

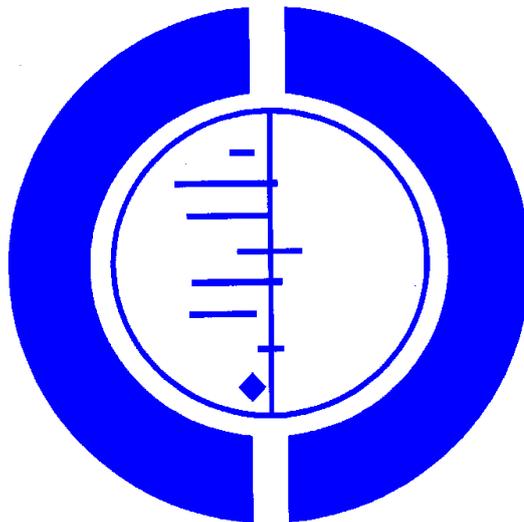
# FINAL REPORT TO THE COCHRANE OPPORTUNITIES FUND

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## A decision tool for updating Cochrane reviews

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## Executive summary

This report describes the development and validation of an updating tool to help assess the need and likely benefits of updating a Cochrane review.

The Cochrane Collaboration has a policy that Cochrane review authors should agree to update their review periodically following its initial publication. Current guidance states this should be done every two years, however, there is limited evidence to suggest the ideal time for updating; too soon may introduce bias, and if too late, the end user may act on out-of-date or potentially misleading information. Given the increasing workload of Cochrane Review Groups and review authors, a change to current procedures for updating Cochrane reviews is needed to replace the *ad hoc* and arbitrary approach that currently exists.

In developing this updating tool an international Steering Committee was established to provide guidance and support to the project. The tool was developed building on existing empirical evidence on updating systematic reviews, guidance in the new *Cochrane Handbook for Systematic Reviews of Interventions* and Review Manager (RevMan) 5, work undertaken by the Cochrane Updating Working Group and existing checklists from other agencies, including Cochrane Review Groups. Formal piloting and input from users and experts involved in updating Cochrane reviews are being used to enhance and refine the tool.

The updating tool is in two parts. Step 1 is a decision tree to identify triggers for updating a Cochrane review. Possible triggers include: new evidence, new methods, response to feedback from users of the review, or other factors such as the age of the review or its use in policy and guidelines. If review authors decide that a trigger is likely to change the conclusions of their review, Step 2 is a checklist designed to help review authors consider which sections of their Cochrane review require updating. It guides review authors step by step through the review process using questions or triggers, which may or may not lead to action and updating of specific sections of the review.

We hope that this updating tool will make it easier to identify which Cochrane reviews are ripe for updating and ensure that the decision-making process is made clearer and more transparent to the end user.

This report describes the development and validation of an updating tool to help assess the need and likely benefits of updating a Cochrane review. The report is presented in five sections. Section 1 describes the background and rationale for the updating tool, including information about when and how to update. Section 2 describes the development of the updating tool and the resulting decision tree and checklist. Section 3 presents the results of the in-house and ongoing formal pilot of the tool, while Sections 4 and 5 provide information about the dissemination of the tool and our key conclusions. This project was funded by the Cochrane Opportunities Fund in 2007.

## **1. Background and rationale for the updating tool**

### **1.1 Definition of updating**

This document and the research underpinning it is predicated on our understanding of what updating means. Moher and Tsertsvadze discussed the definition of an update and suggested that “a distinguishing feature of an updated systematic review from a new review is that during updating the originally formulated protocol (e.g., eligibility criteria, search strategy) is retained, and sometimes extended, to accommodate newly identified information (e.g., new treatment type, diagnostic method, outcome, different population)” (Moher 2006). This is the definition we are proposing to use when discussing updating Cochrane reviews. It draws on the definition used in the new chapter on maintaining and updating Cochrane reviews in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008).

### **1.2 Timeframe for updating**

The Cochrane Collaboration has a policy that Cochrane review authors should agree to update their review periodically following its initial publication. Failure to keep Cochrane reviews up to date may lead to healthcare decision-makers acting on out-of-date or potentially misleading evidence (Shekelle 2001). However, the decision to update a Cochrane review needs to be considered carefully. Updating too soon may introduce time lag or publication bias, as there is evidence that randomized trials with statistically significant results are more likely to be completed sooner and published quicker than trials showing statistically negative or inconclusive results (Hopewell 2007). Also, early terminated trials showing strong benefit, especially those with small numbers of events, may overestimate the underlying treatment effect (Montori 2005). These trials are more likely to be published and included in a systematic review (or meta-analysis) earlier than those with a smaller effect size or a statistically non-significant result. Furthermore, updating a Cochrane review can require a substantial investment in resources and doing this too soon might be an inefficient use of the already limited resources available to prepare and maintain Cochrane reviews.

The current guidance for updating Cochrane reviews is that this should be done every two years, but this guidance is based more on the wish for findings to appear current and up to date by the end user than evidence that this is an appropriate time interval (Middleton 2004). In practice, reviews in rapidly moving fields may need to be updated more often than every two years, and other reviews, where the

evidence is relatively stable, might require updating less often. A recent assessment of 100 systematic reviews, published between 1995 and 2005, found that 57% of reviews required updating within five years (median 5.5, 95% CI 4.6 to 7.6 years), however, 23% of them had signals of being out of date within two years and 15% within one year. The study also found that 7% of reviews had signals for updating at the time of publication (Shojania 2007).

### **1.3 Rationale for updating**

Updating does not just mean adding new research studies. Other factors may need to be considered when updating a Cochrane review (Stead 2001). Such factors might include the need to assess new treatment regimes, specific new subgroups of populations, or drug comparisons, changes to the costs associated with the interventions under review, or the assessment of new outcome measures of more importance to patients and other decision makers (some of which may have been assessed by the studies already included in the review but not yet incorporated within the review itself).

As the science of systematic reviews develops so do their methods; as new methods of analysing and synthesising data become available, the methods of a systematic review need to be assessed to ensure that they are still appropriate and up to date. Finally, and perhaps most importantly, it is necessary to consider whether the topic under review is still relevant and worthy of updating. For example, if a treatment is no longer used for a particular condition or if more effective interventions have been developed. Alternatively, if the efficacy of a given treatment has been well established (i.e., stability of a statistically significant treatment effect estimate), the addition of new studies is less likely to change the pooled results (e.g., effect size, direction) and will result in inefficient use of resources.

### **1.4 Assessing when to update**

Given the workload of Cochrane Review Groups and authors of Cochrane reviews, a more evidence-based approach for updating Cochrane reviews is needed to replace the current ad hoc and arbitrary approach to updating. However, there is limited evidence about how to improve this approach. For example, there is uncertainty about the best methods of assessing when, and if, to update a systematic review (Tsersvadze 2006, Moher 2007) and which criteria could be identified as markers for when results of a review should be considered out of date and misleading. Evidence suggests that it may not be possible to give a predetermined definitive answer to decide when a Cochrane review should be updated (Moher 2007).

To address this uncertainty, we have developed a decision tree (Step 1) and checklist (Step 2) to help review teams assess the need and likely benefits of updating a Cochrane review.

### **1.5 How to update**

Keeping abreast of the literature for a particular Cochrane review helps gauge whether research in a particular content area is moving at a fast or slow pace, thus reflecting the need to update a review more or less frequently. We believe that the best method for deciding whether, and when, to update a

Cochrane review is through continual monitoring of the literature and other sources of information relevant to the objectives of the review.

The following surveillance methods have been shown to be efficient ways of helping review authors to identify whether new studies have been published.

- *Auto Alerts via databases*

Making use of the automatic re-run of the full search strategy by the database service provider every time new studies are added to the database; search results are sent automatically via e-mail.

- *Auto Alerts via electronic journals*

Whenever a known relevant study in a particular journal is cited by others these citing references are sent automatically via e-mail.

- *PubMed 'related articles' feature*

Using a subset of studies (e.g. three largest and three most recent) included in the original Cochrane review as 'seeds' to search for related articles; restricted to material added to the database since the date of the last search and limited to study design (e.g. using the PubMed Clinical Queries option to select the 'therapy' category for randomized controlled trials) (Sampson 2008).

- *Citation tracking in Citation Indexes*

Using the Science Citation Index or Scopus to search for new studies that cite the original Cochrane review; restricted to material added to the database since the date of the last search (Sampson 2008).

- *Searching the Cochrane Review Group's Specialized Register*

Searching using a subject specific search.

It is recommended that the Auto Alerts are set up when the search strategy is first implemented, by the person(s) selected to run the searches (either the review team or the relevant Review Group Trials Search Co-ordinator) as it may be preferable to monitor the literature in this way by receiving a small number of studies regularly, rather than waiting for 12 or 18 months after the review was published and receiving a large number of database records.

To ensure that the auto alerts set up in PubMed/MEDLINE, for example, remain up to date, search terms should be checked on an annual basis by the Trials Search Co-ordinator following the US National Library of Medicine annual file maintenance programme in which the Medical Subject Headings (MeSH) are added to, removed, or amended.

The full search strategy for the review should still be implemented every two years if the auto alert facility is not used or for databases which do not offer an auto alert facility.

## 2. Guide to using the updating tool

### 2.1 Development of the updating tool

This updating tool has been developed building on existing empirical evidence on updating systematic reviews, guidance in the new *Cochrane Handbook for Systematic Reviews of Interventions* and RevMan 5 (Review Manager 2008), work undertaken by the Cochrane Updating Working Group, existing checklists from other agencies (including Cochrane Review Groups) and input from users and experts involved in updating systematic reviews. Experts who provided advice include: Paul Garner and Vittoria Lutje (Cochrane Infectious Diseases Group), Mathew Zacharias, Mike Bennett and Jane Cracknell (Cochrane Anaesthesia Group), Phil Wiffen (Cochrane Pain, Palliative and Supportive Care Group), Liz Paulsen and Andy Oxman (Cochrane Methodology Review Group), Martin Eccles (Cochrane Effective Practice and Organisational Care Group), Jane Clarke (Cochrane Menstrual Disorders and Subfertility Group), Sarah Hetrick (Depression, Anxiety and Neurosis Group), Sonja Henderson (Cochrane Pregnancy and Childbirth Group), Heather Maxwell (Cochrane Peripheral Vascular Diseases Group), Julian Higgins and Sally Green (Handbook Advisory Group), Nandi Siegfried (Cochrane HIV/AIDS Group), Alexander Tsertsvadze (Chalmers Research Group), Phil Alderson (National Institute for Health and Clinical Excellence), Ton Kuijpers and Jako Burgers (Dutch Institute for Healthcare), and Kaveh Shojania (Ottawa Health Research Institute).

### 2.2 Step 1: decision tree

Step 1 of the decision tree (see Appendix 1) is designed to help review authors consider possible triggers for updating and deciding whether or not to update their review or wait for a longer period of time. It is important that the (review team's) decision-making process about updating is transparent so that readers can gain a more complete understanding of the decision-making process regarding updating. However, the decision whether, and when to update, is ultimately down to the judgement of the review team and / or editorial team (depending on the individual Cochrane Review Group policy).

The most likely trigger for updating a Cochrane review is knowledge of the findings of a new study, however, other possible triggers, or combinations of triggers, might include the following:

- *New information*

For example, information about new treatment regimes, new population subgroups, harms, economic data, or outcome measures, including data from studies that were ongoing when the review was prepared previously or data that were missing at that time.

- *New methodology*

For example, new statistical techniques, or changes in the *Cochrane Handbook for Systematic Reviews of Interventions* or RevMan.

- *Response to feedback from users of the review*

- *Other factors*

For example, the age of the review or the imminent use of the review in policy decision-making or the development of clinical practice guidelines or both.

At this stage review authors must make a judgement on whether or not a trigger for updating is *likely* or *unlikely* to change the results or conclusions of a Cochrane review or both. This judgment may involve a degree of subjectivity and it is important that it involves all members of the review team and / or editorial team (depending on the individual Cochrane Review Group policy). Examples of different scenarios where a trigger, such as the identification of a new study, is *likely* and *unlikely* to change the conclusions of a Cochrane review are described below (also see Appendices 2 and 3). Whatever the decision, review authors should briefly describe the process they used. This will provide clarity and transparency for readers.

### **2.2.1 Trigger *unlikely* to change conclusions**

If a trigger is identified and it is deemed *unlikely* to change the conclusions of the Cochrane review, then the authors might decide not to update the review but undertake an amendment. For example, by including the identification of a new study in a Cochrane review whose effect estimate is already stable and highly statistically significant, unless it reports new outcomes or information about harms. In this case, the 'What's new' section of the review should be updated citing any new studies, if appropriate, and why these have not been included at this time. Details of any new studies should also be added to the 'Studies awaiting classification' section of the review. If appropriate, the description of the search methods in both the review's abstract and body of the text, and the search strategies listed in the Appendix should be revised to reflect any amendments to the original search methods and strategies used. Further examples of Cochrane reviews where the inclusion of new studies or information is *unlikely* to change the conclusions of a Cochrane review are given in Appendix 2.

### **2.2.2 Trigger *likely* to change conclusions**

Alternatively, if a trigger is identified which is *likely* to change the conclusions of a Cochrane review, the review should be updated. Examples of such triggers might include the following:

- New study with substantially different results and conclusions than the original Cochrane review.
- New study with a particularly large sample size (especially if the original Cochrane review has inconclusive results or contains only a small number of studies).
- New study with information about an important new comparison, population subgroup, outcome or harms not addressed by the studies in the original Cochrane review.
- New study with a methodological advance not addressed by the studies in the original Cochrane review (e.g. a review where previous studies were at high risk of bias due to problems with blinding, concealment of allocation, or some methodological issue unique to the topic area).

If a trigger is deemed likely to change the conclusions of a Cochrane review, the complete original search strategy should be re-run using at least the same databases, to ensure a systematic and comprehensive search of the literature. Further examples of Cochrane reviews where the inclusion of new studies or information is *likely* to change the conclusions of a Cochrane review are given in Appendix 3.

If the review authors expect that there will never be any further information that could change the findings of the review, this should be discussed with the editorial team and a decision can be made whether or not to mark this review in *The Cochrane Library* as "No longer being updated". This decision should be reported by the review authors.

### **2.3 Step 2: checklist**

If a review team decides that a trigger, for example a new study or information is *likely* to change the conclusions of their review, Step 2, in the form of a checklist, is designed to help them consider which sections of their Cochrane review require updating (see Appendix 4). The checklist aims to guide the review team step by step through the review process using questions or triggers, which may or may not lead to action and updating. The empirical evidence for this action is indicated, where available. We welcome reference to additional evidence to inform the use of the checklist items from review authors and others involved in helping to keep Cochrane reviews up to date.

We believe that to be used optimally the checklist should be completed by the review team for each review and indeed should be seen as an essential part of the review publication procedure (that is, included as part of the review report).

## **3. Validation of the updating tool**

### **3.1 In-house piloting of the updating tool**

During July 2007, we conducted an in-house pilot to test the validity and reliability of the updating tool in assessing the need and likely benefits of updating a Cochrane review. Ten Cochrane reviews from Issue 4, 2007 of *The Cochrane Library*, which had recently been updated, were selected at random: five had been categorised as major updates and five had been categorised as minor. Major indicated a substantive update (i.e. a review that the authors and Review Group wished to highlight as a review that should be read again by people who had read it before, usually because of a change in conclusions). One person (without knowledge of the updated review), used the updating tool to determine if the original version needed updating. The following search strategy was deployed:

- *Phase 1: PubMed 'related articles' feature:* using a subset of studies (e.g. three largest and three most recent) included in the original Cochrane review as 'seeds' to search for related articles; restricted to material added to the database since the date of the last search and

limited to study design (e.g. using the PubMed Clinical Queries option to select the ‘therapy’ category for randomized controlled trials).

If no potential new studies were identified then Phases 2 and 3 of the search strategy were deployed:

- *Phase 2: Citation tracking in Citation Indexes:* using the Science Citation Index to search for new studies that cite the original Cochrane review; restricted to material added to the database since the date of the last search.
- *Phase 3: Searching the Cochrane Review Group’s Specialized Register:* using a subject specific search.

The decision tree (see Appendix 1) was then used to determine possible triggers for updating. If a trigger, for example the availability of a new study, was deemed likely to change the conclusions of the review, the updating checklist (see Appendix 4) was used to help determine which sections of the review required updating. The original version of the review was then compared to the updated version to determine if the updating tool had been successful.

Using the decision tree, six of the ten reviews were deemed as not requiring updating and four should be updated (i.e. the addition of new evidence or new methods was likely to change the conclusions of the review). However, on checking the actual categorisation of the updated review (major or minor) one review had been determined as being a major update but this decision was not confirmed as only one additional study was located and the evidence was inconclusive. We believe the incorrect category had been determined by the review authors on submitting their review. Another review had been correctly determined as requiring an update but there was, in fact, no change in conclusions. Phase 1 of the search strategy picked up 100% of included studies (i.e. no further studies for inclusion were detected through Phase 2 or Phase 3) (Table 1).

Based on the findings of this small in-house pilot, the updating tool appears to be effective in determining whether updating should go ahead. Phase 1 of the search strategy may be sufficient to determine if there are new included studies, especially if there are difficulties getting access to citation tracking. However, Phases 2 and 3 do allow confirmation of Phase 1 and are, therefore, still included as a recommendation for monitoring the literature.

We recommend that two review authors independently read through titles and abstracts to ensure that no included studies are missed. The ‘Criteria for selecting studies for this review’ should also be used carefully to determine the inclusion of any potentially relevant studies, however, it can be hard to detect new data, outcomes or concerns if the review authors are not an expert on the subject. There may also be a problem assessing articles for inclusion because of vague comparison information provided in the review (e.g. “miscellaneous” in one review was not made explicit).

**Table 1: Success of the three different search strategy phases to locate new studies**

Name of Cochrane review	Phase 1	Phase 2	Phase 3	Tool	Updated review
Caesarean delivery for the second twin				Minor	Minor
Calcium antagonists as an add-on therapy for drug-resistant epilepsy				Minor	Minor
Prophylactic antibiotics for preventing early central venous catheter Gram positive infections in oncology patients	√			<b>Minor</b>	<b>Substantive</b>
Mobilisation strategies after hip fracture surgery in adults	√			Substantive	Substantive
Iron-chelating agents for treating malaria	√			Minor	Minor
Conservative management for postprostatectomy urinary incontinence	√			Substantive	Substantive
Cooling for newborns with hypoxic ischaemic encephalopathy	√			Substantive	Substantive
Vitamin A supplementation to prevent mortality and short and long-term morbidity in very low birthweight infants	√			Substantive	Substantive
Complementary and miscellaneous interventions for nocturnal enuresis in children				Minor	Minor
Interventions for asymptomatic retinal breaks and lattice degeneration for preventing retinal detachment				Minor	Minor

√ new studies found

### 3.2 Formal piloting of the updating tool

Following successful collaboration with many entities and input from Cochrane and non-Cochrane experts on updating, we have circulated the updating tool wider to eight Cochrane Review Groups and 14 review authors who have expressed an interest in pilot testing the decision tree and checklist. The following Cochrane Review Groups are participating in the formal pilot: Methodology Review Group, Effective Practice and Organisation of Care, Anaesthesia, Renal, Breast Cancer, Back, Consumers and Communication, and Oral Health.

Testers have been asked to use the updating tool whilst updating any Cochrane reviews in the coming months, telling us how the tool helped or hindered the process. Importantly, as this is part of the piloting process testers are asked to use the tool alongside and not instead of their normal updating process and not necessarily to use the decision tree to decide whether or not to update. Testers have been asked to complete a questionnaire about their experiences of using the tool which they have been asked to return once they have completed their update. We anticipate that the formal pilot will be finished in April 2009, but we may have to wait until July 2009 to receive all feedback from pilot testers updating reviews.

### 4. Dissemination of the updating tool

The initial findings for this project were presented at the Cochrane Colloquium in Freiburg (London 2008) in October this year, where the updating tool was well received and resulted in several more Cochrane Review Groups expressing an interest in piloting the tool.

Following the results of the formal pilot, and any refinement of the tool, we hope to enter into discussions with the Cochrane Editor-in-Chief, the Handbook Advisory Group and the Quality Advisory Group about the possibilities of suggesting changes to updating procedures and incorporating the tool into the *Cochrane Handbook for Systematic Reviews of Interventions*. If appropriate, we should also like to discuss ways of incorporating these recommendations into training programmes for systematic reviews run within The Cochrane Collaboration, such as the updating workshops run by the UK Cochrane Centre and Australasian Cochrane Centre. We will also seek to make the resources available electronically via the internet for review authors to download.

We also plan to make the updating tool available to agencies involved in the production of evidence synthesis, including the Expert Working Group on Updating Systematic Reviews (Thomas Chalmers Research Institute, Canada), the UK Health Technology Assessment Programme and the National Institute for Health and Clinical Excellence (UK) who have all given feedback during the development of the tool. Finally, we intend to publish the updating tool and the results of the formal pilot in a peer-reviewed journal.

In the longer term, further work is needed to develop this tool and to try to incorporate statistical techniques to identify when the addition of new studies is likely change the results of individual meta-analyses within Cochrane reviews. We are in discussion with Alex Sutton (Cochrane Statistical Methods Group) at the University of Leicester about the potential for incorporating a statistical updating prioritisation tool (Takwoingi 2008), which he and colleagues are developing, and which has been piloted by the Cochrane Infectious Diseases Group.

## **5. Conclusion**

The Cochrane Opportunities Fund has enabled this extremely important project to go ahead, which has resulted in the development of an updating tool to produce new methods to guide decisions of whether, and when, to update Cochrane Reviews. We anticipate that this will facilitate updating at the appropriate time and will minimise unnecessary updating. This should lead to improvements in the quality and reliability of healthcare decisions made on the basis of 'current' evidence.

## 6. References

Baum ML, Anish DS, Chalmers TC, Sacks HS, Smith H Jr, Fagerstrom RM. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. *New England Journal of Medicine* 1981; 305: 795-9.

Barrowman NJ, Fang M, Sampson M, Moher D. Identifying null meta-analyses that are ripe for updating. *BMC Medical Research Methodology* 2003; 3: 13.

Bergeroff K, Ebrahim S, Paletta G. Do we need to consider "in process" citations for search strategies? 12<sup>th</sup> Cochrane Colloquium; 2004 Oct 2-6; Ottawa, Ontario, Canada: 179-80.

Berkey CS, Mosteller F, Lau J, Antman EM. Uncertainty of the time of first significance in random effects cumulative meta-analysis. *Controlled Clinical Trials* 1996; 17: 357-71.

Cochrane Infectious Diseases Group Review Update Checklist. [www.liv.ac.uk/evidence/CIDG/checklist-review-update.doc](http://www.liv.ac.uk/evidence/CIDG/checklist-review-update.doc) (accessed 17 September 2007).

Cochrane Consumers and Communication Review Group Resources Authors' Resource Pack D: Updating stage. [www.latrobe.edu.au/cochrane/assets/downloads/AuthorGuideUpdate.doc](http://www.latrobe.edu.au/cochrane/assets/downloads/AuthorGuideUpdate.doc) (accessed 18 October 2007).

Cochrane Pain, Palliative and Supportive Care Group. Information to help review authors update their Cochrane review [updated January 2008].

French SD, McDonald S, McKenzie JE, Green SE. Investing in updating: how do conclusions change when Cochrane systematic reviews are updated? *BMC Medical Research Methodology* 2005; 5: 33.

Higgins JPT, Green S, Scholten RJPM. Chapter 3: Maintaining reviews: updates, amendments and feedback. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1 (updated September 2008). The Cochrane Collaboration, 2008. Available from [www.cochrane-handbook.org](http://www.cochrane-handbook.org).

Hopewell S, Clarke MJ, Stewart L, Tierney J. Time to publication for results of clinical trials. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: MR000011. DOI: 10.1002/14651858.MR000011.pub2.

Ioannidis JP, Contopoulos-Ioannidis DG, Lau J. Recursive cumulative meta-analysis: a diagnostic for the evolution of total randomized evidence from group and individual patient data. *Journal of Clinical Epidemiology* 1999; 52: 281-91.

Ioannidis J, Lau J. Evolution of treatment effects over time: empirical insight from recursive cumulative metaanalyses. *Proceedings of the National Academy of Sciences* 2001; 98: 831-6

Lau J, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers TC. Cumulative meta-analysis of therapeutic trials for myocardial infarction. *New England Journal of Medicine* 1992; 327: 248-54.

Lau J, Schmid CH, Chalmers TC. Cumulative meta-analysis of clinical trials builds evidence for exemplary medical care. *Journal of Clinical Epidemiology* 1995; 48: 45-57.

Linde K. Updating systematic reviews. *Explore* 2006; 2: 363-4.

Loudon K, Hopewell S, Clarke M, Moher D, French S, Scholten R, Eisinga A. Development of a decision tool for updating Cochrane reviews [abstract]. *16<sup>th</sup> Cochrane Colloquium "Evidence in the era of globalisation"*; 2008 Oct 3-7; Freiburg, Germany. *Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen* 2008; 102 (Suppl VI): 24-5.

Middleton P. Life cycle of Cochrane reviews. *Chinese Journal of Evidence-Based Medicine* 2004; 4 (7): 488-92.

Moher D, Tsertsvadze A. Systematic reviews: when is an update an update? *Lancet* 2006; 367: 881-3.

Moher D, Tsertsvadze A, Tricco AC, Eccles M, Grimshaw J, Sampson M, et al. A systematic review identified few methods and strategies describing when and how to update systematic reviews. *Journal of Clinical Epidemiology* 2007; 60: 1095-104.

Montori VM, Devereaux PJ, Adhikari NK, Burns KE, Eggert CH, Briel M, et al. Randomized trials stopped early for benefit: a systematic review. *JAMA* 2005; 294: 2203-9.

Mullen B, Muellerleile P, Bryant B. Cumulative meta-analysis: a consideration of indicators of sufficiency and stability. *Personality and Social Psychology Bulletin* 2001; 27: 1140-62.

Pogue JM, Yusuf S. Cumulating evidence from randomized trials: utilizing sequential monitoring boundaries for cumulative meta-analysis. *Controlled Clinical Trials* 1997;18: 580-93.

Review Manager (RevMan) [computer program]. Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Sampson M, Shojania KG, McGowan J, Daniel R, Rader T, Iansavichene AE, et al. Surveillance search techniques identified the need to update systematic reviews. *Journal of Clinical Epidemiology* 2008; 61: 755-62.

Shekelle PG, Ortiz E, Rhodes S, Morton SC, Eccles MP, Grimshaw JM, et al. Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated? *JAMA* 2001; 286: 1461-7.

Shojania KG, Sampson M, Ansari MT, Jun J, Doucette S, Moher D. Updating Systematic Reviews. Rockville (MD): Agency for Healthcare Research and Quality; 2007 Sep. Technical Review No. 16. (Prepared by the University of Ottawa Evidence-based Practice Centre under Contract No. 290-02-0017.) AHRQ Publication No. 07-0087.

Stead LF, Lancaster T, Silagy CA. Updating a systematic review - what difference did it make? Case study of nicotine replacement therapy. *BMC Medical Research Methodology* 2001; 1: 10.

Takwoingi Y, Sutton AJ, Donegan S, Garner P, Gamble C, Donald A. Prioritising the updating of systematic reviews [abstract]. *16<sup>th</sup> Cochrane Colloquium "Evidence in the era of globalisation"*; 2008 Oct 3-7; Freiburg, Germany. *Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen* 2008; 102 (Suppl VI): 93.

Tsertsvadze A, Moher D, Tricco A, Eccles M, Grimshaw J, Sampson M, et al. When and how to update systematic reviews: a methodological systematic review. *XIV Cochrane Colloquium*; 2006 Oct 23-26; Dublin, Ireland: 61.

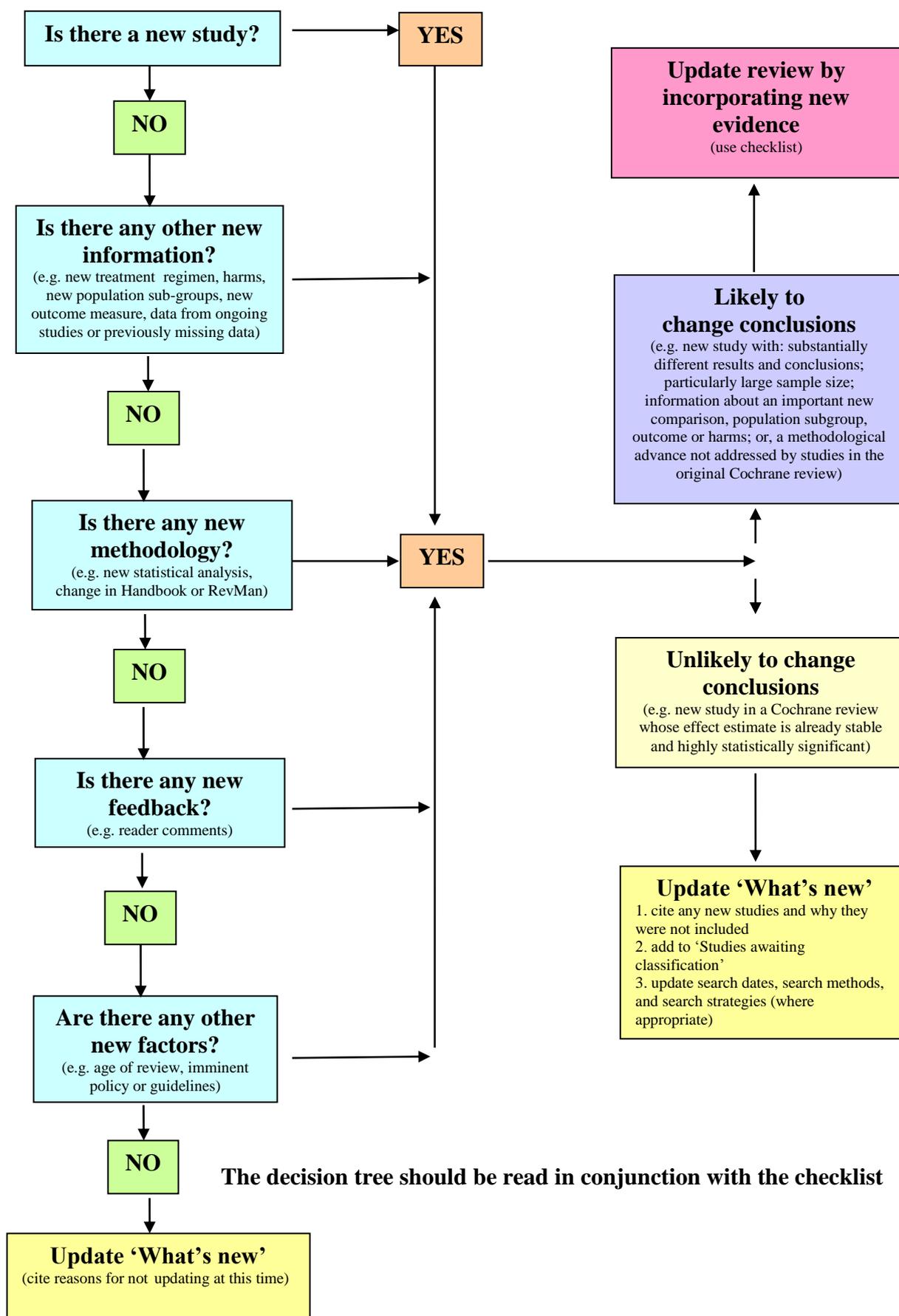
United States National Library of Medicine and the National Institutes of Health. National Library of Medicine (NLM) Annual MEDLINE/PubMed Year-End Processing Activities (YEP) [updated 09 Nov 2006] [www.nlm.nih.gov/bsd/policy/yep\\_activities.html](http://www.nlm.nih.gov/bsd/policy/yep_activities.html) (accessed 6 December 2007).

United States National Library of Medicine and the National Institutes of Health. Medical Subject Headings: Introduction to MeSH - 2008 [updated 1 November 2007] [www.nlm.nih.gov/mesh/introduction2008.html#changes](http://www.nlm.nih.gov/mesh/introduction2008.html#changes) (accessed 6 December 2007).

## **Acknowledgments**

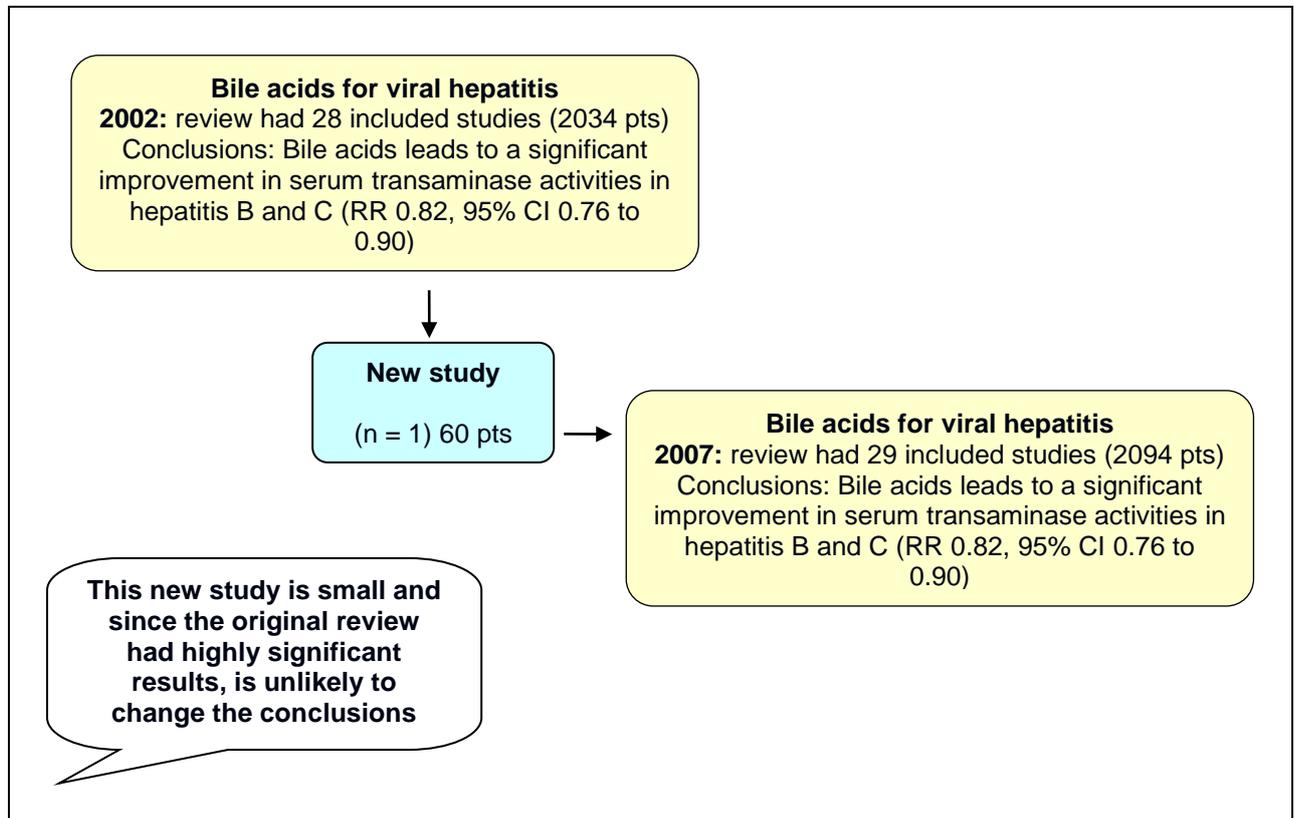
We should like to thank the following individuals for taking time to help us to develop this updating tool: Paul Garner, Mathew Zacharias, Phil Wiffen, Alexander Tsertsvadze, Jane Cracknell, Liz Paulsen, Phil Alderson, Martin Eccles, Jane Clarke, Sarah Hetrick, Andy Oxman, Vittoria Lutje, Ton Kuijpers, Jako Burgers, Kaveh Shojania, Sonja Henderson, Chantelle Garrity, and Heather Maxwell.

## Appendix 1 - Decision tree for whether, and when, to update a Cochrane review



## Appendix 2 - Example of trigger *unlikely* to change conclusions

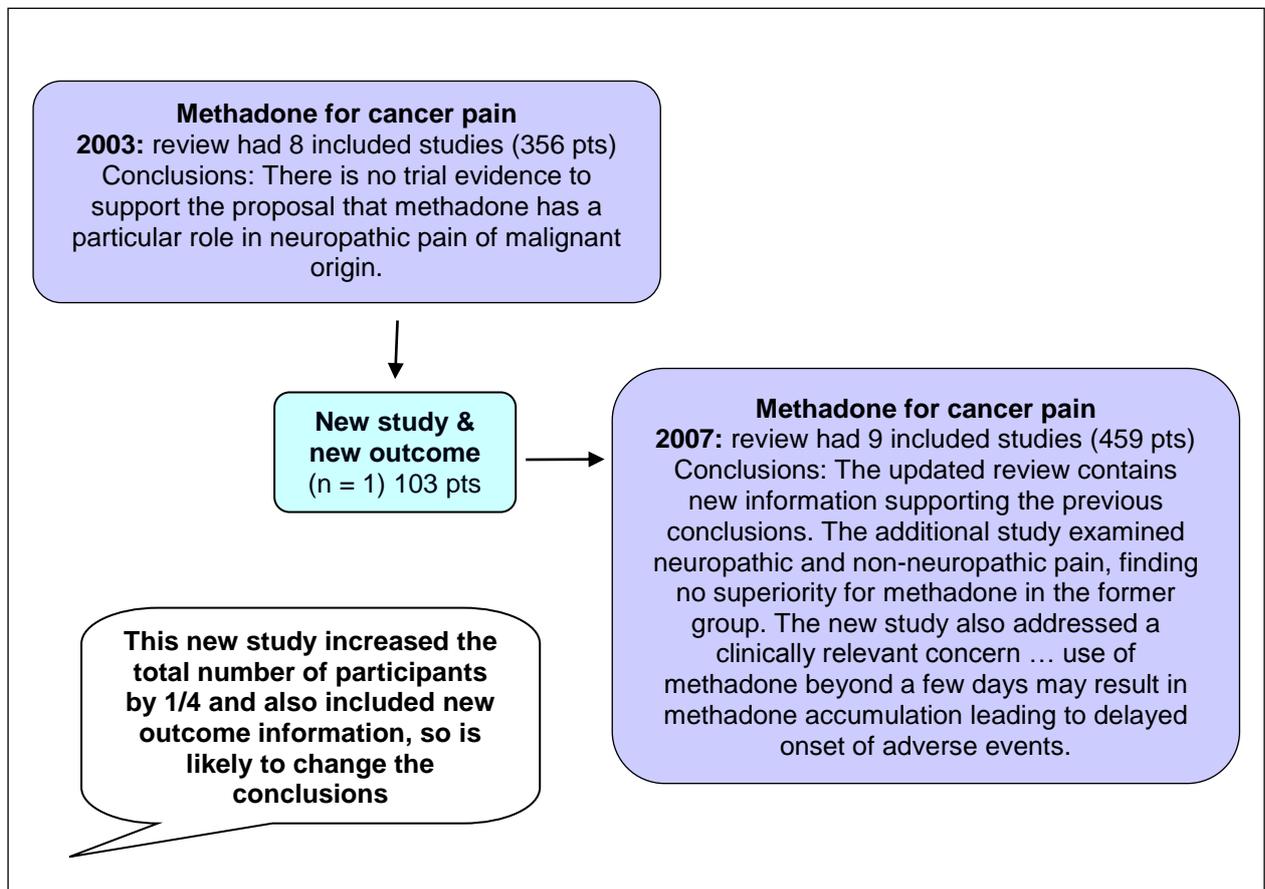
Example of a Cochrane review where the inclusion of new studies or evidence is *unlikely* to change the conclusions of a Cochrane review.



Chen W, Liu J, Gluud C. Bile acids for viral hepatitis. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD003181. DOI: 10.1002/14651858.CD003181.pub2.

### Appendix 3 - Example of trigger *likely* to change conclusions

Example of a Cochrane review where the inclusion of new studies or evidence is *likely* to change the conclusions of a Cochrane review.



Nicholson AB. Methadone for cancer pain. *Cochrane Database of Systematic Reviews* 2007, Issue 4. Art. No.: CD003971. DOI: 10.1002/14651858.CD003971.pub3.

## Appendix 4 - Checklist for updating a Cochrane review

It is recommended that the checklist should be completed by the review team for each review and indeed should be seen as an essential part of the updating review publication procedure.

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
1	Title	Is the review topic still relevant?	If no: do not update the review, merge it with another review, split the review. This should be discussed with the editorial team.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
2					
Review information					
2a	Authors	Are the review authors willing to update the review and do they have time to do so?  Is a new team of review authors needed to update the review?	If a new team of review authors will update the review, any original authors who are not involved in the update should be recorded in the 'Acknowledgements' section.	Cochrane Infectious Diseases Group Review Update Checklist 2007  Linde 2006	
2b	Contact person	Are details correct?	If no: revise or edit as necessary.	Cochrane Infectious Diseases Group Review Update Checklist 2007	
2c	Dates	Do any of the date fields in RevMan need updating?	If yes: edit field date review was last 'Assessed as Up to date', 'Date of Search' and 'Next Stage Expected'.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
2d	What's new section	Has anything new been added to the review? (e.g. new study, new evidence, response to feedback)	If yes: edit 'What's new' field. Select type of 'Event' and 'Description' of what new information has been added to the review e.g. state what has been done (for example, number of studies, participants or extra analyses) and any important changes to conclusions, results or methods of the review. Also insert 'Date'.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Cochrane Infectious Diseases Group Review Update Checklist 2007	
2e	History	Are previous 'What's new' included in this section?	If no: update as necessary.		
3	Abstract	Has review been updated and changed?	If yes: revise the abstract in accordance with changes to the review.  Include an introductory sentence in the Background saying: "This is an updated version of the original Cochrane review published in Issue X, YEAR."  In the Conclusions of the abstract include a sentence saying whether, since the last version of the review, any new studies have been found, if the conclusions have changed, and if the user should re-read the review.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Cochrane Pain, Palliative and Supportive Care Group. Information to help review authors update their Cochrane review 2008	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
4	Plain language summary	Has review been updated?	If yes: revise the summary in accordance with changes to the review.		
5	Background	Are there changes in policy and strategic practice that affect the context of the review?	If yes: revise this section to reflect the changes. Include an introductory sentence saying "This review is an update of a previously published review in The Cochrane Database of Systematic Reviews (Issue X, Year) on 'Title'".	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Cochrane Pain, Palliative and Supportive Care Group. Information to help review authors update their Cochrane review 2008	
6	Objectives	Is the research question still relevant? (e.g. is the intervention still used, has the treatment regime changed, has the health problem been eradicated)	If yes: revise objectives and state the rationale for the change in the 'What's new' section. If no: state this in the 'What's new' section and provide rationale for not updating. This should be discussed with the editorial team.	Cochrane Infectious Diseases Group Review Update Checklist 2007  Linde 2006	
7	Methods	Criteria for selecting studies for this review			
7a	Types of studies	Is the study design still appropriate? (e.g. the inclusion of non-randomized trials for harms)	If no: revise this section, modify the search strategies in the Appendix as necessary and provide the rationale for change.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Linde 2006	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
7b	Types of participants	Is the population still relevant? (e.g. has a study been published which opens up the original question to include all age ranges, less or more specific categories, people from developing countries)  Are important exclusions described?	If no: revise this section, then modify the search strategies in the Appendix as necessary and provide the rationale for change.	Linde 2006  Cochrane Consumers and Communication CRG Checklist 2007	
7c	Types of interventions	Is the intervention(s) still used, or have the treatment or drug comparisons changed?	If changes are needed: revise this section, include new comparisons, modify the search strategy as necessary and provide the rationale for change.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Linde 2006	
7d	Types of outcome measures	Is there evidence which includes important new outcome measures? (e.g. quality of life outcomes, harms, economic analysis)  Are important exclusions described?	If yes: revise this section, modify the search strategy as necessary and provide the rationale for change.	Cochrane Infectious Diseases Group Review Update Checklist 2007  Linde 2006  Cochrane Consumers and Communication CRG Checklist 2007	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
Search methods for identification					
7e	Search methods for identification of studies	Have any new studies been reported?	Rerun full search strategy every two years (if auto alerts are not used or in databases that do not offer an auto alert facility).	<p>These methods have been proposed as triggers for whether new studies have been published:</p> <ul style="list-style-type: none"> <li>• Auto Alerts via databases (i.e. automatic re-run of full search strategy every time new studies are entered into a database, search results automatically sent by e-mail)</li> <li>• Auto Alerts via journals (i.e. whenever a known relevant study in a journal is cited by others the citing references are automatically sent by e-mail)</li> <li>• PubMed 'related articles' feature (e.g using the three largest and three most recent studies included in the original Cochrane review as 'seeds' to search for related articles; restricted to material added to the database since the date of last search and limited to study design publication type (Sampson 2008))</li> </ul> <p>Citation tracking (e.g. using Science Citation Index or Scopus to search for new studies that cite the original Cochrane review; restricted to material added to the database since the date of last search (Sampson 2008))</p> <ul style="list-style-type: none"> <li>• Searching the CRG Specialized Register</li> </ul> <p>The terms in the search strategy should be checked regularly (annually in MEDLINE) for changes introduced by database producers and the strategy amended accordingly to ensure that the auto alerts are kept up to date.</p>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
				<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
		Is original search strategy suitable or does it need to be modified due to changes in criteria for selecting studies or terminology?	If yes: revise the details given for the search methods in the text of the review and for the search strategies in the Appendix.	National Library of Medicine makes changes to MeSH terms annually so may need to modify original search strategy (US National Library of Medicine 2006; US National Library of Medicine 2007)	
		Does the date of last search need updating?	If yes: revise the dates given for each database and other sources as necessary in the text of the review and the Appendix.  Report actual date of search, rather than simply the month and year.  A single date should be given in the 'Date of search' field to indicate when the most recent comprehensive update search was started	Specifying the date, not just month and publication year enables more complete retrieval of records thereby minimizing publication bias (Bergeroff 2004; Moher 2007). It is advisable to seek the guidance of the Trials Search Co-ordinator in selecting the best method to limit the search to the specific date when the search was last re-run for each database.  <i>Cochrane Handbook for Systematic Reviews of Interventions Chapter 3: Section 3.3.3</i>	
<b>Data collection and analysis</b>					
7f	Data collection and analysis	Systematic review methods are susceptible to change based on the findings of methodological research and other developments.  Are the systematic review methods used in the original review still appropriate?	Check <i>RevMan</i> and the <i>Cochrane Handbook</i> to see if there have been changes since the review was last published. If there have been changes, the review authors might wish to revise this section.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>  Linde 2006	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
8	Results				
8a	Description of studies	Have any additional included, excluded or ongoing studies been identified?	If yes: revise accordingly.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
8b	Risk of bias in included studies	Are the methods of assessing methodological quality used in the original review still appropriate? (e.g. the introduction of the new 'Risk of Bias' table)	If no: revise accordingly.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
8c	Effects of interventions	<i>Qualitative analysis</i>  If it was not possible to conduct a meta-analysis, does the addition of new studies change the results in some way?	If yes: describe any changes qualitatively.	Shojania 2007	
		<i>Quantitative analysis</i>  If conducting a meta-analysis, does the addition of new studies change the statistical significance of the results?	If yes: revise accordingly.	There are several statistical methods, using cumulative meta-analysis (CMA), for identifying whether the addition of new studies will change the results of a meta-analysis. Currently no particular tool is recommended, further research is needed (Moher 2007). <ul style="list-style-type: none"> <li>Identifying "null" meta-analysis ripe for updating. A formula based on the number of participants in new included study (Barrowman 2003).</li> <li>Conventional CMA (Baum 1981; Lau 1992; Lau 1995; Berkey 1996; Moher 2007). CMA using the cumulative slope as an indicator of stability. The smaller the magnitude of the slope of the regression line, the greater the confidence that the pooled effect size is becoming stable, suggesting no need for further updating</li> </ul>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
				(Mullen 2001). <ul style="list-style-type: none"> <li>• CMA using sequential monitoring boundaries. Calculating prospectively the amount of additional information needed to determine whether or not to update (Pogue and Yusef 1997).</li> <li>• Recursive CMA (Ioannidis 1999; Ioannidis and Lau 2001; Moher 2007).</li> </ul>	
				Several other quantitative methods have been proposed as triggers for updating: <ul style="list-style-type: none"> <li>• If the sample size of the new study is three times as large as the largest previously published trial (Shojania 2007).</li> <li>• If the relative change in effect magnitude is at least 50% involving one of the primary outcomes of the original review or any mortality outcome (Shojania 2007).</li> </ul>	
9	Discussion	Are there changes in other sections of the review which should be reflected in the discussion?	If yes: revise in light of the new findings.		
10	Authors' conclusions	Are there changes in other sections of the review which should be reflected in the conclusions?	If yes: revise in light of the new findings.	An increase in precision (narrower confidence interval) and change in statistical significance is predictive for changing conclusion of a review (French 2005).	
11	Acknowledgements	Are there new review authors?	If yes: add these and acknowledge the contributions of any previous review authors who have been removed from the by-line.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
12	Contributions of authors	Have there been any changes to the contributions of authors during the update?	If yes: edit the contributions section of the review.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i> Cochrane Infectious Diseases Group Review Update Checklist 2007	
13	Declarations of interest	Are there any changes in conflict of interest?	If yes: include additional information.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
14	Difference between protocol and review	Are there any changes between the original protocol and the updated review?	If yes: include additional information.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
15	Published notes	Are there important editorial changes that should be documented?	If yes: make the necessary changes. (For example, a review might have been suspended, withdrawn, or merged).	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
16	Characteristics of included studies table	Have new included studies been added?	If yes: add details of these to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
17	Characteristics of excluded studies table	Have new excluded studies been identified?	If yes: add details of these to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
18	Risk of bias table	Have new included studies been added?	If yes: add details of these to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
19	Characteristics of ongoing studies table	Have new ongoing studies been identified?	If yes: add details of these to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
20	Summary of findings table	Have new included studies been added?	If yes: add details of these to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
21	Additional tables	Has new data (from new included studies or other sources as relevant) been identified?	If yes: add the data to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
22	References to studies	Are there any additional ongoing trials or trials awaiting assessment, or has a version of the review been published elsewhere?	If yes: add the relevant references. (Knowing when an ongoing trial is due to end may trigger the need for next updating the review.)		
23	Data and analyses	Has data from new included studies been identified?	If yes: add the data to this table.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
24	Figures	Have new included studies been added?	If yes: add details as appropriate.		
25	Sources of support	Are there any changes in sources of support?	If yes: include additional information.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	
26	Feedback	Has there been any feedback (or comments and criticism) on the review?	If yes: address the issue(s) as appropriate.	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	

Number	Section of review	Question / trigger	Updating Action	Source of advice, guidance or evidence	Tick if item updated
27	Appendices	Have new search strategies been required to cover changes to types of participants, interventions, outcomes etc? Or as a result of changes to database subject headings introduced by database providers?	If yes: copy and paste full search strategies as implemented for each database searched, together with the line numbers for each search set, in an appendix to the review	<i>Cochrane Handbook for Systematic Reviews of Interventions</i>	

