Overview and Demo of Apps for Evidence Synthesis Developed by the Complex Review Synthesis Unit (CRSU)

Presented by: **Alex Sutton**

UNIVERSITY OF LEICESTER

CRSU

NIHR | National Institute for Health and Care Research

University of Glasgow

Collaborators / Co-authors / Acknowledgements

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- Additional funding see: https://github.com/CRSU-Apps/.github/blob/main/DetailedFundingStatement.pdf

Complex Review Support Unit

"The CRSU will focus on providing timely and appropriate support for the delivery of complex reviews that are funded and/or supported by NIHR." (Included Cochrane reviews)

- Collaboration between Universities of Leicester and Glasgow
- Funded 2015 – November 2023
- Quickly discovered lack of software for the non-statistic expert systematic reviewer was a limiting factor for data analysis
- Apps developed in response to this need

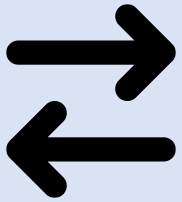
Complex Review Synthesis Unit @ ESG

- CRSU Funding was not renewed
- April 2023 : U o Leicester and Glasgow funded Evidence Synthesis Group (ESG) (5 years)
- App collaboration planned to continue as part of ESG (but work funded from other sources)
- We hope we can use our apps for ESG work!

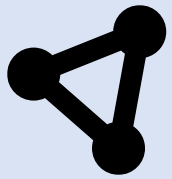
App Principles

- Developed using R and {shiny} (with JAGS and STAN for Bayesian analysis)
- Where possible utilise existing R packages
- Free to use and open source
- Point and click interface
- Built-in example datasets
- Do not replace statisticians
- Provide methods for sensitivity analysis
- Emphasis on visualization
- Export plots of publication quality
- Code is freely available on GitHub
- Can be run locally in R if speed / internet connection / memory / confidentiality concerns are a problem
- Gives a platform to provide methodological developments we develop
- Come with no guarantees

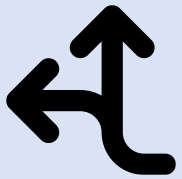
Treatment Effects



- MetaPairwise
  - Pairwise meta-analysis



- MetaInsight
  - Network meta-analysis (NMA)



- MetaCNMA
  - Component network meta-analysis (CNMA)

- MetaImpact
  - Designing studies to contribute to meta-analyses

Diagnostic Test Accuracy

- MetaDTA
  - Frequentist meta-analysis

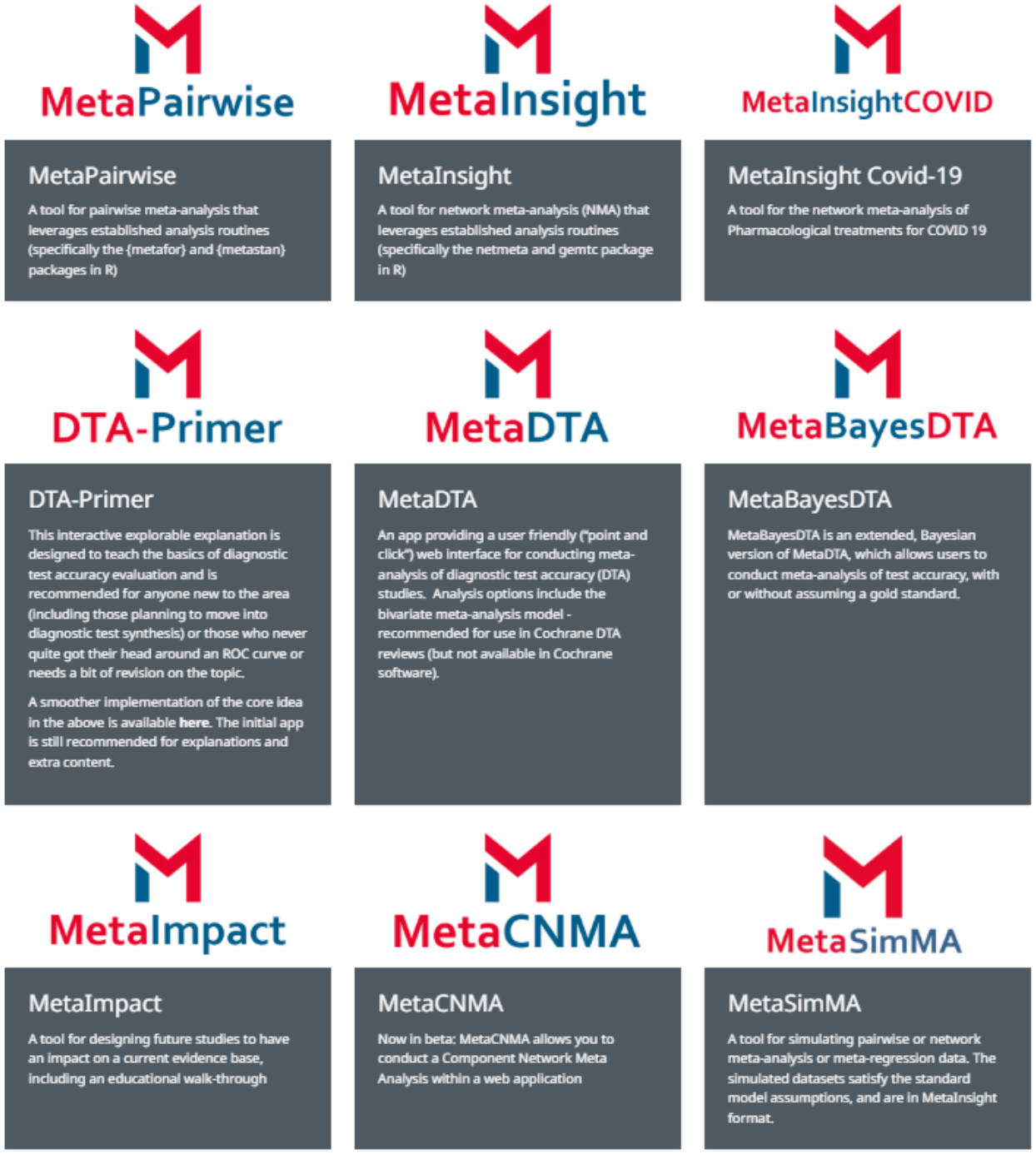
- MetaBayesDTA
  - Bayesian meta-analysis

Other

- DTAPrimer
  - Introduction to DTA

- MetaInsightCOVID
  - Feasibility study for living NMA

- MetaSimMA
  - Tool for simulating MA/NMA datasets



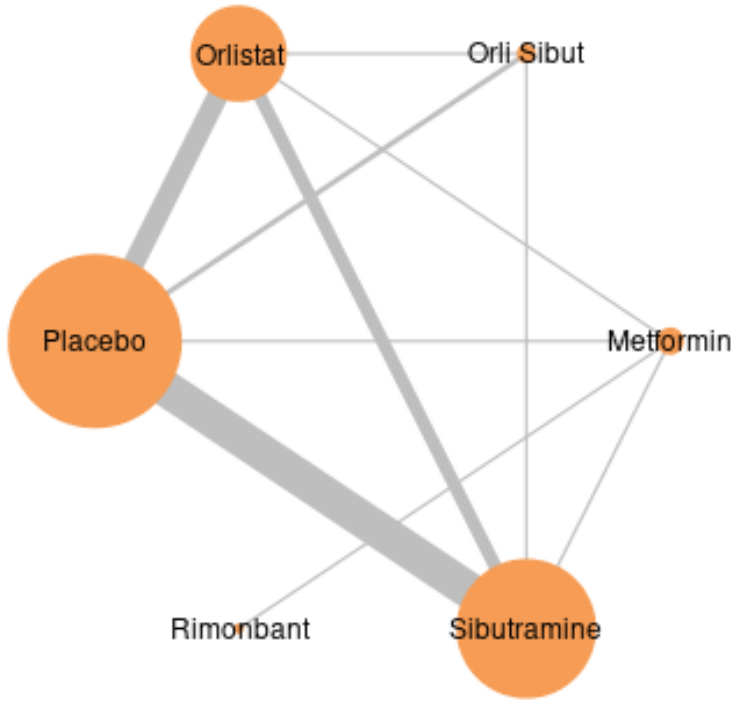
Apps Webpage:

https://www.gla.ac.uk/research/az/crsu/apps/

Network Meta-Analysis

MetaInsight

Extension of pairwise meta-analysis



Direct

Indirect

Component Network Meta Analysis

MetaCNMA

Example questions:

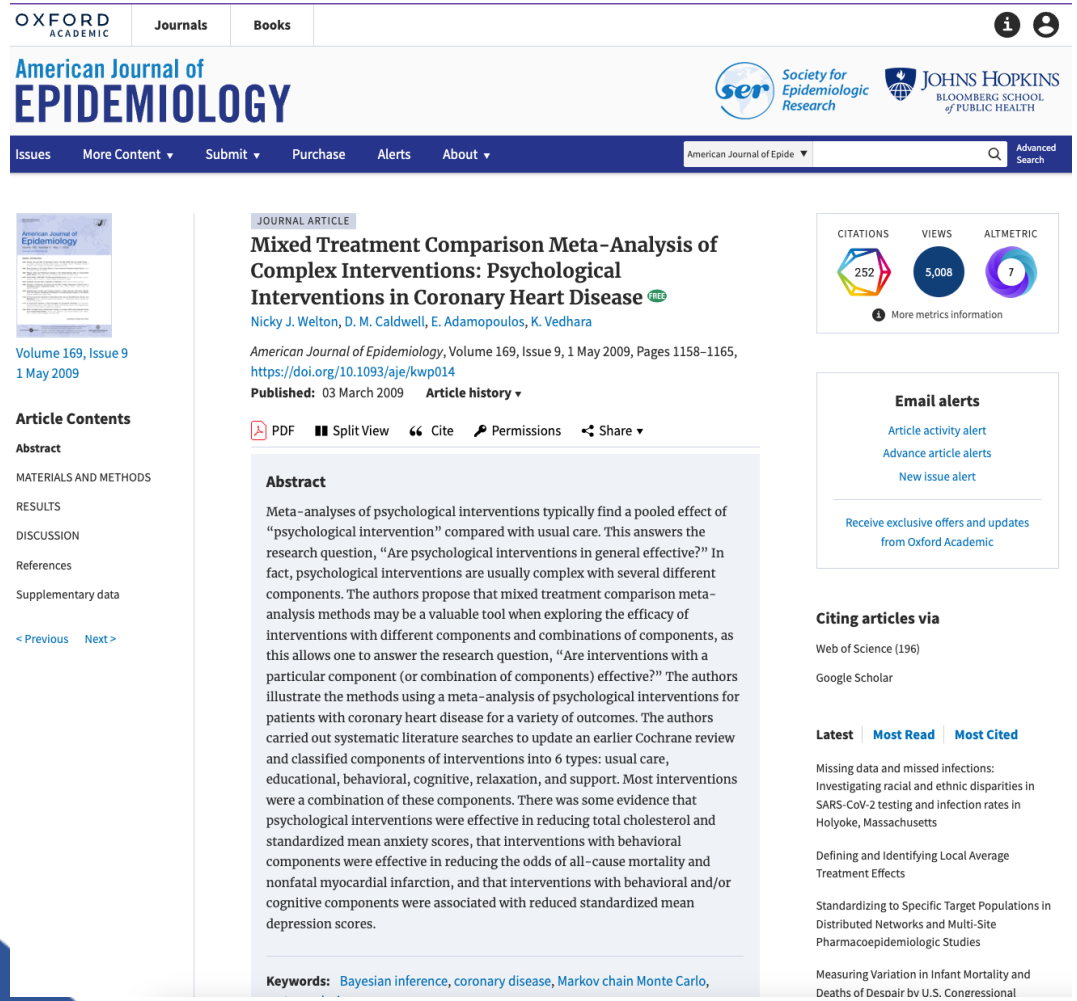
"Which components of these multi-component interventions are most effective?"

or

"What would be the predicted effectiveness of a particular combination?"

Freeman SC, Scott NW, Powell R, Johnston M, Sutton AJ, Cooper NJ. Component network meta-analysis identifies the most effective components of psychological preparation for adults undergoing surgery under general anesthesia. *Journal of Clinical Epidemiology* 2018; 98: 105, https://doi.org/10.1016/j.jclinepi.2018.02.012

CNMA Models



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Volume 169, Issue 9
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JOURNAL ARTICLE

Mixed Treatment Comparison Meta-Analysis of Complex Interventions: Psychological Interventions in Coronary Heart Disease FREE

Nicky J. Welton, D. M. Caldwell, E. Adamopoulos, K. Vedhara

American Journal of Epidemiology, Volume 169, Issue 9, 1 May 2009, Pages 1158–1165,
https://doi.org/10.1093/aje/kwp014
Published: 03 March 2009 **Article history**

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Abstract

Meta-analyses of psychological interventions typically find a pooled effect of "psychological intervention" compared with usual care. This answers the research question, "Are psychological interventions in general effective?" In fact, psychological interventions are usually complex with several different components. The authors propose that mixed treatment comparison meta-analysis methods may be a valuable tool when exploring the efficacy of interventions with different components and combinations of components, as this allows one to answer the research question, "Are interventions with a particular component (or combination of components) effective?" The authors illustrate the methods using a meta-analysis of psychological interventions for patients with coronary heart disease for a variety of outcomes. The authors carried out systematic literature searches to update an earlier Cochrane review and classified components of interventions into 6 types: usual care, educational, behavioral, cognitive, relaxation, and support. Most interventions were a combination of these components. There was some evidence that psychological interventions were effective in reducing total cholesterol and standardized mean anxiety scores, that interventions with behavioral components were effective in reducing the odds of all-cause mortality and nonfatal myocardial infarction, and that interventions with behavioral and/or cognitive components were associated with reduced standardized mean depression scores.

Keywords: Bayesian inference, coronary disease, Markov chain Monte Carlo,

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Missing data and missed infections: Investigating racial and ethnic disparities in SARS-CoV-2 testing and infection rates in Holyoke, Massachusetts

Defining and Identifying Local Average Treatment Effects

Standardizing to Specific Target Populations in Distributed Networks and Multi-Site Pharmacoepidemiologic Studies

Measuring Variation in Infant Mortality and Deaths of Despair by U.S. Congressional

Nicky J. Welton, D. M. Caldwell, E. Adamopoulos, K. Vedhara, Mixed Treatment Comparison Meta-Analysis of Complex Interventions: Psychological Interventions in Coronary Heart Disease, *American Journal of Epidemiology*, Volume 169, Issue 9, 1 May 2009, Pages 1158–1165, https://doi.org/10.1093/aje/kwp014

MetaCNMA

- Implements models from the Welton et al paper.
- Fixed and Random Effects
- Using Stan for Bayesian computation

- Currently in open Beta
- R Package for Bayesian CNMA Analysis based on code developed for the app planned

MetaDTA
and
MetaBayesDTA

Diagnostic tests:

		Reference test: Positive	Reference test: Negative
Index test	Positive	57	14
	Negative	8	33

$$\text{Sensitivity} = \frac{57}{57 + 8}$$

$$\text{Specificity} = \frac{33}{14 + 33}$$

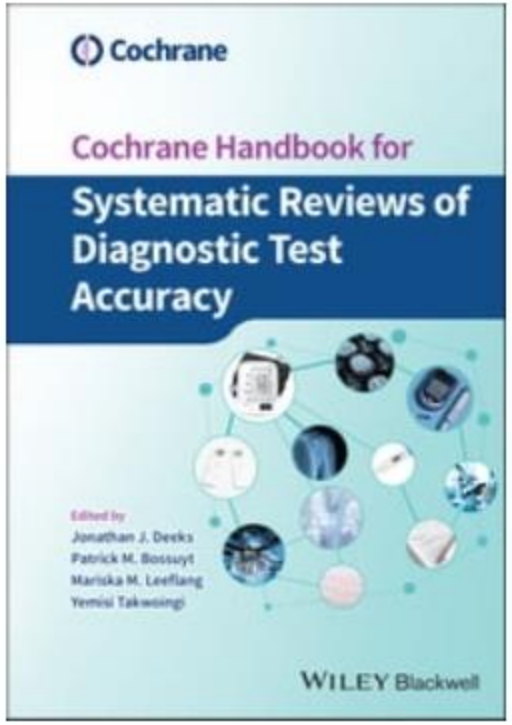
MetaBayesDTA

- Originally written by Enzo Cerullo
- Create an extended version of MetaDTA which fits more complex models - regression models / imperfect gold standards
- Uses Bayesian methods as implemented in STAN software exclusively – bespoke STAN code used throughout
- Encourage good practices
  - Automatically report predictive intervals
  - Prior distributions visualised before model fitting
  - Model and sampler diagnostics automatically presented
- Updated user interface over **MetaDTA**

- Both DTA apps:
  - have links to YouTube tutorials within them
  - code is freely available on GitHub
  - can be run locally in R if speed / internet connection / memory / confidentiality concerns are a problem

- MetaDTA has a manual within app

- A document showing how all possible analyses from the Cochrane Handbook can be replicated in MetaBayesDTA is available within the app



Reproducing analyses from the Cochrane DTA handbook in MetaBayesDTA v1.0

Tom Morris (tm428@leicester.ac.uk)

October 2023

NIHR | National Institute for Health and Care Research

NIHR Complex Reviews Support Unit

University of Glasgow

University of Leicester

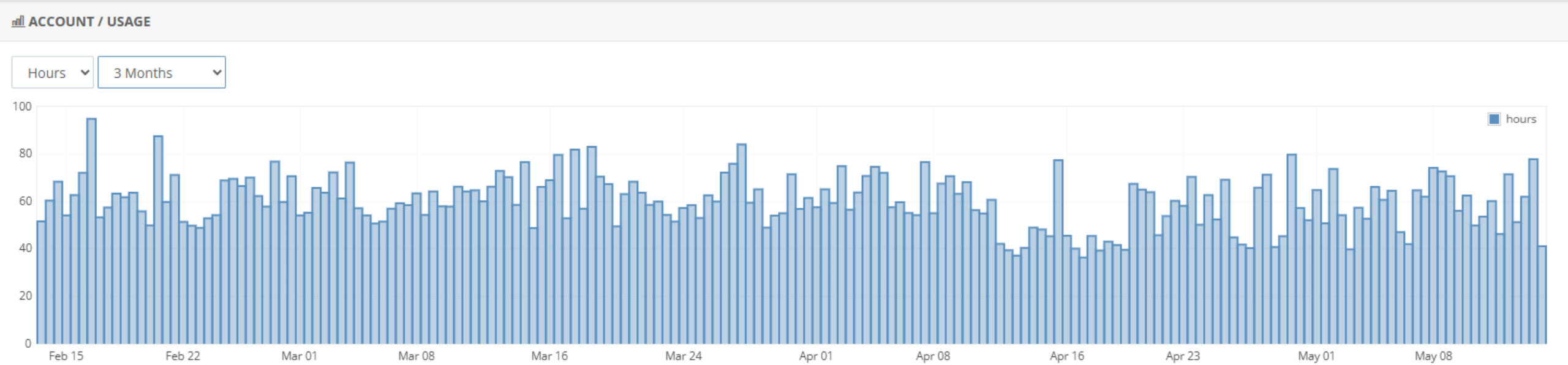
For comments or question on MetaBayesDTA please e-mail apps@crsu.org.uk. For comments or question on this document please e-mail tm428@leicester.ac.uk.

1 Introduction

This guide contains step-by-step instructions on how to reproduce the example meta-analyses in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 2 (https://training.cochrane.org/handbook-diagnostic-test-accuracy/current), using the MetaBayesDTA app (https://crsu.shinyapps.io/MetaBayesDTA/). Six of the examples contained in chapters 9 and 10 of the handbook can be carried out in MetaBayesDTA. Before starting, the reader should familiarise themselves with the example(s) they wish to reproduce and download the accompanying datasets.

App Usage

November 2023 – January 2024

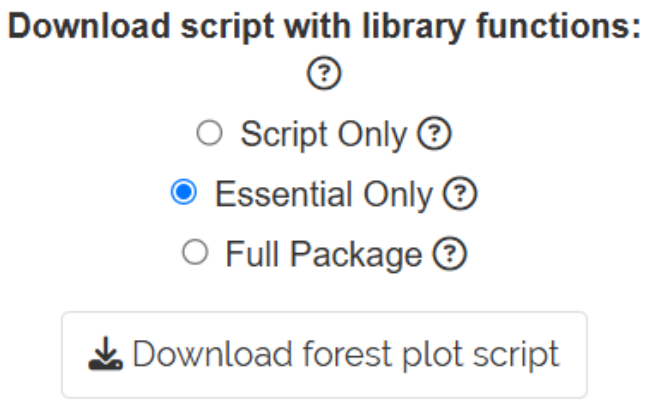


- ~10,500 hours online usage over 3-month period
- Initial app papers for NMA & DTA cited 225+ times each

App Work in Progress (1)

General

- Add more information to the Website
- Add report generation with associated underlying code to analysis apps
    - Adds transparency/reproducibility
    - Allow user to tweak/extend analysis beyond what is possible in the apps in R
    - This has already been done for MetaPairwise
    - Well underway for MetaInsight for NMA



App Work in Progress (2)

MetaInsight

- We have an grant (from Wellcome) to make MetaInsight and CINeMA compatible
- Will allow integrated data analysis and Grade type assessment

https://cinema.ispm.unibe.ch/

- Add generic outcome measure (to allow e.g. Hazard Ratio data from survival outcomes etc)

App Work in Progress (3)

MetaPairwise

- Adding more functionality from the metafor R package

MetaCNMA

- Hope to add more data visualisations in the future

Freeman, S.C., Saeedi, E., Ordóñez-Mena, J.M. *et al.* Data visualisation approaches for component network meta-analysis: visualising the data structure. *BMC Med Res Methodol* **23**, 208 (2023). https://doi.org/10.1186/s12874-023-02026-z

Hopes for the Future:

- Further extend functionality of existing apps
- Integrate with more existing systematic review workflows
  - i.e. Other tools/software
- Do you have any suggestions / requests for analysis apps/features?

Final Points:

Webpage for Apps:
https://crsu.org.uk -> Apps & Materials

@ESG_CRSU

Contact the App Team: apps@crsu.org.uk
GitHub https://github.com/CRSU-Apps/MetaInsight

Interested in learning Shiny/App development?

- MetaPairwise – lots of scope for extension!
- All code open source, CRSU would help where possible

Links to App worksheets (from Cochrane Colloquium 2023):
https://www.gla.ac.uk/research/az/evidencesynthesis/crsu-outputs/cochrane-colloquium-2023/

Thank You For Listening!

References:

Cerullo, E., Sutton, A.J., Jones, H.E. et al. **MetaBayesDTA: codeless Bayesian meta-analysis of test accuracy, with or without a gold standard.** *BMC Med Res Methodol* (2023); 23, 127 https://doi.org/10.1186/s12874-023-01910-y

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