Stages in identifying, evaluating, grading, and implementing methods for systematic reviews

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Acknowledgements: Sue Brennan, Mike Clarke, Jackie Chandler
Evaluation of evidence

Our bread and butter is scrutinising the evidence underpinning clinical interventions
Clinical interventions

- Identification of available interventions
- Development of new/modified interventions
- Evaluation of interventions (primary studies)
- Evaluation of interventions (synthesis)
- Grading the evidence of interventions and formulating recommendations
- Implementation of the interventions
Evaluation of evidence

... but what about the *evidence underpinning methods* used in systematic reviews (SRs)

Why should we care?

- Often many methods to choose from
  - e.g. methods to estimate the heterogeneity variance, calculate confidence interval for the meta-analysis effect
- Our choices have implications (and trade offs) in terms of
  - Performance (bias, efficiency, sensitivity, reliability, validity …)
  - Usability (and implementation)
  - Resource use
- Ultimately, the conclusions of our SRs rest on the methods used
Evaluation of evidence

- Should we use a similar framework for evaluating SR methods as we do clinical interventions?
Identifying, developing, evaluating, grading, and implementing...

**Clinical interventions**

1. Identification of available interventions
2. Development of new/modified interventions
3. Evaluation of interventions (primary studies)
4. Evaluation of interventions (synthesis)
5. Grading the evidence of interventions and formulating recommendations
6. Implementation of the interventions

**SR methods**

1. Identification of available methods
2. Development of new/modified methods
3. Evaluation of methods (primary studies)
4. Evaluation of methods (synthesis)
5. Grading the evidence of methods and formulating recommendations
6. Implementation of the methods
A framework for SR methods

The advantage of using this type of framework is that it makes explicit the steps from identification through to implementation of the SR methods.

This raises a series of questions:

- How should we identify available SR methods?
- How should we evaluate the performance of the SR methods?
- How should we grade resulting evidence and formulate recommendations for SR methods?
- How should we implement recommended SR methods?
Identifying, developing, evaluating, and implementing SR methods

**Step**

- **Identification of available methods**
  - What methods are available?

**Method**

- Ad hoc
  - Scoping reviews/evidence mapping

- Theoretical considerations
  - Existing knowledge
  - Expert opinion

**Step**

- **Development of new/modified methods**
  - (prioritisation)

**Method**

- Expert opinion
  - Theory
  - Existing knowledge
  - Expert opinion

**Step**

- **Evaluation of methods (primary studies)**
  - How do we evaluate the performance of methods?

**Method**

- Informal collation of the evidence
- Simulation studies, randomised trials, empirical evaluations

**Step**

- **Evaluation of methods (synthesis)**
  - How do we evaluate the performance of methods?

**Method**

- Informal recommendation of methods
  - Transparent approach
  - Adapt GRADE?
  - AHRQ approach?

**Step**

- **Grading the evidence of methods and formulating recommendations**
  - (prioritisation)

**Method**

- Implementation strategies
  - Educational strategies
  - Regulation (e.g., MECIR)

**Step**

- **Implementation of the methods**
  - How should we implement recommended methods?
Evaluation of methods (primary studies)

- A range of approaches are available to evaluate SR methods
  - Expert opinion
  - Theory
  - Simulation studies
  - Empirical evaluations
    - Performance of a single method
    - Meta-epidemiological
    - Comparison across methods
  - Randomised trials

- These approaches to have different strengths and weaknesses
Simulation studies

BMC Medical Research Methodology

Research article
The ratio of means method as an alternative to mean differences for analyzing continuous outcome variables in meta-analysis: A simulation study
Jan O Friedrich*1,2,3, Neill KJ Adhikari2,4 and Joseph Beyene5,6

RESEARCH ARTICLE
Characteristics of a loop of evidence that affect detection and estimation of inconsistency: a simulation study
Areti Angeliki Veroniki1, Dimitris Mavridis1,2, Julian PT Higgins3,4 and Georgia Salanti1*

Methods Research Report
Simulation-Based Comparison of Methods for Meta-Analysis of Proportions and Rates

Investigators:
Thomas A. Trikalinos, M.D., Ph.D.
Paul Trow, Ph.D.
Christopher H. Schmid, Ph.D.
Empirical evaluations (performance of a single method)

Poor Reliability between Cochrane Reviewers and Blinded External Reviewers When Applying the Cochrane Risk of Bias Tool in Physical Therapy Trials

Susan Armijo-Olivo¹,², Maria Ospina³, Bruno R. da Costa⁴, Matthias Egger⁵, Humam Saltaji⁶, Jorge Fuentes⁷,⁸, Christine Ha⁹, Greta G. Cummings¹

Testing the Risk of Bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs

Lisa Hartling¹,⁹, Michele P. Hamm¹, Andrea Milne¹, Ben Vandermeer⁴, P. Lina Santaguida¹, Mohammed Ansari³, Alexander Tsertsvadze³, Susanne Hempel¹, Paul Shekelle¹, Donna M. Dryden³

Incorporation of assessments of risk of bias of primary studies in systematic reviews of randomised trials: a cross-sectional study

Sally Hopewell¹,²,³,⁴,⁵ Isabelle Boutron¹,²,³,⁴ Douglas G Altman⁵ Philippe Ravaud¹,²,³,⁴
Empirical evaluations (comparison across methods)

Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes

Jonathan J. Deeks*†

Impact of Adjustment for Quality on Results of Meta-analyses of Diagnostic Accuracy

Mariska Leeflang,* Johannes Reitsma,† Rob Scholten,‡ Anne Rutjes,* Marcello Di Nisio,§ Jon Deeks,‖ and Patrick Bossuyt†

Comparison of statistical inferences from the DerSimonian–Laird and alternative random-effects model meta-analyses – an empirical assessment of 920 Cochrane primary outcome meta-analyses

Kristian Thorlund,a,b* Jørn Wetterslev,b Tahany Awad,c Lehana Thabane,a,d and Christian Gluudb

An empirical comparison of heterogeneity variance estimators in 12894 meta-analyses

Dean Langan,*† Julian P. T. Higginsb and Mark Simmondsa
Randomised trials

A summary to communicate evidence from systematic reviews to the public improved understanding and accessibility of information: a randomized controlled trial

Nancy Santesso, Tamara Rader, Elin Strømme Nilsen, Claire Glenton, Sarah Rosenbaum, Agustín Ciapponi, Lorenzo Moja, Jordi Pardo Pardo, Qi Zhou, Holger J. Schünemann

Comparison between the standard and a new alternative format of the Summary-of-Findings tables in Cochrane review users: study protocol for a randomized controlled trial

Evaluation of methods (synthesis)

- Systematic reviews can be used to collate and synthesize evaluations of methods from:
  - Simulation studies
  - Empirical evaluations
  - Randomised trials
  - Or a mix of the above

E.g. Cochrane Methodology Reviews
Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials  
Andrew Anglemyer, Hacsi T Horvath, Lisa Bero  
Online Publication Date: April 2014

Search strategies to identify observational studies in MEDLINE and EMBASE  
José S Marcano Belisario, Loraine Tudor Car, Tim JA Reeves, Laura H Gunn, Josip Car  
Online Publication Date: December 2013

Strategies to improve retention in randomised trials  
Valerie C Brueton, Jayne Tierney, Sally Stenning, Seeromanie Harding, Sarah Meredith, Irwin Nazareth, Greta Rait  
Online Publication Date: December 2013

Characteristics of randomised trials in ophthalmology using a single eye per person design  
Julio J González-López, Catey Bunce, Fernando Rodriguez-Artalejo  
Online Publication Date: November 2013

Search strategies to identify diagnostic accuracy studies in MEDLINE and EMBASE  
Rebecca Beynon, Mariska M.G. Leeflang, Steve McDonald, Anne Eisinga, Ruth L Mitchell, Penny Whiting, Julie M Glanville  
Online Publication Date: September 2013

Association between personal conflicts of interest and recommendations on medical interventions  
Andreas Lundh, Anders W Jørgensen, Lisa Bero  
Online Publication Date: June 2013
Grading the evidence

Clinical interventions

- GRADE is a transparent and structured process for rating the quality of evidence in SRs and formulating recommendations for guidelines
  - Assess the quality of the evidence (Summary of Findings tables)
  - Formulate and grade strength of recommendations

Methods

- Should we adapt such an approach for grading the evidence of methods and formulating recommendations?
Grading the evidence

Assess the quality of the evidence

<table>
<thead>
<tr>
<th>Clinical interventions</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of bias</td>
<td></td>
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<tr>
<td>Inconsistency of results</td>
<td>Could we adapt this for assessing the quality of the evidence for methods?</td>
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<tr>
<td>Indirectness of evidence</td>
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<tr>
<td>Imprecision</td>
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<td>Publication bias</td>
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</tbody>
</table>
## Grading the evidence

**Formulate and grade strength of recommendations**

<table>
<thead>
<tr>
<th>Clinical interventions</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance between desirable and undesirable outcomes (trade-offs)</td>
<td><strong>Could we adapt this for formulating and grading the strength of recommendations for methods?</strong></td>
</tr>
<tr>
<td>Confidence in the magnitude of estimates of effect of the interventions on important outcomes (overall quality of evidence for outcomes)</td>
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<td>Confidence in values and preferences and their variability</td>
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<tr>
<td>Resource use</td>
<td></td>
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</tbody>
</table>
Towards a framework for communicating confidence in methodological recommendations for systematic reviews and meta-analyses

[Trikalinos, 2013, AHRQ]
Implementation

Clinical interventions

“… guidelines do not implement themselves; they are often not used after dissemination, and implementation activities frequently produce only moderate improvement.”

[Grol 2001 Medical Care]

- This gap between evidence and practice led to implementation science

“… scientific study of methods to promote the update of research findings into routine healthcare in clinical, organisational, or policy contexts.”

[www.implementationscience.com]
## Implementation

<table>
<thead>
<tr>
<th>EPOC taxonomy of implementation strategies</th>
<th>Current strategies Cochrane uses to implement SR methods</th>
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</thead>
<tbody>
<tr>
<td>Audit &amp; feedback</td>
<td>CEU screening of pre-publication drafts of new reviews against MECIR conduct and reporting standards</td>
</tr>
<tr>
<td>Monitoring the performance of the delivery of healthcare</td>
<td>CEU monitoring of review quality (against MECIR) over time</td>
</tr>
<tr>
<td>Educational materials</td>
<td>Training materials</td>
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<tr>
<td>Educational meetings</td>
<td>Workshops</td>
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<tr>
<td>Clinical practice guidelines</td>
<td>Handbook, MECIR conduct and reporting standards</td>
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<tr>
<td>...</td>
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</table>
Methods

- Continuous monitoring of the quality of reviews facilitates the identification of problem areas in the implementation of methods.

- Do we know if our current implementation strategies for increasing the use of recommended methods in Cochrane SRs work?

- Should we be trying to evaluate our implementation strategies?
Key messages

- The conclusions of our SRs rest on the methods used.
- The steps involved in identifying, developing, evaluating, grading, and implementing methods for clinical interventions provide a framework that could be applied to SR methods.
- Is it time to adopt a more transparent and structured approach for recommending methods?
- Cochrane is in a unique position to develop and adopt such an approach.
  - Requires resources.
References
