The Cochrane Collaboration Methods Groups Newsletter

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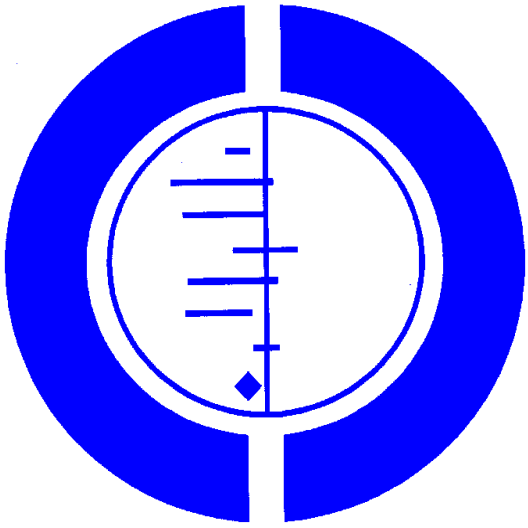

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PURPOSE OF THE NEWSLETTER

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. 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 of 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 Health Service Research and Development Programme in the UK. The Newsletter is distributed to all Methods Group members 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 highlights the wide range and quantity of empirical research being conducted within The Cochrane Collaboration. It also includes a series of articles, which attempt to address some of the more challenging issues in Cochrane reviews. These include discussions about how to include quality of life information in Cochrane reviews, incorporating qualitative research methods in the systematic review process and how to assess the quality of non-randomized studies in a review.

As with previous years, this issue includes structured abstracts and commentaries on topical methodological issues. These include a study looking at different health-related quality of life scales and another, which assesses the quality and reporting of economic evaluations of health care. Other key methodological studies are also discussed, including a study by Egger and colleagues on the importance of comprehensive literature searches and assessment of trial quality in systematic reviews.

As ever, we are always very grateful to the many people who have contributed to this Newsletter. We would 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

Challenging issues in Cochrane reviews: health-related quality of life

Dick Joyce and Donald Patrick

The estimation of Quality of Life (QoL) is receiving steadily increasing attention. Improvement in Health-Related Quality of Life (HRQoL), in particular, is recognised as a valuable outcome indicator of medical and other interventions. Indeed, it is sometimes the primary indicator of outcome and occasionally the only one (e.g., in some psychosomatic or psychiatric conditions; or in general practice, where a specific diagnosis cannot always be established). It is very often, perhaps almost always, the outcome of most significance to the patient.

There is now almost universal agreement about the desirability of incorporating measurements of HRQoL in the overall evaluation of medical, surgical and social interventions. Reports of clinical trials frequently state that HRQoL has been evaluated, although the meaning of this statement varies widely from all psychosocial or patient reported measures to measures previously validated on the population being studied in the clinical trial. Psychometric and other methodological studies are also frequent. Many hundreds of methods and instruments have been, and continue to be, developed and evaluated.

However, there is no final consensus on many important issues, including the DEFINITION of the concept itself. The DOMAINS (e.g., behaviour, cognition, attitude, emotion and belief) that must be considered in an evaluation of HRQoL are less controversial than the primary FACTORS (such as objective physical prowess and subjective appraisal of physical capacity) that enter into them. These are tested by different methods (Sickness Impact Profile, Nottingham Health Profile) and/or described with different terms (such

as affect and emotion). This may raise unfamiliar problems for Cochrane reviewers who do not wish to neglect HRQoL measurements in their overall assessments.

The main purposes of the HRQoL Methods Group are therefore (a) to advise reviewers on the methodological adequacy of HRQoL observations in reports that they are considering for inclusion; (b) to develop and make generally available lexicons of commensurate terms and measurement instruments so that apparently disparate studies may be combined in meta-analyses.

Qualitative research and The Cochrane Collaboration

Jennie Popay

In the lead up to the recent registration of the Cochrane Qualitative Research Methods Group it has been obvious that there is a real demand and enthusiasm within the Collaboration for the type of work the Qualitative Methods Group will be doing. This is very different from the situation I encountered when, with a fellow sociologist Gareth Williams, I attended my first Cochrane Colloquium in Amsterdam in 1997. It was difficult to imagine then that the Collaboration's Review Groups would ever be interested in, and supportive of methodological work on qualitative research. 'What Methods Group?' came the bewildered refrain, as we canvassed support in that vast conference hall. Of course, there have always been enthusiasts within the Collaboration. We were at the conference because Iain Chalmers had talked to us about the enormous potential he saw for qualitative research to increase the breadth and relevance of systematic reviews. Others, like Sandy Oliver, Mike Clarke, Paul Garner, Carl Thompson and Miranda Mugford – to name but a few – also needed no convincing of the value of this development and have provided active support on the road to registration.

At times, however, it has been a lonely road and supporters and activists alike have expressed their frustration at the lack of progress. Time and people are still in short supply but the context within which we are working has changed dramatically making the work easier and more satisfying. Four factors seem to have been particularly important in driving this change: an increasing recognition amongst Cochrane reviewers that qualitative research findings can add to the quality of their reviews; the increasing availability of significant external funding for methodological work on the systematic review of qualitative evidence; and growing numbers of systematic reviews demonstrating the value of including evidence from qualitative research.

The newly registered Qualitative Methods Group will shortly begin a survey of Cochrane reviews to identify those that make some reference to findings from qualitative research. Anecdotal evidence suggests this is increasingly common. Some reviewers are already turning to qualitative research to help them define the question for the review and others are referring to qualitative research in the discussion section of their reviews. One early example of the latter use is the review by Carl Thompson of initiatives providing support for informal carers of people with Alzheimer's type dementia.[1] Work is also underway to extend existing Cochrane reviews to include findings of qualitative research. Noyes and colleagues, for example, with support from the Infectious Diseases Review Group are undertaking methodological work to determine if qualitative research findings can contribute to the systematic review of Interventions for Promoting Adherence to Tuberculosis Management by improving the quality, relevance and scope of the review.[2] Other members of this Review Group are developing protocols to extend a systematic review of malaria treatment interventions to include a review of relevant qualitative research. Similarly, Arai and colleagues [3] have recently reported on exploratory work focusing on the potential for evidence from studies evaluating implementation processes, which include qualitative methods, to improve the utility of a Cochrane review of smoke alarm trials.[4]

There have also been several major funding initiatives in recent years to develop methods for the systematic review of qualitative research, making the type of developments described above more feasible. Perhaps the two most significant developments in the UK are the EPPI centre (http://eppi.ioe.ac.uk/EPPIWeb/home.aspx) at the Institute for Education, funded by the Department of Education, and the Evidence Network (www.evidencenetwork.org), funded by the Economic and Social Research Council (ESRC). Both these initiatives are making important contributions to methodological developments in the systematic review of evidence from studies using diverse designs including, but not restricted to, qualitative methods. Other UK funding initiatives worth noting are the NHS Health Technology Programme support for research to develop 'meta-ethnography' as an approach to the systematic review of qualitative research findings,[5] the Health Development Agency support for the work by Arai and colleagues[3] and a study of existing approaches to the synthesis of qualitative and quantitative data.[6] Additionally, the Cabinet office has funded development work on the critical appraisal of qualitative studies[7] and the ESRC has recently funded a study aiming to develop more systematic approaches to the narrative synthesis of qualitative and quantitative findings.[8] Finally, the inclusion of qualitative research in the allowable areas for the Evidence Synthesis Scientist Awards recently established by the NHS Research and Development capacity building programme, clearly signals that this work is recognised as important.

Partly as a result of the above funding initiatives, an increasing number of systematic reviews of qualitative research are being published and these provide useful exemplars of the way in which qualitative research can extend the relevance and scope of traditional reviews of evidence of effectiveness. Notably, there are the systematic reviews being produced by the EPPI centre and published

on their website. These reviews seek to include evidence on the perspectives of people who are the target of interventions and evidence on factors impacting on implementation (see, for example, the study by Shepherd and colleagues).[9]

There is, then, a growing body of methodological work for the Qualitative Methods Group to build on. We will be collating information about methodological work underway on search strategies, study quality appraisal frameworks and methods for evidence synthesis and posting these on the website. Some protocols for reviews including a focus on qualitative research are already on the website, as are some frameworks for study quality appraisal. A methodological database is being constructed and work will shortly begin on developing initial guidance for reviewers. Given that we are at an early stage in the development of methods for the systematic review of qualitative research, the first iteration of this guidance will not contain definitive statements of best practice but it will help people make choices about approaches to adopt for searching, appraisal and synthesis and offer some advice on the methodological problems they will undoubtedly encounter. It is a challenging agenda but an exciting one.

The group's website is maintained by Peter Finch: http://mysite.freeserve.com/Cochrane_Qual_Method/index.htm

References:

1. Thompson C, Spilsbury K. Support for carers of people with Alzheimer's type dementia (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

2. Volmink J, Garner P. Interventions for promoting adherence to tuberculosis management (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

3. Arai K, Popay J, Roen K, Roberts H. *Preventing accidents in children: how can we improve our understanding of what really works? Exploring methodological and practical issues in the systematic review of factors affecting the implementation of child injury prevention initiatives.* (Health Development Agency research Programme). Child Health Research and policy Unit Project, City University, London. [ongoing research]. Available: www.city.ac.uk/barts/chrpu/projects/childinjuryprevention/index.htm (accessed 19 May 2003).

4. DiGuiseppi C, Higgins JPT. Interventions for promoting smoke alarm ownership and function (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

5. Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, Donovan J. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. *Social Science and Medicine* 2003; 56:671-684.

6. Dixon-Woods M, Smith JA, Booth A, Young B, Jones DR, Miller T, Sutton A, Shaw RL. *How can systematic reviews incorporate qualitative research?* (ESRC Research Methods Programme). Department of Epidemiology and Public Health, University of Leicester, Leicester. [ongoing research]. Available: www.prw.le.ac.uk/research/qualquan/esrcsummary.htm (assessed 19 May 2003).

7. Spencer L, Ritchie J, Lewis J, Dillon L. *Assessing Quality in Qualitative Evaluations*. London: Cabinet Office, in press.

8. Popay JM, Baldwin S, Petticrew M, Roberts H, Sowden A. *Narrative synthesis of quantitative and qualitative data in systematic reviews*. (ESRC Research Methods Programme). Institute for Health Research, Lancaster University, Lancaster. [ongoing research].

9. Shepherd J, Oliver S, Harden A, Rees R, Brunton G, Garcia J, Oakley AS. How can different types of evidence be synthesised in a systematic review? *4th Symposium on Systematic Reviews*: *pushing the boundaries*; 2002 Jul 2-4; Oxford, UK. P18.

Illustrating Cochrane reviews with narrative clips describing patients' experiences of the interventions

Andrew Herxheimer and Sue Ziebland

An important characteristic of randomized trials is that they describe the results of using an intervention in groups of people, and compare the outcomes in groups treated in different ways. Such comparisons give us reliable information about the relative value of the interventions that are compared, even though there are often large differences between the individuals within each group in a randomized trial. Since Cochrane reviews are based mainly on the data from randomized trials, their conclusions can also tell us only about groups and averages. The results are, therefore, difficult to apply to individual patients, and their implications for consumers remain unclear.

Clinicians have a further difficulty when they want to explain to patients how a particular intervention may affect their disease and their life, because randomized trials and systematic reviews rarely describe these in human terms that people can understand. For example, survival of an otherwise fatal disease is always reported in trials, but most reports say little or nothing about what kind of survival – about the quality of life during and after the intervention. Even when quality of life or performance measures are used in a trial, the results can be applied to individuals in only broad and vague terms. That is bound to be so because all such measurements refer to averages, not individuals. An

unfortunate consequence is that Cochrane reviews are dry and technical, and lack human interest. This limits their appeal. DIPEx, a database of personal experiences of health and illness, can help to bridge this gap between number-based science and patients' stories.

The primary aim of DIPEx is to describe the widest practicable range of individual experiences from the patients' points of view, in order to provide a rich information resource for patients affected by the diseases and for those who look after them. DIPEx studies use qualitative narrative interview methods, which encourage people to talk without interruption about all aspects that mattered to them, from the point when they first started to suspect a problem. Only then are they asked to talk about additional areas that they may not have covered in depth, including what they knew about the condition before the diagnosis, how they sought information and chose between options, ideas about causes, and their experiences of treatments and side effects. These accounts of what it is like to undergo different interventions provide a valuable and compelling perspective which, gathered together and analysed as topic summaries on the DIPEx site, can be used to illustrate reviews of those interventions. DIPEx aims to convey a broad range of experiences, both positive and negative, and to describe important effects that the intervention and the disease had on those people's lives.

DIPEx now includes collections of experiences of hypertension, epilepsy and of five common cancers – of the prostate, breast, bowel, testis and cervix. Work is proceeding on ten further modules: rheumatoid arthritis, parents of children with congenital heart disease, heart failure, chronic pain, lung and ovarian cancer, palliative care, depression, young people's sexual health and people with dementia and their carers.

We envisage using a DIPEx topic summary and up to six clips from the interviews in a module to illustrate one Cochrane review. A poster at the Cochrane Colloquium in Stavanger in 2002 showed two examples demonstrating graphically how the illustrations might be linked with a Cochrane review.[1] The two reviews chosen were on 'Chemotherapy for advanced colorectal cancer' and 'Tamoxifen for early breast cancer'. The summary of what DIPEx participants had said about the intervention, and three clips from individual interviews were juxtaposed with the synopsis or abstract of the review. As more DIPEx modules are completed, we will identify Cochrane reviews that they might be used to illustrate, and discuss the possibilities with the editors of the Collaborative Review Groups responsible for them. We could also begin to look at Cochrane protocols, so that we can let reviewers know what issues patients are raising about the interventions. This would enable them to consider these aspects in their review.

The technical means of linking the DIPEx material to the Cochrane review still remain to be worked out with the publishers of Cochrane reviews. The text summary would be easy to add to a review as hypertext, and so would the transcript of the clips, but video or audio versions of the clips would be more demanding and might be more appropriately put in as links to the particular page on the DIPEx website.

More information about DIPEx is available from their website www.dipex.org. For more information about how individual experiences can be linked to Cochrane reviews please contact Andrew Herxheimer (Andrew_Herxheimer@compuserve.com).

Reference:

1. Herxheimer A. Illustrating Cochrane reviews with narrative clips describing patients' experiences of the intervention. *10th Cochrane Colloquium*; 2002 Jul 31 – Aug 3; Stavanger, Norway. Poster 63, p58.

Quality assessment of non-randomized studies

Jon Deeks, Nandi Siegfried and Martie Muller

There are many more ways in which non-randomized studies can produce misleading results than randomized trials. Consequently, assessment of the quality of non-randomized studies is more difficult.

The Cochrane Reviewers' Handbook lists selection, performance, detection and attrition biases as aspects of quality that should be assessed for randomized trials. Selection bias is prevented by properly concealed randomisation, performance and detection biases by masked interventions and outcome assessments, whilst attrition bias is minimised by complete follow-up. Non-randomized studies suffer from all the same potential biases but are far more susceptible; as randomization does not occur, blinding is rare and follow-up is often poor.

In a review of Male Circumcision for Prevention of Transmission of HIV,[1] soon to be published in *The Cochrane Library*, data from non-randomized studies were considered as there are currently no completed randomized trials for this intervention (three are currently in progress). The observational studies were of three different designs:

- Cross-sectional surveys: participants were tested for HIV and risk factors were elicited at the same time.
- Cohort incidence studies: risk factors for infection were elicited in a known HIV negative group who were followed, with new HIV cases identified by repeated testing.
- Case-control studies: the prevalence of risk factors in an HIV positive sample was compared with the prevalence in an HIV negative sample.

'Bespoke' quality assessment forms were developed for the quality assessment. We approached this task in collaboration with epidemiologists and clinical experts, learning what we could from existing quality tools reviewed in a forthcoming UK Health Technology Assessment

report.[2] We briefly summarise some issues which differ from those encountered with randomized trials.

The intervention occurred before the study commenced
The intervention (circumcision) was carried out in all participants before the studies commenced, most commonly during childhood or adolescence. Performance bias relates to the correct classification of individuals into intervention and control groups (and not whether interventions were masked) and we found a difference between studies in which circumcision status was determined by direct observation and those where it was based on self-report.

Some studies are prospective, others retrospective
The outcome (HIV infection) occurred in cross-sectional and case-control studies before the study commenced. Thus in case-control and cross-sectional studies it was possible for the assessment of the intervention allocation to be biased by knowledge of the outcome - another source of performance bias.

Evaluation of the intervention was not the aim of these studies
Circumcision was one of many risk factors investigated in these studies. None attempted to create comparable circumcised and non-circumcised groups, so all had potential for selection bias and confounding. A critical part of the quality assessment involved judging whether the circumcision analysis could be confounded. We first produced a list of potential confounders with the help of our clinical experts. We had ten: age, urban or rural study location, religion, markers of socioeconomic status, marital status, sexual history, STD history, condom use, migration and travel, and other possible HIV exposures. Each study report was examined to note whether these factors could be ruled out as possible confounders, i.e. if (a) all participants had the same value, (b) the study design had matched on the factor, (c) the distribution of the factor was similar in circumcised and non-circumcised groups, or (d) a statistical adjustment had been made to compensate for the difference.

Interventional effects or associations?
The epidemiological studies answered the question "are circumcised men less likely to contract HIV?". The studies concluded that there is an association between circumcision and HIV transmission. However, the Cochrane review asked a different question: "will use of circumcision as an intervention reduce transmission of HIV?". Beyond the issues addressed by the quality assessment, there are several ways in which evidence of an association may not lead to an interventional effect: the association may be (a) related to age at circumcision, or (b) influenced by aspects of adulthood initiation ceremonies other than circumcision (e.g. teaching of penile hygiene practices); and (c) circumcision as an adult intervention may induce changes in sexual behaviour that may possibly increase risk.

Key lessons we have learnt are:

- Quality assessment is more challenging for non-randomized studies than for randomized trials.
- Existing quality checklists make good starting points, but think carefully as to how the particular clinical situations affect the study features you should look for, and consider developing bespoke checklists
- Different study designs need different checklists (although they have common items)
- Potential confounding factors should be pre-specified, and not limited to the factors adjusted for in the studies.
- Involve expert epidemiologists and clinicians in the discussions about quality assessment and potential confounders
- Think clearly about the differences between observing an association and having evidence of an interventional effect

Full details of our quality assessment are published in the forthcoming review.[1] We look forward to receiving comments on the approach we have adopted.

References:

1. Siegfried N, Muller M, Volmink J, Egger M, Low N, Weiss H, Walker S, Deeks J, Williamson P. Male circumcision for prevention of heterosexual acquisition of HIV in men (Protocol for a Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

2. Deeks JJ, Dinnes J, D'Amico RA, Sowden AJ, Sakarovitch C, Song F, Petticrew M, Altman DG. Evaluating non-randomized intervention studies. *Health Technology Assessment*, in press.

Why we still ask 'should Cochrane reviews include non-randomized studies?'

Tom Jefferson and Deirdre Price

This question has surfaced innumerable times in many guises. It is sometimes posed by the audience at a conference presentation: "is it true that Cochrane reviews only include randomized trials"? or "why does Cochrane only include trials in its reviews?". Sometimes it appears as a sweeping statement by (alas) members of the Collaboration, "we only review randomized data" and its variant: "Cochrane is about effectiveness". *The Cochrane Library* has included systematic reviews of non-randomized data since 1992 and the Non-randomized Studies Methods Group has been registered for over three years.

Doubts over the inclusion of non-randomized studies, are in part, based on a misunderstanding of the role of our Collaboration, of systematic reviews specifically, and of the role of randomization in reducing bias.

The Collaboration's mission is to "…help people make well-informed decisions about healthcare…". We do this "… by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions".[1] Readers will notice that the word used in

our mission statement is 'effects', not 'effectiveness'. Effectiveness is the prime effect, but not the only one. There are other effects of an intervention such as unintended, unexpected and harmful ones, as well as economic and social ones.

Cochrane systematic reviews are aimed at answering relevant questions about healthcare interventions "…using outcomes that matter to people making choices in health care".[1] The questions posed by reviewers cannot be justified by their ability to be answered comfortably within the current established methodological framework.

Some questions are not amenable to being answered by trials because there are none available, or because the effects to be assessed are rare, or long term, or because the conduct of a trial to answer that particular question would be unethical.

If we accept that to address some questions we may have to look for and include studies of non-randomized design (either exclusively or alongside trials) we move away from the comforts and certainty of the 'randomized' world. We move into a relatively unknown and unexplored territory for reviewers, populated by cohorts, case-controls and epidemiological studies but also by more obscure study designs such as case-crossovers and self-controlled case series.

Moving away from well-trodden paths engenders fear and apprehension. But, if we can understand what benefits randomization offers, we will be better able to judge when observational studies offer similar advantages. Randomization offers two very useful things. The first is unbiased allocation (through concealed application of an unbiased allocation schedule). Treatment choice is not influenced by patient variables. And, second, the application of statistical theory allows testing and calculation of confidence intervals. Differences between patient groups will be dispersed in such a way to conform to the laws of chance.[2,3]

In certain instances, observational studies may confer these benefits and there are many examples from the vaccines field. Dourado et al investigated an outbreak of aseptic meningitis after a mass vaccination campaign with MMR (Urabe mumps strain) in Salvador, Brazil.[4] Virtually all of the 1-11 year olds were vaccinated during a two-week period. Thus, the first benefit of randomization is met - unbiased allocation - as treatment is allocated to the total population. Cases both pre- and post-vaccination were identified from the city's sole neurological hospital with clinical and laboratory confirmation and exclusion of all cases with prior neurological disorders or uncertain vaccination histories. Comparisons were made utilising the same population before and after vaccination. Therefore, statistical calculations based on assumption about the random allocation of differences between the populations apply. Elevated relative risks in the post-vaccination period suggest a causal link between MMR (Urabe mumps strain) and aseptic meningitis. In certain cases, such as Dourado et al, observational studies can provide certainty equivalent to a randomized trial and thereby merit inclusion in systematic reviews.

So far, the methodology to incorporate observational studies into systematic reviews is underdeveloped. Recognition is needed to confirm that complex, important questions such as: 'what are the effectiveness and safety profiles of vaccine X in children?' can only be answered with a mix of study designs – randomized trials and observational studies. In order to progress, the Collaboration, entities and individuals, need to focus not on 'should' but 'when' and 'how' to include non-randomized studies in systematic reviews.

References:

1. The Cochrane Brochure. Available: www.cochrane.org./cochrane/cc-broch.htm (accessed 19 May 2003).

2. Vandenbroucke J. *Under what circumstances can observational studies achieve the same type of unbiasedness as randomised studies?* UK Cochrane Centre, 2003 25 Mar; Oxford, UK. [Oral presentation].

3. Altman DG, Bland M. Treatment allocation in controlled trials: why randomise? *BMJ* 1999; 318:1209.

4. Dourado I, Cunha S, Teixeira MG, Farrington CP, Melo A, Lucena R, Barreto ML. Outbreak of aseptic meningitis associated with mass vaccination with a urabe-containing measles-mumps-rubella vaccine: implications for immunization programs. *American Journal of Epidemiology* 2000; 151:524-530.

Cochrane systematic reviews of diagnostic test accuracy

Jon Deeks, Constantine Gatsonis, Mike Clarke and Jim Neilson

The Steering Group in April 2003 accepted a proposal to take forward a programme of work to extend the definition of Cochrane reviews to include systematic reviews of diagnostic test accuracy. Diagnostic tests fall within the ethos of the Collaboration, as they relate to healthcare management decisions, and they need to be empirically evaluated to determine whether their use causes more benefit than harm. Healthcare professionals, policy makers, carers and consumers are regularly faced with decisions concerning the selection and timing of diagnostic tests, and the interpretation of their results. Now that the infrastructure and mechanisms for producing systematic reviews of healthcare interventions are established within the Collaboration, it is timely to start the second decade of the Collaboration with the new challenge of developing Cochrane reviews of diagnostic test accuracy.

Systematic reviews of diagnostic test accuracy will not be included in *The Cochrane Library* overnight. There is much work to be done in deciding methodological standards, developing publication formats and software, and considering questions such as the role of handsearching and development of databases of primary studies. Of paramount importance will be working out how this new challenge can interleave with current functions of Centres and Review Groups, as well as Fields and Methods Groups, without creating unmanageable demands, and ensuring that all involved will be able to obtain training and the necessary methodological and software support. It will be an opportunity to work in partnership with several groups currently not as yet directly involved in the work of The Cochrane Collaboration. We will also be looking outside the Collaboration for financial resources to support these developments.

To take this programme forward, a new subgroup jointly chaired by Jon Deeks (Methods Group representative on the Steering Group) and Constantine Gatsonis (convenor of the Screening and Diagnostic Tests Methods Group) is being created, who will work with key people in the Collaboration to manage the development of Cochrane diagnostic test accuracy reviews. Currently, they are producing a document, which outlines key issues and tasks that need to be explored, which will be circulated for consultation within the Collaboration. We look forward with excitement to this new development within the work of The Cochrane Collaboration.

Assessing statistical heterogeneity: chi^2 or I^2?

Julian Higgins

A generally desirable attribute of a meta-analysis is that the results of the studies *agree*. This may be important irrespective of how clinically or methodologically diverse the studies are. For example, consistent results across studies in different populations, with different methodologies and with slight variations on the outcome definition can add considerable weight to the generalizability of the findings. In statistical terms, we define consistency across studies in terms of *homogeneity*. We say there is homogeneity of effect across studies if every study is estimating the same magnitude of effect (for example, a common odds ratio or a common standardized mean difference). Whenever homogeneity does not exist, we say there is *heterogeneity*. This article discusses how we should assess heterogeneity in a particular meta-analysis.

The traditional test: Chi^2
Meta-analyses in Cochrane reviews, RevMan or MetaView include a statistical test that aims to answer the question of whether studies have homogenous effects. This is displayed below a meta-analysis, for example as:

- Test for heterogeneity: chi-squared=12.44 df=7 p=0.09

In this case, the test produces a chi-squared value of 12.44 on 7 degrees of freedom (df), the latter obtained as the number of studies minus one. (In the example, there were eight studies). The resulting p value is 0.09, which would not be deemed statistically significant using the conventional cut-off of 0.05.

Is this a useful test? A well-known problem with the test is that it typically has low power, meaning that it is unlikely to yield a statistically significant result when there is genuinely some heterogeneity of effect. This is because it is difficult to demonstrate variation across studies when there aren't many of them. Thus a non-significant test result should not be taken as evidence of homogeneity. A more fundamental problem, however, concerns the whole notion of testing for heterogeneity. Since systematic reviews inevitably bring together studies in different populations, in different settings, using different methods, with different outcome definitions (and the list goes on…), we might reasonably always expect heterogeneity of underlying effects to be present. In that case we shouldn't be interested in determining *whether* heterogeneity is present, but instead should focus attention on how large it is and how much it impacts on the conclusions of the review.

The new addition in RevMan 4.2: I^2
RevMan 4.2 supplements the test for heterogeneity with a new quantity that describes the impact of heterogeneity on the meta-analysis. The quantity is called I^2, and it is displayed thus:

- Test for heterogeneity: chi-squared=12.44 df=7 (p=0.09) I^2=44%

I^2 measures the degree of *inconsistency* across studies. It is calculated as follows:

- $100\% \times (\text{Chi}^2 - \text{df})/\text{Chi}^2$

Its lowest possible value is 0%, and its highest is 100%. It may be interpreted approximately as the proportion of total variation in the observed results of the studies that may be explained by heterogeneity rather than chance variation. Thus, if I^2 = 0%, then there is no apparent heterogeneity, whereas in the example I^2 = 44% so almost half of the variability in effect estimates was due to genuine variation in the underlying effects. In practice, I^2 will never reach 100%, but values in excess of 70% would usually inspire particular caution in interpreting a meta-analysis.

Some useful properties of I^2 are:

- I^2 may be bigger than zero even if the test result is not statistically significant.
- I^2 will be bigger than zero if, and only if, a random effects meta-analysis differs from a fixed effect meta-analysis.
- Larger values of I^2 indicate greater heterogeneity, and less easily generalized conclusions.

To read more about I^2, look out for: Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency is preferable to testing for heterogeneity in meta-analysis (to appear in *BMJ*), or consult the following more technical paper: Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002; 21:1539-1558.

Searching the SCI for journal articles which cite Cochrane reviews and Cochrane methodology reviews

Mike Clarke and Liz MacKinnon

One way to assess the influence of Cochrane reviews would be to identify the number of articles which cite them, and to look at why they are cited in these articles. A few months ago, the UK Cochrane Centre asked Liz MacKinnon from the Clinical Trial Service Unit in Oxford to help us to see how feasible it would be to do this using the Science Citation Index (SCI), which can be used to search for journal articles, which cite other articles (including Cochrane reviews and Cochrane methodology reviews). At the moment, Cochrane reviews do not have their own entries in SCI (The Cochrane Collaboration Steering Group is hopeful that they will be added soon) but they can still appear as part of the reference lists for articles that do have their own entries.

The Science Citation Index is available in various ways. Some of the ways that we know about are on CD-ROM via SciSearch from www.isinet.com/ with author abstracts, updated monthly, back years to 1991; without author abstracts, updated quarterly, back years to 1980. SciSearch is also available ONLINE via DIALOG (www.dialog.com/), DIMDI (www.dimdi.de/) and STN (www.stn-international.de/): updated weekly, back years to 1974 and via DATASTAR (www.datastarweb.com/): updated weekly, back years to 1980. In the UK, the SCI is available via the ISI Web of Science (http://wos.mimas.ac.uk/) using an ATHENS username and password.

This project used the latter and a cited reference query involved entering text into one or more of the following fields: 'cited author', 'cited work' and 'cited year'. Unfortunately, based on our experience of searching SCI for citations to a number of reviews in December 2002 to February 2003, we advise that anyone planning to use SCI in this way should be cautious. This is because:

a) As a 'cited work' (this would be the name of the journal for cited articles that were published in a 'traditional' scientific journal), the *Cochrane Database of Systematic Reviews* in *The Cochrane Library* appears in SCI in several different ways, so your query needs to take account of all the possible variations.

b) Because Cochrane reviews are republished with each issue of *The Cochrane Library*, their recommended citation changes every three months. This means that the cited review might appear in SCI with different publication years and, even though Cochrane reviews do not have start and finish pages, digits sometimes appear in the page field in SCI.

c) If the first author of a review has ever changed, then all relevant first authors will need to be searched for and the results combined. This is because the searches can only look for the first author.

d) Titles are not included in the cited reference information on SCI, so if you find citations for a particular author, and that author is (or has been) first author for more than one Cochrane review, you cannot identify which of their reviews is being cited without checking the references list of the article citing it.

On a more positive note, although it is difficult to identify articles citing specific, individual Cochrane reviews in SCI, the total number of citations to all Cochrane reviews can be obtained (again, though, with some difficulty). Based on searches of SCI (via the Web of Science) that were done between 20 January and 5 February 2003, articles included in SCI up to that time included the following numbers of citations to articles and other documents which appear to be Cochrane reviews or other publications of The Cochrane Collaboration (such as the Cochrane Reviewers' Handbook):

- 195 citations of Cochrane works published in 1995
- 211 citations of Cochrane works published in 1996
- 324 citations of Cochrane works published in 1997
- 716 citations of Cochrane works published in 1998
- 919 citations of Cochrane works published in 1999
- 3000 citations of Cochrane works published in 2000
- 1394 citations of Cochrane works published in 2001
- 439 citations of Cochrane works published in 2002

This gives a total of 7198 citations of Cochrane works that had been published between 1995-2002 and had been cited before February this year.

We should be pleased to hear from anyone who has found easier ways to identify articles that cite Cochrane reviews. If you would like any further information relating to this project, please contact Liz (liz.mackinnon@ctsu.ox.ac.uk).

Using a Cochrane methodology review to inform practice

Elizabeth Pienaar

In 2002, the Cochrane Information Management System commissioned a survey of reviewers living in developing or low-resourced countries.[1] The reason for the survey was the recognition that people living in these countries face problems different from those of people living in places such as Europe or the United States of America. The survey

was based on the Collaboration-wide survey conducted the year before. In the first survey the response rate was low and it was suggested that some way must be sought to increase this. In the initial survey, the sample population was large but the current survey only dealt with a small proportion of this group. The initial survey was sent via email and also made available on the internet. For the developing country survey it was decided not to make it available through the internet. The reason for this was that in most of the relevant countries the access speed is slow and the connection not always reliable. Postal questionnaires were considered, but it was decided not to use that route, as this would have meant increased cost not only for sending out survey documents, but also for return postage. Postal services are also not always very reliable in some countries.

It is a known fact that non-response reduces the effective sample size and can also lead to the introduction of bias.[2] In epidemiological studies non-response can have a large impact on the result of the research. Because of the latter, researchers conducting surveys are always looking for ways and means by which the response rate may be increased to an acceptable level.

In a recent Cochrane methodology review on how to increase the response rate to postal questionnaires, Edwards and colleagues came to the conclusion that there are several ways in which to do this. [3] Strategies may, or may not, mean extra cost, material and time to the researcher. It was found that putting certain questions first might also influence the response rate. Providing an incentive was found to be another way of increasing the response rate and the provision of a monetary incentive more than doubled the odds of response.

There is also the question of when to offer the incentive. If it is provided with the questionnaire it has a higher impact on response than when it is given for the return of the questionnaire. In an attempt to keep cost low it was decided to go with the latter, namely an incentive to those who return the questionnaire. The incentive decided on is a one-year subscription to *The Cochrane Library*. The names of all persons who return their questionnaires will be put onto a numbered list. From this list two numbers will then be randomly selected. The UK Cochrane Centre has offered to provide me with not one, but two, subscriptions, for which I am extremely grateful.

The incentive was announced in the first reminder. The paragraph with the announcement was put in bold type so as to attract the attention of the reader immediately. Care was also taken to send the reminders only to those persons who had not yet returned a completed questionnaire. With this being an email survey, it is possible to know from which email a response is still outstanding. On the days following the first reminder there was a sharp increase in the number of responses. The trend was again noticeable after the second and the final reminder. By the end of March, completed surveys had been returned by 80 persons out of the 355; this is a response rate of 22%.

I have come to the conclusion that the provision of the incentive had an effect on response, as well as the sending of reminders. The latter was made easier because this was an email survey and not a postal survey. My experience has shown that the results of the Cochrane methodology review are not only applicable to postal surveys, but also to electronic surveys.

References:

1. Clarke M, Higgins J, Moore T, Wiffen P. *Report on the Cochrane Software Needs Assessment Survey*. Oxford, March 2002.

2. Armstrong BK, White E, Saracci R. *Principles of exposure measurement in epidemiology* (Monographs in Epidemiology and Biostatistics, 21). New York: Oxford University Press, 1995:294-321.

3. Edwards P, Roberts I, Clarke M, DiGuiseppi C, Pratap S, Wentz R, Kwan I. Methods to influence response to postal questionnaires (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

Evidence-based information science: using empirical evidence to inform practice

Carol Lefebvre

In the same way that evidence-based medicine is the use of the best evidence in making decisions about the care of individual patients, evidence-based information science makes use of the best evidence from information science research to guide information practice.

The UK Cochrane Centre is currently handsearching the information science literature to improve access to methodological research in this field, by incorporating reports to relevant studies in the *Cochrane Methodology Register*, published in *The Cochrane Library*.

Some examples of evidence-based information science research within the Collaboration include:

- Assessing which bibliographic databases to search by recording and comparing reports of randomized trials identified in each database and analysing the overlap.[1]
- Evaluating whether searching MEDLINE is as effective as handsearching MEDLINE-indexed journals to retrieve randomized trials for possible inclusion in systematic reviews.[2]
- Evaluating the comparative effectiveness of handsearching versus electronic searching of a variety of biomedical databases to identify reports of randomized trials for possible inclusion in systematic reviews.[3]

- Comparing cover-to-cover searching of journals by hand with searching the full-text of journal articles electronically on screen and with keyword searching of the full-text of journal articles electronically.[4]
- Designing objectively-derived highly sensitive search strategies for identifying reports of randomized trials in MEDLINE and EMBASE and reports of systematic reviews / meta-analyses in MEDLINE by identifying terms which occur frequently in 'gold-standards' of known reports but which do not occur frequently in other records in the databases.[5]

The above are examples, which indicate ways in which empirical research is currently being conducted to inform best practice in work associated with information retrieval within the Collaboration. (See also information about the proposed Cochrane Information Retrieval Methods Group under Possible Methods Groups).

References:

1. McDonald S, Taylor L, Adams C. Searching the right database. A comparison of four databases for psychiatry journals. *Health Libraries Review* 1999; 16:151-156.

2. Hopewell S, Clarke M, Lusher A, Lefebvre C, Westby M. A comparison of handsearching versus MEDLINE searching to identify reports of randomized controlled trials. *Statistics in Medicine* 2002; 21:1625-1634.

3. Hopewell S, Clarke M, Lefebvre C, Scherer R. Handsearching versus electronic searching to identify reports of randomized trials (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

4. Weir E. Comparing methods of electronic versus paper searching of online journals (Ongoing research project). In: *The Cochrane Methodology Register* in *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

5. White, VJ, Glanville JM, Lefebvre C, Sheldon TA. A statistical approach to designing search filters to find systematic reviews: objectivity enhances accuracy. *Journal of Information Science* 2001; 27:357-370.

The new Cochrane information management system: what does it mean for Methods Groups?

Monica Kjeldstrøm

The Cochrane Collaboration has embarked on the development of a new Information Management System (IMS). The main purpose of the new IMS is to support a more efficient preparation, maintenance and publication of high quality Cochrane reviews, by allowing members to share relevant material more easily, and to act on the most accurate and up-to-date information available. The new IMS will be built around a central system accessible via the internet.

Obviously, it will be the Review Groups and their reviewers who will be the most active users of the system, but also convenors and members of Methods Groups will also use it. Already, Methods Group convenors are preparing their modules via the new web-based Contact Database. With this system, convenors are less likely to forget where to go and what to do when updating their modules…… *as has happened in the past!* It will also be easier to implement structural changes to the module for Methods Groups, as the new IMS will not require an update to be installed on a local PC. Other members of Methods Groups will over time be able to look up contact details of co-members (if permission has been given to share their contact details), and to contribute online to the preparation of reviews through Review Groups. For instance, a member of the Statistical Methods Group may be asked for advice on the use of a particular method in a review and could be provided access to the relevant data directly on the new IMS so as to gain a better understanding of the question being asked.

The concepts behind the new system are based on the results of the software needs assessment survey that was carried out in 2000 and on discussions by the Information Management System Group and its advisory groups. If you would like to learn more about the results of the survey and the plans for the new IMS (and what it could mean for other user groups, such as reviewers), you should visit the IMS website: www.cc-ims.net. Look under 'Projects'. Here you can also share your thoughts on the plans, pose questions, and let us know what you think would be particularly important to address in the development. We look forward to hearing from you!

The Cochrane Methodology Register

Marit Johansen

What it is

The *Cochrane Methodology Register* (CMR) is a bibliographic collection of studies relevant to the methods of systematic reviews of healthcare and social interventions. The register includes journal articles, book chapters, conference proceedings, conference abstracts and reports of ongoing methodological research. Relevant records are identified primarily through a programme of handsearching, undertaken by the UK Cochrane Centre, and through the development of a series of search strategies run in MEDLINE. The register aims to include all published reports of empirical methodological studies that could be relevant for inclusion in a Cochrane methodology review, along with comparative and descriptive studies relevant to conduct a systematic review of healthcare interventions. While the register's primary focus is on bias, the more general scope is on the conduct and critical appraisal of reviews of healthcare evaluations. In Issue 2, 2003 of *The Cochrane Library*, CMR contains 4553 records. All records

include a range of bibliographic details such as where and when the study was published and one or more CMR index terms, named 'CMR keywords' in the records field. A large number of records also contain an abstract.

Who it's for
The register is relevant to all who are about to do a Cochrane methodology review as well as those who have methodology questions when conducting a systematic review or a healthcare evaluation.

Where and how to search
The *Cochrane Methodology Register* is published in *The Cochrane Library*. To search the register, use the 'search Phrase' box on the opening screen. More information about CMR and details of the indexing terms assigned to the records can be found by clicking on 'Using *The Cochrane Library*' on the opening screen. From the page, 'Searching *The Cochrane Library*', go to the link CMR. To use an index term as a search term it must be edited before searching. Be aware of punctuation marks that are non-searchable; such as colons, commas, hyphens, numbers etc.

The future
The intention of the Cochrane Methodology Review Group is to develop the register to include all relevant methodological articles. A complete register would then be the only resource needed when looking for an article concerning methodology questions. The register is not there yet. To make a user-friendly register, the records should be well-indexed to ease the retrieval. MEDLINE indexing terms do not reflect methodological questions satisfactorily and this makes searching for records to be included in the register a challenge. The UK Cochrane Centre is working to develop further and refine the list of useful index terms to make up for the rather poor MEDLINE indexing.

Help
You should contact the Methodology Review Group Co-ordinator, Elizabeth Paulsen (elizabeth.paulsen@shdir.no), if you are conducting or about to conduct a Cochrane methodology review and need help to search the register. Elizabeth will forward your request to the Group's Trials Search Co-ordinator, Marit Johansen (marit.johansen@shdir.no), who will be happy to help.

PUBLISHED METHODOLOGICAL RESEARCH - structured abstracts and commentaries

How objective are systematic reviews? Differences between reviews on complementary medicine

Linde K and Willich SN. *Journal of the Royal Society of Medicine* 2003; 96:17-22.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Systematic reviews are designed to minimize biases and make results and conclusions as objective as possible. However, they depend on the quality of the primary studies, the findings can be influenced by decisions made in the review process and reviewers with prior views of the topic may draw different conclusions from the same data.

Objective: To compare systematic reviews in complementary medicine which address the same questions to determine whether they produce different answers.

Design: An empirical study.

Data collection and analysis: Systematic reviews of herbal medicines, homeopathy and acupuncture published between 1989 and 2001 addressing the same topic were identified from the Cochrane Complementary Medicine Field database. Information on literature searching, inclusion criteria, selection process, quality assessment, data extraction, methods to summarize primary studies, number of included studies, results and conclusions was compared qualitatively.

Main results: Seventeen topics (eight on acupuncture, six on herbal medicines, three on homeopathy) had been addressed by two to five systematic reviews each. The number of primary studies in the reviews varied greatly within most topics. The most obvious reason for discrepancies between the samples was different inclusion criteria (in 13 topics). For example, the restriction to trials published in English in one review explains the exclusion of 12 of 17 trials included in another review. Methods of literature searching may have contributed with some topics but the equivalence of the searches was difficult to assess, as the strategies were not described in sufficient detail to allow a comparison. Methods for quality assessment of studies in the reviews differed considerably (a wide variety of scores and checklists were used) but major disagreements about overall quality were rare. The exception was for back pain trials where the majority of studies were described in one review as 'good' and in two other reviews as 'poor'. Because of the heterogeneity of the studies, the variability of outcome measures and insufficient reporting, only 20 reviews contained a quantitative meta-analysis. Only in three reviews (on whether homeopathy is any different from placebo) did the meta-analytic methods differ fundamentally and this, together with differences in study samples, led to discrepant conclusions. More subtle differences in conclusions were common and seemed to depend more on the prior beliefs of the reviewers than on the data.

Conclusions: This qualitative analysis indicates that systematic reviews of herbal medicine, homeopathy and acupuncture can differ greatly in their conclusions. In the large part, these discrepancies are traceable to the multiple decisions taken in the review process rather than to differences in the quality of the reviews themselves. The methodology of systematic reviews has developed considerably over the past ten years and recent guidelines (QUORUM) should help to improve the reporting in future years but caution will still be needed in their interpretation.

COMMENTARY
Prepared by Peter Gøtzsche

The authors identified 17 topics in alternative medicine (eight on acupuncture, six on herbal medicines, three on homeopathy) that had been addressed by at least two systematic reviews and noted whether the reviews gave different answers.

Different inclusion criteria were an important reason for discrepancies and the conclusions seemed to depend more on the prior beliefs of the reviewers than on the data. Some differences were pronounced, e.g. for homeopathy, but it is difficult to know what this means, since meta-analysis was rarely used, e.g. for acupuncture for back pain, the original authors had used vote counting which is a very unreliable method. An additional weakness of the reviews is that a wide variety of quality scores had been used, and it is not clear from the paper whether the reviews took account of elementary criteria such as the quality of the allocation concealment.

It is not unexpected that poor methods for research synthesis lead to considerable discrepancies and misleading answers. But, indirectly, this result gives support to the rigorous methods we use in Cochrane reviews.

I feel the topic addressed in this paper would be more interesting to study in areas where empirically-based methods for assessing the quality of the trials have been used and where there are summary estimates based on adequate meta-analytic methods.

How important are comprehensive literature searches and the assessment of trial quality in systematic reviews?

Egger M, Jüni P, Bartlett C, Holenstein F, Sterne J. *Health Technology Assessment* 2003; 7:1-76.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Extensive literature searches, which cover the grey literature and all relevant languages and databases, are normally recommended to minimize reporting biases in systematic reviews and meta-analyses. However, the size and direction of these effects is unclear at present. There may be trade-offs between timeliness, cost and the quality of systematic reviews.

Objectives: (a) To examine the characteristics of clinical trials that are difficult to locate (unpublished trials, trials published in languages other than English, trials published in journals not indexed in MEDLINE) and of trials of lower quality. (b) To compare within meta-analyses the treatment effects reported in trials that are difficult to locate with trials that are more accessible, and of trials of lower with trials of higher quality. (c) To assess the impact of excluding trials that are difficult to locate and of trials of lower quality on pooled effect estimates, p-values and the shape of funnel plots.

Design: An empirical study.

Data collection and analysis: Systematic reviews from the *Cochrane Database of Systematic Reviews*, the *Database of Abstracts of Reviews of Effects*, eight medical journals and *Health Technology Assessment* reports were searched for meta-analyses based on comprehensive literature searches and which combined the binary outcomes of at least five trials. Comprehensive searches were defined as not restricted to the English language; the *Cochrane Central Register of Controlled Trials* or at least two other electronic databases had been searched; and at least one indicator of searches for unpublished trials was present (e.g. conference proceedings). Quality assessment was restricted to trials included in Cochrane reviews.

Within each meta-analysis pooled effect estimates were calculated separately for the trials that were difficult to locate and the remaining trials, applying the same statistical model used by the original authors. For each meta-analysis, a ratio of the pooled estimates was derived. A weighted average for all these ratios was calculated using random-effects meta-analysis. The percentage change in the pooled effect estimate, which occurred when trials that are difficult to locate were excluded, was also calculated and changes in p-values and the impact on the shape of the funnel plot were examined.

Main results: 159 systematic reviews met the inclusion criteria. Comparisons of treatment effects were based on: unpublished versus published (60 meta-analyses); other languages versus English (50); non-indexed versus MEDLINE-indexed (66). Analyses of trial quality were based on: inadequately concealed/unclear versus adequately concealed (39); not double-blind versus double-blind (45).

The importance of trials that were difficult to locate appeared to vary across medical specialties and between complementary and conventional medicine. Unpublished trials showed less beneficial effects than published trials. Trials published in languages other than English and trials not indexed in MEDLINE tended to show larger treatment effects. Trials that were difficult to locate tended to be smaller and of lower methodological quality than trials that

were easily accessible and published in English. Trials with inadequate or unclear concealment of allocation showed more beneficial effects than adequately concealed trials. Open trials tended to be more beneficial than double-blind trials.

Including unpublished trials in the meta-analyses reduced funnel plot asymmetry. Inclusion of trials published in languages other than English and of trials not indexed in MEDLINE increased the degree of asymmetry in the funnel plot. The impact of trials of lower methodological quality on the funnel plot was substantial for trials with inadequate or unclear concealment of allocation.

Conclusions: Systematic searches of English language literature, accessible in the major bibliographic databases, will often produce results that are close to those obtained by reviews based on more comprehensive searches free of language restriction. However, the importance of trials that are difficult to locate appears to vary across medical specialty and between complementary and conventional medicine. Further research is required to clarify this issue, for example comparing the results from rapid reviews restricted to English language with meta-analyses based on extensive searches without language restrictions.

The inclusion or exclusion of trials of low methodological quality has a substantial impact on the results of meta-analyses. Thorough trial quality assessments should, therefore, be a priority in order to avoid introducing bias. Further methodological research into markers of trial quality in different areas of medicine is required.

COMMENTARY
Prepared by Brenda Thomas and Peter Sandercock

A systematic and comprehensive search for trials minimises bias in systematic reviews. This report on searching for systematic reviews is a 'must read' for systematic reviewers; it focuses on how to ensure that the resources invested in searching are put to best use.

One of the aims was to examine, using a selection of meta-analyses, the characteristics and impact of trials published in journals not indexed in MEDLINE. The study sample met strict inclusion criteria and the 66 meta-analyses containing trials published in both MEDLINE and non-MEDLINE journals were eligible for the analysis of MEDLINE bias. Although there were obvious differences in the characteristics of the trials in the two groups, the principal findings indicated that excluding non-MEDLINE trials did not markedly affect the estimate of treatment effects. However, the impact varied across specialties. Of the eight neurology meta-analyses included, seven related to pharmacological interventions. It is likely that the results here may not apply to trials, for example, in rehabilitation, many of which are published in journals not indexed in MEDLINE and are to be found in specialist databases and by handsearching.

The authors suggest that trials, which are 'difficult to locate', are often of lower quality. So, if time or resources for searching are limited, thorough quality assessment should probably take precedence over obsessively extensive literature searches and translations of articles in languages other than English. Since the contribution of studies, which are 'difficult to locate', will vary between different specialties and topics, it will be difficult for reviewers to decide in advance how comprehensive their search for such studies needs to be.

The Cochrane Collaboration has a support network for reviewers, which means that in many Collaborative Review Groups, the effort of locating trials is substantially reduced; nonetheless, anyone who is interested in systematic reviews should have a look at this very informative report.

Can we individualize the 'number needed to treat'? An empirical study of summary effect measures in meta-analyses

Furukawa TA, Guyatt G, Griffith LE. *International Journal of Epidemiology* 2002; 31:72-76.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Meta-analyses summarize the magnitude of treatment effect using measures of associations such as odds ratio (OR), risk ratio (RR), risk difference (RD) and number needed to treat (NNT). When applying results to individual patients, measures of association like RR from studies/meta-analyses have been combined with patient's expected event rate (PEER) to obtain an individualized NNT. This is based on the assumption that RR is constant even when the baseline risk differs.

Objective: To examine empirically the generalizability of the most commonly used measures of association for summarizing treatment effects in meta-analyses.

Design: An empirical study.

Data collection and analysis: A random selection of 55 meta-analyses, from *The Cochrane Library*, where the summary measure was based on the pooling of three or more randomized trials, were evaluated. The OR, RR and RD of each randomized trial were compared with the corresponding pooled OR, RR and RD from the meta-analyses of all the other randomized trials. For the meta-analyses that produced statistically significant results, the individualized NNTs were calculated over a range of baseline risks. The agreement of the individualized NNT based on the fixed effect or random effects model OR, or the random effects model RR was calculated.

Main results: The fixed effect and random effects model OR and the random effects model RR appear to be reasonably constant across different baseline risks. The RD

was less constant. The individualized NNTs calculated from fixed effect and random effects model OR and from the random effects model RR all produced good to excellent agreement, and were unlikely to lead to differing clinical decisions.

Conclusions: Clinicians may wish to rely on the random effects model RR (easier to interpret and use for calculations than ORs) and use the PEER to individualize NNT when they apply the results of a meta-analysis in their practice.

COMMENTARY
Prepared by Shah Ebrahim

Presenting the effects of treatments can be done using measures of relative or absolute effect, but all methods can confuse clinicians. The number needed to treat (NNT), unlike relative measures of effect, provides an indication of the workload implications and is popular in the evidence-based medicine world. NNTs use the relative risk derived from a meta-analysis or large trial and the patient's expected event rate (PEER). The authors do not elaborate on why the risk difference estimated from meta-analyses - easily, but often misleadingly, derived from Cochrane software - should not be used to derive NNTs. Nor do they consider where data on PEER should be obtained - trial event rates would be a poor choice.

In the meta-analyses examined, relative measures of effect are broadly constant - that is the relative effects, but not risk differences, of individual trials were concordant with the pooled estimate - and therefore applicable to most patients. Concordance may be inflated in systematic reviews in which clinical heterogeneity has been reduced by asking a tightly focused question, and reviews with heterogeneous effects may well avoid producing a pooled effect estimate. Detecting non-constant relative treatment effects is difficult without large trials and a growing list of conditions where effects are not constant now exists. Research comparing predicted and observed NNTs would be useful.

Health-related quality of life in Parkinson's disease: a systematic review of disease specific instruments

Marinus J, Ramaker C, van Hilten JJ, Stiggelbout AM.
Journal of Neurology, Neurosurgery and Psychiatry 2002; 72:241-248.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Health-related quality of life can be assessed with both generic and disease specific instruments. In Parkinson's disease several disease specific instruments have been developed and, as such, investigators need to decide which one to use.

Objective: To compare and contrast disease-specific quality of life instruments in Parkinson's disease and assess their clinimetric properties.

Design: An empirical study.

Data collection and analysis: Studies were identified by searching MEDLINE, EMBASE, SCIsearch, *The Cochrane Library* and conference reports. Two reviewers independently evaluated the thoroughness and results of the identified studies and the clinimetric characteristics of the scales they used.

Main results: Twenty studies were found reporting on the clinimetric properties of four scales. The content validity of the Parkinson's disease questionnaire-39 item version (PDQ-39), the Parkinson's disease quality of life questionnaire (PDQL), and the Fragebogen Parkinson LebensQualitat (Parkinson quality of life questionnaire; PLQ) was adequate to good, but for the Parkinson's impact scale (PIMS) it was insufficient. Construct validity of both the PDQ-39 and the PDQL was good, but for the PLQ and the PIMS this was insufficiently evaluated. Internal consistency of all scale totals and of subscale totals of the PDQL was good, whereas for the social support subscale of the PDQ-39 and four subscales of the PLQ this was inadequate. Test-retest reliability was not evaluated for the PDQL and was adequate in the other scales. Responsiveness was partially established for the PDQ-39, and not assessed for the other scales. The number of available translations, as well as the number of studies in which these instruments were used, differed considerably.

Conclusions: The selection of an instrument partially depends on the goal of the study. In many situations however, the PDQ-39 will probably be the most appropriate HRQoL instrument. The PDQL may be considered as an alternative, whereas the PLQ may be considered in studies involving German-speaking patients with Parkinson's disease. Use of the PIMS should be considered only as a means of identifying areas of potential problems.

COMMENTARY
Prepared by Zbys Fedorowicz

This elegant paper by Marinus et al, consisting of a comprehensive systematic review of 20 identified studies, delves into the minutiae of four Quality of Life (QoL) instruments utilised in Parkinson's disease. The reviewers stated objectives were, to "compare contrast and assess the clinimetric properties" of these four QoL's, which they undertook with clarity of purpose.

Alas, strident efforts to contrast and compare these QoLs only serve as a self-fulfilling prophecy that they cannot be adequately 'compared' and that they 'contrast' significantly with each other. Comparisons confirming the inability to match up or achieve balance, and contrasts that are distinct, disparate, or dissimilar only further energize the dichotomy

in opinion apropos the acceptability and perceived utility of QoLs as self reported outcomes indicators.

These QoLs assess cognitive and physical domains of quality of life in patients suffering with Parkinson's disease. However, in a meta-assessment of the quality of these instruments, should we consider employing Donabedian's [1] time-honoured and tested domains of *structure*, *process* and *outcomes*? Should our objective be not only to assess their structure and outcomes quality but also to chase that elusive goal of process quality with a view to its improvement?

Deming, [2] the Quality Improvement 'heavyweight', in his *System of Profound Knowledge* defined 'variation' as a barrier to quality improvement and quite remarkably this reduction in 'variation' is emphasized by the evidence based paradigm in health care. Therefore, possible implications for practice are that, in pursuing the incorporation of QoLs into the evolving paradigm of patient-centred care, we should redirect our focus from *contrast* and *compare* to merge and unify by reducing variation in their structure and process.

Reduction in variation will safeguard the 'quality' in Quality of Life instruments but it is equally important that this 'process' is not confused with 'standardization' and its consent to a more permissive approach in quality.

Subsequent systematic reviews of QoLs should perhaps aim to synthesise, rather than to endorse further, already well documented divergent contrasts and comparisons.

References:

1. Donabedian A. *The Definition of Quality and Approaches to its Assessment*. Ann Arbor, Michigan: Health Administration Press, 1980.

2. Deming WE. *The New Economics for Industry, Education and Government*. Cambridge, Massachusetts: Center for Advanced Engineering Study, 1993.

Scope and impact of financial conflicts of interest in biomedical research: a systematic review

Bekelman JE, Li Y, Gross CP. *JAMA* 2003; 289:454-465.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Despite increasing awareness about the potential impact of financial conflicts of interest on biomedical research, no comprehensive synthesis of the body of evidence relating to financial conflicts of interest has been performed.

Objective: To review original, quantitative studies on the extent, impact and management of financial conflicts of interest in biomedical research.

Design: A systematic review.

Data collection and analysis: Studies were identified by searching MEDLINE (January 1980 to October 2002), the Science Citation Index via the Web of Science citation database, references of articles, letters, commentaries, editorials, books and by contacting experts. All English-language studies containing original, quantitative data on financial relationships among industry, scientific investigators, and academic institutions were included. A total of 1664 citations was screened, 144 potentially eligible full articles were retrieved, and 37 studies met the inclusion criteria. One investigator extracted data from each of the 37 studies. The main outcomes were the prevalence of specific types of industry relationships, the relation between industry sponsorship and study outcome or investigator behaviour, and the process for disclosure, review, and management of financial conflicts of interest.

Main results: Approximately a quarter of investigators have industry affiliations, and roughly two thirds of academic institutions hold equity in start-ups that sponsor research performed at the same institutions. Eight articles, which together evaluated 1140 original studies, assessed the relation between industry sponsorship and outcome in original research. Aggregating the results of these articles showed a statistically significant association between industry sponsorship and pro-industry conclusions (pooled Mantel-Haenszel odds ratio, 3.60; 95% confidence interval, 2.63-4.91). Industry sponsorship was also associated with restrictions on publication and data sharing. The approach to managing financial conflicts varied substantially across academic institutions and peer reviewed journals.

Conclusions: Financial relationships among industry, scientific investigators and academic institutions are widespread. Conflicts of interest arising from these ties can influence biomedical research in important ways.

COMMENTARY
Prepared by Mike Clarke

During recent years, there have been increasing worries about conflicts of interest in research. This concern is not solely a feature of The Cochrane Collaboration and our desire to minimise bias. It is a concern within scientific and healthcare research more generally. Within the Collaboration, one of the ways it is being addressed is through a plenary session at the Cochrane Colloquium in Barcelona in October 2003.

This recent report by Justin Bekelman and colleagues is a timely contribution to this debate. Although their systematic review is, itself, open to the possibility of bias through a restriction to published articles and, more so, those in English only; it provides a detailed account of relevant studies. Although there are conflicts of interest that are not financial, the focus on the possible impact that money might have is appropriate.

The consistent link, across several studies, between pharmaceutical industry sponsorship and a research conclusion that favours industry is important. The fact that this was also true when it was investigated in the context of randomized trials should be of particular concern to those involved in the preparation and maintenance of Cochrane reviews. It highlights the need for Cochrane, and other, reviewers of healthcare interventions to consider the potential for conflicts of interest in eligible studies when deciding on the best way to minimise bias within their review. It is also important for readers of reviews to consider this when they use a review to help make a decision about health care.

Quality of systematic reviews of economic evaluations in health care

Jefferson T, Demicheli V, Vale L. *JAMA* 2002; 287:2809-2812.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: Initiatives aimed at increasing the uniformity, quality, and reporting of economic evaluations of healthcare interventions were undertaken during the last decade in response to reviews which illustrated variability in the methods used to conduct and report economic evaluations.

Objective: To assess the quality of methods used in systematic reviews of economic evaluations in health care and the quality of conducting and reporting economic evaluations in health care and to determine if initiatives during the last decade led to an increase in the quality of economic evaluations.

Design: A systematic review.

Data collection and analysis: Full-text searches were conducted for the period 1990 to March 2001, as well as correspondence with researchers and handsearching issues of *Health Economics* (1992 to March 2001). Systematic reviews of economic evaluations of healthcare interventions assessing methodological quality using explicit criteria were included. A total of 102 reviews were identified, but only 39 met the inclusion criteria. The quality of the reviews was assessed using a six-item checklist. Two reviewers extracted data on methods of assessing the quality of economic evaluations included in each of the reviews. Grouped items were further subdivided into methodological quality and reporting quality items.

Main results: Quality of the reviews was satisfactory but more focus is needed on search strategies and standardization of evaluation instruments. Serious methodological flaws were found in a significant number of economic evaluations. These included lack of clear description of methods, lack of explanation and justification for the framework and approach used, and low quality estimates of effectiveness for the interventions evaluated. Reviews identified a proportion of evaluations of unclassifiable study design, studies that ignored basic research and economic methodological principles, and ones that reported results lacking clarity. Evaluations that were published in specialty journals and unpublished evaluations submitted by the pharmaceutical industry within a reimbursement scheme were found to be of lower quality. Overall, there appear to have been some modest improvements in quality of conducting and reporting economic evaluations in the last decade.

Conclusions: Care should be taken when deciding or justifying allocation of resources on the basis of economic evaluations of healthcare interventions. Economic models used in evaluations should be made more readily accessible to reviewers and readers, basic formal training should be given to all those involved in conducting and assessing economic evaluations, and a validated and accepted instrument for quality assessment of economic evaluations is needed.

COMMENTARY
Prepared by Miranda Mugford

There have been many empirical studies of the quality of economic evaluations, but this study pulls them together in a systematic review of the state of the art in economic evaluation in health care, and allows some uncomfortable conclusions to be drawn. The paper, by three members of the Cochrane Economics Methods Group, is extremely valuable for defining the future agenda for the group, and for defining further empirical study of methods of economic evaluation.

The Cochrane Brochure makes clear that the evidence of effectiveness is not enough for a judgement about whether to adopt or abandon the form of care.[1] The question policy makers and managers and users of care must ask is not just whether something works but whether it is worthwhile and adds value.

Economic evaluation compares the outcomes (effectiveness and value) and resource costs of two (or more) forms of care. An important feature of economic evaluation is that it is a decision analysis technique for pooling or modelling the available evidence. It is therefore a method for synthesis of evidence rather than a single primary research technique, like a clinical trial.[2]

Many have warned of bias in economic evaluations and, indeed, there are tongue in cheek guides on how to make economic evaluations say what you wish.[3] To counteract this trend, both in North America and in the UK, in the mid 1990s checklists of quality of economic evaluations were developed.[4,5]

This review shows there have been a large number of reviews of economic evaluations. Thirty-nine met criteria

for reviews intended to assess quality of economic evaluations of health care. A wide range of tools for quality assessment had been used in the reviews. The reviews were grouped into reviews with broadly similar intentions. In each subgroup the conclusion was that very few studies met 'good' standards, and that there was only slight evidence of improvement over time.

What are the implications of this review for The Cochrane Collaboration? Most of us make economic decisions and judgements in daily life and so it is not surprising to find many authors and Cochrane reviewers using terms such as 'cost effectiveness' in discussing their results. Frequently, however, the terminology is used misleadingly or confusingly. It is important that a common language of economic discourse is used, especially as there are international differences in terminology. One way towards this is for reviewers to take part in workshops on the subject of economic evaluation methods and understanding economic studies. Another is for wider circulation in the Collaboration of materials produced by the Cochrane Economics Methods Group and other groups.[6,7] Methods recommended for economic evaluation have also continued to develop and need to be evaluated and incorporated.[8]

Few checklists have been formally validated, but the BMJ list has received more scrutiny than most. There is scope for further research on the value of these for peer review and screening studies for reviews. The danger of the checklist approach to reviewing is to assume 'one size fits all'. Economic evaluations are constructed differently for different purposes and may not always conform to a specific quality checklist. But even where the criteria are clear and studies are scored, we have not yet arrived at a method for rejecting studies on quality grounds. We need further validations of the effects of rejecting studies, which meet some but not all criteria.

In this paper, the authors point out that peer reviewers for most journals do not have the skills to judge quality of economic submissions. This clearly results in much poor analysis being published. However, it is also possible that less well-informed editors and reviewers may reject good analyses as irrelevant to their journals. In the light of recent moves by the BMJ to publish economic studies only if they are sent the primary research papers as well, it may become more difficult to get even good economic studies into the press.[9] Publication bias in economic evaluation is still a topic for research in the Cochrane Economics Methods Group and beyond.

A great deal of work has been done by the Centre for Reviews and Dissemination at the University of York in establishing the NHS Economic Evaluation Database. This provides critical abstracts and commentaries of economic evaluations. A programme of research is underway to assess the quality and usefulness of the abstracts. The database is currently published as part of *The Cochrane Library*, but in future, as The Cochrane Collaboration publishing moves to Wiley, this is in doubt. Given the demonstrated poor quality of much so-called economic literature, as demonstrated by this review by Tom Jefferson, Vittorio Demicheli and Luke Vale, it seems all the more important for those reviewing evidence in health care to have easy access to critical reviews of economic studies.

References:

1. Cochrane Brochure. Available: www.cochrane.org/cochrane/cc-broch.htm (assessed 19 May 2003).

2. Rennie D. Commentary – Cost-effectiveness analysis: making a pseudoscience legitimate. *Journal of Health Politics Policy and Law*. 2001; 26:383-386.

3. Goodacre S, McCabe C. Being economical with the truth: how to make your idea appear cost effective. *Emergency Medicine Journal* 2002; 19:301-304.

4. Drummond MF, Jefferson TO, on behalf of the *BMJ* Economic Evaluation Working Party. Guidelines for authors and peer-reviewers of economic submissions to the *BMJ*. *BMJ* 1996; 313:275-283.

5. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in health and medicine*. New York: Oxford University Press, 1996.

6. Jefferson T, Demicheli V, Mugford M. *Elementary economic evaluation in health care*. 2nd edition. London: BMJ Books, 2000.

7. Donaldson C, Mugford M, Vale L (editors). *Evidence-based health economics: from effectiveness to efficiency*. London: BMJ Books, 2002.

8. Drummond M, McGuire A (editors). *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press, 2001.

9. Smith R. New *BMJ* policy on economic evaluations. *BMJ* 2002; 325:1124.

Individual patient- versus group-level data meta-regressions for the investigation of treatment effect modifiers

Berlin JA, Santanna J, Schmid CH, Szczech LA, Feldman HI. *Statistics in Medicine* 2002; 21:371-387.

STRUCTURED ABSTRACT
Prepared by the Cochrane Methodology Review Group

Background: When performing a meta-analysis, interest often centres on finding explanations for heterogeneity in the data, rather than on producing a single summary estimate. Such exploratory analyses are frequently undertaken with published, study-level data, using techniques of meta-analytic regression.

Objective: To explore a real-world example, for which both published group-level and individual patient-level data were available, and to compare the substantive conclusions reached by both methods.

Design: An empirical study.

Data collection and analysis: The authors studied the benefits of anti-lymphocyte antibody induction therapy among renal transplant patients in five randomized trials, focusing on whether there were subgroups of patients in whom therapy might prove particularly beneficial. Allograft failure within five years was the endpoint studied. A variety of analytic approaches to the group-level data were studied, including weighted least-squares regression (n=5), logistic regression (n=628, the total number of subjects), and a hierarchical Bayesian approach. Logistic regression models were fitted to the patient-level data.

Main results: In the patient-level analysis, treatment was significantly more effective among patients with elevated (20 per cent or more) panel reactive antibodies (PRA) than among patients without elevated PRA. These patients comprised a small (about 15 per cent of patients) subgroup of patients that benefited from therapy. The group-level analyses failed to detect this interaction.

Conclusions: The authors recommend using individual patient data, when feasible, to study patient characteristics, in order to avoid the potential for ecological bias introduced by group-level analyses.

COMMENTARY
Prepared by Paul Glasziou

It has been known for some time that results from meta-regressions, by analysing the effects of covariates at the trial level, may be potentially confounded by design features. The basic mechanism here is that there may be confounding between the feature of interest, take gender as an example, and design features that may modify the treatment effect, the dose of the drug, for example. Then, if the trials of low dose medication had predominantly female participants and the trials of high dose medication had predominantly male participants, if only high dose medication were truly effective, it may appear that medication is only effective in males.

Of course, a good meta-regression should adjust for all the potential design confounders. These could include features such as the nature of the intervention (dosage, duration, timing, route of administration, etc), the comparator, the way that the outcome was measured, or the duration of the study and timing of the outcome measurement. This paper by Berlin et al is the first empirical demonstration that such confounding by design tends to substantially alter the interpretation of the effect modification. The question arises now as to how often such a problem occurs and the extent to which it occurs. This can be approached through simulation studies but it would be good to have further empirical evidence. For example, a collaborative group of all those who have done individual patient reviews coming together and performing both forms of analysis would give a more systematic picture of the problem. In the meantime, Berlin and colleagues have demonstrated that the theoretical fear is a potential reality, and that we should do individual patient based meta-analyses wherever possible. However, we also need to recognise that this is hard and expensive and not always doable. The alternative then is to ensure that we add a substantial pinch of salt to the interpretation of meta-regressions.

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.

Effects of adjusting for censoring in meta-analyses of time-to-event outcomes

Claire Vale

Title: The effects of adjusting for censoring in meta-analyses of time-to-event outcomes.

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Date of study: 2000-2001.

Background: For meta-analyses of time-to-event outcomes such as survival or time to recurrence, the most appropriate outcome statistic is the hazard ratio. This takes account of both the number of events and the time to these events and so also allows for censoring. However, the hazard ratio can only be calculated directly if individual patient data has been collected. Alternatively, it can be estimated provided that sufficient statistical information is presented in the trial reports. The former approach is quite rare and the latter often practically difficult. More commonly, meta-analyses of time-to-event outcomes rely on estimating odds ratios (ORs) at fixed points in time. If these trials have been published at different stages in follow-up, censoring patterns will vary from trial to trial, and may affect the comparability and possibly the reliability of the different results. Methods

are available to adjust (reduce) the numbers of patients at risk to allow for variable follow-up, but these are rarely applied.

Objective: To look at the effect of using a simple method to adjust for variable follow-up on the survival results of meta-analyses in cancer.

Location: Meta-analysis Group, MRC Clinical Trials Unit, London, UK.

Methods: Meta-analyses of survival data for five meta-analyses of published trials in cancer were conducted. ORs and associated statistics were calculated based on unadjusted total numbers of participants and events. These were compared with calculations that first adjusted the numbers at risk for censoring using a simple model.

Summary of main results: Adjusting for censoring changed the pooled ORs in 17/24 cases. On average there was a 2.6% difference between the adjusted and the unadjusted OR. Confidence intervals were frequently wider for the adjusted OR. Adjusting also reduced weighting of individual trials with immature follow-up. In 18/24 cases, adjusting reduced statistical heterogeneity and affected the associated p-values.

Conclusions: The standard (unadjusted) method for carrying out a meta-analysis of published time-to-event data assumes that follow-up is complete at the time point of analysis (e.g. at three years all patients have been followed to three years), yet trial reports may state otherwise. Adjusting the numbers at risk and the numbers of events ensures that trials are weighted according to the information they contribute, such that a large trial with poor follow-up is not given undue weight. It also means that ORs, confidence intervals and p-values reflect the uncertainty of curves extrapolated to distant time points.

Recommendations: Reviewers conducting meta-analyses of published time-to-event data, where actual numbers at risk are not available, should adjust the numbers at risk estimated from total numbers analysed, to account for immature data and censoring.

Dissemination of findings: A full report of this study has been published.[1] If anyone would like a copy of this report, please contact Claire Vale. Aspects of the study were presented at the Cochrane Colloquium in 2000 and 2001.

Reference:

1. Vale C, Tierney J, Stewart L. Effects of adjusting for censoring on meta-analyses of time-to-event outcomes. *International Journal of Epidemiology* 2002; 31:107-111.

The typical Cochrane review

Sue Mallett and Mike Clarke

Title: The typical Cochrane review: how many trials? How many participants?

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Date of study: 2001-2002.

Objective: To describe the number of trials and participants in a typical systematic review from the *Cochrane Database of Systematic Reviews*.

Location: UK Cochrane Centre, Oxford, UK.

Methods: The number of studies was counted for three categories within Cochrane reviews: included studies, ongoing studies and studies awaiting assessment. 1000 reviews from the *Cochrane Database of Systematic Reviews* in *The Cochrane Library*, Issue 1, 2001 were analysed. The number of participants was extracted for a sample of reviews.

Summary of results: 9778 studies were included in 989 Cochrane reviews. In addition there were 356 that were listed as ongoing and 1138 awaiting assessment for inclusion. A typical review contained six included studies (range 0 to 136). Forty percent of the reviews listed ongoing and/or studies awaiting assessment for inclusion. This research shows that if ongoing studies were included in the 171 reviews where they are listed, they would, on average contribute, 17% of the total number. Based on a sample of 258 reviews, the median number of participants per review was 945 (interquartile range 313 to 2511) and the median number of participants per study was 118 (interquartile range 60 to 241). There were no included studies in 48 reviews.

Conclusions: This report provides a descriptive study of the number of studies and participants in a typical Cochrane review from *The Cochrane Library*, Issue 1, 2001.

Recommendations: A typical Cochrane review included six studies. However, 40% of reviews listed an important number that were either ongoing or awaiting assessment. It will be important that reviews are kept up-to-date to include these studies as they become available or are assessed as suitable.

Dissemination of findings: A full report of this study has been published.[1]

Reference:

1. Mallett S, Clarke M. The typical Cochrane review. How many trials? How many participants? *International Journal of Technology Assessment in Health Care* 2002; 18:820-823.

Meta-analyses involving cross-over trials

Diana Elbourne

Title: Meta-analyses involving cross-over trials: methodological issues

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Date of study: 2001-2002.

Objective: To find ways to incorporate two-period, two-treatment cross-over trials into the synthesis of quantitative data (statistical meta-analysis), and to establish whether this is appropriate.

Location: London School of Hygiene and Tropical Medicine, London, UK.

Methods: The characteristics of these trials were outlined, with detailed examples of methods for analysis for both continuous and binary data. These case studies were then extended into the context of a meta-analysis. *The Cochrane Library* was surveyed to assess current practice for synthesis. The *Cochrane Controlled Trials Register* and the *Cochrane Database of Systematic Reviews* (Issue 1, 2001) were searched using the free-text terms 'cross-over' or 'crossover'.

Summary of main results: The survey suggested that about 8% (24,710 out of 294,369) of trials and 315 out of 1000 complete reviews in *The Cochrane Library* contained these terms, of which 184 (18%) referred to cross-over trials. There was no consistent approach to their inclusion in the reviews: 11 (6%) specifically excluded cross-over trials from consideration; 21 (11%) reviews excluded them from analysis, but considered their results separately in the review text; 95 (52%) sought data from the first period of the trial only (and when data were unavailable, 54 excluded the trials, 13 included the data from both periods, and 28 gave no clear policy); and 56 (30%) included data from both periods as though a parallel group design had been used. Only one review (1%) incorporated the paired data into the meta-analysis.

On the assumption that the cross-over and the parallel group trials are estimating the same treatment effect and the choice of trial design has not been dictated by differences which could influence the observed treatment effect, synthesis methods using an estimate of treatment effect and its standard error from each study are described for continuous and binary data, both when the necessary paired data are given and also when they need to be calculated or imputed.

Conclusions: Methods do exist for including valuable information from two-period, two-treatment cross-over trials into quantitative reviews. However, poor reporting of cross-over trials will often impede attempts to perform a meta-analysis using the available methods.

Recommendations: Before using these methods for the synthesis of data from cross-over trials into meta-analyses, meta-analysts may first wish to consider the following questions:

- Are all the trials addressing a similar enough question in terms of populations, interventions and outcomes?
- Is there sufficient statistical homogeneity between the trials (or between parallel group and cross-over trials)?
- Are the individual trials of adequate quality to be considered for inclusion, including whether a cross-over design was appropriate, in particular whether the likelihood of substantial carry-over could be excluded?
- Are appropriate (paired) data available or calculable for each patient?

Disseminations of findings: A full report of this study has been published.[1]

References:

1. Elbourne DR, Altman DG, Higgins JP, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. *International Journal of Epidemiology* 2002; 31:140-149.

Number and size of randomized trials reported in general healthcare journals

Steve McDonald

Title: Number and size of randomized trials reported in general healthcare journals from 1948 to 1997.

Contact: Steve McDonald, Australasian Cochrane Centre, Monash Institute of Health Services Research, Monash Medical Centre, Locked Bag 29, Clayton, VIC 3168, Australia. Tel: +61 3 95947529; Fax: +61 3 95947554; Email: steve.mcdonald@med.monash.edu.au.

Objective: To investigate trends in the number and size of randomized trials reported in general healthcare journals from 1948 to 1997.

Location: UK Cochrane Centre, Oxford, UK.

Methods: Journals were handsearched for the 50 years from 1948 to 1997 for all reports of trials in which participants were randomly (or quasi-randomly) assigned to alternative forms of care. Trial reports published as letters, conference abstracts and news items were excluded from this study. Data were collected on the number of reports of randomized trials in each journal per year and the number of participants in each trial.

Summary of main results: 5503 reports of trials were identified in 18 general healthcare journals. Fifteen journals were searched for the entire period from 1948-1997. Seven

were published in English, three in German, and one each in Danish, Dutch, Finnish, French, Italian, Norwegian, Spanish and Swedish. More than a third of the trial reports appeared in the *BMJ* (2016, 37%). The peak period for trial reports was the mid-1980s, with more in 1986 than any other year (242). By the mid-1990s the number per year had declined by a third to levels similar to the 1970s. Trials with fewer than 100 participants accounted for most of the reports (69%). In spite of the overall decline in the number of trial reports, those involving 100 participants or more continued to increase throughout the period studied.

Conclusions: The downturn in trial reports seen in these journals is unlikely to reflect a wider trend to conduct fewer randomized trials. Competition from specialist journals is likely to be most keenly felt by the general journals with smaller circulations. Decreases in the number of trial reports in general journals may indicate changing editorial policies and author preferences. The continued increase in the number of larger trials reported is encouraging, especially if it represents an increase in the size of trials more generally.

Recommendations: Further research is needed to determine whether the trends over time identified here are reflective more of trends in the actual conduct of rather than simply the reporting of randomized trials.

Dissemination of findings: A full report of this study has been published.[1]

Reference:

1. McDonald S, Westby M, Clarke M, Lefebvre C and the Cochrane Centres' Working Group on 50 Years of Randomized Trials. Number and size of randomized trials reported in general health care journals from 1948 to 1997. *International Journal of Epidemiology* 2002; 31:125-127.

Publishing protocols of systematic reviews

Chris Silagy, Philippa Middleton and Sally Hopewell

Title: Publishing protocols of systematic reviews: comparing what was done to what was planned.

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Date of study: 2000-2001.

Objective: To assess the extent to which the content of published Cochrane reviews had changed compared with their previously published protocols and to assess any potential impact these changes may have had in introducing bias to the study.

Location: Australasian Cochrane Centre, Melbourne, Australia and UK Cochrane Centre, Oxford, UK.

Design: A retrospective comparative study.

Methods: Previously published protocols were identified for all new Cochrane reviews appearing in *The Cochrane Library* Issue 3, 2000. The texts of published protocols and completed reviews were compared. Two raters independently identified changes to the different sections of the protocol and classified the changes as none, minor, or major.

Main results: Of the 66 new Cochrane reviews, a previously published protocol was identified for 47 reviews. Of these, 43 reviews had at least one section that had undergone a major change compared with the most recently published protocol. The greatest variation between protocols and reviews was in the methods section, in which 68% of reviews (n=32) had undergone a major change. Changes made in other sections that may have resulted in the introduction of bias included narrowing of objectives, addition of comparisons or new outcome measures, broadening of criteria for the types of study design included, and narrowing of types of participants included.

Conclusions: Research protocols, even if published, are likely to remain, at least to some extent, iterative documents. A large number of changes were made to Cochrane reviews, some of which could be prone to influence by prior knowledge of results.

Recommendations: Even if many of the changes between protocol and review improve the overall study, the reasons for making these should be clearly identified and documented within the final review.

Dissemination of findings: A full report of this study has been published.[1]

Reference:

1. Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. *JAMA* 2002; 287:2831-2834.

Thomas C Chalmers M.D. Award - 2002

The Thomas C Chalmers M.D. prize is awarded annually for the best oral or poster presentation at the Cochrane Colloquium. Last year in Stavanger it was awarded to Pamela Royle for her study entitled "Obtaining published errata to randomized controlled trials: is it worth the effort?"

Obtaining published errata to randomized controlled trials

Pamela Royle and Norman Waugh

Title: Obtaining published errata to randomized controlled trials: is it worth the effort?

Contact: Pamela Royle, Department of Public Health, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, UK. Tel: +44 1224 55172; Email: p.royle@abdn.ac.uk.

Date of Study: 2001-2002.

Objective: To do a pilot study to determine characteristics of published errata linked to randomized controlled trials (RCTs) in the MEDLINE database, and to estimate the proportion that are worthwhile obtaining when doing a systematic review.
Location: Wessex Institute for Health Research and Development, University of Southampton, UK.

Methods: MEDLINE (SilverPlatter) was searched from 1995 to June 2001 for records that had both 'randomized-controlled-trial' in the publication type field and 'erratum' in the comments field. Records from four journals (*Lancet, BMJ, New England Journal of Medicine* and *JAMA*) were downloaded. 100 were randomly selected and examined independently from different perspectives by the two authors:

1. An information specialist, asking whether it seem worthwhile spending the time and money acquiring the errata for the reviewers, in order to minimise their time spent on trying to interpret erroneous or confusing data. Those errors that appeared trivial (such as errors in authorship or contact details) were classified as not worthwhile. All other errors (including those in data in tables and figures, and errors in the text) were considered as worthwhile obtaining.

2. An experienced reviewer and public health consultant, asking whether the error would be significant enough to affect either the interpretation of the paper, or results of a systematic review which used the study.

Also measured were: the number of citations to the RCT and its erratum in the Science Citation Index; the time between publication of the RCT and its erratum; and indexing of errata in the *Cochrane Controlled Trials Register* (CENTRAL).

Summary of main results: From the perspective of the information specialist, 74% of the errata were considered worthwhile obtaining. These were mainly errors in tables or figures, leading to inconsistencies with data in the text. Another 9% described less serious errors, but were considered worth obtaining if easily available; they mainly consisted of errors in the introduction or discussion. The final 17% were considered trivial in this context and not worthwhile acquiring for systematic reviewers. They mainly consisted of errors in authorship (such as omissions of authors' names, incorrect spellings or errors in their contact details). From the perspective of the experienced reviewer/ public health consultant; 5% of errata were classified as likely to affect a meta-analysis (and more likely if only a few RCTs are included in the review); 10% as having significant errors that would affect the interpretation of the RCT (but no effect on a meta-analysis); and 85% were not considered important enough to affect either of the above. Errata were published for an average of 8% of RCTs in the four journals. The mean number of months between publication of the RCT and its erratum was 3.5. The mean number of citations per year to the RCTs was 28, whereas for the errata it was 0.6. At least one copy of all RCTs with the errata information was in CENTRAL, but 77% of the RCTs checked had one or more extra copies in CENTRAL, but with the errata information missing. The *Lancet*, *BMJ*, *New England Journal of Medicine* and *JAMA* all provided free electronic access to errata, but many other journals did not.
Conclusions: About 5% of the errata to RCTs in this pilot study appeared to matter in terms of changing the final conclusions of a systematic review. However, the majority (74%) of errata appeared to contain information important enough to be worthwhile obtaining, on the basis that they concerned errors in data in tables or figures. Although the errors reported are only significant in a minority of instances, in the majority of cases knowing them can save the reviewers time in trying to resolve inconsistencies and discrepancies in the data. Relative to citations to the RCTs, most errata were never cited, which suggests they were largely overlooked.
Recommendations: To ensure that reviewers have access to as complete and accurate a data set as possible, it is recommended that information specialists should endeavour to identify errata to RCTs in the search step, and ensure that reviewers obtain them, especially in those reviews when only a few trials are available. Where duplicates of RCTs exist in CENTRAL, and one copy contains the errata reference, this copy should remain in CENTRAL, and the copies lacking the errata reference should be removed. This would help ensure that the errata are not missed when searching. To facilitate access to errata, it is recommended that all journals provide free electronic access to errata to RCTs they have published.

Dissemination of findings: A poster was presented at the Cochrane Colloquium in Stavanger in 2002.[1] A fuller report is being prepared for submission to a journal.

Reference:

1. Royle P. Obtaining published errata to randomized controlled trials: is it worth the effort? *10th Annual Cochrane Colloquium*; 2002 Jul 31 – Aug 3; Stavanger, Norway. P6.

NEW COCHRANE METHODOLOGY REVIEWS

This section aims to highlight new Cochrane methodology reviews, which have been conducted by members of the Cochrane Methodology Review Group and published in the *Cochrane Database of Methodology Reviews* in *The Cochrane Library*. Information on the current status of all Cochrane methodology reviews and protocols, completed and ongoing, is available on page 43.

Cochrane Methodology Review Group

Elizabeth Paulsen

The Cochrane Methodology Review Group (CMRG) was formally re-registered from a Methods Group to a Collaborative Review Group in February 2003. Beginning with Issue 4, 2003 the CMRG module will be published together with other Collaborative Review Group modules in *The Cochrane Library*. The CMRG will otherwise continue to prepare, maintain and make available Cochrane methodology reviews. These will continue to be published in the *Cochrane Database of Methodology Reviews* (and not the *Cochrane Database of Systematic Reviews*) in *The Cochrane Library*. The CMRG's register of studies will also continue to be published in *The Cochrane Library* as the *Cochrane Methodology Register*.

The CMRG will continue to contribute to the Methods Groups Newsletter and maintain close contact with the Cochrane Methods Groups. The advisory board will continue to be composed of the convenors for Methods Groups.

In October 2002, Elizabeth Paulsen took over as the new co-ordinator for the Group. After six years of excellent work for the Group, Kirsty Louden Olsen left the position to return to Scotland. Kirsty is still maintaining her ties with The Cochrane Collaboration by working on the copy-editing project. Marit Johansen also joined the Group in November as the Trials Search Co-ordinator. Both Elizabeth and Marit are based in Oslo at the Norwegian branch of the Nordic Cochrane Centre. Mike Clarke and Andy Oxman continue as Co-ordinating Editors. The other editors are Fiona Godlee, Peter Gøtzsche, Philippa Middleton, and Karen Robinson.

In Issue 2, 2003 of *The Cochrane Library*, there were nine reviews and seven protocols in the *Cochrane Database of Methodology Reviews*. Abstracts of methodology reviews published in *The Cochrane Library* are now available free of charge on the internet at www.cochrane.de/cochrane/mrabstr/.

The CMRG currently has 71 members registered on the group's electronic discussion list. For information about the list and to subscribe, go to: www.cochrane.de/mailman/listinfo/ems-mg.

The next meeting of the CMRG will be at the Cochrane Colloquium in October in Barcelona. The meeting is open to all members of the Group.

Summaries of new and recent Cochrane methodology reviews are presented below:

Editorial peer review for improving the quality of reports of biomedical studies

Tom Jefferson, Phil Alderson, Frank Davidoff and Liz Wager

Title: Editorial peer review for improving the quality of reports of biomedical studies.

Contact: Dr Tom Jefferson, Health Reviews Ltd, Via Adige 28/a, 00061 Anguillara, Roma, ITALY. Tel: +39 6 49902982; Fax: +39 6 49387173; Email: TOJ1@aol.com.

Date of study: 1999-2002.

Objective: To estimate the effects of processes in editorial peer review.

Location: UK Cochrane Centre, Oxford, UK.

Methods:

Search Strategy

The search is detailed in the Cochrane review. It was restricted to health literature, but involved database searches, handsearches, personal communication and reference list searches.

Selection Criteria

We included prospective or retrospective comparative studies, with two or more comparison groups, generated by random or other methods, reporting original research regardless of publication status. We hoped to find studies identifying good submissions on the basis of importance of the topic dealt with, relevance of the topic to the journal, usefulness of the topic, soundness of methods, soundness of ethics, completeness and accuracy of reporting.

Data collection and analysis

We identified 135 reports of studies, which could possibly fulfil our inclusion criteria. Twenty-one of these fulfilled our criteria. Because of the diversity of study questions, viewpoints, methods and outcomes we carried out a descriptive review of included studies, grouping them by broad study questions.

Summary of main results: The practice of concealing the identities of peer reviewers or authors appears to have little effect on the outcome of the quality assessment process (nine studies). Checklists and other standardisation media have little reliable evidence to support their use (two studies). There is no evidence that referees' training has any effect on the quality of the outcome (two studies). Electronic communication media do not appear to have an effect on quality (two studies). On the basis of one study little can be said about the ability of the peer review process to detect bias against unconventional drugs. Validity of peer review was tested by only one small study in a specialist area. Editorial peer review appears to make papers more readable and improve the general quality of reporting (two studies), but the evidence for this may be of limited generalisability.

Conclusions: At present there is little empirical evidence to support the use of editorial peer review as a mechanism to ensure quality of biomedical research, despite its widespread use and costs. A large, well-funded programme of research on the effects of editorial peer review is needed.

Dissemination of findings: This review has been published as a Cochrane methodology review and in *JAMA*.[1,2]

References:

1. Jefferson TO, Alderson P, Davidoff F, Wager E. Editorial peer-review for improving the quality of reports of biomedical studies (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

2. Jefferson T, Alderson P, Wager E, Davidoff F. Effects of editorial peer review: a systematic review. *JAMA* 2002; 287:2784-2786.

Grey literature in meta-analyses of randomized trials

Sally Hopewell, Steve McDonald, Mike Clarke and Matthias Egger

Title: Grey literature in meta-analyses of randomized trials of healthcare interventions.

Contact: Sally Hopewell, UK Cochrane Centre, Summertown Pavilion, Middle Way, Oxford, OX2 7LG. Tel: +44 1865 516300; Fax: +44 1865 516311; Email: shopewell@cochrane.co.uk

Date of Study: 2001-2002.

Objective: To review systematically research studies, which have investigated the impact of grey literature in meta-analyses of randomized trials of healthcare interventions. A study was considered eligible for this review if it compared the effect of the inclusion and exclusion of grey literature on the results of meta-analyses of randomized trials.

Location: UK Cochrane Centre, Oxford; UK, Australasian Cochrane Centre, Melbourne, Australia; Department of Social and Preventative Medicine, University of Berne, Switzerland.

Methods: We searched the *Cochrane Methodology Register* (*The Cochrane Library*, Issue 1, 2002), MEDLINE (1966 to February 2002), the Science Citation Index (1981 - April 2002) and contacted researchers who may have carried out relevant studies. The main outcome measure was an estimate of the impact of trials from the grey literature on the pooled effect estimates of the meta-analyses.

Summary of main results: Eight studies meeting the inclusion criteria were identified. Four studies contained multiple meta-analyses and four contained single meta-analyses. Of the included studies, four multiple and three single meta-analyses, found that published trials showed an overall greater treatment effect than grey trials. This difference was statistically significant in two of the four multiple meta-analyses. The remaining single meta-analysis found that published trials showed no effect of treatment and that grey trials showed a negative treatment effect; this difference was not statistically significant. Overall, there were more published trials included in the meta-analyses than grey trials (median 46 (IQR 4-300) versus 5.5 (IQR 4-88)). Published trials had more participants on average. In the two studies that assessed methodological quality of the included trials, the published trials were of higher quality than the grey trials. The most common types of grey literature were abstracts (49%) and unpublished data (33%).

Conclusions: This review suggests that published trials are generally larger and may show an overall greater treatment effect than grey trials.

Recommendations: This has important implications for reviewers who need to ensure they identify grey trials, in order to minimise the risk of introducing bias into their review.

Dissemination of findings: This review has been published as a Cochrane methodology review.[1]

Reference:

1. Hopewell S, McDonald S, Clarke M, Egger M. Grey literature in meta-analyses of randomized trials of healthcare interventions (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

Handsearching versus electronic searching to identify reports of randomized trials

Sally Hopewell, Mike Clarke, Carol Lefebvre and Roberta Scherer

Title: Handsearching versus electronic searching to identify reports of randomized trials.

Contact: Sally Hopewell, UK Cochrane Centre, Summertown Pavilion, Middle Way, Oxford, OX2 7LG, UK. Tel: +44 1865 516300; Fax: +44 1865 516311; Email; shopewell@cochrane.co.uk.

Objective: To review systematically empirical studies, which have compared the results of handsearching with the results of searching one or more electronic databases to identify reports of randomized trials.

Location: UK Cochrane Centre, Oxford, UK and University of Maryland, Baltimore, USA.

Methods: Studies were sought from the *Cochrane Methodology Register* (*The Cochrane Library*, Issue 2, 2002), MEDLINE (1966 to Week 1 July 2002), EMBASE (1980 to Week 25 2002), AMED (1985 to June 2002), BIOSIS (1985 to June 2002), CINAHL (1982 to June 2002), LISA (1969 to July 2002) and PsycINFO (1972 to May 2002). Researchers who may have carried out relevant studies were contacted. The main outcome measure was the number of reports of randomized trials identified by handsearching as compared to electronic searching.

Main summary of results: Thirty-four studies were identified. Handsearching identified 92-100% of the total number of reports of randomized trials found. The Cochrane Highly Sensitive Search Strategy (HSSS) identified 80% (14 studies) of the total number of reports of trials found. Electronic searches categorised as 'complex' found 65% (30 studies). Those categorised as 'simple' found 42% (nine studies). The retrieval for an electronic search was higher when the search was restricted to English language journals; 62% (29 studies) versus 39% (three studies) for journals published in other languages. When searching was restricted to full reports, the retrieval for complex searches (including the HSSS) improved to 82%.

Conclusions: Searching electronic databases using the Cochrane HSSS, or other complex searches, identifies the majority of trials published as *full* reports in English language journals and indexed in those databases. Handsearching is still required for more complete identification.

Recommendations: Where resources are limited, they are best concentrated on handsearching the non-indexed parts of a journal (e.g. abstracts and journal supplements), issues of a journal published prior to the introduction of appropriate indexing terms, in addition to journals not indexed in databases such as MEDLINE. However, before searching these sources, the list of journals already searched, or being searched, by The Cochrane Collaboration should be checked.

Dissemination of findings: This review has been published as a Cochrane methodology review.[1]

Reference:
1. Hopewell S, Clarke M, Lefebvre C, Scherer R. Handsearching versus electronic searching to identify reports of randomized trials (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

Peer review for improving the quality of grant applications

Vittorio Demicheli and Carlo Di Pietrantonj

Title: Peer review for improving the quality of grant applications.

Contact: Vittorio Demicheli, Director Servizio Sovrazonale di Epidemiologia ASL 20, Via Venezia 6, Alessandria 15100, Piemonte ITALY. Tel. +39 131 307821; Fax: +39 131 307847; Email: demichelivittorio@asl20.piemonte.it.

Date of Study: 2002.

Background: Grant-giving relies heavily on peer review for the assessment of the quality of proposals but the evidence of effects of these procedures is scarce. Researchers and grant-giving bodies have expressed concern about the amount of time spent writing and reviewing grants. A number of criticisms about peer review of grant applications have focused on the reliability of the process and the existence of a number of biases. Descriptive evidence of gender bias was provided by a study at the Swedish Medical Research Council but a number of other studies carried out in similar contexts found no evidence of it. Similarly, contrasting findings are available on other investigated biases of peer review; age, institution, 'cronyism', discipline, gender, etc. An extensive, although non-systematic, review of existing studies on grant-giving peer review has been published. In spite of these concerns and limitations very little has been done to address aspects such as the equity, effectiveness and efficiency of the process. The availability of a growing amount of original research on the effect of peer review allows a systematic review of studies comparing the effectiveness of peer review processes of research grant applications in terms of identifying high quality proposals for potential funding.

Objective: To estimate the effect of grant-giving peer review processes on importance, relevance, usefulness, soundness of methods, soundness of ethics, completeness and accuracy of funded research. These processes are grouped as: different ways of screening, assigning or masking submissions; different ways of eliciting internal or external opinions; different decision-making procedures (group or single person); different types of feedback to author(s) and subsequent revision of submissions.

Methods:
Search Strategy
Electronic database searches and citation searches, and researchers in the field were contacted.

Selection Criteria
Prospective or retrospective comparative studies with two or more comparison groups assessing different interventions or one intervention against doing nothing. Interventions may regard different ways of screening, assigning or masking submissions, different ways of eliciting opinions or different decision-making procedures. Only original research proposals and quality outcome measures were considered.

Data collection and analysis
Studies were read, classified and described according to their design and study question. No quantitative analysis was performed.

Summary of main results: Ten studies were included. Two studies assessed the effect of different ways of screening submissions, one study compared open versus blinded peer review and three studies assessed the effect of different decision-making procedures. Four studies considered agreement of the results of peer review processes as the outcome measure. Screening procedures appear to have little effect on the result of the peer review process. Open peer reviewers behave differently from blinded ones. Studies on decision-making procedures gave conflicting results. Agreement among reviewers and between different ways of assigning proposals or eliciting opinions was usually high.

Conclusions: There is little empirical evidence on the effects of grant-giving peer review. No studies assessing the impact of peer review on the quality of funded research are presently available.

Recommendations: Experimental studies assessing the effects of grant-giving peer review on importance, relevance, usefulness, soundness of methods, soundness of ethics, completeness and accuracy of funded research are urgently needed. Practices aimed to control and evaluate the potentially negative effects of peer review should be implemented meanwhile.

Dissemination of findings: This review has been published as a Cochrane methodology review.[1]

Reference:
1. Demicheli V, Di Pietrantonj C. Peer review for improving the quality of grant applications (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

Randomization to protect against selection bias in healthcare trials

Regina Kunz, Gunn Vist, and Andy Oxman

Title: Randomization to protect against selection bias in healthcare trials.

Contact: Regina Kunz, Arbeitsgemeinschaft Koordinierungsausschuss e.V., Auf dem Seidenberg 3a, 53721 Siegburg, Germany. Tel: +49 2241 938848; Fax: +49 2241 938835; Email: regina.kunz@arge-koa.de.

Date of study: 1998 to 2002.

Objective: To assess the effects of randomization and concealment of allocation on the results of healthcare trials.

Location: German Cochrane Centre, Siegburg, Germany and Norwegian Branch of the Nordic Cochrane Centre, Oslo, Norway.

Methods: This is a conversion and update of a previously published review.[1] Fourteen newly identified studies have been added to the 18 studies included in the original review. Studies were identified by searching the *Cochrane Methodology Register*, MEDLINE, SciSearch, reference lists and personal communication. Eligible studies included cohorts of trials, systematic reviews or meta-analysis of healthcare interventions that compared outcomes or prognostic factors for one of the following comparisons: randomized versus non-randomized trials, randomized trials with adequate versus inadequate concealed allocation, or high versus low quality trials where selection bias could not be separated from other sources of bias. Tabular summaries of the results were prepared for each comparison and the results across studies were assessed qualitatively to identify common trends or discrepancies.

Summary of main results: Thirty-two studies including over 3000 trials were identified (54 comparisons). In 22 of 35 comparisons of randomized and non-randomized trials of the same intervention, estimates of effects were larger in non-randomized trials. Eight were similar, four comparisons showed smaller treatment effects in non-randomized trials. One comparison found reversed effects (randomized trials indicated a harmful effect while non-randomized trials using historic controls suggested a beneficial effect). The deviation of the effect estimate for non-randomized compared with randomized trials ranged from 76% smaller to 400% larger effect. Seven studies compared randomized and non-randomized trials across different interventions across different clinical conditions using standardised effect sizes. The results of these studies are unclear. Three studies compared adequately and inadequately concealed allocation within randomized trials of the same intervention. All three detected larger effect sizes with inadequate concealment. Nine studies compared high and low quality trials and found important differences in estimates of effect, but it is not possible to determine the extent to which these differences can be attributed to randomization or concealment of allocation.

Conclusions: Non-randomized trials and randomized trials with inadequate concealment of allocation tend to result in larger estimates of effect than randomized trials with adequately concealed allocation. It is generally not possible to predict the magnitude, or even the direction, of possible selection biases and consequent distortions of treatment effects.

Recommendations: This review supports the argument for using random allocation and ensuring that randomization schedules are concealed in healthcare trials.

Dissemination of findings: This review has been published as a Cochrane methodology review.[2]

Reference:

1. Kunz R, Oxman AD. The unpredictability paradox: review of empirical comparisons of randomized and non-randomized clinical trials. *BMJ* 1998; 317:1185-1190.

2. Kunz R, Vist G, Oxman AD. Randomization to protect against selection bias in healthcare trials (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

Technical editing of research reports in biomedical journals

Liz Wager and Philippa Middleton

Title: Technical editing of research reports in biomedical journals

Contact: Liz Wager, Sideview, 19 Station Road, Princes Risborough, HP27 9DE, UK. Tel: +44 1844 275814; Fax: +44 1844 275034; Email: liz@sideview.demon.co.uk.

Objective: To examine the evidence about the effects of technical editing in medical journals.

Methods: Standard Cochrane methodology review (see published review for details).[1]

Summary of main results: We used a broad definition of technical editing to cover anything that happens to a research paper between acceptance and publication. A separate review considered effects of editorial peer review (i.e. changes occurring between submission and acceptance).[2] We found 18 studies on technical editing, and 35 about reference accuracy. Only two of these were randomized trials. A 'package' of largely unspecified processes applied between acceptance and publication was associated with small but statistically significant improvements in readability (measured by Gunning and Flesch readability scores) in two studies and improved reporting quality in another two studies. One study showed mixed results (good and bad) after stricter editorial policies were introduced. More intensive editorial processes were associated with fewer errors in abstracts and references. Providing instructions to authors was associated with improved reporting of ethics requirements in one study, and fewer errors in references in two studies, but no difference was seen in the quality of abstracts in one randomized trial. Structuring generally improved the quality of abstracts, but increased their length. The reference accuracy studies showed a median citation error rate of 36% (range across journals 4-67%) and a median quotation error rate (i.e. misrepresenting quoted work) of 20% (range 0-44%).

Conclusions: We know surprisingly little about the effects of technical editing. Our review suggests that the 'package' of activities between acceptance and publication does improve papers to some extent.

Recommendations: Our review found 39 papers about reference accuracy, which had surveyed over 15,000 references in over 100 journals. We therefore suggest that no further surveys are needed. More interesting was the single before-and-after study that examined the effects of an intervention to improve accuracy (asking authors to supply copies of the first pages of all references). Most studies have compared versions of papers at acceptance and publication without attempting to define key steps in technical editing (such as author's corrections, editing for house style, scrutiny by a professional copy-editor, and proof reading). It would be interesting to learn more about the separate effects of these processes. We found no published evidence that any journal 'house style' is based on evidence from journal readers about readability, etc. We hope that journals might undertake such research.

Dissemination of findings: This review has been published as a Cochrane methodology review.[1]

Reference:

1. Wager E, Middleton P. Technical editing of research reports in biomedical journals (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.

2. Jefferson TO, Alderson P, Davidoff F, Wager E. Editorial peer-review for improving the quality of reports of biomedical studies (Cochrane Methodology Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford, Update Software.

INFORMATION FROM THE METHODS GROUPS

It's not a rumour … good things are happening in the Methods Groups

Jon Deeks
Steering Group Methods Groups Representative

Methods Groups in the Collaboration don't always feel like they are keeping their head above water. They are a self-critical lot, bent on underestimating the importance of their work and always thinking that they should do more, more quickly and better. If the Collaboration had an annual prize for feelings of guilt, the entries from the methodologists would be very competitive.

But it's time to stop for a moment to recognise the fantastic achievements that Methods Groups have made to the Collaboration, often on the basis of very limited resources. Also, to thank the individuals and many institutions that have dedicated their time over many years to the support of Cochrane activities. Thank you!

Methods Group functions can be divided into support activity and research work. The support work is usually evident to the Collaboration, through numerous courses and workshops, methodological input into editorial groups and individual reviews, the development of Collaboration training materials, and representation on advisory groups and Colloquium planning groups.

However, the research activities of the Methods Groups are not always identifiable or noticed. Research is often done by individual members of Methods Groups rather than by the group as a collective entity and is published under the name of the institution to whom they belong. And their work is published in the traditional competitive and secretive manner that paper journals demand, as there is no opportunity for publication in *The Cochrane Library*. The magnitude of their research achievements is therefore not visible to others in the Collaboration. Maybe the new publishing arrangement with Wiley will open the way for new opportunities to address this.

There are also many important indirect ways in which members of Methods Groups have influence on research. Cochrane methodologists have often been able to influence work done elsewhere, and to put forward a Cochrane perspective when advising funders on priority agendas, peer reviewing grant applications and submitted papers, persuading colleagues of critical research questions and the importance of obtaining pragmatic and usable solutions, and encouraging wider debate amongst the academic community.

Like all Cochrane entities, Methods Groups struggle for resources, especially for their support activities, which are not attractive to funders. Many funders prefer to include the costs of methodological support as part of their grants for healthcare research projects. Although Methods Groups should not give up trying, it is important for the other entities within the Collaboration to look to request the resources needed for methodological support in their funding applications wherever possible.

Keep up the good work!

There are now ten registered Methods Groups and one new possible Methods Group. Reports from most of these Groups follow.

Registered groups
Applicability and Recommendations
Economics
Health-Related Quality of Life
Individual Patient Data Meta-analysis
Non-randomised Studies
Prospective Meta-analysis
Qualitative Research
Reporting Bias
Screening and Diagnostic Tests
Statistical

Possible group
Information Retrieval

REGISTERED GROUPS

Cochrane Applicability and Recommendations Methods Group

Paul Glasziou

2002 has been a productive year for the Applicability and Recommendations Methods Group. With funding from the Australian Government, we have established an electronic discussion list and have updated our review of studies of applicability.[1] Articles identified during the update are being summarised by various Group members (currently 24) and are forwarded to the discussion group each month. We'd welcome new members – sign up at: http://sun21.imbi.uni-freiburg.de/mailman/listinfo/applicabilitygroup. We have also developed training materials that are currently being tested by group members: a brief lecture, tutorial and guide to the five-step process for applying the results of systematic reviews. Following further revision, these materials will be made more widely available. We are working with the Cochrane Acute Respiratory Infections Review Group to identify and understand difficulties reviewers experience in applying review results and are conducting a survey to canvass their opinions and practices with regard to the use of non-randomized evidence in their reviews.

Empirical work on applicability is progressing well. Led by Jesse Berlin, a proposal has been submitted to the US Agency for Healthcare Quality and Research to undertake Empirical Studies of Trials that Estimate Effect Modification (ESTEEM). The main question being asked is

whether meta-regression analyses of aggregate-level data give correct answers to questions about individual patient characteristics that may modify the effect of treatments. An empirical comparison using patient-level data from eight previously conducted individual patient data analyses in cancer and epilepsy is proposed. Simulation studies to identify situations in which it is clearly likely or clearly unlikely that the aggregate-level data will give the correct answer are also planned. On recommendations, the GRADE working group, led by Andy Oxman, who offered two workshops and a plenary session at the Cochrane Colloquium in Stavanger, are conducting empirical research on grading evidence and recommendations. The group plan to provide the Collaboration with policy advice on how to grade evidence (across studies for each outcome) in Cochrane reviews and to develop new guidelines for discussion sections of Cochrane reviews for the *Cochrane Reviewers' Handbook*.

Reference:

1. Stevens A, Abrams K, Brazier J, Fitzpatrick R, Lilford, R (editors). *The Advanced Handbook of Methods In Evidence Based Healthcare.* London: SAGE, 2001.

Cochrane Economics Methods Group

Miranda Mugford, Luke Vale and Cam Donaldson

A summary of the state of thinking about economics and systematic reviews in general, and Cochrane reviews in particular, is now published. In May 2002, BMJ publishing group published the book based on a workshop held in Banff, Alberta in February 2001. Fuller details are given below:

Donaldson C, Mugford M, Vale L (editors). *Evidence-based health economics: the role of economics in systematic review*. London: BMJ Publishing Group, 2002.

Chapter headings and authors:

1. From effectiveness to efficiency: an introduction to evidence-based health economics. Cam Donaldson, Miranda Mugford and Luke Vale
2. Using systematic reviews in economic evaluation: the basic principles. Cam Donaldson, Miranda Mugford and Luke Vale
3. Reviewing economic evidence alongside systematic reviews of effectiveness: example of neonatal exogenous surfactant. Miranda Mugford
4. The place of economic analyses in systematic reviews: a clinician's viewpoint. Cindy Farquhar and Paul Brown
5. Evidence-based economic evaluation: how the use of different data sources can impact results. Douglas Coyle and Karen M. Lee
6. Methodological quality of economic evaluations of healthcare interventions – evidence from systematic reviews. Tom Jefferson, Luke Vale and Vittorio Demicheli
7. Effectiveness estimates in economic evaluation. Vittorio Demicheli, Tom Jefferson and Luke Vale
8. Criteria list for conducting systematic reviews based on economic evaluation studies - CHEC, Andre Ament, Silvia Evers, Marielle Goossens, Henrica de Vet and Maurits van Tulder
9. Evaluating economic interventions: a role for non-randomised designs? Ivar Sønbø Kristiansen and Toby Gosden
10. Making the problem fit the solution: evidence-based decision-making and 'Dolly' economics. Stephen Birch
11. Evidence-based medicine meets economic evaluation – an agenda for research. Michael Drummond
12. Glossary of terms for economics and systematic review. Gillian Currie and Braden Manns

The main activity of the Group during the year has been in preparation of registration as a joint Campbell and Cochrane Methods Group. This is progressing slowly and will be followed by a newsletter describing the changes and plans.

The Cochrane Economics Methods Group has been commissioned by the Cochrane Collaboration Steering Group to survey a sample of Review Groups and reviewers to assess the cost of doing an individual Cochrane review. We hope to report results at the Cochrane Colloquium in Barcelona in October.

Cochrane Health-Related Quality of Life Methods Group

Catherine Acquadro, Dick Joyce, Lucile Lapalus and Donald Patrick

The Cochrane Health-Related Quality of Life (HRQL) Methods Group held two meetings in 2002; one was at the Cochrane Colloquium in Stavanger and the other was in Orlando at the annual ISOQOL conference.

In Stavanger, 11 active members were able to attend. Each subgroup defined their 2002-2003 objectives knowing that the main mission of the Group is to advise Cochrane reviewers on how to integrate HRQL outcomes into Cochrane reviews.

The three subgroups were renamed:

- Terminology subgroup became HRQL Concepts and Methods Review
- Quality and Validity subgroup became HRQL Review Design
- Statistics subgroup became HRQL Analysis

The first subgroup, chaired by Elaine McColl, decided to complete the HRQL glossary by September 2003 and to post it on the website. Xavier Badia, chair of the second subgroup could not attend. In his absence, participants proposed to go over chapters 1-7 of the *Cochrane*

Reviewers' Handbook in order to produce for each chapter a specific text on HRQL issues and submit them to the Handbook Advisory Group. Jeff Sloan, chair of the last subgroup, proposed to: develop a set of guidelines for examining the statistical components of HRQL studies that might be included in a systematic review; and produce examples of a complete statistical review by ISOQOL 2002. It was also decided to create our own website by December 2002.

In addition, two workshops on HRQL were held using an interactive learning method called the Workmats. Both workshops were a great success. At the Cochrane Colloquium in Barcelona, it is planned to hold three HRQL workshops open to all Cochrane reviewers.

The second meeting held at the ISOQOL 2002 conference in Orlando enabled us to follow up on the objectives defined in Stavanger.

For more information, please contact Lucile Lapalus, Co-ordinator: llapalus@mapi.fr.

Cochrane Individual Patient Data Meta-analysis Methods Group

Lesley Stewart, Jayne Tierney and Mike Clarke

There are currently 42 members from 12 countries in the Group.

We are currently developing a website for the Group which we hope will improve communication between the members of the Group and with other Cochrane entities. The site will provide general information about individual patient data (IPD) meta-analyses and resource material for anyone planning to start an IPD project or who wants to learn more about them. This will include details of relevant references, a frequently asked questions list and PowerPoint presentations. We hope that the website will provide an easy way for Collaborative Review Groups to contact us for advice and, to help with this, there will be an on-line form that will go directly to the Group convenors. The site will also have a searchable database of IPD meta-analyses carried out by Group members (and, in future, also those done by others) and a searchable database of methodological projects carried out by Methods Group members. A pilot version will be released to members of the Group in June and will go 'live' later in the year.

This year we are planning to run two workshops at the Cochrane Colloquium in Barcelona, one on IPD methodology and the other on practical methods for estimating hazard ratios from published summary statistics.

Cochrane Non-randomized Studies Methods Group

Barney Reeves

The main task for the Group remains the production of guidance on the inclusion of non-randomized studies in Cochrane reviews. Research by Jon Deeks and colleagues, soon to be published in a monograph (www.ncchta.org.uk), has been important in informing the developing guidance. The monograph includes a review of tools for assessing the quality of non-randomized studies, evidence about the true uncertainty of effect estimates from non-randomized studies and the ability of statistical methods to adjust for confounding.

The Group met once in Oxford (July 2002) during the last year. This was the first time that the Adverse Events Subgroup, co-ordinated by Andrew Herxheimer, had met as part of the larger Group. Reviews of adverse events are crucial to the Collaboration since reviews need to include evidence about harm as well as benefit. Because adverse events are usually rare, they are only likely to be studied in non-randomized studies. The subgroup has recently prepared recommendations about including adverse events in reviews and plans to submit these to the editors of the *Cochrane Reviewers' Handbook*, for inclusion.

Other work of Group members deserves mention. Martie Muller's review of the effect of circumcision to reduce the risk transmission of HIV (see page six) shortly to appear in *The Cochrane Library*, highlights many of the problems of reviewing non-randomized studies, for example judging the susceptibility of studies to confounding and the importance of investigating heterogeneity even when not formally pooling results. The good news is randomized trials of circumcision are underway. Lee Hooper has a protocol in *The Cochrane Library* for a review of prophylactic antibiotics, including adverse effects and would welcome comments.

One thing is now clear – carrying out a review of non-randomized studies is much more difficult than a review of randomized trials. Reviewers, keen to include non-randomized studies in reviews, should recognise that the effort required is likely to be much greater and the conclusions weaker. The rewards may be greatest for reviews of non-randomized studies of adverse, long-term and rare outcomes. As mentioned above, there is a pressing need to supplement traditional reviews of randomized trials of effectiveness with reviews of non-randomized studies of adverse or unintended effects. Such reviews may require specialist reviewers, for example when considering side effects of drugs.

The Non-randomized Studies Methods Group will meet next in Barcelona, which promises to be an interesting Colloquium for reviewers who are interested in non-randomized studies. The organisers have scheduled a plenary session on non-randomized studies and the Non-

randomized Studies Methods Group will be offering a training workshop for the first time.

Cochrane Qualitative Research Methods Group

Jane Noyes, Jennie Popay and Katrina Roen

After a long period of gestation (perhaps unparalleled within the Collaboration), The Cochrane Collaboration has a Qualitative Research Methods Group. A letter confirming our registration was received on 24 April 2003 and we would like to take this opportunity to thank all the people who have helped us to get to this point. Whilst we have been waiting to hear about registration, we haven't been idle! Thanks to Jane Noyes and Peter Finch we have a new website receiving 80 hits, registering around 10 new members a month, three committed convenors and 125 people in 12 countries wanting to get involved in the work of the group. Janice Morse has agreed to act as a co-convenor in Canada and we are looking to recruit other convenors from outside the UK – volunteers welcome! Whilst we know we have a long way to go before we are making a significant contribution to the work of the Collaboration, we have made a start. But what about the future!

As Jennie Popay argues in an earlier article in this Newsletter (see page 4), there seems to be a lot of demand within the Collaboration for guidance on how to approach the systematic review of evidence from qualitative research, so that is going to be an early priority for the Group. We plan to establish four subgroups in the near future focusing on:

- Producing preliminary guidance for Cochrane reviewers.
- Developing a training strategy for the future.
- Developing databases of methodological references and examples of systematic reviews including qualitative evidence.
- Establishing mechanisms for dissemination and discussion of the group's work.

Watch this space and if you are keen to get involved do contact us: Jane Noyes at jn109@york.ac.uk; Jennie Popay at j.popay@lancaster.ac.uk; or Katrina Roen at k.roen@lancaster.ac.uk.

Cochrane Reporting Bias Methods Group

Chris Bartlett, Matthias Egger, David Moher and Jonathan Sterne

The Group is now in its third year of official existence and has 59 members. A comprehensive review of membership will take place this year and the membership list will be revised if necessary. Chris Bartlett (Bristol) will be stepping down as co-ordinator in mid 2003 and we are currently considering how the co-ordinator's role might change, who will perform it and where it will be based. It is probable that this function will move across the Atlantic to Ottawa. The co-ordinator's part-time post has been supported by the UK MRC Health Services Research Collaboration. However, this block of funding, at present the only official financial support for the Group, is now coming to an end. Some major changes for the Group will therefore be in prospect this year.

A meeting of the Group was held on 2 July 2002 at St Catherine's College, Oxford, UK as a satellite meeting to the fourth Symposium on Systematic Reviews. The meeting included a discussion led by Iain Chalmers on the prospective registration of trials, the promotion of which would aid in lessening the effects of reporting bias. There was also a demonstration by Michael Borenstein of the 'Comprehensive Meta-analysis' software package and an introduction to the 'Handbook of Publication Bias' from Hannah Rothstein. There were also contributions from John Ioannidis, An-wen Chan, Martie Muller, Julie Milton, Sally Hopewell and Lesley Wood. Other members of the Group also contributed to the main Symposium.

POSSIBLE METHODS GROUPS

Cochrane Information Retrieval Methods Group

Carol Lefebvre, Steve Pritchard and Alison Weightman

(The following text is based on the Draft Module of the proposed Group and is therefore still under discussion).

Background

The importance of a broad and sensitive literature search to retrieve the maximum number of relevant published and unpublished studies is a crucial component of an unbiased systematic review. A discussion with the Vice Chancellor of the University of Wales College of Medicine about the Library's wish to develop further its support for the evidence-based healthcare agenda led to an exploration of the potential for a Cochrane Information Retrieval Methods Group. Colleagues at the UK Cochrane Centre and elsewhere expressed support for the concept and offered advice and guidance on the way forward. It was suggested that the Group would complement the work of other Groups, notably the Cochrane Reporting Bias Methods Group, and draw from the remits of two Groups that are no longer active: The Cochrane Informatics Methods and Cochrane Information Retrieval Methods Groups.

An initial pre-exploratory meeting was held at the University of Wales College of Medicine in Cardiff on 31

May 2002. A further international exploratory meeting was held in London at the Health Development Agency on 2 December 2002. This resulted in the establishment of an international body of collaborators who have refined the scope and functions of the Group.

Scope
The Group will seek to provide advice and support, to conduct research and to facilitate information exchange regarding methods to support the information retrieval activities of The Cochrane Collaboration. Members will concentrate on providing practical support for the development of information retrieval techniques and facilities for information searchers. Close links will be forged with Cochrane and other groups to minimise duplication of effort. These aims will be realised by the following activities:

Providing policy advice
- Offering policy advice on information retrieval issues to the Steering Group and other parts of the Collaboration, in conjunction with other Cochrane Advisory and Methods Groups, including contributing to the updating of Section 5 of the *Cochrane Reviewers' Handbook.*

Providing training and support
- Providing training and support in effective information retrieval skills and the appraisal and evaluation of search strategies for those undertaking Cochrane reviews, in particular the Trials Search Co-ordinators, and those who critique these reviews.
- Offering training programmes for new searchers and for those involved in training others, including workshops at the Cochrane Colloquia.
- Developing a web resource, identifying and evaluating databases of potential value to those preparing Cochrane reviews.

Conducting empirical research including systematic reviews
- Contributing information on ongoing and completed information retrieval research to the *Cochrane Methodology Register.*
- Carrying out, supporting and encouraging research, including conducting and maintaining systematic reviews of information retrieval methods.
- Developing and evaluating retrieval strategies for research evidence to support the systematic review process (systematic reviews, randomized controlled trials and other types of research evidence) for use by The Cochrane Collaboration.
- Encouraging improvements to indexing and abstracting tools for the identification and retrieval of trials and other research evidence - this will involve liaison with, and persuasion of, publishers, database producers and database suppliers.
- Liasing with the Cochrane Library Users' Group to see how these findings might be of relevance to *The Cochrane Library*.

Helping to monitor the quality of systematic reviews
- Working together with the Trials Search Co-ordinators, the Cochrane Quality Advisory Group, the Handbook Advisory Group and others to: advise on good practice in reporting search methods; formalise a method for monitoring the quality of searching techniques employed in Cochrane reviews.

Serving as a forum for discussion
- Liaising and co-operating with Advisory Groups within the Collaboration such as the CENTRAL/CCTR Advisory Group, the Handbook Advisory Group, the Quality Advisory Group and the Cochrane Library Users' Group as well as other relevant national and international groupings; in particular, groupings of health librarians and information professionals.
- Acting as a forum for discussion and exchange of views regarding the contribution of information retrieval methods to the goals of the Collaboration.
- Disseminating the work of the Group to relevant international groups to encourage further discussion and the development of its agenda.
- Hosting an e-mail discussion group and holding open meetings at Cochrane Colloquia.

Issues relating to information retrieval methods are not currently the specific focus of an existing Cochrane Methods Group, but this is a topic of interest to many Cochrane reviewers, those supporting the review process such as the Trials Search Co-ordinators and other individuals and groups. The Group will liaise closely with all relevant parties to ensure that its rationale, scope and objectives are appropriate to the developing needs of The Cochrane Collaboration.

If the Group is successful in registering with The Cochrane Collaboration, the Group Co-ordinator will contact all Collaborative Review Groups, Fields, Networks and Centres and other relevant parties, to alert them to the existence of the Group and to invite them to collaborate actively with the Group. For further information about the proposed Group, please contact Carol Lefebvre (clefebvre@cochrane.co.uk), Steve Pritchard (Pritchard@cardiff.ac.uk) or Alison Weightman (WeightmanAL@cardiff.ac.uk).

CAMPBELL COLLABORATION METHODS GROUPS (C2)

Jeff Valentine

The Campbell Collaboration (C2) aims to utilize scientific standards in conducting systematic reviews of research on social and behavioral policies and programs and make the

findings easily available to policy makers, practitioners, and the public. Within this framework, the C2 Methods Group (a) provide expertise to researchers conducting systematic reviews, (b) improve systematic review methods, (c) offer training on how to conduct reviews, and (d) facilitate the use of systematic reviews in policy-making and practice, particularly as this relates to the end-user's understanding of methodology and how to assess evaluations of policies and practices.

There have been several exciting developments during the past year:

C2 was part of a group that successfully bid on a major contract from the U.S. Department of Education's Institute for Education Sciences to establish the What Works Clearinghouse (WWC). The WWC was established to provide educators, policymakers, and the public with a central, independent, and trusted source of scientific evidence of what works in education. The WWC will produce syntheses of the research on educational interventions. The results of these syntheses will be available to the public through an on-line, searchable database.

The C2 Methods Group serves as the 'quality control' unit for the WWC. In particular, members of the Methods Group have been involved in (a) designing an instrument for evaluating the quality of study design and implementation, (b) designing an instrument for describing the confidence with which inferences can be drawn from a body of literature, and (c) setting up standardized procedures for conducting research syntheses.

The first Campbell Collaboration Methods Conference was held in Baltimore in September 2002. Over 80 participants from the U.S. and Europe attended. The second C2 Methods Conference will be held in Barcelona in conjunction with the annual Cochrane Collaboration meeting.

C2 approved two policy briefs during the past year. The Research Design policy brief addresses the following key question for Campbell Collaboration (C2) reviews: *What should be C2 policy concerning acceptable methodologies used in primary studies when a systematic review concerns the effectiveness of an intervention*? The Brief (a) identifies the key issues that are confronted by C2 systematic reviewers who find a variety of study designs in their literature; (b) outlines possible ways to represent this diversity in their work; (c) proposes agreed-upon guidelines that C2 may wish to promulgate; and (d) provides exemplars that demonstrate how these guidelines might be implemented in practical ways.

The Statistical Analysis Policy Brief identifies the key issues that are confronted by C2 systematic reviewers who want to synthesize the results of studies statistically; outlines possible ways that statistical procedures might be used, and provides exemplars of how these methods might be used.

C2 also established two new Methods Groups during the year. The Training Group (convened by Betsy Becker and Terri Pigott) will address C2's goals of providing training and support for the Review Groups within C2. The Information Retrieval Group (convened by Hannah Rothstein, Darcy Strouse, and Julia Lavenberg) will provide advice, training, and support on information retrieval issues (e.g. search strategies, assessment of publication bias) as well as conduct formal research on information retrieval strategies.

Further information on the Campbell Collaboration Methods Groups, including contact information for convenors, can be obtained from: www.missouri.edu/~c2method/.

PAST MEETINGS

10th Cochrane Colloquium

Stavanger, Norway
31 July – 3 August 2002

Janet Wale

As the second International Colloquium that I have attended, it would be hard to choose the most important personal take-home message. The first plenary launched us into the Colloquium itself and into cyclical themes that also presented themselves in following sessions. These were of timeliness (availability of information needed), and the message that evidence is not the final outcome. Valued decisions, relevance, implications, and implementation follow.

For me, key messages from the plenary sessions were:

- Grading the quality of evidence and the strength of recommendations – moving toward quality of outcome – in that the quality of a study does not directly translate into implications or outcome.
- Improving the quality of Cochrane reviews – providing utility of information by being interactive, or sexy if you are wearing a rosy shirt as Richard Smith was. Next, pre-specifying what is a significant treatment effect, so that 'consumers are the beneficiaries of improved quality of health care' – a nice return to single-mindedness by Julian Higgins.
- Looking back and looking forward – by Steering Group past and present members. This was a call for succinct titles, many more reviews, mixed funding of entities, decentralisation, more formal structures and people care, a new decade of delivery and access to review information.

Days were extremely busy, with a succession of meetings and workshops, all of them worthwhile in widening my experience and perspective.

2nd Campbell Collaboration Colloquium

Stockholm, Sweden
27 – 28 February 2003

Peter Tugwell

I attended the second Campbell Collaboration Colloquium in Stockholm (my first). There were over 300 participants. It was reminiscent of early Cochrane Colloquia with the high levels of volunteerism and enthusiasm by impressive individuals for developing the evidence-based building blocks to ensure rigor whilst allowing flexibility. They have five Co-ordinating Groups; Crime and Justice (25 review titles registered), Education (10 review titles registered), Social Welfare (17 review titles registered), Methods (two policy briefs published, and Communication and Dissemination, and the first regional Campbell centre - the Nordic Campbell Center - opened at the end of 2002. *The Campbell Library* has been established and contains two components: C2-SPECTR: the Social, Psychological, Educational and Criminological Trials Register; C2-RIPE: The register of C2 Systematic Reviews of Interventions and Policy Evaluation.

The meeting format is similar to Cochrane Colloquia with a few plenaries and many workshops. Iain Chalmers gave the keynote Jerry Lewis Lecture - excellent as always. A key message of his talk was the potential for mutual synergistic benefit between Campbell and Cochrane for the two Collaborations as well as the well-being of those to whom the results are applied. Reasons include similarity in objectives, the fact that people contributing to both Collaborations face similar challenges in securing ongoing funding for preparing and maintaining systematic reviews and for editorial and organisational infrastructure, face similar challenges in securing academic recognition of systematic reviews and face many of the same methodological challenges, and because the underlying principles of both Collaborations include 'fostering collaboration' and 'reducing duplication'. Dialogue is happening already between the Steering Groups, the Nordic Cochrane and Campbell Centres, the Social Welfare and Developmental, Psychosocial and Learning Problems Group, Cluster/Place Randomization Methods Groups, Economics Methods Groups, the Implementation/ Qualitative Methods Groups, the group to become an Equity Methods Group.

Phil Davies from the UK Government Chief Social Researcher's Office and Cabinet Office Strategy Unit gave another excellent presentation on internationalism. One of his key points was to encourage the Campbell Collaboration to look further at external validity and multi-method evaluation incorporating both qualitative and quantitative methods in looking at five aspects of interest to users of effectiveness syntheses: intervention effectiveness – 'what works', implementation effectiveness – 'how it works', resource effectiveness – 'at what cost/benefit?', experiential effectiveness – 'users' views', and likely diversity of effectiveness. Responding appropriately to users' needs for evidence and systematic reviews was also mentioned as an important feature in the international development of the Campbell Collaboration.

A presentation by Angela Harden illustrated well how qualitative evidence could be helpful in interpreting a systematic review of randomized trials of strategies to influence the eating habits of school children. This is one example of the likely value of joint sessions at coming Cochrane and Campbell Colloquia involving Methods Groups from both Collaborations.

FUTURE MEETINGS

11th Cochrane Colloquium

Barcelona, Spain
26 – 31 October 2003

The Iberoamerican Cochrane Centre will host the 11th Cochrane Colloquium at Barcelona from 26 – 31 October 2003.

The aims of the 11th Colloquium are to focus on available scientific evidence, healthcare provision and global sociocultural diversity. The Colloquium aims to study the process of producing quality healthcare information and explore its availability and application, bearing in mind the different circumstances faced by citizens, healthcare professionals and governments around the world.

The first part of the Colloquium (26 - 28 October) will mostly be dedicated to activities of methodological training, co-ordination of groups and committee meetings. The second part (29 - 31 October) will focus on the application of scientific evidence, bearing in mind different needs, circumstances and perspectives.

More information is available at: www.colloquium.info/.

International Society for Clinical Biostatistics and the Society of Clinical Trials

London, UK
20 – 24 July 2003

The meeting will include topics of interest to researchers in academia, private industry and government, focusing on trial design, analysis, organization and management; methodological and regulatory issues; technology and data management; and quality control and cost issues in clinical trials. The programme consists of plenary, contributed paper, poster and pre-conference workshop sessions. More information is available at: www.sctweb.org/meeting2.cfm.

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AVAILABILITY OF THE NEWSLETTER

Additional copies of the MG Newsletter may be obtained from the UK Cochrane Centre, which is based at:

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The Newsletter is also available on The Cochrane Collaboration websites.

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MORE INFORMATION

The Cochrane Library

The Cochrane Library contains five main databases: the *Cochrane Database of Systematic Reviews* (CDSR), the *Database of Abstracts of Reviews of Effects* (DARE), the *Cochrane Central Register of Controlled Trials* (CENTRAL), the *Cochrane Database of Methodology Reviews* (CDMR), and the *Cochrane Methodology Register* (CMR). In addition, *The Cochrane Library* contains information about the Collaboration, complete contact details for all Cochrane entities, and links to the *Cochrane Reviewers' Handbook* and a glossary of Cochrane and methodological jargon. Information about how to subscribe is available from:

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Cochrane Internet Sites

A wide range of Cochrane Collaboration information is available from the following WWW sites, including the abstracts from all the completed reviews in the current issue of *The Cochrane Library*, details of Cochrane email lists, opportunity to download Cochrane software, contact details for all Cochrane entities and much more. A leaflet, available from these sites, provides a concise overview of the Cochrane Collaboration, while the brochure provides more detailed information.

Germany
www.cochrane.de

UK
www.update-software.com

USA
www.cochrane.org

International Cochrane email list: CCINFO

This moderated list offers an excellent means of keeping informed of the activities and policies of The Cochrane Collaboration. The list is used for announcements and discussion of matters relevant to the Collaboration as a

whole. To subscribe send an email to: ccinfo@mcmaster.ca with the message:

subscribe ccinfo firstname lastname

Do not fill in the subject or add a signature. You will receive confirmation that you have been added to the list.

Cochrane Centre Internet Sites

Australasian Cochrane Centre
www.cochrane.org.au

Brazilian Cochrane Centre
www.centrocochranedobrasil.org

Canadian Cochrane Centre
www.cochrane.McMaster.ca/

Chinese Cochrane Center
www.chinacochrane.org

Dutch Cochrane Centre
www.cochrane.nl

German Cochrane Centre
www.cochrane.de

Iberoamerican Cochrane Centre
www.cochrane.es

Italian Cochrane Centre
www.areas.it

Nordic Cochrane Centre
www.cochrane.dk

South African Cochrane Centre
www.mrc.ac.za/cochrane/cochrane.html

United States Cochrane Center
www.cochrane.us

APPENDIX

Previous structured abstracts and commentaries

Methods Groups Newsletter Volume 6, June 2002
(www.cochrane.org/newslett/MGnews6_2002.pdf)

Devereaux PJ, Manns BJ, Ghali WA, Quan H, Guyatt GH. Reviewing the reviewers: the quality of reporting in three secondary journals. *CMAJ* 2001; 164:1573-1576.

Kjaergard LL, Villumsen J, Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Annals of Internal Medicine* 2001; 135:982-989.

Devereaux PJ, Manns BJ, Ghali WA, Quan H, Lacchettti C, Montori VM, Bhandari M, Guyatt GH. Physician interpretations and textbook definitions of blinding terminology in randomized controlled trials. *JAMA* 2001; 285:2000-2003.

Braunholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a trial effect. *Journal of Clinical Epidemiology* 2001; 54:217-224.

Reidpath DD, Allotey PA. Data sharing in medical research: an empirical investigation. *Bioethics* 2001; 15:125-134.

Villar J, Mackey ME, Carroli G, Donner A. Meta-analyses in systematic reviews of randomized controlled trials in perinatal medicine: a comparison of fixed andrandom effects models. *Statistics in Medicine* 2001; 20:3635-3647.

Methods Groups Newsletter Volume 5, June 2001
(www.cochrane.de/newslett/mgnews5.pdf)

McAuley L, Pham B, Tugwell P, Moher D. Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? *Lancet* 2000; 356:1228-1231.

Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA* 2001; 285:1987-1991.

Sutton AJ, Duval SJ, Tweedie RL, Abrams KR, Jones DR. Empirical assessment of effect of publication bias on meta-analyses. *BMJ* 2000; 320:1574-1577.

Ioannidis JP, Lau J. Completeness of safety reporting in randomized trials: an evaluation of 7 medical areas. *JAMA* 2001; 285:437-443.

Petrosino A, Boruch R, Rounding C, McDonald S, Chalmers I. The Campbell Collaboration Social, Psychological, Educational and Criminological Trials Register (C2-SPECTR). *Evaluation and Research in Education* 2000; 14:206-219.

Clarke M, Clarke T. A study of the references used in Cochrane protocols and reviews: three bibles, three dictionaries and nearly 25,000 other things. *International Journal of Technology Assessment in Health care* 2000; 16:907-909.

Benson K, Hartz AJ. A comparison of observational studies and randomized controlled trials. *New England Journal of Medicine* 2000; 342:1878-1886.

Concato J, Shah N, Horwitz RI. Randomized controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine* 2000; 342:1887-1892.

Methods Groups Newsletter Volume 4, June 2000
(www.cochrane.de/newslett/mgnews4.htm)

McAlister FA, Clark HD, van Walraven C, Straus SE, Lawson FM, Moher D, Mulrow CD. The medical review article revisited: has the science improved? *Annals of Internal Medicine* 1999; 131:947-951.

Langham J, Thompson E, Rowan K. Identification of randomized controlled trials from the emergency medicine literature: comparison of handsearching versus MEDLINE searching. *Annals of Emergency Medicine* 1999; 34:25-34.

Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999; 282:1054-1060.

Poole C, Greenland S. Random-effects meta-analyses are not always conservative. *American Journal of Epidemiology* 1999; 150:469-475.

McGettigan P, Sly K, O'Connell D, Hill S, Henry D. The effects of information framing on the practices of physicians. *Journal of General Internal Medicine* 1999; 14:633-642.

Spiegelhalter DJ, Myles JA, Jones DR, Abrams KR. An introduction to Bayesian methods in health technology assessment. *BMJ* 1999; 319:508-512.

Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H. The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review. *Health Technology Assessment* 1999; 3:1-96.

Stroup DF, Berlin JA, Morton SC, Olkin I et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000; 283:2008-2012.

Katerndahl DA, Lawler W. Variability in meta-analytic results concerning the value of cholesterol reduction in coronary heart disease: a meta-analysis. *American Journal of Epidemiology* 1999; 149:429-441.

Methods Groups Newsletter Volume 3, June 1999
(www.cochrane.de/newslett/1999mg.pdf)

Thornley B, Adams C. Content and quality of 2000 controlled trials in schizophrenia over 50 years. *BMJ* 1998; 317:1181-1184.

Cholesterol Treatment Trialists' (CTT) Collaboration. Protocol for a prospective collaborative overview of all current and planned randomized trials of cholesterol treatment regimens. *American Journal of Cardiology* 1995; 75:1130-1134.

Clarke M, Stewart L, Pignon JP, Bijnens L. Individual patient data meta-analysis in cancer. *British Journal of Cancer* 1998; 77:2036-2044.

Boynton J, Glanville J, McDaid D, Lefebvre C. Identifying systematic reviews in MEDLINE: developing an objective approach to search strategy design. *Journal of Information Science* 1998; 24:137-157.

Demissie K, Mills OF, Rhoads GG. Empirical comparison of the results of randomized controlled trials and case-control studies in evaluating the effectiveness of screening mammography. *Journal of Clinical Epidemiology* 1998; 51:81-91.

Ioannidis JP, Cappelleri JC, Lau J. Issues in comparisons between meta-analyses and large trials. *JAMA* 1998; 279:1089-1093.

Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, Tugwell P, Klassen TP. Does quality of reports of randomized trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998; 352:609-613.

Methods Groups Newsletter Volume 2, June 1998
(www.cochrane.de/newslett/1998mg.pdf)

Mulrow CD. The medical review article: state of the science. *Annals of Internal Medicine* 1987; 106:485-488.

Scherer RW, Dickersin K, Langenberg P. Full publication of results initially presented in abstracts. *JAMA* 1994; 272:158-162.

Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. *BMJ* 1994; 309:1286-1291.

Dickersin K, Min YI. NIH clinical trials and publication bias. *Online Journal of Current Clinical Trials* 1993; Doc No. 50.

Moher D, Jadad AR, Nichol G, Penman M, Tugwell P, Walsh S. Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. *Controlled Clinical Trials* 1995; 16:62-73.

CURRENT STATUS OF COCHRANE METHODOLOGY REVIEWS

Published reviews	
Jefferson T, et al.	Editorial peer-review for improving the quality of reports of biomedical studies
Scherer R, et al.	Full publication of results initially presented in abstracts
Hopewell S, et al.	Grey literature in meta-analyses of randomized trials of healthcare interventions
Hopewell S, et al.	Handsearching versus electronic searching to identify reports of randomized trials
Edwards P, et al.	Methods to influence response to postal questionnaires
Demicheli V, et al.	Peer review for improving the quality of grant applications
Kunz R, et al.	Randomization to protect against selection bias in healthcare trials
Wager E, et al.	Technical editing of research reports in biomedical journals
Hopewell S, et al.	Time to publication for results of clinical trials
Reviews currently undergoing editing following peer review	
Vale L, et al.	Quality of systematic reviews of economic evaluations in health care
Reviews currently undergoing peer review	
Mapstone J, et al.	Strategies to improve recruitment to research studies
Reviews in progress	
Ghersi D, et al.	Impact of shared scientific or ethical review of multicentre clinical research on the quality of clinical research and the clinical research process
Clarke M, et al.	Individual patient data meta-analyses compared with meta-analyses based on aggregate data
Edwards P, et al.	Methods to influence the completeness of response to self-administered questionnaires
Villanueva E, et al.	N-of-1 trials for making therapy decisions
Vist G, et al.	Outcomes of patients who participate in randomized controlled trials versus those of similar patients who do not participate
Olsen K, et al.	Publication bias in clinical trials
Protocols in progress	
Westby M, et al.	The effect of masking reviewers at the study inclusion stage of a systematic review
Song F, et al.	Validity of indirect comparisons for estimating relative efficacy of competing healthcare interventions
Proposed titles for reviews	
Oxman A, et al.	What proportion of randomized controlled trials are positive?

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