Developing methods for Cochrane DTA reviews – a perspective based on the DTA editorial process

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Outline

• What is the Cochrane DTA editorial process?
• Identifying and addressing a research need
• Adopting and implementing a new method
Editorial Process of Diagnostic Test Accuracy reviews

The publication of Cochrane systematic reviews differs from that of print journals. Cochrane Review Groups (CRGs) manage the process from the consideration of the proposal for a new DTA review through to publication including peer review. During this life cycle CRGs also support authors in use of RevMan software and some systematic review methods.

Additional to that, all protocols and full text systematic reviews of Diagnostic Test Accuracy are peer reviewed both by the Coordinating editor of the CRG and the DTA Editorial Team and they are required to agree that protocols and reviews are of a suitable standard for publication.

Full details of the editorial processes for systematic reviews of diagnostic test accuracy are provided in this document DTA Editorial process. Details about the DTA Editorial Team can be found here (DTA Editorial Team).
Cochrane DTA editorial process

Cochrane Review Group

Quality of clinical aspects and reporting of review

Sign off for publication in Cochrane Library

DTA Editorial Team

Quality of methods and methodological reporting
Cochrane DTA Editorial Team

DTA-ET

ET 1  ↔  ET 2
<table>
<thead>
<tr>
<th>Date</th>
<th>Team</th>
<th>Issues raised</th>
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<tr>
<td>2th April 2013</td>
<td>ET2</td>
<td>QUADAS-2 presentation in a protocol...</td>
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<td>14th July 2015</td>
<td>ET1</td>
<td>Performance of methods for meta-analysis of diagnostic accuracy with few studies or sparse data</td>
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<td>We discussed a protocol today that mentioned their planned strategy for meta-analysis if they have few included studies. Please see the attached paper:</td>
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<td>[PDF] Takwoingi et al 2015 - Performance of met</td>
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<td>11th August 2015</td>
<td>ET1</td>
<td>Watch out for ...</td>
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Methods for DTA meta-analysis

• Simple meta-analytic models have weaknesses
  – fail to account for heterogeneity or
  – correlation between sensitivity and specificity not accounted for
  – may require zero cell adjustments

• Hierarchical models do not have these limitations

• Bivariate and HSROC models are the two approaches recommended
  – Basic model requires estimation of 5 parameters
  – Too little data plus too many parameters = problems!
Analysis with few studies – a discussion from 2008

• Should we advise in the Handbook a minimum number of studies?
• Should we alter RevMan so that it only allows hierarchical model parameters to be entered when this number is reached?
• What can we say in the Handbook about pooling when there are few studies?
• Personally I think that the "don't pool " approach is not right
• If we do pool, what methods can we use?
• Real case to discuss soon in DTA-ET
**The Cochrane Methodology Register (CMR) 2012 Issue 3**
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<table>
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<tr>
<th>Title</th>
<th>Performance of methods for meta-analysis of diagnostic test accuracy studies when few studies are available. Oral presentation at the 17th Cochrane Colloquium; 2009 Oct 11-14, Singapore [abstract] Links Export Citation</th>
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<tr>
<td>Author(s)</td>
<td>Takwoingi Y, Guo B, Riley R, Deeks J</td>
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<tr>
<td>Source</td>
<td>Cochrane Database of Systematic Reviews, Supplement</td>
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<td>Date of Publication</td>
<td>2009</td>
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<td>Volume</td>
<td>Suppl</td>
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<td>Issue</td>
<td>CD000001</td>
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| Abstract | Background. Hierarchical methods recommended (Lee et al. 2006) for meta-analyses of diagnostic test accuracy studies are complex, relying on iterative procedures for the estimation of multiple model parameters. In certain circumstances, for instance when there are few studies in a meta-analysis, such models may not converge or produce unstable parameter estimates. Objectives: To evaluate the performance of meta-analytic approaches for test accuracy studies when few studies are available, and to develop recommendations for proceeding with meta-analysis when the suggested hierarchical methods fail. Methods: Ten-thousand meta-analysis datasets were simulated for each of a range of realistic scenarios that varied according to selections of the accuracy of diagnostic tests to important factors, including: the number of studies, number of patients within studies, disease prevalence, and heterogeneity in threshold and accuracy across studies. A variety of meta-analysis models were fitted and performance was assessed according to the bias, mean-square error and coverage of parameter estimates. Results: Irrespective of disease prevalence, estimation of hierarchical model parameters and their standard errors often fail in the absence of heterogeneity in threshold and accuracy. For example, in one scenario, the proportion of convergence failures for the hierarchical summary ROC model were 65%, 59% and 54% for 5, 10 and 15 studies respectively. Even given substantial heterogeneity, the models may still fail to converge when studies are few (e.g. 8 or less). Simpler models converge more easily but are clearly biased in a number of scenarios. Conclusions: Hierarchical methods are complex and their model convergence is sensitive to the number of studies in a meta-analysis and a variety of data characteristics. Where hierarchical methods fail, researchers may be forced to use simpler but...
Section 10.5.6 Approaches to analysis with small numbers of studies

• Difficult to decide on terms to include in a model and ‘best’ model
• No hard and fast rules about how to proceed
• Some strategies outlined

“Academic illustrations of the application of hierarchical methods have typically involved large meta-analyses. In contrast, our experience of supporting Cochrane and non-Cochrane diagnostic test accuracy review authors suggest that small meta-analyses or sparse data often occur and pose a challenge to these data hungry hierarchical models...”
7.6 Analysis with small number of studies

Cochrane Collaboration DTA Online Learning Materials
Module 7: Analyse and present results
QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies

Penny F. Whiting, PhD; Anne W.S. Rutjes, PhD; Marle E. Westwood, PhD; Susan Mallett, PhD; Jonathan J. Deeks, PhD; Johannes B. Reitsma, MD, PhD; Mariska M.G. Leeﬂang, PhD; Jonathan A.C. Sterne, PhD; Patrick M.M. Bossuyt, PhD; and the QUADAS-2 Group*

In 2003, the QUADAS tool for systematic reviews of diagnostic accuracy studies was developed. Experience, anecdotal reports, and feedback suggested areas for improvement; therefore, QUADAS-2 was developed. This tool comprises 4 domains: patient selection, index test, reference standard, and flow and timing. Each domain is assessed in terms of risk of bias, and the first 3 domains are also assessed in terms of concerns regarding applicability. Signalling questions are included to help judge risk of bias.

The QUADAS-2 tool is applied in 4 phases: summarize the review question, tailor the tool and produce review-specific guidance, construct a flow diagram for the primary study, and judge bias and applicability. This tool will allow for more transparent rating of bias and applicability of primary diagnostic accuracy studies.

For author afﬁliations, see end of text.
* For members of the QUADAS-2 Group, see the Appendix (available at www.annals.org).
Implementation of QUADAS-2

“Is it possible for you to ask ASAP if we shall use QUADAS-2 or we shall stick to the QUADAS referred to on the website and used so far? This is a very important question for us so that we can revise and finalise the protocols we are working on.”

Message from a CRG ME on 31st October 2011

SDTMG Business meeting

Version 5.2 released 9th Nov 2012

Visit IMS Team 24th Feb 2012

DTA-ET, CEU, CRGs, IMS, Wiley, etc.
Implementation and application of QUADAS-2

Off the shelf

Bespoke
Finally...
thank you!