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# Innovating Complex Evidence Synthesis Modelling Through Interactive Shiny Applications

Alex Sutton, Prof Medical Statistics, University of Leicester, UK  
(ajs22@le.ac.uk) (intermediate R user overseeing others more experienced)

Clareece Nevill, Suzanne Freeman, Enzo Cerullo, Nicola Cooper on behalf of  
the NIHR Complex Review Support Unit (CRSU)



# BACKGROUND

- Work conducted largely fund by National Institute for Health Research (NIHR) UK Complex Review Support Unit (CRSU) (<http://www.nihrcrsu.org/>)

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

- Provide flexible, timely and appropriate response to specific requests, to support successful delivery of the complex reviews
- Contribute to building capacity and capability within the research community

# BACKGROUND (cont.)

- Many reviews don't have experienced statistical support
- We identified two barriers:
  - Lack of awareness more sophisticated / appropriate synthesis methods existed
    - But that's a different talk
  - Lack of statistical software expertise to implement methods
    - Solutions:
      - Run training using advanced software (e.g. in R / WinBUGS etc)
      - Create user-friendly software for the non-expert

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# PRE-HISTORY: TIDI

HEALTH POLICY ANALYSIS | VOLUME 14, ISSUE 5, P768-776, JULY 01, 2011



PDF [1 MB]



Figures



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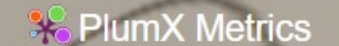
## Development of a Transparent Interactive Decision Interrogator to Facilitate the Decision-Making Process in Health Care

Sylwia Bujkiewicz, PhD • Hayley E. Jones, PhD • Monica C.W. Lai, MSc • Nicola J. Cooper, PhD

Neil Hawkins, PhD • Hazel Squires, MSc • Keith R. Abrams, PhD • David J. Spiegelhalter, PhD

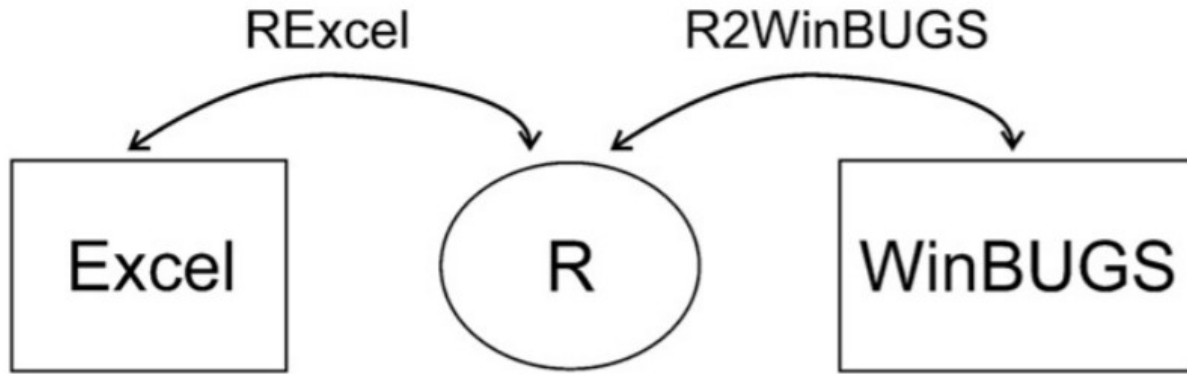
Alex J. Sutton, PhD • [Show less](#)

[Open Access](#) • Published: May 02, 2011 • DOI: <https://doi.org/10.1016/j.jval.2010.12.002>

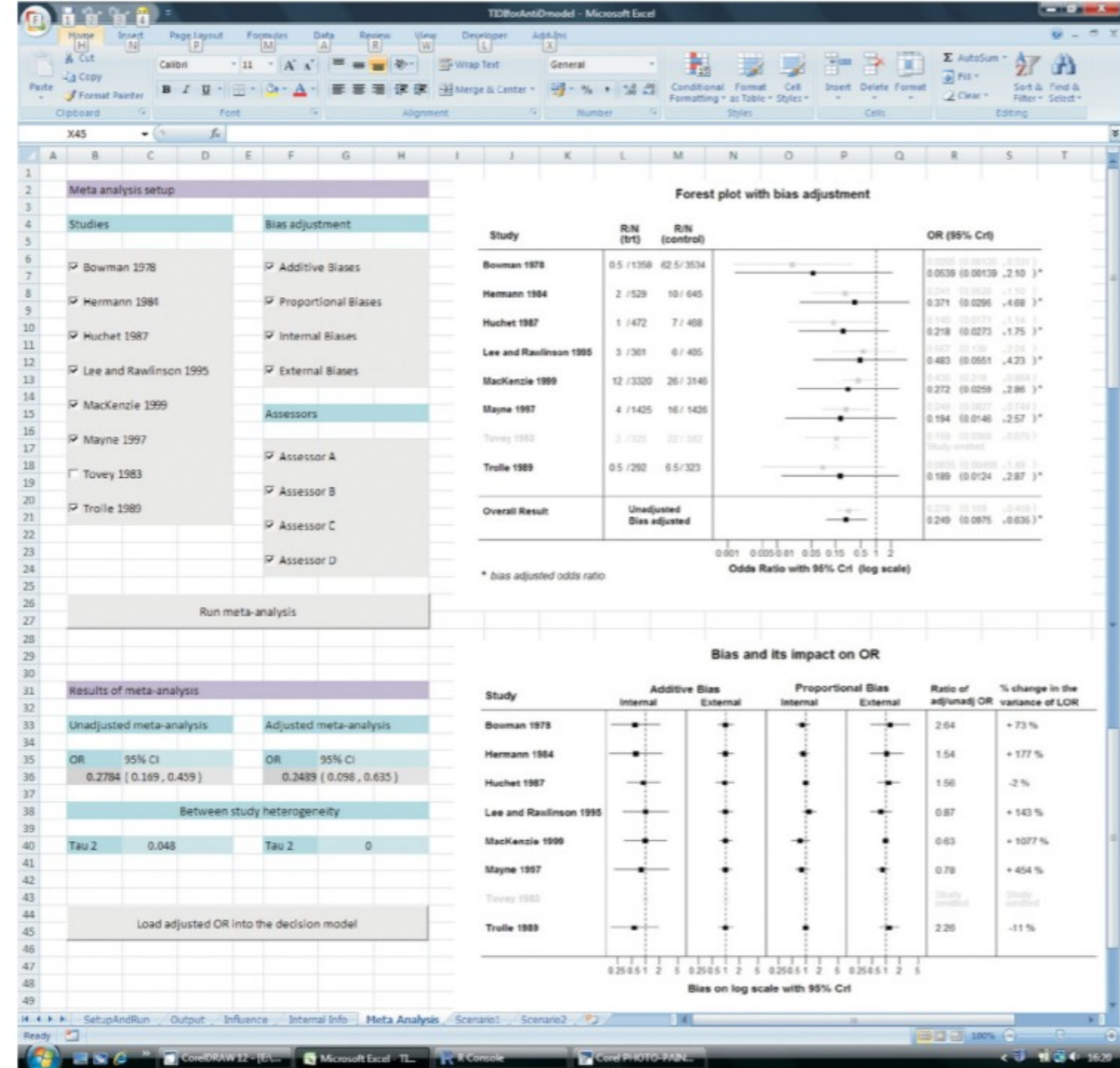


- Allowed on-the-fly exploration of linked meta-analyses and decision model to explore impact of assumptions on results

# PRE-HISTORY: TIDI



- Hard to install
- Bespoke programming
- Used in a real NICE HTA Appraisal Meeting(!)
- Ahead of its time? (2011)



# THE CRSU APPS (

<http://www.nihrcrsu.org/guidance/apps/>)

- **MetaInsight:** Conducts Network Meta-Analysis
- **MetaDTA:** Conducts Meta-Analysis of Diagnostic Test Accuracy Studies
- **MetaInsight:** Covid-19: Proof of concept - tool for exploration, re-analysis, sensitivity analysis, and interrogation of published meta-analysis. Shadowed a living systematic review of Covid treatments
- **DTA primer:** interactive explorable explanation is designed to teach the basics of diagnostic test accuracy evaluation



# THE CRSU APPS (Cont.) (

<http://www.nihrcrsu.org/guidance/apps/>)

## General Principles of Apps:

- All developed using the R package Shiny
- Started small and expanded continuously by multiple people over time
- Where possible utilise existing R packages
- Free to use and open source
- Point and click interface

## Principles of Analysis Apps:

- Bayesian models fitted via Jags/STAN simulation engines
- Emphasis on visualization and methods for sensitivity analysis
- Implement new methodological developments by authors over time

# MetaInsight: For conducting NMA

## Core features:

- Conducts NMA of binary and continuous outcomes
- Frequentist and Bayesian analysis
- Inconsistency / model fit assessments

## Coming soon:

- Novel graphical representations of the results and their implications for practice

## Wish list:

- Other outcomes (inc. survival)
- Inclusion of covariates

Owen RK, Bradbury N, Xin Y, Cooper N, Sutton A. MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. *Res Synth Methods*. 2019;10(4):569-581. doi:10.1002/irsm.1373

You have selected **Continuous** outcome on the 'Home' page. The analysis page for **Continuous** outcomes are now displayed.

**Outcome for continuous data:**

Mean Difference (MD)

Standardised Mean Difference (SMD)

**For treatment rankings, smaller outcome values (e.g. smaller mean values for continuous data, or ORs less than 1 for binary data) are:**

Desirable

Undesirable

**Model:**

Random effect (RE)

Fixed effect (FE)

**Select studies to exclude:**

Tips: you can use the data table to help find the study that you want to exclude.

[Open the data table](#)

Kuo 2006

Ozcelik 2004

Turker 2006

Wang 2005

Schechter 2006

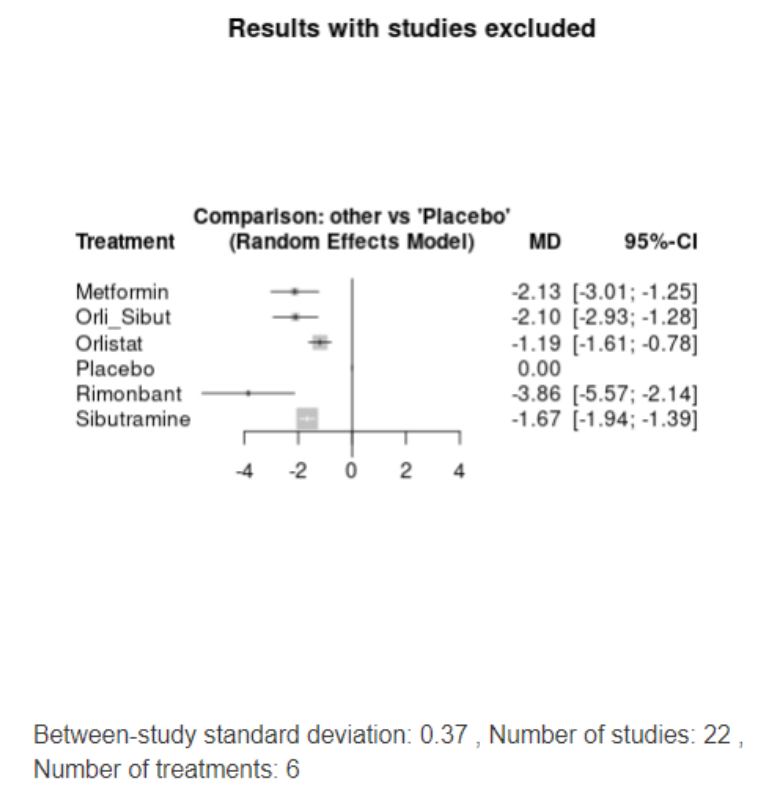
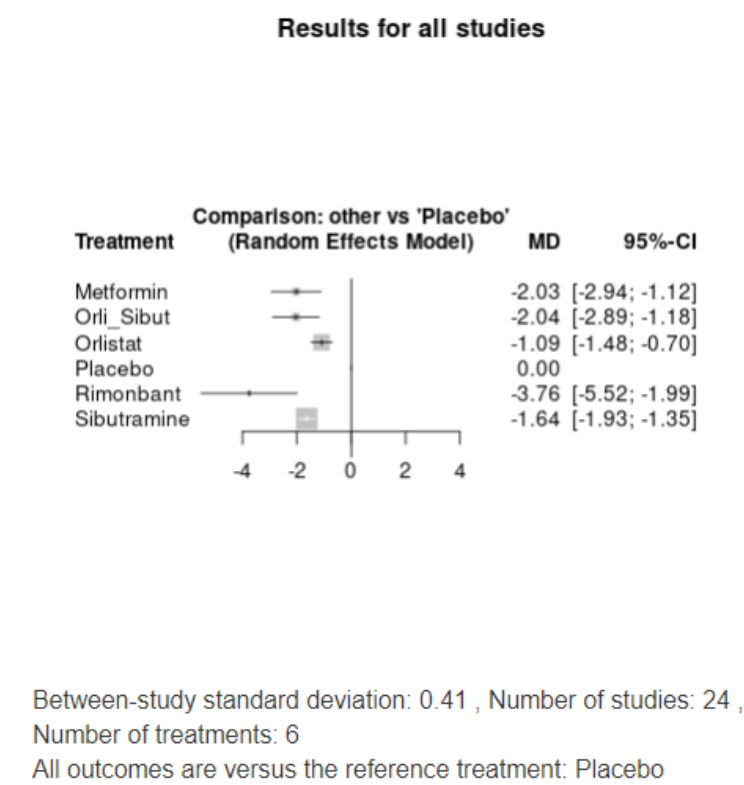
Aydin 2004

Data table (Click to open / hide this panel)

1. Data summary    **2. Frequentist network meta-analysis**

3. Bayesian network meta-analysis

2a. Forest Plot    2b. Comparison of all treatment pairs    2c. Inconsistency



# MetaDTA: For Conducting Diagnostic Test Accuracy Meta-Analysis

Core features:

- Conducts bivariate analysis
- Can plot covariates / quality on ROC plot
- Graphic for clinical impact for a given disease prevalence

Coming soon:

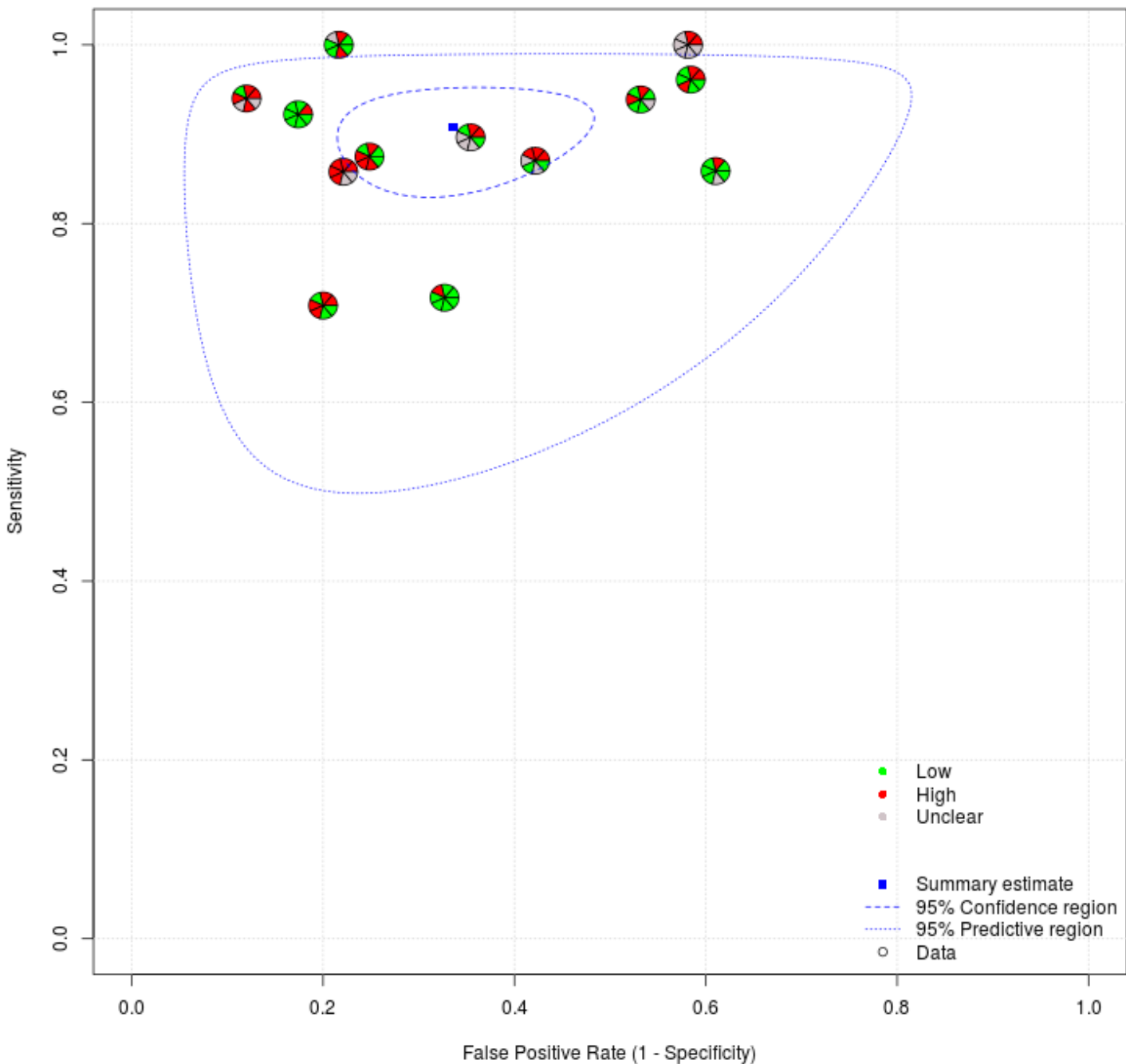
- Inclusion of covariates in the analysis
- Bayesian analysis
- Analysis allowing for an imperfect gold standard
- Interface overhaul

Wish list:

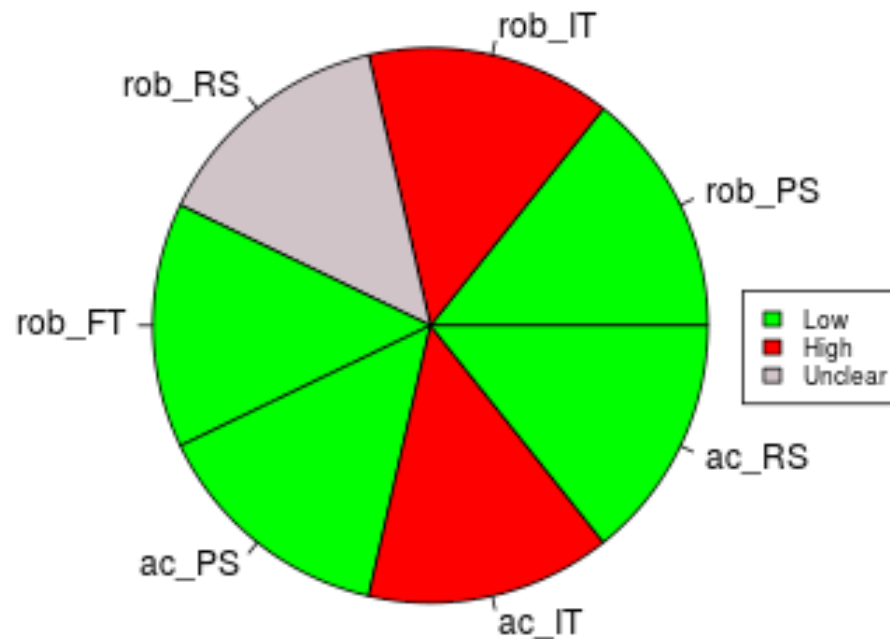
- Inclusion of multiple thresholds per study

Freeman SC, Kerby CR, Patel A, Cooper NJ, Quinn T, Sutton AJ. Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. *BMC Medical Research Methodology* 2019; **19**: 81 +

### Random Effects Meta-Analysis



### Scores from each element of the QUADAS-2 tool



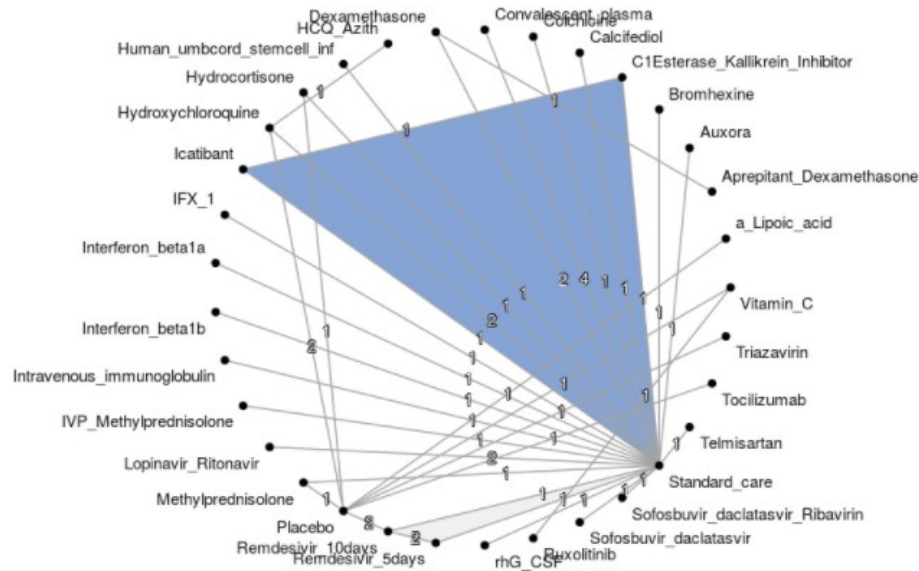
Patel A, Cooper NJ, Freeman SC, Sutton AJ. Graphical enhancements to summary receiver operating characteristic plots to facilitate the analysis and reporting of meta-analysis of diagnostic test accuracy data. *Research Synthesis Methods* 2020, <https://doi.org/10.1002/jrsm.1439>.

# MetaInsight Covid-19:

## Network plot

Please note: there exist two separate networks. The primary network is displayed below. If you would like to view the overall disconnected network, please click the link below.

[View the disconnected overall network \(Click to open / hide this panel\)](#)



**Abbreviations:** IFN: Interferon; LopRitIFNa: Lopinavir + Ritonavir + Interferon-alpha; LopRitRibIFNa: Lopinavir + Ritonavir + Ribavirin + Interferon-alpha; LopRitRibIFNb1b: Lopinavir + Ritonavir + Ribavirin + Interferon-beta-1b; LopRitDarCobUmilIFNa: Lopinavir + Ritonavir or Darunavir/Cobicistat + Umifenovir + Interferon-alpha; HCQ: Hydroxychloroquine; HCQ\_Azith: Hydroxychloroquine + Azithromycin; Human\_umbcord\_stemcell\_inf: Human umbilical cord mesenchymal stem cell infusion; rhG\_CSF: Recombinant human granulocyte colony-stimulating factor; Interferon\_kappa\_TFF2: Interferon-kappa + Trefol-factor-2

The trials that contain zero outcome (i.e. missing treatment effect) on both arms are not displayed in this style. For the default analysis, trials that become disconnected after removal of such trials are also not displayed. Please switch to style 2 to view the full network.

Numbers on the line indicate the number of trials conducted for the comparison. The shaded areas (if there are any) indicate there exist multi-arm trials between the comparisons.

- Exploration into publishing meta-analysis using MetaInsight allowing exploration, re-analysis, sensitivity analysis, and interrogation of data
- Open & reproducible science

# CHALLENGES AND LIMITATIONS

- Support for user base
  - Apps get used worldwide for approx. 800 hours a month total (mostly MetaInsight and MetaDTA)
  - We get 2/3 queries a week from non NIHR researchers
    - Currently support but may struggle in future to sustain
- Shiny account incurs a modest cost that needs finding annually
  - Ring-fenced money for 3 years
  - Set up our own Shiny server?
- Scaling analyses plots to always be legible / making static versions of interactive plots available for download

# THE FUTURE

- Current funding ends November 2021 but hope to find further funds
- Development of an app for component NMA
- Keep adding features to existing analysis apps
  - Script of R commands used “behind the scenes” created to improve transparency/reproducibility and as an educational resource
- Produce educational materials linked to versions of the app
- Tool to allow others to publish meta-analyses using versions of apps as viewer + for user analysis



THANK YOU

<http://www.nihrcrsu.org/guidance/apps>

Or Google “CRSU apps”