



Editorial considerations for reviews that compare multiple interventions

Saïd Business School, Oxford, UK

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Handout E2

The Current Situation with Cochrane Overviews

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Objectives for this session

- Review some history
 - the Comparing Multiple Interventions Methods Group
 - Guidance for Overview authors
- Approaches taken in the first 10 published Cochrane Overviews
 - Search
 - Analysis/Synthesis
 - Indirect comparisons
- Learn from your experiences to date
- Identify your burning questions

What exactly are Cochrane Overviews?

- Possible answers (all different)
 1. What the Handbook suggests they should be
 2. What subsequent guidance from the CMIMG suggests they should be
 3. What actual Overviews in The Cochrane Library look like
- What should be the new guidance for the next revision of the Handbook?

2008 - Chapter 22 of the Handbook

- **Key characteristic of an Overview**
 - Reviews rather than trials are the focus of analysis & the target of search.
 - Authors discouraged from searching for or examining trials
- **Primary purpose of Cochrane Overviews**
 - To summarize evidence from more than one systematic review of **different interventions** for the same condition or problem.
- ***Misconception***
 - *Any review that compares interventions must use the Overview format*

Handbook - Some Overviews might not compare different interventions

- Different outcomes of a single intervention
 - E.g. Hormone Replacement Therapy
- Different conditions, problems, or populations
 - E.g. – Aspirin to prevent stroke after ...
- Adverse effects of an intervention used for more than one condition.
 - NSAIDs for rheumatoid arthritis or osteoarthritis

These other uses for Overviews are still valid, but today's discussion will focus on comparing interventions

Handbook – Indirect comparisons

- Not dealt with in depth
 - “may include meta-analyses across reviews to provide indirect comparisons of the effects of different interventions on a given outcome”
 - “seek appropriate statistical and methodological support”
- Informal indirect comparisons subtly encouraged
 - “Authors should be cautious when comparing absolute effects across reviews if there are differences in control group risks ”

Pharmacological interventions for alcohol withdrawal

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Treatments versus Placebo				
Alcohol withdrawal seizures - Benzodiazepine objective Follow-up: mean 10 days	Study population		RR 0.16 (0.04 to 0.69)	324 (3 studies)	■■■■ moderate ¹	
	80 per 1000	13 per 1000 (3 to 55)				
	Medium risk population					
	69 per 1000	11 per 1000 (3 to 48)				
Alcohol withdrawal seizures - Anticonvulsants objective Follow-up: mean 10 days	Study population		RR 0.52 (0.25 to 1.07)	1108 (10 studies)	■■■■ moderate ²	
	101 per 1000	53 per 1000 (25 to 108)				
	Medium risk population					
	150 per 1000	78 per 1000 (38 to 161)				
Adverse events - Benzodiazepine subjective Follow-up: mean 10 days	Study population		RR 3.28 (0.31 to 34.52)	71 (2 studies)	■■■■ moderate ³	
	28 per 1000	92 per 1000 (9 to 967)				
	Medium risk population					
	46 per 1000	151 per 1000 (14 to 1000)				
Adverse events - Anticonvulsant subjective Follow-up: mean 10 days	Study population		RR 1.56 (0.74 to 3.31)	663 (7 studies)	■■■■ moderate ⁴	
	50 per 1000	78 per 1000 (37 to 165)				
	Medium risk population					
	34 per 1000	53 per 1000 (25 to 113)				

Handbook – Primary Overview purpose was comparison of multiple interventions

- Attractive because
 - Might provide a way to “lump”
 - Potentially reader friendly
- Some problems flagged for later development
 - Out of date reviews
 - Key interventions with no Cochrane Review
 - Reviews with varying approaches to populations, comparators, or outcomes
 - Trials included in more than one review
 - Multi-arm trials
 - Updating

2010 - Comparing Multiple Interventions

Methods Group

- Continued development of network meta-analysis methods
 - Formal statistical approaches to comparing interventions
 - Which treatment is most effective, has fewest adverse effects?
 - Reader friendly (if not necessarily author friendly)
- How should NMA be used in Cochrane Reviews?
 - Of all sorts, not just Overviews
- How do Overviews and NMA fit together?
- Willing to assist CRGs with individual Overviews or NMAs

Overviews and NMA

Can this marriage be saved?

- Handbook Chapter 22
 - Overview authors should look at Reviews, not at trials
- NMA – Trials are ***really important***
 - Individual trial data used in the analysis
 - use of summary statistics from a meta-analysis may be possible in some instances
 - Conditions and assumptions to be met before including a trial in the analysis
 - Would the trial descriptions in reviews be detailed enough to assess this?

CMIMG – 2011 Milan Meeting

Evolution of Cochrane Intervention Reviews and Overviews of Reviews to better accommodate comparisons among multiple interventions

- 5 Co-ordinating Editors
- 1 Managing Editor
- 1 Trials Search Coordinator
- 1 Field Convener
- 1 Centre Director
- Authors of Overviews and Intervention Reviews
- The Editor in Chief.

2011 Milan meeting – Recommendations

Which we have now revised!!!

- ~~• Encouraged use of NMA in both Intervention Reviews & Overviews~~
- ~~• A recommendation to include trials in Overviews~~
- ~~• Hybrid approach to search~~
 - ~~— Start with reviews~~
 - ~~— Update if needed~~
 - ~~— Find trials for missing interventions~~
- ~~• Synthesis~~
 - ~~— Might include both trials and reviews~~
- A sequential process from Overview to Intervention Review

2012 - Paris meeting

- The meeting
 - Open meeting – 26 people + 6 CMIMG co-convenors
 - Lively half-day discussion
 - Informed by a discussion among the Co-Eds earlier that week

The message

- A clear message that the Milan recommendations were confusing & needed rethinking

The follow-up

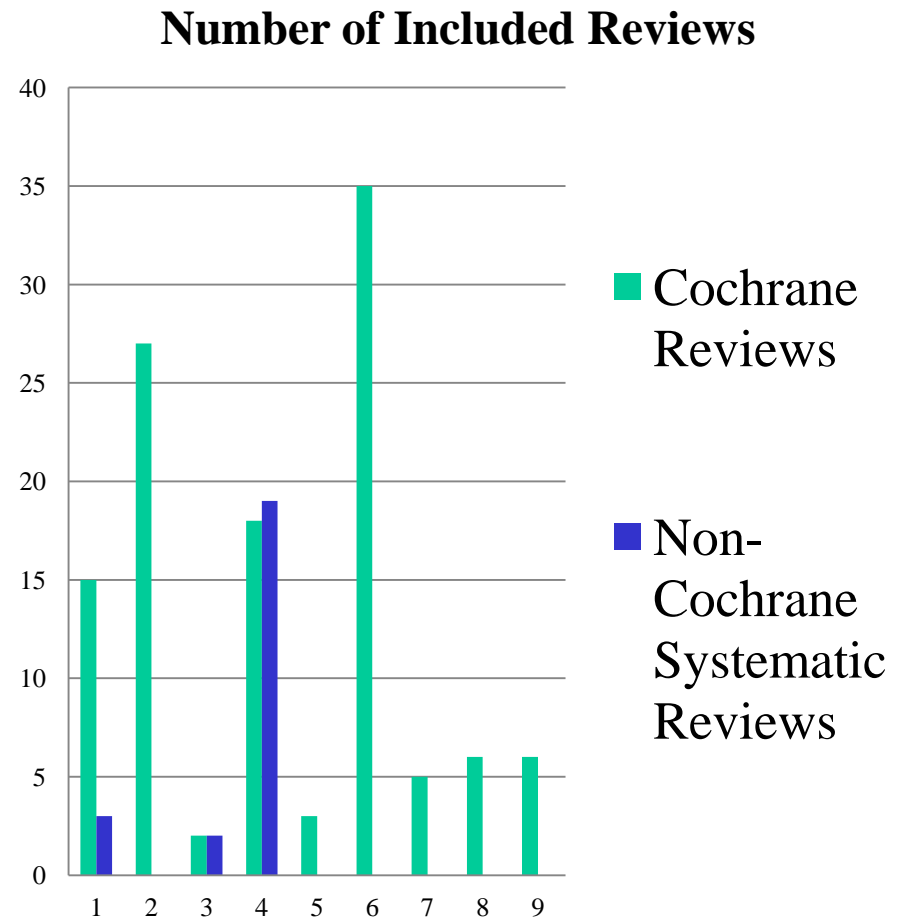
- CMIMG discussion leading to the current paper
- Also being considered by Methods Exec, MARS and Coeds
- New Handbook guidance planned

2013 – Oxford Meeting

- Coordinating Editors
 - Recommended a new review type clearly distinguishable from Overviews or Intervention Reviews
 - Not sure what we'll call these
 - “NMA Reviews” for our discussions today
 - OK to have overlap between NMA reviews & Intervention Reviews
- MARS & Methods Exec
- All of you
 - Recommendations and suggestions for the CMIMG as we prepare new handbook guidance

Ten Published Cochrane Overviews

- Approaches to search
 - Cochrane Reviews only
 - 4 Overviews
 - Cochrane and non-Cochrane reviews
 - 3 Overviews
 - Cochrane Reviews with updating search
 - 1 Overview
 - Trials only
 - 1 Overview



Ten Published Cochrane Overviews

- Approaches to analysis
 - Direct comparisons only
 - 1 Overview

Surgical Approaches to Cholecystectomy

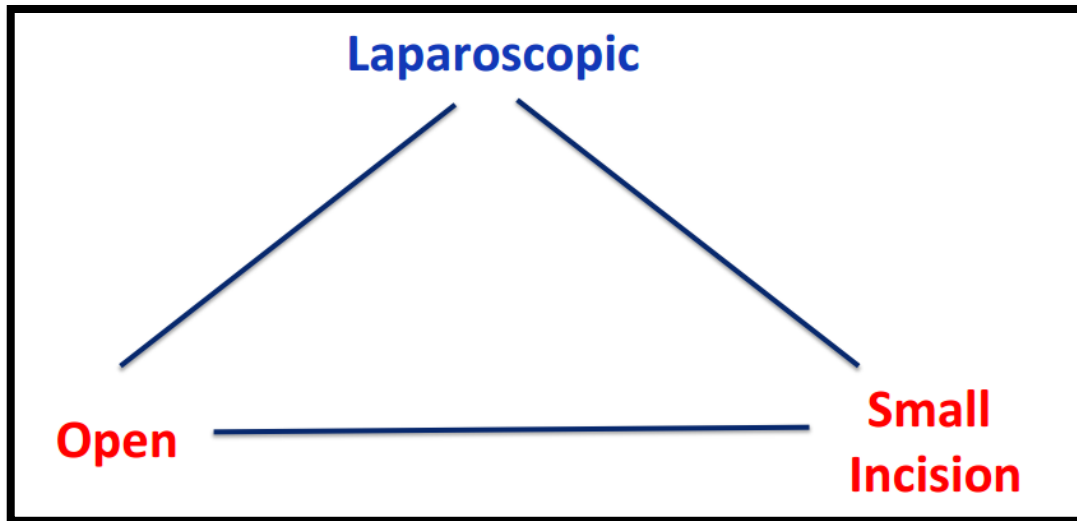


Table 5. Summary of Findings table: OC vs SIC

Table 6. Summary of Findings table: OC vs LC

Table 7. Summary of Findings table: LC vs SIC

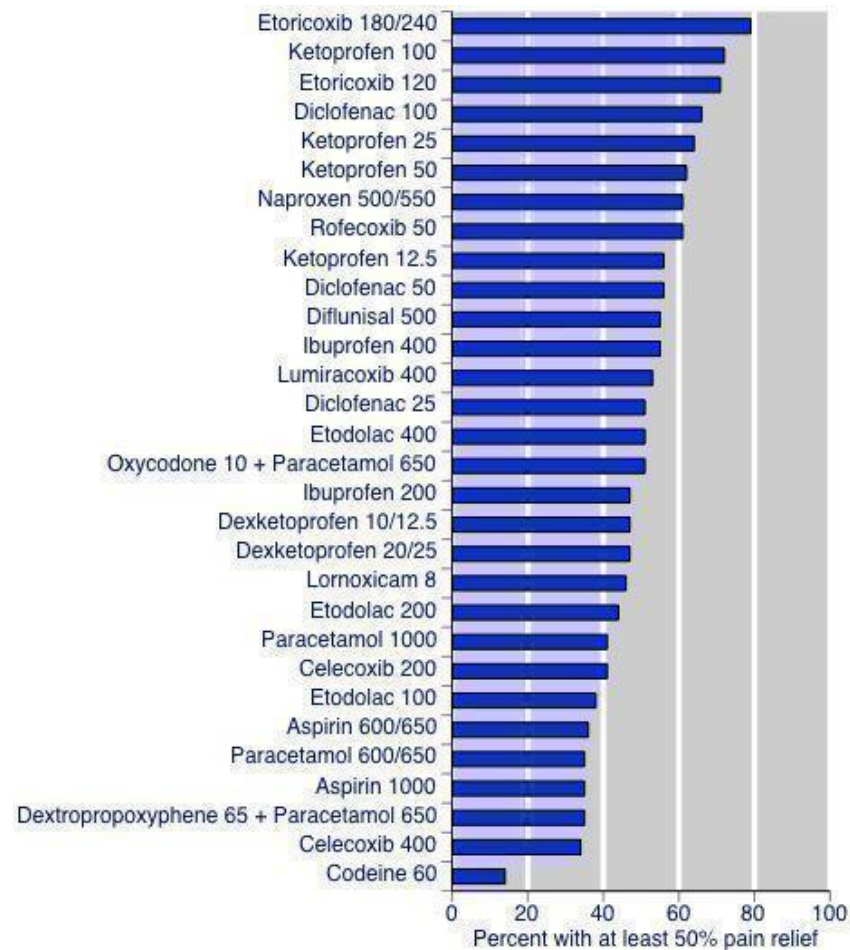
Ten Published Cochrane Overviews

- Approaches to analysis
 - Direct comparisons only
 - 1 Overview
 - Formal statistical indirect comparisons
 - 3 Overviews

Ten Published Cochrane Overviews

- Approaches to analysis
 - Direct comparisons only
 - 1 Overview
 - Formal statistical indirect comparisons
 - 3 Overviews
 - “Informal” indirect comparisons
 - 2 Overviews

Single dose oral analgesics for acute postoperative pain in adults



Ten Published Cochrane Overviews

- Approaches to analysis
 - Direct comparisons only
 - 1 Overview
 - Formal statistical indirect comparisons
 - 3 Overviews
 - “Informal” indirect comparisons
 - 2 Overviews
 - Evidence map
 - 4 Overviews

Effectiveness of financial incentives

- Outcomes of interest
 - Healthcare professional behavior
 - Patient outcomes
- Reviews included
 - 2 Cochrane reviews
 - 2 non-Cochrane reviews

A Priori Classification of Types of Incentives

- **Payment for working for a specified time period** (e.g. salary, sessional payment)
- **Payment for each service/episode/visit** (fee-for-service)
- **Payment for providing care for a patient or specific population** (e.g. capitation)
- **Payment for providing a pre-specified level or change in activity or quality of care** (e.g. includes target payments, bonuses)
- **Mixed and other** (comprising more than one of the above groups or not classifiable)

Outcomes From The 4 Reviews

- **Consultation/Visit rates**
- **Processes of care**
- **Referrals/Admissions**
- **Compliance with guidelines**
- **Prescribing costs**

Data on Incentive-Outcome Pairs Review G

Outcome	Consultation or Visit rates	Processes of care	Referrals or Admissions	Compliance with guidelines	Prescribing costs
Intervention					
Payment for working for a specified time period					
Payment for each service/episode/visit					
Payment for providing care for a patient or a specific population					
Payment for providing a pre-specified level or providing a change in activity or quality					
Mixed or other systems					

Data on Incentive-Outcome Pairs Review A

Outcome	Consultation or Visit rates	Processes of care	Referrals or Admissions	Compliance with guidelines	Prescribing costs
Intervention					
Payment for working for a specified time period					
Payment for each service/episode/visit					
Payment for providing care for a patient or a specific population					
Payment for providing a pre- specified level or providing a change in activity or quality					
Mixed or other systems					

Data on Incentive-Outcome Pairs Study Level Analysis

Outcome	Consultation or Visit rates	Processes of care	Referrals or Admissions	Compliance with guidelines	Prescribing costs	Overall effect within intervention
Intervention						
Payment for working for a specified time period						
Payment for each service/episode/visit						
Payment for providing care for a patient or a specific population						
Payment for providing a pre-specified level or providing a change in activity or quality						
Mixed or other systems						
Overall effect within outcomes						

Pain management for women in labour

Table 13. (1.) Results by individual review - hypnosis

Table 14. (2.) Results by individual review - biofeedback

Table 15. (3.) Results by individual review - sterile water

Table 16. (4.) Results by individual review - immersion in water

Table 17. (5.) Results by individual review - aromatherapy

Table 18. (6.) Results by individual review - relaxation techniques

Table 19. (7.) Results by individual review - acupuncture

Table 20. (8.) Results by individual review - massage, reflexology and other manual methods

Table 21. (9.) Results by individual review - TENS

Table 22. (1.) Results by individual review - inhaled analgesia

Table 23. (2.) Results by individual review - parenteral opioids versus placebo/IM opioids versus different IM opioids

Table 24. (2.) Results by individual review - parenteral opioids - IV opioids versus different IV opioids/parenteral opioids versus different intervention

Recommendations

- For discussion this afternoon
- From the background paper
 - Overviews should return to being reviews of reviews (and rarely include indirect comparisons)
 - Indirect Comparisons require examination of individual trials
- From the Coordinating Editors
 - NMA should be done in a new Review type

Your turn!

- Other issues in the authoring & editorial process
 - for Overviews
 - For Reviews that compare multiple interventions



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