



Learning *Live*

Data Synthesis and Rating the Certainty of Evidence in Rapid Reviews

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January 25, 2024

The Goal of Today's Webinar

To present considerations and recommendations on how to accelerate the synthesis of evidence and rating the certainty of evidence (COE) for rapid reviews (RRs) of interventions.

RESEARCH METHODS & REPORTING

 Check for updates

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Updated recommendations for the Cochrane rapid review methods guidance for rapid reviews of effectiveness

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Cochrane Rapid Review - Definition

‘A type of evidence synthesis that brings together and summarises information from different research studies to produce evidence for people such as the public, healthcare providers, researchers, policymakers, and funders in a systematic, resource-efficient manner. This is done by **speeding up the ways** we **plan, do** and/or **share the results** of conventional structured (systematic) reviews, **by simplifying or omitting** a variety of methods that should be **clearly defined** by the authors.’

Evidence Synthesis

Cochrane Rapid Reviews Methods Group

General Considerations

- In general, the synthesis of evidence in RRs follows similar principles as in systematic reviews (SRs).
- At the outset of the rapid review, working with end-users to understand their goals and develop an analysis plan is crucial.
- If changes in the analysis plan are necessary during the conduct of the RR, make sure to amend the protocol and document the changes.

Recommendations to Accelerate the Evidence Synthesis in Rapid Reviews



Focus on the Most Important Comparisons and Outcomes

- Focus on the most important interventions, comparators, and outcomes for end-users.



Consider Whether a Meta-analysis is Appropriate

- A meta-analysis is often the most useful and efficient way of providing data synthesis in an RR.
- The methodological standards for conducting a meta-analysis apply equally to SRs and RRs, and authors should consult the Cochrane Handbook for the full details regarding metanalytic techniques.

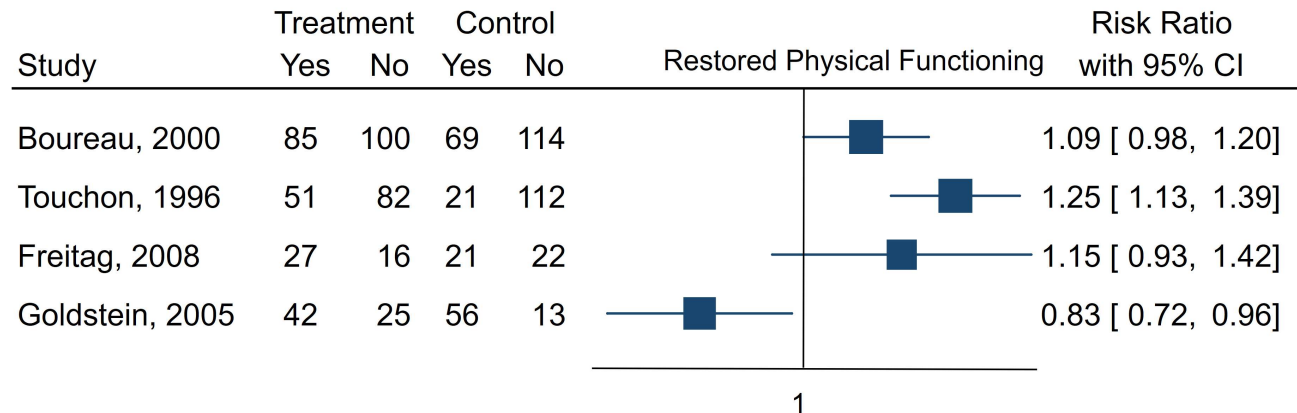
Cochrane Handbook for
Systematic Reviews of
Interventions



Chapter 10: Analysing data and undertaking meta-analyses

Use Non-Quantitative Methods to Present Results

- If resources do not allow for a meta-analysis, use non-quantitative methods, such as tables or other visual displays of results to present effect estimates.



- We strongly recommend against vote counting based on statistical significance or subjective rules such as a combination of direction, statistical significance and magnitude of effect.

Consider How to Synthesize Evidence When Including One or More SRs

- Building on an existing SR is challenging.
- Carefully match PICO (**P**opulation-**I**ntervention-**C**omparator-**O**utcomes) and key questions to decide whether to use a systematic review as a base.
- Consider the most recent, methodologically robust, and comprehensive SR(s) as a base for the RR.
- Update the included SR(s) searches to detect new studies.
- Update the meta-analysis of the SRs, if appropriate.
- An alternative strategy is to use identified studies of reviews but conduct your own risk of bias ratings and evidence synthesis.

Recommendations to Present the Evidence in a Rapid Review



Provide a Descriptive Summary of Study Characteristics

- Provide a descriptive summary of the characteristics of the included studies at the beginning of the Results chapter.
- Use tables, text, or graphs for descriptive summaries.


<u>First author, Year:</u> Boureau, 2000 ¹⁵	<u>N of participants:</u> 405	<u>Interventions:</u> G1: Sumatriptan 20 mg, nasal G2: DHE, nasal 1 mg plus optional 1 mg	<u>Mean age (years):</u> Overall: NR G1: 41 G2: 40	<u>Attacks per month:</u> NR	<u>Primary outcome:</u> Headache relief at 1 hour
<u>Trial name:</u> NR	<u>Study duration:</u> 24 hours	<u>Timing of interventions:</u> NR	<u>Females:</u> Overall: 84% G1: 83%* G2: 85%*	<u>Migraine with aura:</u> Overall: 21% G1: 22% G2: 21%	
<u>Setting, Country:</u> Outpatient setting, France, Portugal, Belgium, Switzerland	<u>Diagnostic tool:</u> ICHD, 1st edition		<u>Non-white:</u> NR		
<u>Funding:</u> Industry, Glaxo Wellcome					


* Number self-calculated

Perform a Synthesis of Findings

- Perform a synthesis of the findings, i.e., do not solely present data and do not catalogue studies (e.g., the first study showed, the second study showed...).
- Always provide a narrative interpretation of the findings regardless of whether a meta-analysis can be conducted.
- If a meta-analysis is not possible, consider using the Synthesis Without Meta-analysis (SWiM) reporting guidelines to present findings.

RESEARCH METHODS AND REPORTING

 OPEN ACCESS



Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline

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Additional material is published online only. To view please visit the journal online.
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In systematic reviews that lack data amenable to meta-analysis, alternative synthesis methods are commonly used, but these methods are rarely reported. This lack of transparency in the methods can cast doubt on the validity of the review findings. The Synthesis Without Meta-analysis (SWiM) guideline has been developed to guide clear reporting in reviews of interventions in which alternative

item checklist, was developed to facilitate improved reporting of systematic reviews.² Extensions are available for different approaches to conducting reviews (for example, scoping reviews³), reviews with a particular focus (for example, harms⁴), and reviews that use specific methods (for example, network meta-analysis.⁵) However, PRISMA provides limited guidance on reporting certain aspects of the review, such as the methods for presentation and synthesis, and no reporting guideline exists for synthesis without meta-analysis of effect estimates. We estimate that 32% of health related systematic reviews of interventions do not do meta-analysis,⁶⁻⁸ instead using alternative approaches to synthesis that

Summary of the Main Recommendations

To accelerate the synthesis of evidence, consider:

- Focusing on the most important interventions, comparators, and outcomes.
- Using non-quantitative methods, such as tables or other visual displays of results instead of formal meta-analyses.
- Including well-conducted systematic reviews as the base for the RR.

When synthesizing the evidence in RRs, always:

- Add a descriptive summary of the characteristics of the included studies.
- Provide a narrative interpretation of the findings, with or without meta-analysis.
- Apply the same methodological standards as in systematic reviews when conducting a meta-analysis.

Paper Forthcoming



RR SYNTHESIS PAPER

Research Methods and Reporting Article (BMJ Evidence-Based Medicine Journal)

TITLE: Rapid Reviews Methods Series: Guidance on Evidence Synthesis

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On behalf of the Cochrane Rapid Reviews Methods Group

Rating the Certainty of Evidence

Cochrane Rapid Reviews Methods Group

















Rating the Certainty of Evidence (COE)

- Do not omit rating the COE.
- For SRs and RRs, Cochrane recommends the **Grading of Recommendations Assessment, Development and Evaluation (GRADE)** approach to describe the level of confidence that investigators have in estimates of effects.
- If time and other resources permit, we encourage investigators to use the full GRADE approach as recommended for Cochrane systematic reviews.

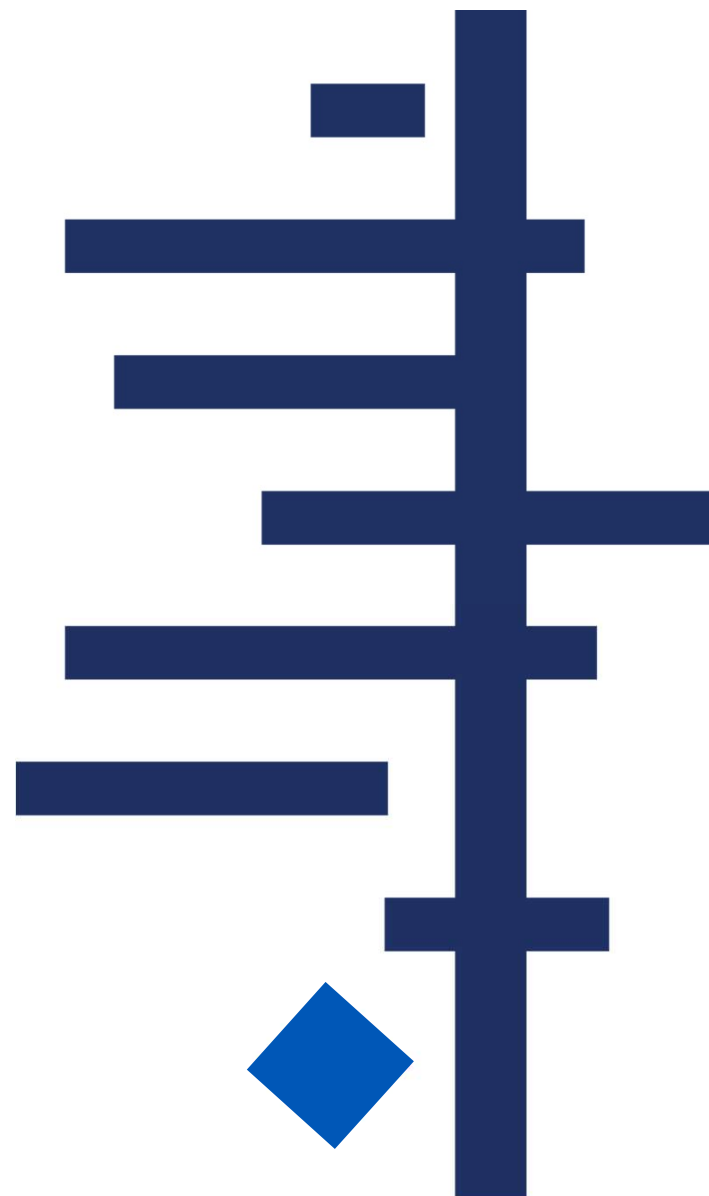
Cochrane Training

Cochrane and the GRADE Working Group provide extensive training resources on the application of GRADE.

<https://training.cochrane.org/introduction-grade>

 GRADE 1. The GRADE approach and 'Summary of findings' tables Introduction 	 GRADE 2. Choosing comparisons and outcomes for 'Summary of findings' table 	 GRADE 3. Applying the 'Risk of bias' assessments to GRADE 
 GRADE 4. How to GRADE the evidence: Inconsistency 	 GRADE 5. How to GRADE the evidence: Indirectness 	 GRADE 6. How to GRADE the evidence: Imprecision 
 GRADE 7. How to GRADE the evidence: Publication bias 	 GRADE 8. Other factors – upgrading the quality of evidence 	

Recommendations When Applying GRADE in a Rapid Review



Maintain Consistency with GRADE

- Rate the COE at the outcome level (not at the study level).
- Do not modify the categories of COE ratings (high, moderate, low, very low).
- Do not modify the domains that determine the COE for an outcome.

Domains that can reduce the COE	Domains that can increase the COE
<ul style="list-style-type: none">➤ Limitations in study design and execution*➤ Inconsistency in results➤ Indirectness of evidence (PICO and applicability)➤ Imprecision➤ Publication bias	<ul style="list-style-type: none">➤ Dose-response gradient➤ Large magnitude of effect➤ All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed*

*This domain becomes part of the 'limitations in study design and execution' domain if Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) is used to assess risk of bias.

Maintain Consistency with GRADE

- Use Summary of Findings tables (and Evidence Profiles) with explanatory footnotes that justify uprating and downrating.

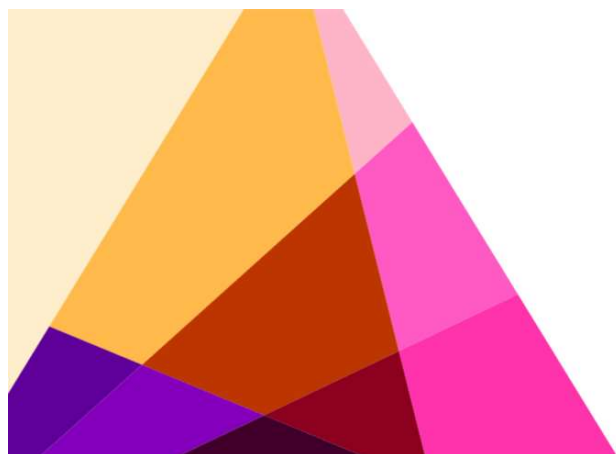
Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cognitive behavioral therapy	SGA	Relative (95% CI)	Absolute (95% CI)	
Response (follow-up: range 8 weeks to 16 weeks; assessed with: HAM-D)											
5	randomised trials	not serious	not serious	not serious	serious ^a	none	231/413 (55.9%)	300/542 (55.4%)	RR 0.96 (0.76 to 1.21)	22 fewer per 1 000 (from 133 fewer to 116 more)	⊕⊕○ Moderate
Serious adverse events (follow-up: range 8 weeks to 16 weeks)											
2	randomised trials	not serious	not serious	not serious	very serious ^c	serious ^b	Serious adverse events were 0% with CBT and ranged from 0.8% to 1% with SGA..			○○○ Very Low	

Explanations

- Confidence interval crosses decision threshold; downgraded 1 step for imprecision
- Outcomes reporting bias; most trials did not report on serious adverse events, downgraded 1 step for risk of bias

Use GRADEPro (<https://grade.pro.org>)

- Use GRADEpro to increase efficiency and consistency when rating the COE.

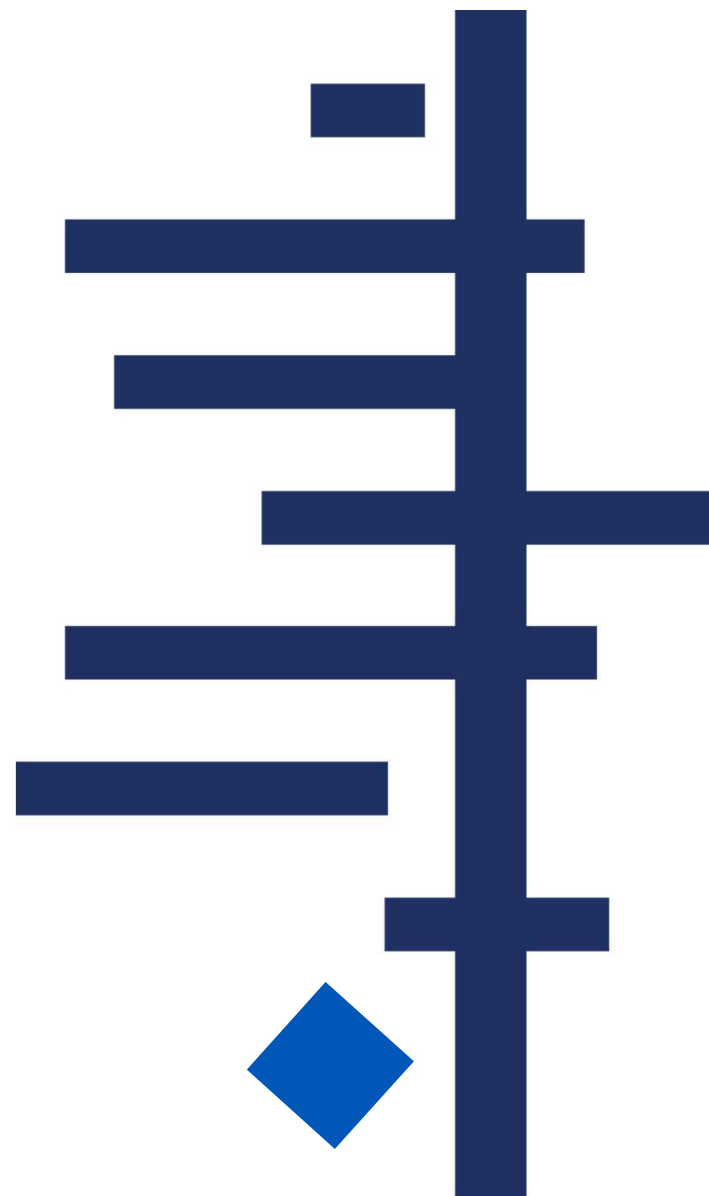


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Creating guidelines with GRADEpro GDT is easy! Today with over 40,000 users GRADEpro has become a reference point for on how to enable and aid collaboration and management in both small and large distributed teams.

Recommendations for Accelerating the Application of GRADE



Use Informal Judgments to Rate the Importance of Outcomes

- GRADE guidance recommends a literature review or a formal Delphi approach to rate the importance of outcomes for decision-making.

RATING SCALE:								
1	2	3	4	5	6	7	8	9
↑ of least importance						↑ of most importance		
of limited importance for making a decision (not included in evidence profile)			important, but not critical for making a decision (included in evidence profile)			critical for making a decision (included in evidence profile)		

- To accelerate the process, consider using informal judgements of knowledge users, topic experts (including people who live with the condition), or internal team members to prioritize the outcomes to grade.

Links to Free Software

<https://www.surveymonkey.com>

<https://www.guru99.com/best-free-online-survey-tools.html>

<https://blog.capterra.com/best-free-survey-tools-power-your-research/>

<https://www.guru99.com/best-free-online-survey-tools.html>

Limit the Number of Comparisons and Outcomes for Which the Certainty of Evidence is Assessed

- Prioritize interventions, comparators, and outcomes most pertinent to knowledge users.
- The GRADE guidance recommends limiting the number of graded outcomes to a maximum of seven.
- Consider fewer than seven outcomes.
- Outcomes should include benefits and harms.

1. How important are the following outcomes for preoperative evaluation of the adult patient undergoing non-cardiac surgery?

	1	2	3	4	5	6	7	8	9
Bleeding	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Blood transfusions	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Coagulation disorders	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Acute kidney injury/failure	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
All-cause mortality	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Mental state postoperatively	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Delirium	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Postoperative pain (Numeric Rating Scale)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Health related quality of life (EuroQoL, EQ5D)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Health and disability (12item WHODAS 2.0)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Postoperative recovery	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Postoperative mobility	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients satisfaction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Discharge destination	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Heart failure	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hepatic failure	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Use a Single Reviewer to Rate COE and a Second Reviewer to Verify Decisions

- GRADE guidance recommends that two reviewers independently rate the COE and then agree on a final rating.
- To accelerate the process, consider using a single reviewer to rate the certainty of evidence and verify all decisions (and footnoted rationales) by a second reviewer.



Rely on COE Grades from Well-Conducted Systematic Reviews

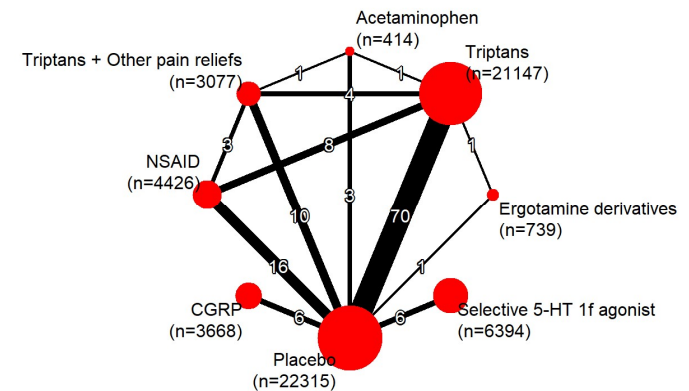
- If effect estimates of a well-conducted systematic review, meta-analysis, or network meta-analysis are incorporated to address parts of a key question of the RR, we advise using existing COE grades from such reviews.



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Rating the Certainty of Evidence for a Network Meta-analysis

- GRADE recommends rating the COE for direct and indirect estimates separately. To accelerate the process, rate only the COE of the direct estimate. If there is incoherence with the indirect estimate, rate down further.
- If a network meta-analysis presents only indirect estimates, use standard GRADE guidance and rate down for indirectness.



Summary of Main Recommendations

When using GRADE for the COE in RRs, always:

- Maintain consistency with GRADE domains and definitions of the COE.
- Rate the COE at an outcome level, not at a study level.
- Use Summary of Findings tables with explanatory footnotes.

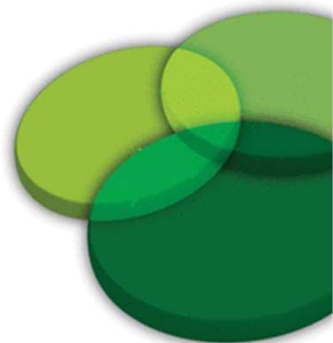
To accelerate the application of GRADE, consider:

- Focusing on the most important comparisons and outcomes.
- Employing informal judgments of knowledge users, experts, or team members to rate the importance of outcomes.
- Using fewer than seven outcomes for rating the COE.
- Relying on COE ratings of well-conducted system reviews if used as the base for a rapid review.

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Research methods and reporting



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Rapid reviews methods series: Guidance on assessing the certainty of evidence

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 **Cochrane Methods**
Rapid Reviews

Questions?





Thanks for taking part

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