity ($I^2 \geq 50\%$). Of the meta-analyses where the I^2 is $\geq 50\%$ (large heterogeneity), 67% (168/249) in the Cochrane and 52% (11/21) of the genetic risk factor meta-analyses have lower 95% confidence intervals that cross into the range of little heterogeneity ($I^2 \leq 25\%$). The uncertainty for the upper 95% confidence interval of I^2 for the two large data sets limited to those meta-analyses that have $I^2=0\%$ ($n=373$ Cochrane and $n=12$ genetic) is in all cases larger than 33% in all these meta-analyses. For 81% of the meta-analyses with $I^2=0\%$, the 95% confidence intervals extend to $I^2=50\%$ and higher [81% (303/373) and

83% (10/12) in the two data sets]. Of the 11 reviews published in the *BMJ*, eight systematic reviews performed quantitative syntheses; one did not test for between-study heterogeneity at all. I^2 was measured for at least one data synthesis in six of them and all of them performed statistical significance-testing for heterogeneity, apparently using the Q statistic. A total of eight statements were made trying to interpret heterogeneity in the text of these reviews and for seven of them, sufficient information was provided so that we could calculate the 95% confidence interval of I^2 . The lower 95% confidence interval in all cases went to as low as 0% (rounded to integer percentage) with one exception. The upper 95% confidence interval in all cases exceeded the 50% threshold and in 4/7 cases it also exceeded the 75% threshold.

Conclusions: Under the current research circumstances, in most meta-analyses, the presence of considerable between-study heterogeneity cannot be excluded with confidence. This is an important lesson about the potentially ubiquitous presence of some between-study heterogeneity. Claims for homogeneity may sometimes be stronger than the evidence allows and may lead to spurious certainty about the comparability of study results and the generalizability of treatment effects.

Reference:

Patsopoulos N, Ioannidis J, Evangelou E. Uncertainty of heterogeneity in meta-analysis. *XV Cochrane Colloquium*; 2007 Oct 23-27; São Paulo, Brazil:157-158.



Cochrane Methodology Review Group

Elizabeth Paulsen

The Cochrane Methodology Review Group (CMRG) is made up of editors, referees and authors interested in collecting empirical studies of methodological questions. We summarize the empirical basis for decisions about methods for systematic reviews and evaluations of health care, including preventive, diagnostic, therapeutic, rehabilitative and educational interventions.

A dedicated editorial team co-ordinated by Mike Clarke and Andy Oxman makes this possible. The other editors are Philippa Middleton, Peter Götzsche, Karen Robinson, Paul Glasziou, Peter Jüni and Gordon Guyatt (Criticism Editor). Other members of the editorial team based in Oslo are Marit Johansen (Trials Search Co-ordinator), Jan Ødegaard-Jensen (Statistician), Elizabeth Paulsen (Review Group Co-ordinator). A methodology register was developed and is maintained by Sally Hopewell and Anne Eisinga at the UK Cochrane Centre. Currently, the register contains more than 10,000 references to methodology studies.



At the start of this year, a total of 10 protocols, and 13 methodology reviews were published in *The Cochrane Library* (Issue 2, 2008). Information on all the Cochrane methodology reviews and protocols is available on page 38.

The CMRG participated in the piloting of RevMan 5 at the end of 2007. Feedback has been positive and all authors of methodology reviews are now using RevMan 5 for new reviews and updates.

We would love to have more people from low- and middle-income countries participating or developing methodology reviews. For more information on how you can participate, contact the Review Group Co-ordinator (elizabeth.paulsen@nokc.no).

The next meeting of the CMRG editorial team will be in October 2007 at the Cochrane Colloquium in Freiburg, Germany.

A summary of the most recent Cochrane methodology review is presented below:

When and how to update systematic reviews

David Moher, Alexander Tsertsvadze, Andrea Tricco, Martin Eccles, Jeremy Grimshaw, Margaret Sampson and Nick Barrowman

Background: Systematic reviews are most helpful if they are up to date. We did a systematic review of strategies and methods describing when and how to update systematic reviews.

Objectives: To identify, describe and assess strategies and methods addressing: 1) when to update systematic reviews and 2) how to update systematic reviews.

Search strategy: We searched MEDLINE (1966 to December 2005), PsycINFO (1955 to June 2005), the Cochrane Methodology Register (Issue 1, 2006), and handsearched the 2005 Cochrane Colloquium proceedings.

Selection criteria: We included methodology reports, updated systematic reviews, commentaries, editorials, or other short reports describing the development, use, or comparison of strategies and methods for determining the need for updating or updating systematic reviews in health care.

Data collection and analysis: We extracted information from each included report using a 15-item questionnaire. The strategies and methods for updating systematic reviews were assessed and compared descriptively with respect to their usefulness, comprehensiveness, advantages, and disadvantages.

Main results: Four updating strategies, one technique, and two statistical methods were identified. Three strategies

addressed steps for updating and one strategy presented a model for assessing the need to update. One technique discussed the use of the 'entry date' field in bibliographic searching. Statistical methods were cumulative meta-analysis and predicting when meta-analyses are outdated.

Authors' conclusions: Little research has been conducted on when and how to update systematic reviews and the feasibility and efficiency of the identified approaches is uncertain. These shortcomings should be addressed in future research.

Reference:

Moher D, Tsertsvadze A, Tricco A, Eccles M, Grimshaw J, Sampson M, Barrowman N. When and how to update systematic reviews. *Cochrane Database of Systematic Reviews* 2008, Issue 1. Art. No.: MR000023. DOI: 10.1002/14651858.MR000023.pub3.



INFORMATION FROM THE METHODS GROUPS

News from the Steering Group

Jon Deeks
Steering Group Methods Groups Representative

The Steering Group has been dealing with some strategic planning issues during the past year.

The Cochrane Library has a very clear place in the evidence-based medicine market, and a very distinctive brand. Our publishers have been considering alternative products which can be generated from Cochrane reviews. At its next meeting during the Cochrane Colloquium in October 2008, the Cochrane Collaboration Steering Group (CCSG) will be debating the direction in which our publication policy should develop - whether we should stick to doing what we know we are good at, or move into new areas.

The CCSG has been supporting Co-ordinating Editors of the Cochrane Review Groups in co-ordinating their activities, with the aim of improving the quality of Cochrane reviews. Much has yet to be decided, including how this 'editorial board' initiative can best work with the existing quality improvement and assurance activities in the Collaboration (such as the Handbook) and benefit from the input of the talented methodologists within the Methods Groups.

This year sees a lot of outputs from Methods Groups reaching Cochrane Review Groups. These include the new RevMan 5 software, the new version of the *Cochrane*



Handbook for Systematic Reviews of Interventions, Risk of Bias assessments, Summary of Findings tables, and diagnostic test accuracy reviews. Whilst there are numerous individuals and Methods Groups to thank for their hard work in producing these new developments, the work is not over. Many Methods Groups will have high demands for providing training to support these developments, and the Steering Group is considering how these activities can best be supported and organized.

At this point I can say farewell as your representative on the Steering Group, as my six year sentence comes to an end at the Colloquium in Freiburg.

My time has been a valuable and enjoyable experience, and I wish my successor well in taking on this role.

There are 13 registered Methods Groups. Reports from most of these Groups are given below.

Registered groups

Adverse Effects
 Applicability and Recommendations
 Bias
 Economics
 Individual Patient Data Meta-analysis
 Information Retrieval
 Non-Randomised Studies
 Patient Reported Outcomes
 Prognosis
 Prospective Meta-Analysis
 Qualitative Research
 Screening and Diagnostic Tests
 Statistical Methods

REGISTERED GROUPS

Cochrane Adverse Effects Methods Group

Andrew Herxheimer

Until now systematic reviews have been focusing predominantly on evidence of effectiveness of interventions; their adverse effects have had much less attention and space. Yet clinicians and patients decide to use an intervention only when its likely benefits outweigh the harms it may cause. If the harms are not properly assessed they are liable to be underestimated, leading to a bias in favour of the intervention. This imbalance between the assessments of therapeutic effectiveness and of harms was an unforeseen consequence of a pragmatic decision made soon after The Cochrane Collaboration began - the decision to concentrate on randomized controlled trials in reviews because they provided the soundest evidence of effectiveness. Much less reliable study designs, such as case-control and cohort studies - and case reports - were usually excluded, at least until the vast numbers of randomized trials had been reviewed. Otherwise the workload and costs would have

been unmanageable. It seemed that the adverse event data in randomized trials would give sufficient and reliable information. However, rare and unexpected events are seriously underrepresented in randomized trials, and other types of study are more appropriate for analysing such adverse effects. Jan Vandembroucke has now elegantly explained why: for discovery and explanation, the hierarchy of evidence is the reverse of that for evaluation, where randomized trials are at the top.¹

The Adverse Effects Methods Group (AEMG) was registered in July 2007. Its central aim is to help Cochrane Review Groups and review authors to deal with adverse effects as rigorously as with evidence of effectiveness.² We plan to do this through a link person in each Cochrane Review Group, who will keep the editors and authors in touch with the AEMG. The work of incorporating adverse effects into reviews will take some years, and each Cochrane Review Group will need to consider the urgency of this updating for its reviews, and to decide on priorities among the new protocols, new reviews, reviews being updated and others. The need will be most urgent for reviews of interventions that are important for patients/consumers and widely used in practice. Input from the consumer members of Cochrane Review Groups will thus be important, and of course the AEMG will also be glad to help.

References:

1. Vandembroucke JP. Observational research, randomised trials, and two views of medical science. *PLoS Medicine* 2008; 5:e67.
2. Loke Y, Herxheimer A, Golder S. Cochrane Adverse Effects Methods Group. *About The Cochrane Collaboration (Methods Groups)* The Cochrane Library 2008, Issue 1. Art. No.: CE000150 (also on www.aemg.cochrane.org).

Cochrane Applicability and Recommendations Methods Group

Holger Schünemann and Gordon Guyatt

The Applicability and Recommendations Methods Group continues to work closely with the GRADE working group; indeed, the activities of the two groups are largely overlapping. The Applicability and Recommendations Methods Group is largely responsible for two chapters in the new *Cochrane Handbook for Systematic Reviews of Interventions*: 'Presenting results and Summary of Findings tables' and 'Interpreting the results and drawing conclusions'. These chapters contain much new material. This is especially true of the introduction of the Summary of Findings (SoF) tables (see also page 4).

The SoF tables will go a long way in helping with the planning of reviews and summarizing the often overwhelming information in Cochrane reviews. When planning the review, the approach encourages review



authors to identify all patient-important outcomes. The SoF tables provide a structure for considering the quality of evidence for each important outcome. This involves considering issues of study design, limitations in planning and conducting studies, precision, consistency and directness of results, and the likelihood of publication bias. The information in the tables, including the quality of evidence for each outcome and the key results for each outcome, will provide extremely useful summaries for users of Cochrane reviews.

All authors of Cochrane reviews are strongly encouraged to complete SoF tables, which will be placed directly after the abstract in the review. The first SoF tables have appeared already. To develop these tables review authors can use the GRADEpro software that contains instructions and was released together with RevMan 5.0 in March 2008.

In addition to the information in the *Cochrane Handbook for Systematic Reviews of Interventions*, Cochrane review authors may find it useful to access a five-part series regarding GRADE that will appear in the *BMJ* over the next few months. Ultimately, they will also benefit from a series of detailed papers regarding GRADE that will appear in the *Journal of Clinical Epidemiology* in the next year or so.

Cochrane Bias Methods Group

Jennifer Tetzlaff, David Moher, Jonathan Sterne and Doug Altman

The Bias Methods Group (BMG) continues to raise awareness of bias in systematic reviews and included studies via teaching and workshops, and to conduct methodology research to identify prominent issues and develop methods to avoid and detect bias. The BMG membership consists of approximately 85 members from over 15 countries.

In December 2007, we hosted our first BMG-specific workshop in Edmonton, Canada. The day-and-a-half course, facilitated by our convenors, addressed bias in randomized trials, the new Cochrane Risk of Bias tool, selective outcome reporting, and publication bias. We are also helping to disseminate and provide practical training on the Risk of Bias tool, and leading and participating in numerous workshops. We continue to host general bias workshops at symposia and Cochrane Colloquia including one facilitated by Peter Jüni and Simon Wandel at the Cochrane Colloquium in São Paulo, Brazil in 2007.

Our members have been integral in developing methods to assess risk of selective outcome reporting bias and have facilitated advanced training sessions to disseminate this work. Other ongoing initiatives include the BRANDO project (*Bias in Randomised AND Observational studies*), the PRISMA Statement (*Preferred Reporting Items for Systematic reviews and Meta-Analyses*) and two meta-epidemiological research projects focused on bias in

intervention studies (Leslie Wood) and systematic reviews (Andrea C. Tricco). Recent Cochrane methodology reviews by our members (completed or in progress) include: when and how to update systematic reviews; blinded versus unblinded assessments of Risk of Bias in studies included in a systematic review; publication bias in clinical trials; and tests for funnel plot asymmetry (see page 5).

One of our major contributions to the Collaboration in this past year was to the revised *Cochrane Handbook for Systematic Reviews of Interventions*. Specifically, members contributed to new chapters on ‘Assessing Risk of Bias in included studies’ (edited by Higgins and Altman) and ‘Addressing reporting biases’ (edited by Sterne, Moher and Egger), and assisted in updating other chapters. We thank all who contributed their time and expertise.

We are hosting a substantive meeting at the Cochrane Colloquium in Freiburg in October 2008 and invite all those interested to join us. The BMG expresses our sincere gratitude to our funders, the Canadian Institutes of Health Research and the Canadian Agency for Drugs and Technologies in Health, without whom our continued progress would not be possible. Finally, we thank all of our current members for your continued interest and look forward to seeing you in Freiburg! For further information please visit www.chalmersresearch.com/bmg.

Campbell and Cochrane Economics Methods Group

Ian Shemilt and Miranda Mugford

The Campbell and Cochrane Economics Methods Group (CCEMG) is an international network of researchers, practitioners, policy-makers and consumers with a shared interest in approaches to research synthesis that combine systematic review and economics methods.

CCEMG has been registered as a methods group of The Cochrane Collaboration since 1998 and was co-registered in 2003 as a methods group of Cochrane’s sister organization, The Campbell Collaboration. Our joint role reflects the commitment of both Collaborations to develop jointly their methodological approach to systematic reviews, as well as reflecting the broad interests of our co-convenors and members in evidence-based economics methods, encompassing education, social care, criminal justice and cross-sector evaluation, alongside health care.

We recently contributed a new chapter on ‘Incorporating economics evidence’ to the new *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 15, available online at www.cochrane-handbook.org). Our chapter provides initial guidance on methods for including economics perspectives and evidence in Cochrane reviews, with a focus on critical review and synthesis of evidence from published and unpublished studies. A series of



workshops and open learning materials based on the new guidance are planned.

CCEMG currently has 134 members based in 28 countries, with several new members in countries not previously represented, including Argentina, Chile, Israel and Norway. Our membership includes economists willing to provide advice and peer review for economics components of Cochrane and Campbell reviews in topic areas falling within the scope of over thirty Cochrane Review Groups and Campbell Co-ordinating Groups. During 2008 and 2009, we plan further work to consolidate links between Review Groups, authors and our economist members who can help with reviews or provide specialist advice.

Other activities planned for 2008 and 2009 include our ongoing contribution to the work of the GRADE Working Group (www.gradeworkinggroup.org/) on incorporating economics evidence into evidence profiles and Summaries of Findings tables, publication of our new *Campbell Methods Policy Brief on Economics Methods* and development of material for a new book aiming to profile and evaluate recent developments, proposals and controversies in methods at the interface of systematic reviews, research synthesis and economic evaluation.

Further information and resources can be found on the CCEMG website at www.c-cemg.org or by contacting Ian Shemilt (Research Co-ordinator) at research@c-cemg.org.

Cochrane Individual Patient Data Meta-analysis Methods Group

Larysa Ryzewska, Jayne Tierney, Lesley Stewart and Mike Clarke

The Individual Patient Data (IPD) Meta-analysis Methods Group currently has 65 members (28 active, 37 passive) from 17 countries with interests spanning a wide range of healthcare areas. The Group did not meet at the Cochrane Colloquium in São Paulo, as relatively few Methods Group members attended, but we are hoping to meet at the Colloquium in Freiburg in 2008. If you would like to join the Group or are interested in finding out more please contact Larysa Ryzewska (lhr@ctu.mrc.ac.uk) or visit our website (www.ctu.mrc.ac.uk/cochrane/ipdmg).

We ran a training workshop on IPD methodology during the São Paulo Colloquium and also plan to run a new training workshop on statistical methods for meta-analysis of individual patient data at the forthcoming Colloquium in Freiburg. This workshop, led by Richard Riley (University of Liverpool, England) will cover methods for modelling IPD, combining IPD and aggregate data, and estimating treatment-covariate interactions.

A Cochrane Collaboration Steering Group funded project to improve the quality of Cochrane reviews that include time-to-event outcomes has now been completed. Last year we

published an open access, step-by-step guide to the methods, which is geared towards non-statisticians. This user friendly guide to the methodology is freely accessible on the *Trials* journal website¹ and is accompanied by an Excel spreadsheet for performing the associated calculations. We also held an in-depth workshop on the methods at the MRC Clinical Trials Unit in London in November 2007. Finally, we plan to convert queries we have received on the methods and calculations spreadsheet into Frequently Asked Questions. These will be made available via our website.

Two of the co-conveners (JT, LS), together with a SAS consultant, have been involved in the re-development of SCHARP, a SAS-based application with a point-and-click interface that facilitates the analysis and plotting of IPD. SCHARP produces forest plots, Kaplan Meier curves (if appropriate) and corresponding summary statistics for time-to-event, dichotomous and continuous outcome data. It also facilitates the interactive analysis of many trials and multiple outcomes overall or by trial or patient subgroup, from a single flat data file. In the absence of dedicated funding, it has taken longer than we had hoped to finalise SCHARP, but seven groups involved in the production of Cochrane reviews and methodological research will receive the software this year.

Finally, we would like to remind everyone that our website contains searchable databases of both completed and current IPD meta-analyses and methodology research projects. The website also provides general information about IPD meta-analyses, along with resource materials (including relevant references, PowerPoint presentations and an FAQ section) for anyone planning an IPD project or wanting to learn more about them. It provides an easy way for Cochrane Review Groups to contact us for advice and allows them to check whether a proposed review topic has already been covered by an IPD review.

Reference:

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Cochrane Information Retrieval Methods Group

Carol Lefebvre, Jessie McGowan, Alison Weightman and Bernadette Cole

There are approximately 150 members of the Information Retrieval Methods Group (IRMG), many of whom have been active in a number of the projects outlined below.

The co-conveners and members of the Group have continued to serve on various Cochrane Collaboration policy advisory groups relevant to information retrieval including the Handbook Advisory Group, the Monitoring and Registration Group, the Publishing Policy Group, the



Quality Advisory Group, the Trials Search Co-ordinators Working Group and the newly-established Trials Search Co-ordinators Executive.

One of the co-convenors (CL) led the work on the new chapter on 'Searching for Studies' in the *Cochrane Handbook for Systematic Reviews of Interventions*, together with two other members of the IRMG.¹ All members of the Group were invited to contribute to the chapter and a number did so. The new chapter is a considerably expanded version of the equivalent chapter in the previous version of the Handbook and contains information on search methods and sources to search, together with revised versions of the Cochrane Highly Sensitive Search Strategies for identifying randomized trials in MEDLINE.

Members of the IRMG have been active in areas of development within The Cochrane Collaboration including adverse effects and diagnostic test accuracy. Co-convenors and members of the Group conducted a number of workshops at the Cochrane Colloquium in São Paulo in 2007 and further workshops have been accepted for the Colloquium in Freiburg in 2008.

Filters for importing records from *The Cochrane Library* into ProCite and Reference Manager are updated on our website (www.cochrane.org/docs/import.htm). The Group is looking at adding information about EndNote filters to this site.

The web resource of methodological search filters compiled by the Information Specialists associated with InterTASC (most of whom are members of the Group) continues to be extended and updated. Appraisals for some of the filters are available (www.york.ac.uk/inst/crd/intertasc/index.htm).

The PRESS project (Peer Review of Electronic Search Strategies), previously known as EHTAS (Evaluating HTA Searches), led by one of the co-convenors (JM) together with other Group members, to develop a checklist for search strategies for systematic reviews has been published as a report by the Canadian Agency for Drugs and Technologies in Health (CADTH)² and a manuscript including an evidence-based practice guideline for peer-reviewing search strategies has been submitted for publication.³ All members of the Group were invited to contribute to the survey that underpinned this project.

A proposal was accepted for funding through the Collaboration's Opportunities Fund in April 2008 for a project entitled: 'Beyond the database search: developing inclusive global registers of studies'. This project aims to develop a framework and methodology for locating evaluation studies that have previously been identified as hard to access, particularly from low- and middle-income countries. The project is led by one of the co-convenors (AW) and involves three other Cochrane entities in addition to the IRMG.

Funding has also been sought from the UK Medical Research Council methodological funding call for a collaborative project to develop public health search filters.

The IRMG discussion list is used to notify members of activities such as the annual IRMG meeting at Cochrane Colloquia, to circulate the minutes etc. It has been used to find possible contributors for projects associated with information retrieval, including those listed above.

An open meeting of the Group was held during the Colloquium in São Paulo in 2007 and a further meeting is planned for the Freiburg Colloquium in October 2008.

Infrastructure support for the time of the co-convenors is provided by Cardiff University, the UK Cochrane Centre and the University of Ottawa. Support for the time of the coordinator and administrative assistance is provided by Cardiff University.

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1. Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.0 (updated February 2008). The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org. (accessed 30 April 2008).
2. Sampson M, McGowan J, Lefebvre C, Moher D, Grimshaw J. *PRESS: Peer review of electronic search strategies (Technology report number 477)*. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2008.
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Cochrane Non-Randomised Studies Methods Group

Barney Reeves

The main achievement of the Non-randomised Studies Methods Group (NRSMG) this year is the contribution of Chapter 13 to the *Cochrane Handbook for Systematic Reviews of Interventions* on 'Including non-randomized studies'. This forms part of the section on special topics of version 5 of the Handbook which will also be published in book form later this year; until then, it can be 'browsed' online (www.cochrane-handbook.org). The chapter aims to highlight aspects of reviews that may be different when including non-randomized studies, compared to randomized trials, in systematic reviews. As well as summarizing what is currently known, it tries to point out the uncertainties that remain. We hope that it will breathe new fire into the bellies of NRSMG members – to do the research to address these uncertainties.



Last year also saw the publication of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (see page 14). Poor reporting is a major obstacle to review authors who wish to include non-randomized studies in reviews, so the statement is clearly important to the NRSMG. The STROBE authors welcome the development of modifications of the Statement for particular types of observational study. Analyses of data from clinical registries or other routinely collected data sets, with the objective of estimating the relative effectiveness of two or more treatments, constitute one type of design of obvious relevance to NRSMG members, which may need to be distinguished from the three designs currently covered by STROBE.

The NRSMG was represented at the Colloquium in São Paulo and again presented its workshop on extracting data from non-randomized studies. Although attendance at this workshop continues to be good, it is time to develop new workshops – suggestions from both review authors and NRSMG members would be welcome (barney.reeves@bristol.ac.uk). The Colloquium in Freiburg is going to have a major focus on methodology and the NRSMG will meet there as usual. Registration is open – so see you there.

Cochrane Prognosis Methods Group

Katrina Williams, Jill Hayden, Sue Woolfenden, Doug Altman, Richard Riley and Riekie de Vet

The Prognosis Methods Group was recently registered as the newest Cochrane Methods Group. During the exploratory meetings at the Cochrane Colloquia in Ottawa (2004), Melbourne (2005) and Dublin (2006) it became evident that many researchers are performing systematic reviews of prognostic studies. The majority of the attendees expressed strong interest in pursuing further discussions around the methodology of systematic reviews of prognostic studies. At the Colloquium in Dublin, the establishment of a Prognosis Methods Group was unanimously agreed upon. Six convenors prepared the application last year. The convenors aim to establish ‘working groups’ to focus on the different stages of prognostic systematic reviews.

The aim of prognostic research

Prognostic research provides information about the long-term health and well-being of individuals with specific diseases or conditions. Prognostic studies can provide information on the likelihood of a particular outcome or disease recurrence; they can identify target groups for treatment or intervention strategies to modify factors associated with poor outcomes. Such information is required for healthcare decision making and is not always available from clinical trials. Prognostic information may also inform diagnosis by identifying relevant classifications. Moreover, the clinical course (i.e. prognosis) may be used to validate a

diagnostic test in the absence of a ‘gold standard’ or reference test.

The role of the Prognosis Methods Group in The Cochrane Collaboration

The official registration of the Prognosis Methods Group does not mean that prognostic reviews will be undertaken within the Collaboration, at least not currently. Rather, the Methods Group will assess the feasibility of systematic reviews of prognostic studies and undertake methodological research to improve prognostic reviews. It will also facilitate those encountering prognostic information in Cochrane reviews of randomized trials and diagnostic studies to help provide best evidence for healthcare decision making relevant to diagnosis, therapy and service delivery. In particular, the Prognosis Methods Groups will have two primary roles:

(1) Conducting research to advance the methods of prognostic reviews. The most important challenges are to identify prognostic studies, assess their methodological quality, and combine results across different research designs, analyses, and presentations of results.

(2) Working with existing Cochrane entities, including Methods Groups to ensure the best use of prognostic evidence in Cochrane reviews. For example, Cochrane Review Groups may want to relate treatment effectiveness to the ‘baseline’ event rate that is obtained from prognostic studies. Another example: analyses of reviews of diagnostic studies that include a large number of tests to examine which combination of tests best predict the presence of the target disease is similar to the analysis of prognostic studies. This prompts combined action of the Screening and Diagnostic Tests Methods Group and the Prognosis Methods Group.

Activities of the Prognosis Methods Group

Advice on methods: The Prognosis Methods Group will give methodological advice by developing and disseminating appropriate methodological standards for prognostic systematic reviews and by providing training and support through workshops at Cochrane Colloquia, and other relevant conferences.

Serving as a forum for discussion: The Prognostic Review Network provides an open forum for all those interested in prognostic research and provides opportunities for researchers to collaborate and share information regarding reviews or methodological studies that are currently in progress.

Conducting methodological research: Members of the Prognostic Review Network are active researchers on many of the methods projects that form our research agenda. During the first twelve months after the Prognosis Methods Group is registered as a Cochrane entity, the group’s research agenda will be developed and priorities set.



Cochrane Prospective Meta-analysis Methods Group

Davina Gherzi and Lisa Askie

A key activity of the Prospective Meta-analysis Methods Group (PMA MG) over the past year has been the development of a chapter (Chapter 19) on prospective meta-analysis for the *Cochrane Handbook for Systematic Reviews of Interventions*. Our hope is that this new chapter will help those embarking on prospective meta-analysis to plan adequately the considerable amount of work and collaboration necessary for these projects to be successful. A training workshop, based on the new chapter, will be run at this year's Colloquium in Freiburg.

With the help of resources provided to all Methods Groups by The Cochrane Collaboration, and matching funds provided by the NHMRC Clinical Trials Centre in Sydney, Australia, the Group has been able to employ a part-time research assistant (Henry Ko). With Henry's support, the Group's convenors will now be able to hold regular teleconferences and develop a research agenda. The intention is also to organize an e-mail discussion list and make sure the information on the Group's website is up to date.

Included on the group's 'to do' list are plans to develop a checklist for those wanting to critically appraise published prospective meta-analyses. An increasing number of projects being labelled as prospective meta-analysis are being published, although it is not at the moment clear if they meet the necessary requirements.

Lisa Askie has joined the Prospective Meta-analysis Methods Group as co-convenor, replacing John Simes who has stepped down as co-convenor but will remain involved in the group. Lisa is Research Fellow at the NHMRC Clinical Trials Centre at the University of Sydney, and lead investigator on a number of ongoing prospective meta-analyses including a number in the area of paediatrics.

For more information about the PMA MG please visit our website www.cochrane.org/docs/pma.htm.

Cochrane Qualitative Research Methods Group

Jane Noyes

Developments from the Cochrane Qualitative Research Methods Group (CQRMG) (www.joannabriggs.edu.au/cqrmg) include the new *Cochrane Handbook for Systematic Reviews of Interventions* chapter on the 'Inclusion of qualitative evidence and Cochrane intervention reviews'. This chapter acknowledges that evidence from qualitative studies has an

important role in ensuring that systematic reviews are of maximum value to policy, practice and consumer decision making. Many authors of Cochrane intervention reviews have identified qualitative studies associated with included trials, but have not known what role (if any) qualitative evidence could play. The new chapter outlines that qualitative research can contribute to Cochrane intervention reviews in four ways:

- Informing reviews by using evidence from qualitative research to help define and refine the question, and to ensure the review includes appropriate studies and addresses important outcomes;
- Enhancing reviews by synthesizing evidence from qualitative research identified whilst looking for evidence of effectiveness;
- Extending reviews by undertaking a search specifically to seek out evidence from qualitative studies to address questions directly related to the effectiveness review;
- Supplementing reviews by synthesizing qualitative evidence within a stand-alone, but complementary, qualitative review to address questions on aspects other than effectiveness.

We recognize that the synthesis of qualitative research is an area of debate and evolution. Authors can use the CQRMG as a forum for discussion and further development of methodology in this area.

Recently, a preliminary toolkit has been launched on the CQRMG's website. It contains PowerPoint presentations from convenors and/or affiliates, to be used by colleagues who are teaching in the area of qualitative evidence synthesis. Anyone willing to contribute to the further development of the toolkit is welcome to e-mail presentations to nathan.tan@adelaide.edu.au. Please fill in the written statement posted on the website, which declares that the CQRMG is allowed to publish your material.

One major change of the CQRMG website is that the Qualitative Reference Review Database (CQRMG1) has now been populated - 485 records and counting. If you would like to contribute more generally to the Group's trial register activities, Andrew Booth (a.booth@sheffield.ac.uk) will be glad to hear from you.

Finally, we should like to offer a sincere thank you to Dr. Mary Dixon-Woods, who recently stepped down from co-chairing the CQRMG's Communications and Dissemination Sub-Group. Dr Dixon-Woods' insights and contributions have been invaluable to the development of the CQRMG. We should like to wish her all the best for all her future undertakings.



Cochrane Screening and Diagnostic Tests Methods Group

Petra Macaskill, Constantine Gatsonis and Roger Harbord

The past year (2007 to 2008) saw the establishment of the UK Support Unit (UKSU, located in Birmingham) and the Continental Europe Support Unit (CESU, located in Amsterdam) to support Cochrane reviews of diagnostic test accuracy, which has provided additional impetus to key projects relating to the *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*, pilot reviews, extensions to RevMan 5 and training. Statistical methods have now been implemented in RevMan 5, testing has been undertaken and the software released. We are now hoping to see the first diagnostic test accuracy reviews published in *The Cochrane Library* in Issue 4, 2008. Cochrane Review Groups are starting to register new titles.

Five training workshops were again offered at the Colloquium in São Paulo in 2007 to cover major aspects of a diagnostic review. Several workshops were able to demonstrate how RevMan 5 software can be used for diagnostic reviews and discussed the interpretation of output. The sessions were well attended and similar training sessions will be offered again at the Colloquium in Freiburg. Outside the Colloquium, training courses have been run for Cochrane Editorial Groups in Amsterdam in November 2007 and June 2008, as well as events for individual Cochrane Review Groups and at regional meetings in the UK and India.

The business meeting held at the Colloquium in São Paulo attracted a diverse group of people engaged in the conduct of diagnostic reviews, and individuals who are interested in becoming involved in such reviews. Attendees were very interested to hear about ongoing developments and the role of the support centres. We are expecting a larger presence of methodologists at the next meeting in Freiburg. The next meeting will also provide an opportunity to consider feedback from review authors and support centres on methodological and software issues. Before that, a symposium 'Methods for Evaluating Medical Tests' to be held at the University of Birmingham on 24 to 25 July 2008 will provide a longer forum for some members of the Methods Group and others to meet to discuss methodological research.

We should like to thank everyone who has contributed to the activities of our Methods Group over the past year, and we look forward to seeing many of you in Freiburg.



CAMPBELL COLLABORATION METHODS GROUPS (C2)

Jeff Valentine

The Campbell Collaboration (C2) aims to utilize scientific standards in the conduct of systematic reviews of research on social and behavioural policies and programmes, and to make the findings easily available to policy makers, practitioners, and the public. Within this framework, the C2 Methods Group (1) provides expertise to researchers conducting systematic reviews, (2) improves systematic review methods, (3) offers training on how to conduct reviews, and (4) facilitates the use of systematic reviews in policy making and practice, particularly as this relates to the end-users' understanding of methodology and how to assess evaluations of policies and practices.

This past year has largely been spent on organizational activities. For the first time, the Methods Group established a formal membership policy that is inclusive and allows for broad participation while at the same time helping to ensure that the voting members of the Group are active and well-qualified. In addition, a proposal to establish an advisory board for the Methods Group is currently being considered. Finally, an election is being held for a new co-chair to replace Jeff Valentine, who is stepping down after four years. The new co-chair will be one of two representatives from the Methods Group on C2's Steering Group, and will be the first co-chair elected by the membership of the Methods Group. Taken together, we are pleased with the organizational progress made over the last year, and will work to ensure that the momentum continues.

Therese Pigott was named editor for the Methods Group by the C2 Steering Group, for a term running from 2008 to 2010. Jeff Valentine served in that role from 2006 to 2008.

The C2's Training Group received funding for the development of several training modules, and a commitment from C2 to fund training activities in conjunction with the C2 Colloquium. In addition, C2 has committed to funding one two-and-a-half day training session in Europe and one in North America each year. Our hope is that we can begin to address the capacity issues that have been confronting the co-ordinating groups since the formation of C2.

The affiliation between C2 and the American Institutes for Research (AIR) formally ended as of June 2007. A significant investment in C2 was subsequently made by the Norwegian Knowledge Information Centre, part of the Ministry of Health in Norway. As part of that move, a new Executive Director has been hired. This development has been very helpful and is largely responsible for C2's ability to expand training activities.



FUTURE MEETINGS

16th Cochrane Colloquium

Freiburg, Germany
3 to 7 October 2008

The team from the German Cochrane Centre cordially invites you to come to Freiburg in October 2008 to participate in the 16th International Colloquium of The Cochrane Collaboration.

The Cochrane Colloquium 2008 offers an outstanding opportunity to interact with central players active in evidence-based health care, global knowledge management and systematic reviews. Catch up on current international developments and perspectives and attend workshops to delve further into individual topics.

More information is available at www.colloquium.info.

Sixth International Congress on Peer Review and Biomedical Publication

Vancouver, Canada
10 to 12 September 2009

The Sixth International Congress on Peer Review and Biomedical Publication will be held from 10 to 12 September 2009 in Vancouver. As with the previous Congresses, the aim will be 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.

More information is available at www.jama-peer.org.



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AVAILABILITY OF THE NEWSLETTER

Additional copies of the Methods Groups Newsletter may be obtained free of charge from the UK Cochrane Centre, which is based at:

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The Newsletter is also available from The Cochrane Collaboration website at www.cochrane.org/newslett/index.htm



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APPENDIX

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