

Draft minutes GRADE working group meeting Barcelona

Barcelona, October 30, 2003

Present: Pablo Alonso, David Atkins, Malgorzata Bala, Denise Campbell, Jonathan Craig, Inday Dans, Tony Dans, Ben Djulbegovic, Yngve Falck, Cindy Farquhar, Signe Flottrop, Paul Glasziou, Gordon Guyatt, Margaret Haugh, Mark Helfand, Suzanne Hill, Gillian Leng, Wiktorina Lesniak, Anne Lethaby, Alessandro Liberati, Nicola Magrini, Merce Marzo, James Mason, Susan Norris, Wytze Oosterhuis, Andy Oxman, Vivian Robinson, Holger Schunemann, Peter Tugwell, Helena Varonen, Gunn Vist

Regrets: Peter Briss, Martin Eccles, Francoise Cluzeau, Dianne O'Connell, Robin Harbor, David Henry, Andrea Horvath, Robert Phillips, Haruko Shimamura, Tessa Tan-Torres, John Williams,

1. Conduct of the meetings

To allow continued progress while accommodating people who have not attended previous meetings it was agreed that discussions from previous meetings will not be revisited unless new arguments are brought forward. When previously discussed issues are raised these will be tabled until after the person raising the issue has the opportunity to discuss it with someone who participated in the earlier discussion. If they find that there are new arguments, the issue can then be added to the agenda.

2. The minutes from Krakow were approved without further comment.

3. Including balance sheets in Cochrane reviews

During the GRADE workshop on 28 October it was pointed out that the table with instructions for grading the quality of evidence needs improvement. Its current form does not accommodate 'poisoning fatalities' in the SSRI examples that was used as the workshop example (both serious flaws and strong association of observational study). Sue H volunteered to make a new suggestion for the table before next meeting. Ben D suggested not using 'some' in 'some uncertainty' about the directness in the evidence summary, which he found confusing.

Action: Sue Hill

The meeting at the Cochrane Colloquium on 29 October was successful. There was nearly unanimous agreement among those who attended the meeting that Cochrane reviews should include balance sheets. Tony D disagreed based on the opinion that balance sheets should be prepared locally rather than in the context of a Cochrane review. Andy O's presentation and Paul G's summary of the meeting are attached. Tony D will look for examples where including a balance sheet in a Cochrane review would pose a problem..

Action: Tony Dans

It was agreed that it is necessary to specify the population of interest for the question. When reliable data are available different balance sheets should be prepared for different populations within a review. The population of interest needs to be clearly labeled in balance sheets.

It is possible that some Cochrane reviews may require a number of different balance sheets for different populations and settings, or an interactive balance sheet that allows users to specify population or setting characteristics. This might result in many empty cells because important information will often be lacking. However, this makes the lack of important information clear and it may help to prompt reviewers or others to seek this information.

It was suggested that the term 'balance sheet' is associated with costs and may be confusing. The following suggestions were offered. These will be considered at the next meeting along with any other suggestions that are offered.

- Clinical balance sheet
- Considered judgement form/table
- Evidence table
- Benefits/harms table
- Clinical impact table
- Clinical balance table
- Cost and consequences
- Evidence profile
- GRADE table

The following agreed to prepare one or more examples of balance sheets that could be included in a Cochrane review:

<u>Group</u>	<u>Contact/volunteer</u>
ARI	Paul Glasziou (Editor)
Back	Victoria Pennick (Co-ordinator) Lex Bouter (Co-ordinating Editor)
Breast Cancer	Merce Marzo (reviewer) Centro Iberoamericano Pablo Alonso Coello (reviewer)
EPOC	Andy Oxman (editor)
Menstrual disorders	Cindy Farquhar (Co-ordinating Editor)
Musculoskeletal	Vivian Robinson (reviewer) Peter Tugwell (Co-ordinating Editor)
Renal	Jonathan Craig (Co-ordinating Editor)

Paul G and Andy O volunteered to coordinate this work.

Action: Paul Glasziou, Andy Oxman

4. Examples of evidence summaries, balance sheets and judgments

- Valve anticoagulation (observational evidence)

It was agreed that when there is high quality randomised evidence for a similar population (with some uncertainty about directness) and a consistent strong association with no plausible confounders, as in this example, this constitutes strong evidence.

The timeframe for outcomes needs to be included in GRADE tables.

The baseline risk of bleeding was missing from the balance sheet. The inconvenience of anticoagulation was considered as a potentially important consequence and should perhaps be included in the balance sheet.

It was agreed that the absolute effect should be presented as the risk difference (number of events per 100 or 1000) rather than as NNT's and NNH's.

Gordon G and Holger S will edit this example.

Action: Gordon G, Holger S

Gunn V and Andy O will make the relevant changes in other GRADE documents.

Paul G suggested that there is a simulation study that provides a basis for considering relative risks between 2 and 10 as strong and over 10 as very strong, based on the likelihood of confounding explaining the relationship: Bross I. Pertinency of an Extraneous Variable. J Chron Dis, 1967: 487-95. Bross has a nice table on p490 on what could be explained, and says in the conclusions: "Only an occasional variable will be as large as 2 and the chance of a larger variable diminishes rapidly ... a value of 9 would be extremely unlikely." But he uses a working rule of an RR of 5 for a single cutoff point. We will revisit this after the Bross article is circulated.

Action: Gunn G

- Colon cancer screening (diagnostic test accuracy)

This example was too complicated. It was agreed that only pair wise comparisons should be considered in GRADE tables. This example will be redone to only include FOBT versus Colonoscopy. It was suggested to label false negatives and false positives with the consequences of these. It was debated whether it would be better to use modeling to estimate the consequences of false negatives and false positives without reaching agreement. It was agreed that a cross-sectional study can be appropriate for evaluating test accuracy and that when such evidence is considered appropriate, the quality of the evidence should not be lowered based on study design (i.e. observational studies could start out as high quality evidence). This needs to be clearly labeled in evidence summaries and explained in instructions for grading evidence of test accuracy.

It has been difficult to find good examples of evidence of test accuracy for which there is sufficient information to prepare evidence summaries and balance sheets. Everyone was requested to send systematic reviews of test accuracy that could be used to Gunn, or better yet, to prepare evidence summaries and balance sheets.

Action: All

- Licensing of retailers of tobacco (costs)

We agreed that the quality of evidence was very low for all of the outcomes, all of the outcomes were considered critical to the recommendation, the overall quality of evidence was very low and there were uncertain net benefits. The majority voted for 'no recommendation'. Andy O voted for 'Do it' as all the costs can be put on private costs and he did not see any harms or 'Evaluate it', which would be consistent with the majority.

There was agreement that disaggregated costs or resource utilization should be included for important costs only. It was agreed that the quality of evidence for disaggregated costs or resource utilisation should be judged similarly to judgments of other consequences. It was suggested that we should confer with the Cochrane Economics Methods Group regarding appropriate study designs and quality criteria for assessing the quality of evidence for costs.

Action: Andy

5. Observational studies and harm

Possible situations where there is consistent observational evidence of no effect were discussed. Examples might be rare serious adverse effects of vaccines that are postulated or connective tissue disease from breast implants. It was agreed that consistent observational evidence of little or no effect with narrow confidence intervals and no plausible confounders could potentially be considered moderate quality evidence for harms. We need some examples to examine before finalizing this.

Action: All

We discussed situations when a new drug is compared to an old drug for which there is much more experience and evidence documenting its safety. Possibilities for grading the quality of the evidence for safety in such situations that were considered included:

- Leave it up to the panel to decide (?)
- Make separate judgments for the old and new drug (e.g. high for the old and low for the new)
- Judge the quality of evidence for the comparative safety of the two drugs to be low (based on low quality evidence for safety for the new drug)
- Judge the quality of evidence for the comparative safety of the two drugs to be high (based on the high quality evidence for safety for the old drug)

We did not reach agreement on how to handle situations such as this. We need some examples to work through. David A suggested that statins and cancer might be an example.

Action: David A, Sue H, Peter T, All

6. Diagnostic tests

This will be discussed further pending some better examples to work through.

Action: All

7. Costs

More examples are needed.

Action: All

8. Equity

Andy presented suggestions for how to take account of equity in grading evidence and recommendations from discussion at a WHO workshop in September. Tony and Inday distributed an example where equity is an issue. "Can long-term reduction or modification of dietary fat prevent cardiovascular disease?" with evidence summaries and balance sheets for both the 'general population (similar to trial populations)' and a disadvantaged population. In this example the balance sheets were clearly affected by the different baseline risks in the two populations.

Tony volunteered to prepare more examples where equity is an important consideration. It was recognized that considerations of equity in this context simply represent taking into

account specific conditions for a disadvantaged population. Nonetheless, it was considered important to highlight these considerations. Inday, Tony, Peter, Vivian et al will prepare a document for circulation describing equity considerations.

Tony, Inday, Peter, Vivian et al.

9. BMJ article

David Henry and Andy are revising the article. Some decisions subsequent to the submitted draft should be considered in the revision, such as revising the table to clarify judgments about the quality of observational evidence. It was suggested to change the wording of the GRADE recommendations from Do it to, for example, Offer it or Recommended and Strongly recommended. This will be discussed further at future meetings.

10. Next meeting

We ran out of time and the following items on the agenda were not discussed:

- Other articles
- Reliability and sensibility study
- Presentation study
- Future meetings
- Review key decisions and action items

Next meeting: Birmingham 30th November and 1st December 2003.

11. Other business

Holger suggested that we should consider having a website. He will prepare a suggestion for the website.

Action: Holger