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

2015 Annual Cochrane Methods Symposium, Vienna

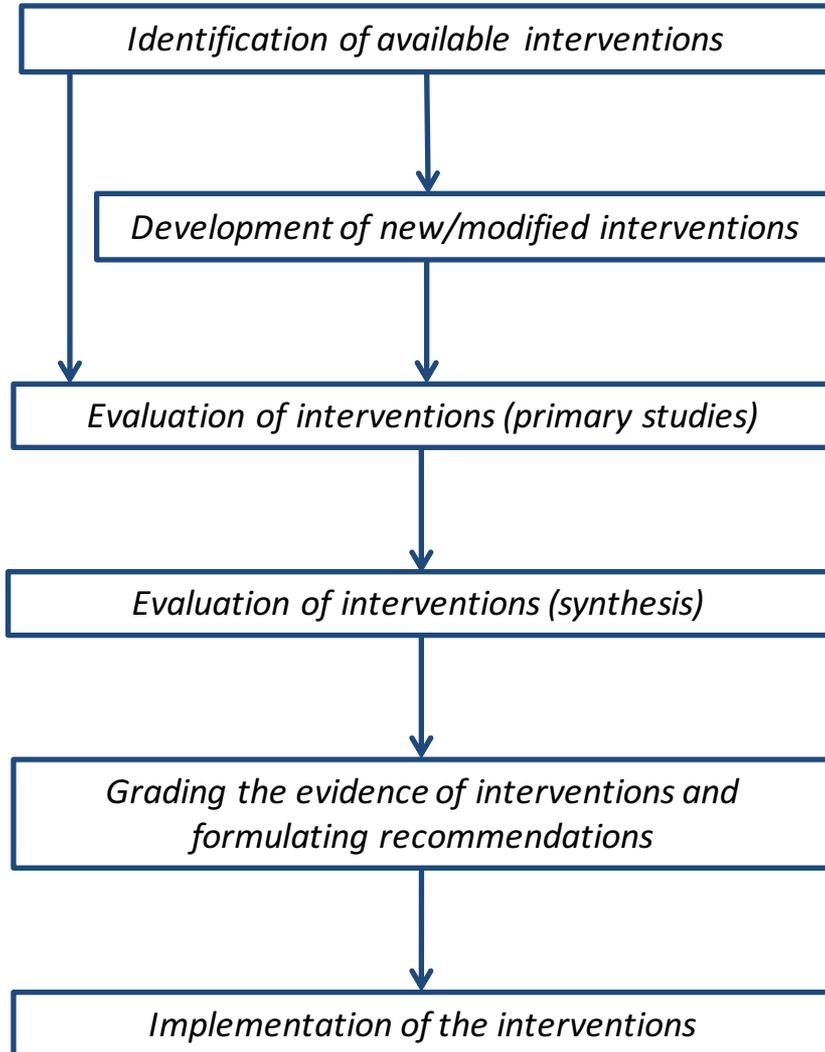## 2nd October 2015

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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*

Identifying, developing, evaluating, grading, and implementing…

Clinical interventions

Evaluation of evidence

… but what about the *evidence underpinning methods* used in systematic reviews (SRs)
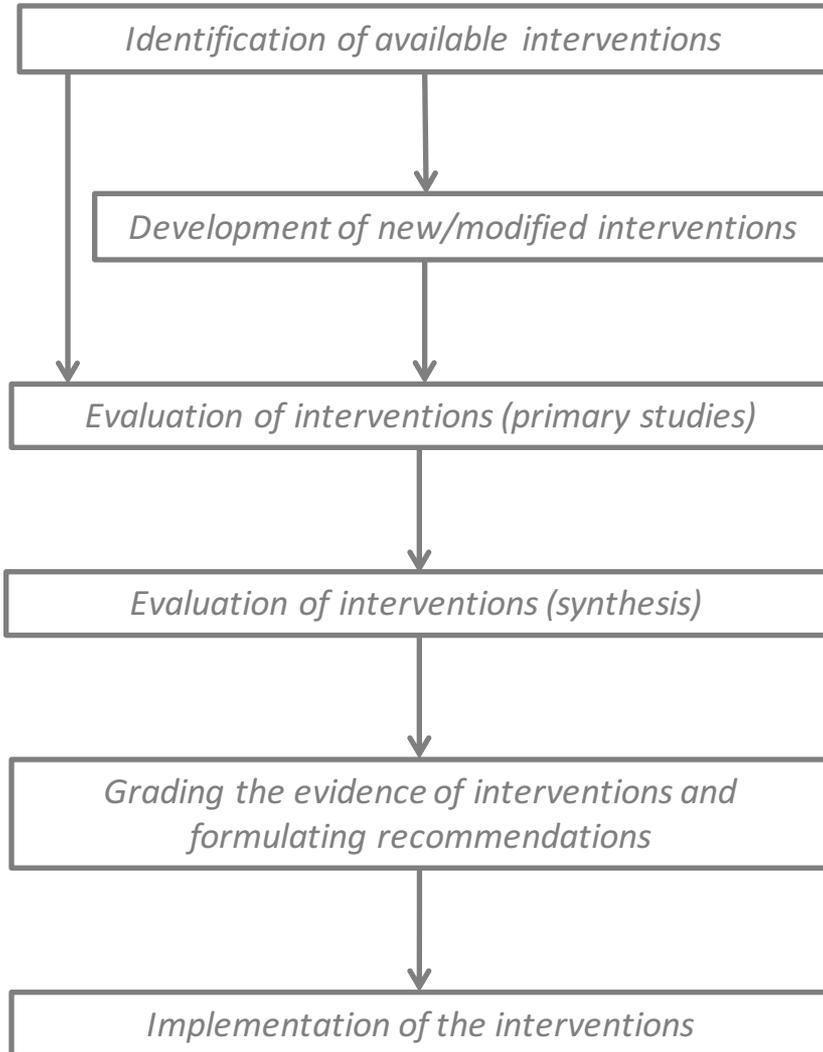
Why should we care?

- 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
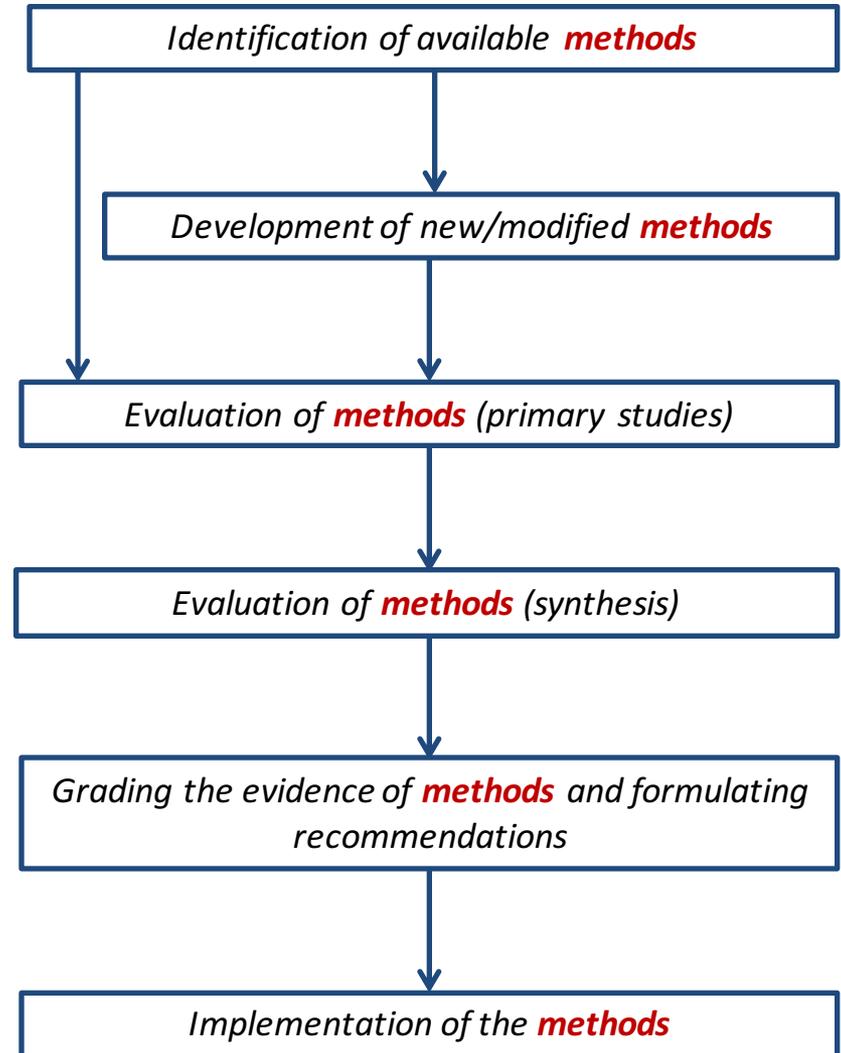
Evaluation of evidence

- Should we use a similar framework for evaluating SR methods as we do clinical interventions?

Identifying, developing, evaluating, grading, and implementing...

Clinical interventions

SR methods

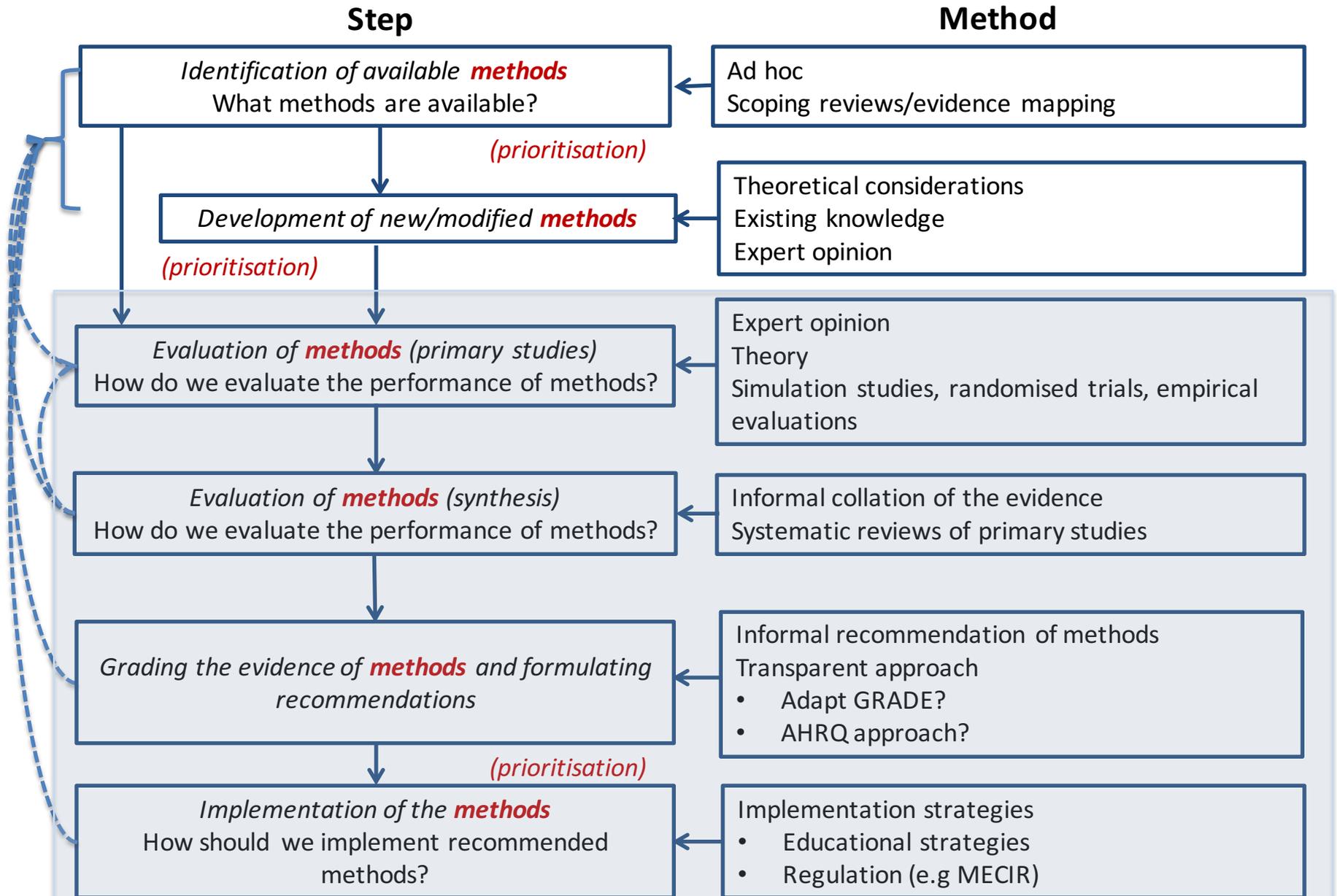| Clinical interventions	SR methods
Identification of available interventions	Identification of available **methods**
Development of new/modified interventions	Development of new/modified **methods**
Evaluation of interventions (primary studies)	Evaluation of **methods** (primary studies)
Evaluation of interventions (synthesis)	Evaluation of **methods** (synthesis)
Grading the evidence of interventions and formulating recommendations	Grading the evidence of **methods** and formulating recommendations
Implementation of the interventions	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	**Method**
Identification of available **methods** What methods are available?	Ad hoc Scoping reviews/evidence mapping
(prioritisation)	
Development of new/modified **methods**	Theoretical considerations Existing knowledge Expert opinion
(prioritisation)	
Evaluation of **methods** *(primary studies)* How do we evaluate the performance of methods?	Expert opinion Theory Simulation studies, randomised trials, empirical evaluations
Evaluation of **methods** *(synthesis)* How do we evaluate the performance of methods?	Informal collation of the evidence Systematic reviews of primary studies
Grading the evidence of **methods** *and formulating recommendations*	Informal recommendation of methods Transparent approach • Adapt GRADE? • AHRQ approach?
(prioritisation)	
Implementation of the **methods** How should we implement recommended methods?	Implementation strategies • Educational strategies • Regulation (e.g MECIR)

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

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Simulation studies

Research article

Open Access

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 Adhikari[2,4] and Joseph Beyene[5,6]

BMC
Medical Research Methodology

RESEARCH ARTICLE   **Open Access**

Characteristics of a loop of evidence that affect detection and estimation of inconsistency: a simulation study

Areti Angeliki Veroniki[1], Dimitris Mavridis[1,2], Julian PT Higgins[3,4] and Georgia Salanti[1*]

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)

PLOS | ONE

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

Susan Armijo-Olivo[1,2]*, Maria Ospina[3], Bruno R. da Costa[4], Matthias Egger[5], Humam Saltaji[6], Jorge Fuentes[7,8], Christine Ha[9], Greta G. Cummings[1]

ELSEVIER

Journal of Clinical Epidemiology

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

Lisa Hartling[a,*], Michele P. Hamm[a], Andrea Milne[a], Ben Vandermeer[a], P. Lina Santaguida[b], Mohammed Ansari[c], Alexander Tsertsvadze[c], Susanne Hempel[d], Paul Shekelle[d], Donna M. Dryden[a]

BMJ open

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

Sally Hopewell,[1,2,3,4,5] Isabelle Boutron,[1,2,3,4] Douglas G Altman,[5] Philippe Ravaud[1,2,3,4]

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[*,†]

Review

Impact of Adjustment for Quality on Results of Metaanalyses of Diagnostic Accuracy

Mariska Leeflang,[1*] Johannes Reitsma,[1] Rob Scholten,[2] Anne Rutjes,[1] Marcello Di Nisio,[3] Jon Deeks,[4] and Patrick Bossuyt[1]

Original Article

Research Synthesis Methods

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 Gluud[b]

Original Article

Research Synthesis Methods

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

Dean Langan,[a*†] Julian P. T. Higgins[b] and Mark Simmonds[a]

Randomised trials

ORIGINAL ARTICLE

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

Nancy Santesso[a,*], Tamara Rader[b], Elin Strømme Nilsen[c], Claire Glenton[c], Sarah Rosenbaum[c],
Agustín Ciapponi[d], Lorenzo Moja[e,f], Jordi Pardo Pardo[b], Qi Zhou[a], Holger J. Schünemann[a,g]

TRIALS

STUDY PROTOCOL   **Open Access**

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

Alonso Carrasco-Labra[1,2], Romina Brignardello-Petersen[3,4], Nancy Santesso[1], Ignacio Neumann[5], Reem A Mustafa[1,6], Lawrence Mbuagbaw[1], Itziar Etxeandia Ikobaltzeta[7], Catherine De Stio[8], Lauren J McCullagh[8], Pablo Alonso-Coello[1,9], Joerg J Meerpohl[10], Per Olav Vandvik[11], Jan L Brozek[1,12], Elie A Akl[1,13], Patrick Bossuyt[14], Rachel Churchill[15], Claire Glenton[16,17], Sarah Rosenbaum[16,17], Peter Tugwell[18], Vivian Welch[19], Gordon Guyatt[1,12] and Holger Schünemann[1,12*]

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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

`Review` `Methodology`

Search strategies to identify observational studies in MEDLINE and EMBASE

José S Marcano Belisario, Lorainne Tudor Car, Tim JA Reeves, Laura H Gunn, Josip Car

Online Publication Date: December 2013

`Protocol` `Methodology`

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

`Review` `Methodology`

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

`Protocol` `Methodology`

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

`Review` `Methodology`

Association between personal conflicts of interest and recommendations on medical interventions

Andreas Lundh, Anders W Jørgensen, Lisa Bero

Online Publication Date: June 2013

`Protocol` `Methodology`

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

GRADE

Assess the quality of the evidence

Clinical interventions	Methods
Risk of bias	
Inconsistency of results	**Could we adapt this for assessing the quality of the evidence for methods?**
Indirectness of evidence	
Imprecision	
Publication bias	

Grading the evidence

Formulate and grade strength of recommendations

Clinical interventions	Methods
Balance between desirable and undesirable outcomes (trade-offs)	**Could we adapt this for formulating and grading the strength of recommendations for methods?**
Confidence in the magnitude of estimates of effect of the interventions on important outcomes (overall quality of evidence for outcomes)	
Confidence in values and preferences and their variability	
Resource use	

Figure 1. Overview of the proposed framework for rating the strength of methodological recommendations

1. Define the *background context*

Define:
- the *setting*
- the methodological *problem*
- the available *choices*
- the recommendation's *perspective*
- the *measures* to optimize

2. Decompose the recommendation into *testable* and *nontestable* statements

3. Describe statements in four dimensions:

a. Evidentiary basis (testable statements)
- mathematical & technical arguments
- empirical evidence of large scale
- case study
- expert opinion

OR

a. Face validity (nontestable statements)

b. Feasibility of implementation (all statements)

c. Expected practical impact of implementation (all statements)

d. Congruence with context-specific requirements (all statements)

4. Opine on whether the recommendation constitutes a mandatory item, a desirable but not mandatory item, or something in between, based on all testable and nontestable statements it includes

Mandatory item:
Most peers agree that SRs not following the recommendation are likely to be misleading

Desired but not mandatory item :
Most peers agree that
(i) it is desirable to follow the recommendation
(ii) failure to do so is unlikely to render the SR misleading

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

EPOC taxonomy of implementation strategies	Current strategies Cochrane uses to implement SR methods
Audit & feedback	CEU screening of pre-publication drafts of new reviews against MECIR conduct and reporting standards
Monitoring the performance of the delivery of healthcare	CEU monitoring of review quality (against MECIR) over time
Educational materials	Training materials
Educational meetings	Workshops
Clinical practice guidelines	Handbook, MECIR conduct and reporting standards
…	

Implementation

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

Grol R. Successes and failures in the implementation of evidence-based guidelines for clinical practice. Medical care. 2001 Aug;39(8 Suppl 2):II46-54.

Trikalinos TA, Dahabreh IJ, Wallace BC, Schmid CH, Lau J. Towards a Framework for Communicating Confidence in Methodological Recommendations for Systematic Reviews and Meta-Analyses. AHRQ Methods for Effective Health Care. Rockville (MD)2013.

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