



**a fully interactive web-application for producing and visualising network meta-analyses**

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Joint work with Anna Chaimani

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**Cochrane Learning Live Webinar, 10<sup>th</sup> February 2022**



- 1 Introduction & overview of NMAstudio functionalities
- 2 Live demonstration: built-in data and example of user data set
- 3 Final considerations and forthcoming updates

INTRO

A **web app** to enhance and facilitate interpretation of **Network Meta Analysis - NMA**

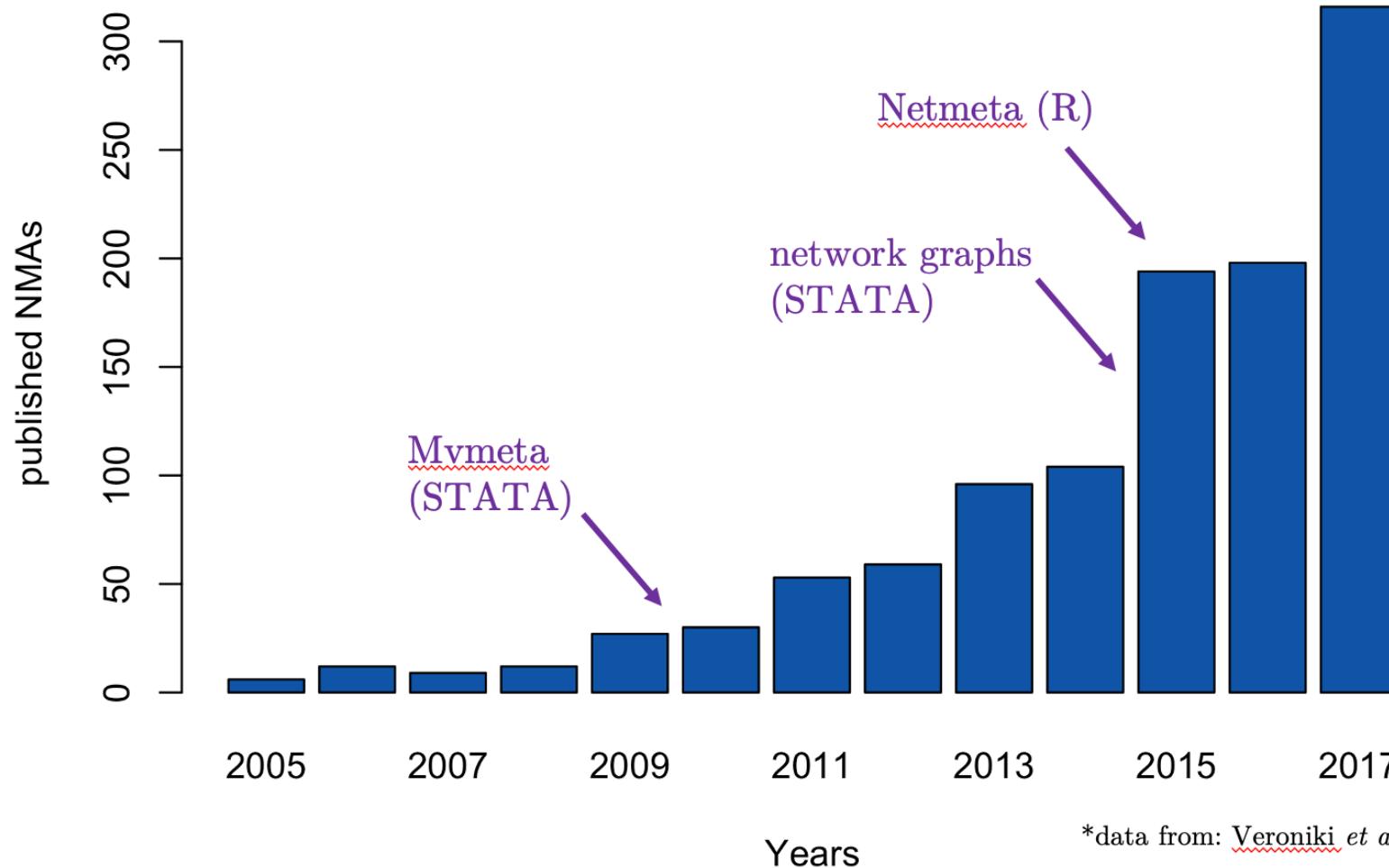
NMAs simultaneously compare multiple treatments forming a ‘network’ of treatments



- All relative effects between treatments → large number of results produced
- Visualisation is challenging, [especially with large networks](#)
- Think of the long Supplementary materials of published NMAs etc

- Software has played a role in the growth of published NMAs

# Why an online tool?

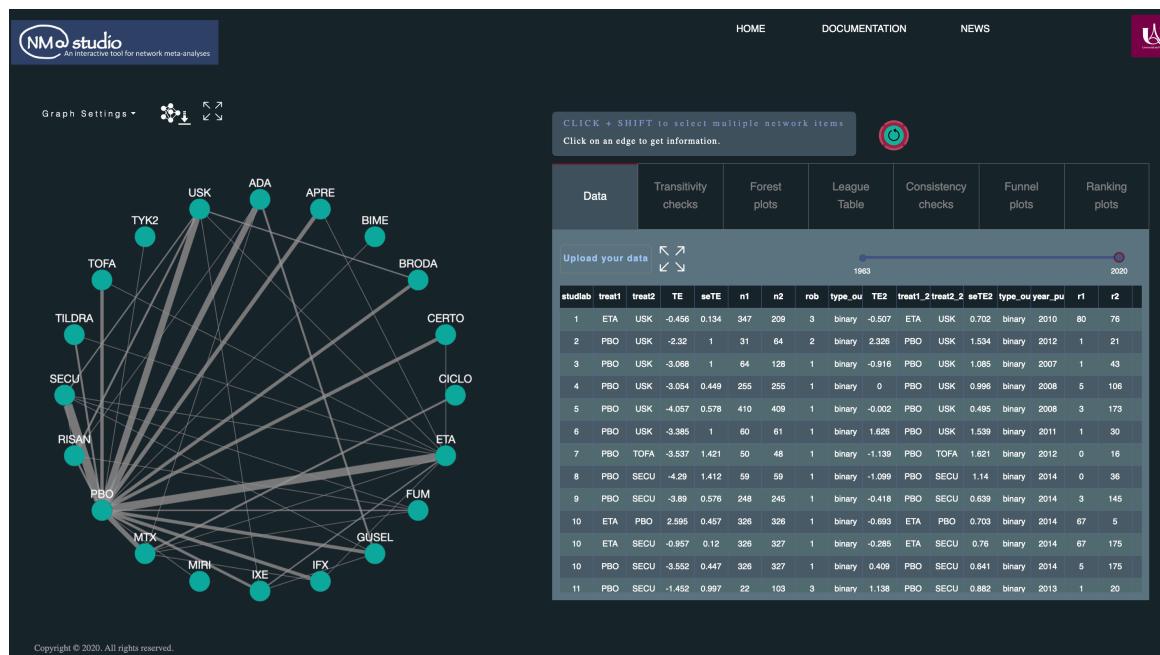


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- Software has played a role in the growth of published NMAs
- We are moving to online/ living evidence (e.g. Covid evidence) -> flexible, user-friendly software is needed to keep up with fast-production of new evidence
- Existing software not *fully* interactive

- Core idea: ‘interactivity’ between the typical NMA network plot and the NMA outputs
  - 1. Users upload data and interact with a [network plot](#) clicking treatments or comparisons
  - 2. Based on their selection, different outputs and information are displayed

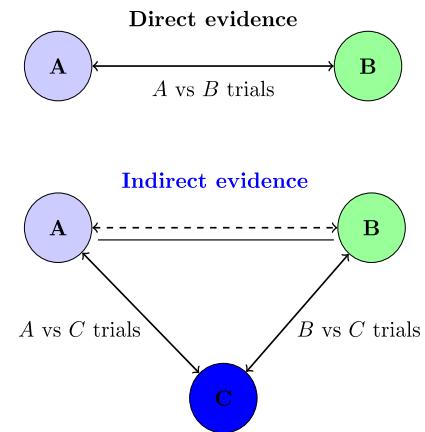
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Webpage: <https://www.nmastudioapp.com>

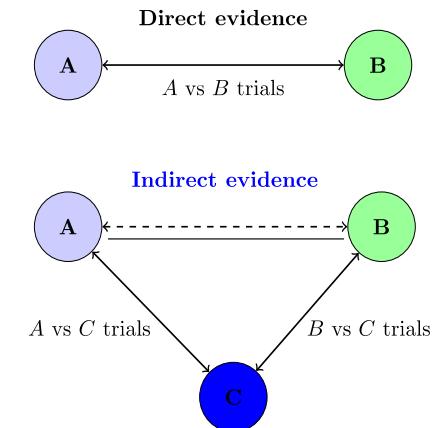
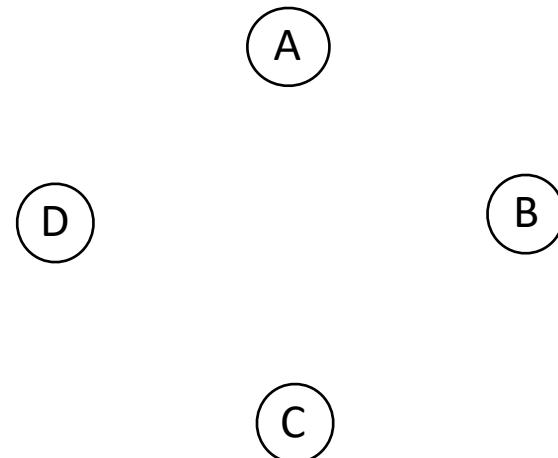
Simultaneous comparison of multiple treatments integrating **direct** with **indirect** evidence in a network of studies

Which treatment works best? (in terms of e.g. efficacy/safety)



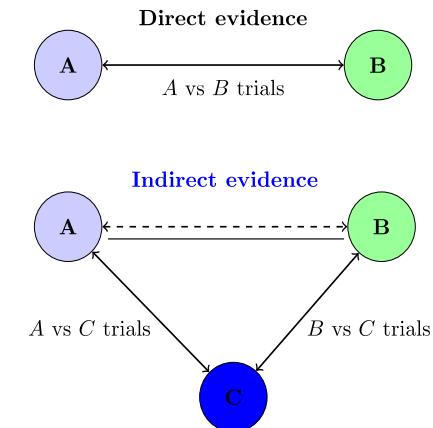
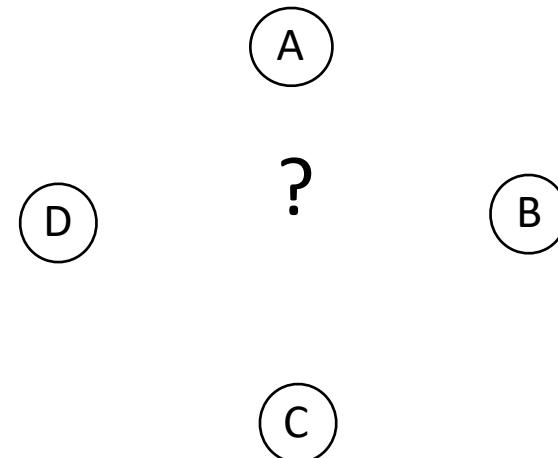
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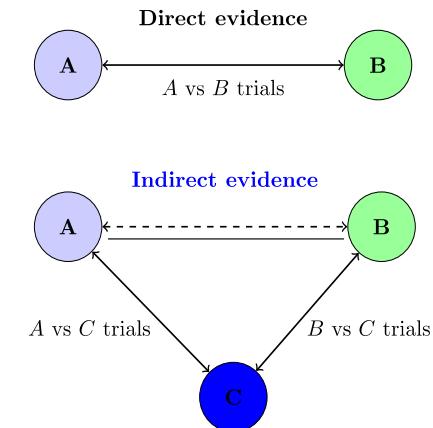
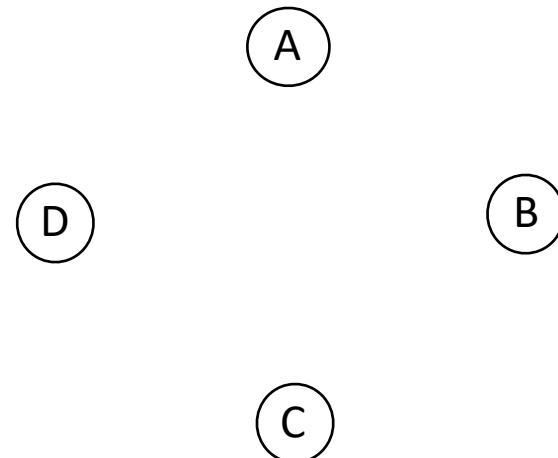
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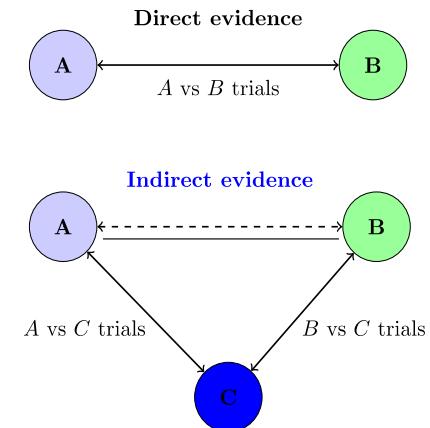
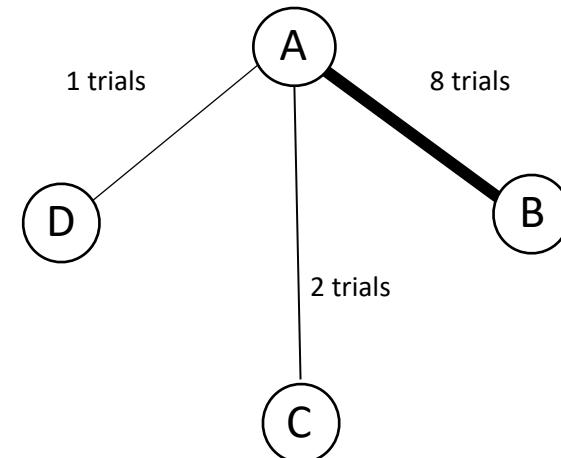
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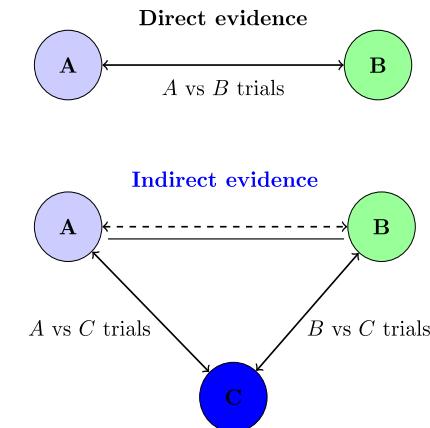
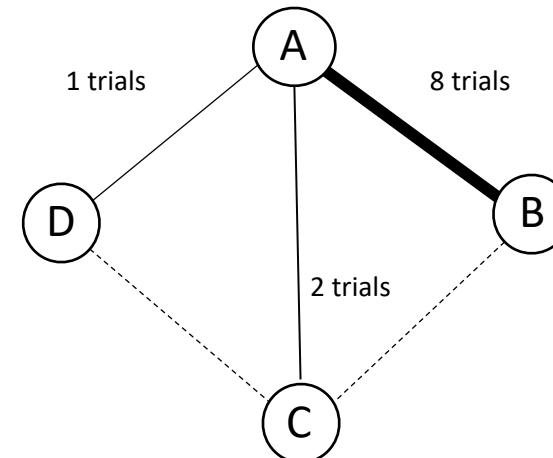
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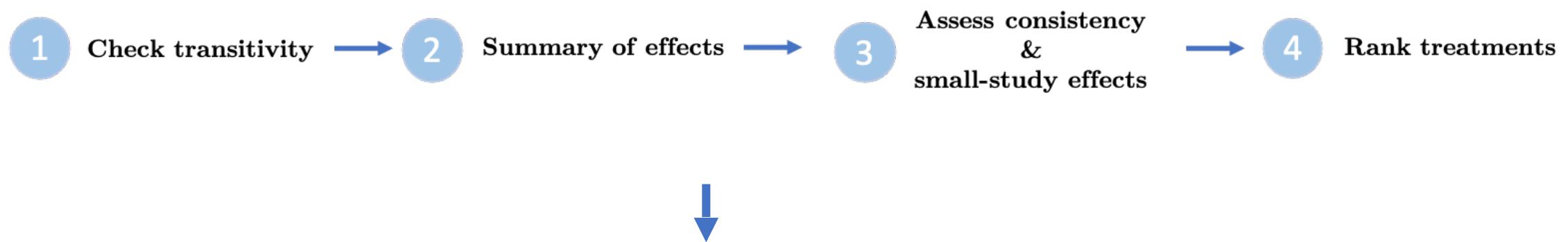


Simultaneous comparison of multiple treatments integrating **direct** with **indirect** evidence in a network of studies

Which treatment works best? (in terms of e.g. efficacy/safety)



Check that the underlying assumptions which make indirect evidence valid are met in your network



## How does it work?

- ❖ Fully built in Python (Dash environment, Plotly for visualisation)
- ❖ Connected to R-package netmeta<sup>1</sup> to produce NMA results
- ❖ Can analyse two outcomes at a time
- ❖ Can read-in CINeMA<sup>2</sup> report file to provide additional visualisations
- ❖ Flexibility on data formats, outcome type etc..
- ❖ A built-in example is permanently loaded (to ease exploration)
- ❖ Works with any browser but Chrome, Mozilla preferred

<sup>1</sup>G. Rücker, U. Krahn, J. König, O. Efthimiou, A. Davies, T. Papakonstantinou & G. Schwarzer. netmeta: Network Meta-Analysis using Frequentist Methods, 2021. R package version 2.0-1. <https://CRAN.R-project.org/package=netmeta>.

<sup>2</sup>A. Nikolakopoulou, J.P.T. Higgins, T. Papakonstantinou, A. Chaimani, C. Del Giovane, M. Egger & G. Salanti. CINeMA: An approach for assessing confidence in the results of a network meta-analysis PLOS Medicine 2020 17 1-19

LIVE DEMONSTRATION

## Two examples

1. Built-in example (chronic plaque psoriasis data)
2. A user data set (major depressive disorders data)

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1. Built-in example (chronic plaque psoriasis data)  To demonstrate main functionalities
  
2. A user data set (major depressive disorders data)  To demonstrate data upload process

158 RCTs comparing 20 drugs



Trusted evidence.  
Informed decisions.  
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

## Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis

Emilie Sbidian<sup>1,2,3</sup>, Anna Chaimani<sup>4,5</sup>, Ignacio Garcia-Doval<sup>6</sup>, Liz Doney<sup>7</sup>, Corinna Dressler<sup>8</sup>, Camille Hua<sup>1,3</sup>, Carolyn Hughes<sup>9</sup>, Luigi Naldi<sup>10</sup>, Sivem Afach<sup>3</sup>, Laurence Le Cleach<sup>1,3</sup>

<sup>1</sup>Department of Dermatology, Hôpital Henri Mondor, Créteil, France. <sup>2</sup>Clinical Investigation Centre, Hôpital Henri Mondor, Créteil, France. <sup>3</sup>Epidemiology in Dermatology and Evaluation of Therapeutics (EpiDermE) - EA 7379, Université Paris Est Créteil (UPEC), Créteil, France. <sup>4</sup>Université de Paris, Centre of Research in Epidemiology and Statistics (CRESS), INSERM, F-75004, Paris, France. <sup>5</sup>Cochrane France, Paris, France. <sup>6</sup>Department of Dermatology, Complexo Hospitalario Universitario de Vigo, Vigo, Spain. <sup>7</sup>Centre of Evidence Based Dermatology, Cochrane Skin Group, The University of Nottingham, Nottingham, UK. <sup>8</sup>Division of Evidence Based Medicine, Department of Dermatology, Venerology and Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany. <sup>9</sup>c/o Cochrane Skin Group, The University of Nottingham, Nottingham, UK. <sup>10</sup>Centro Studi GISED (Italian Group for Epidemiologic Research in Dermatology) - FROM (Research Foundation of Ospedale Maggiore Bergamo), Padiglione Mazzoleni - Presidio Ospedaliero Matteo Rota, Bergamo, Italy

Two outcomes:

- **EFFICACY:** PASI 90 - Psoriasis Area and Severity Index (RR)
- **SAFETY:** SAE - Serious Adverse Events (RR)

# Let's have a first look



[Link to NMAs studio](#)

## Outcome:

- **EFFICACY:** Response Rate as total n. of patients with  $\geq 50\%$  reduction of the total score on a standardised observer-rating scale for depression (OR)

Articles

432 RCTs comparing 21 drugs



focus on head-to-head comparisons



179 RCTs comparing 19 drugs

## Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis



Andrea Cipriani, Toshi A Furukawa\*, Georgia Salanti\*, Anna Chaimani, Lauren Z Atkinson, Yusuke Ogawa, Stefan Leucht, Henricus G Ruhe, Erick H Turner, Julian P T Higgins, Matthias Egger, Nozomi Takeshima, Yu Hayasaka, Hissei Imai, Kiyomi Shinohara, Aran Tajika, John P A Ioannidis, John R Geddes



### Summary

**Background** Major depressive disorder is one of the most common, burdensome, and costly psychiatric disorders worldwide in adults. Pharmacological and non-pharmacological treatments are available; however, because of inadequate resources, antidepressants are used more frequently than psychological interventions. Prescription of these agents should be informed by the best available evidence. Therefore, we aimed to update and expand our previous work to compare and rank antidepressants for the acute treatment of adults with unipolar major depressive disorder.

*Lancet* 2018; 391: 1357–66

Published Online  
February 21, 2018  
[http://dx.doi.org/10.1016/S0140-6736\(17\)32802-7](http://dx.doi.org/10.1016/S0140-6736(17)32802-7)

See *Comment* page 1333

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University of Oxford, Oxford,  
United Kingdom

**Methods** We did a systematic review and network meta-analysis. We searched Cochrane Central Register of Controlled Trials, CINAHL, Embase, LILACS database, MEDLINE, MEDLINE In-Process, PsycINFO, the websites of regulatory agencies and international registers for published and unpublished double-blind randomised

What you need:

1. A .csv file containing main data set
2. A .csv file containing CINeMA report (optional)

In the data selection process, you will choose:

- **Data Format:** long, wide, wide inverse variance (iv)
- **Outcome type:** continuous vs binary
- **Effect size:** OR, RR, MD, SMD

## 1. Data set: long-format

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	studyID	armID	manga	drug_name	Responders	Ntotal	age_mean	age_sd	pub_year	RoB	_Female	Dosing_sche	Dose_range	Spons
2	8	1	0	agom	177	252	42	11	2008	I		1	Flexible	Licensed Yes
3	8	2	0	fluo	164	263	43	12	2008	I		1	Flexible	Licensed No
4	10	1	0	agom	106	167	43	14	2001	I			Fixed	Licensed Yes
5	10	2	0	paro	120	168	42	13	2001	I			Fixed	Licensed No
6	11	1	0	agom	113	137	40	10	2004	I		1	Fixed	Licensed Yes
7	11	2	0	venl	111	140	42	10	2004	I		1	Flexible	Licensed No
8	12	1	0	agom	127	213	69	6	2008	I			Flexible	Licensed Yes
9	12	2	0	paro	118	199	68	6	2008	I			Flexible	Licensed No
10	13	1	0	agom	205	314	39	13	2014	I		1	Flexible	Licensed Yes
11	13	2	0	fluo	209	314	39	13	2014	I		1	Flexible	Licensed No

## 2. CINeMA report (optional)

- as it is saved from CINeMA -

A	B	C
Comparison	Confidence rating	
agom:amit	Moderate	
agom:bupr	Moderate	
agom:cita	Moderate	
agom:clom	Moderate	
agom:dulo	Low	
agom:esci	Moderate	
agom:fluo	Low	

## 1. Data set: long-format

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5	10	2	0 paro		120	168	42	42	13	2001	I			
6	11	1	0 agom		113	137	40	40	10	2004	I			
7	11	2	0 venl		111	140	42	42	10	2004	I			
8	12	1	0 agom		127	213	69	69	6	2008	I			
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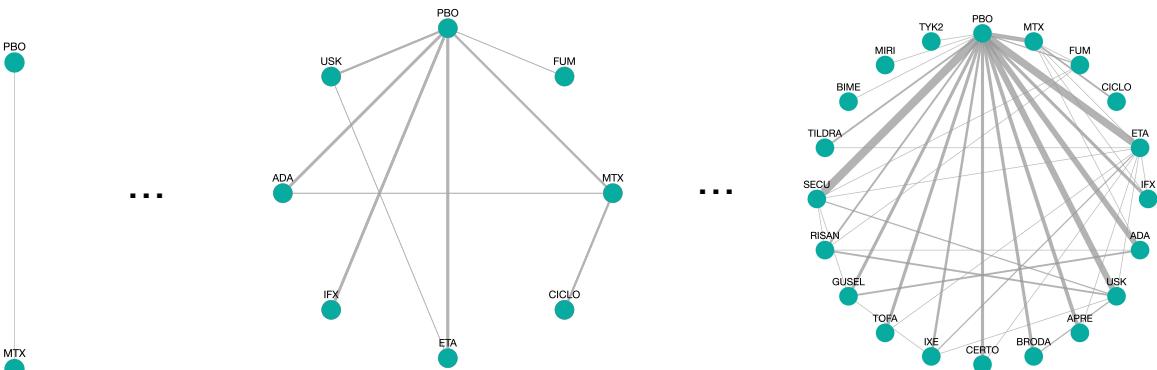
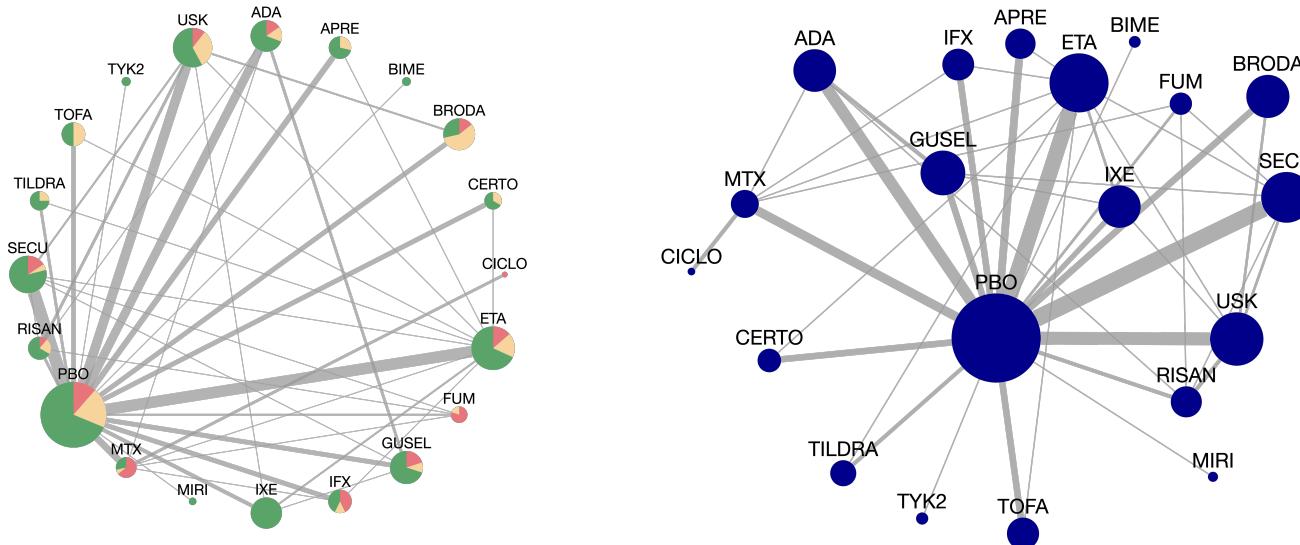
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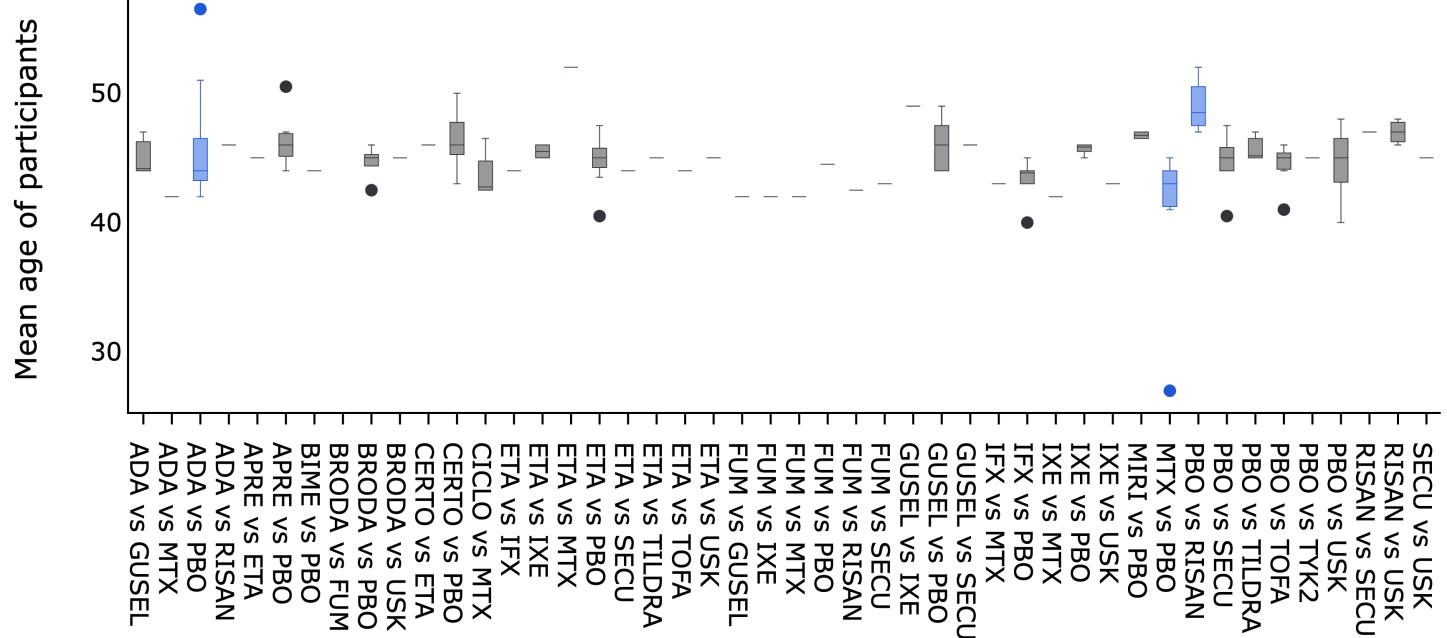
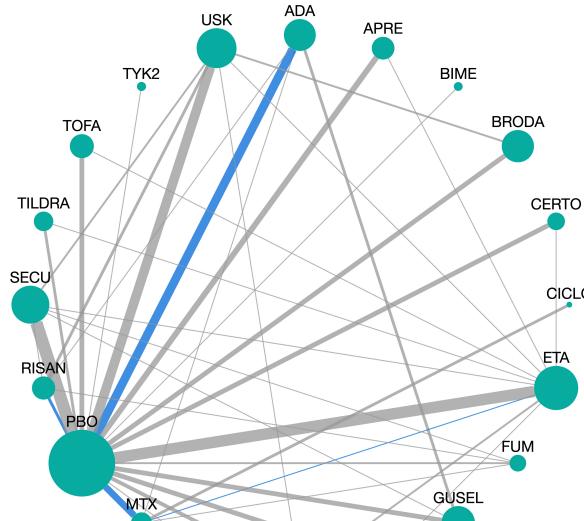
[Link to NMAstudio](#)

## CONSIDERATIONS & FINAL REMARKS

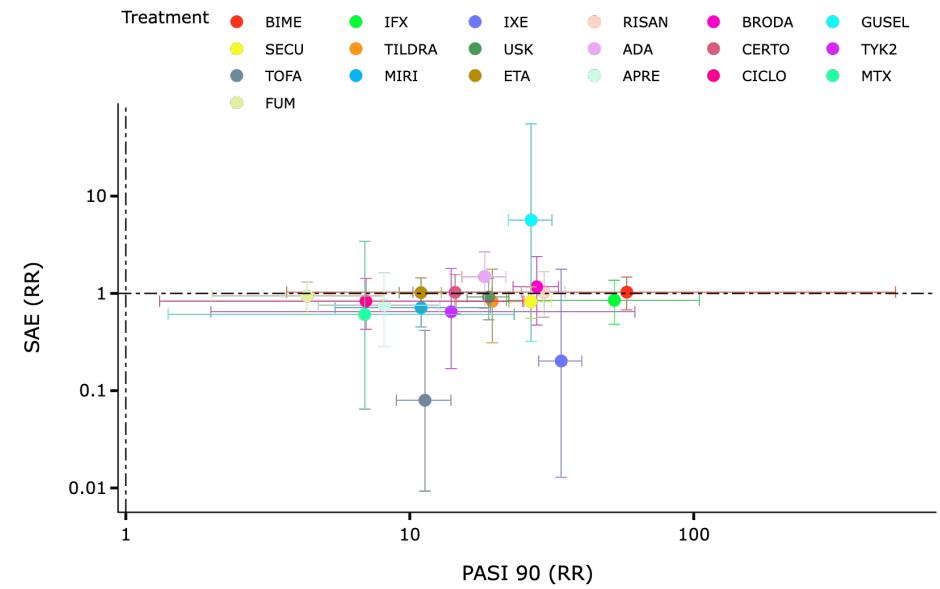
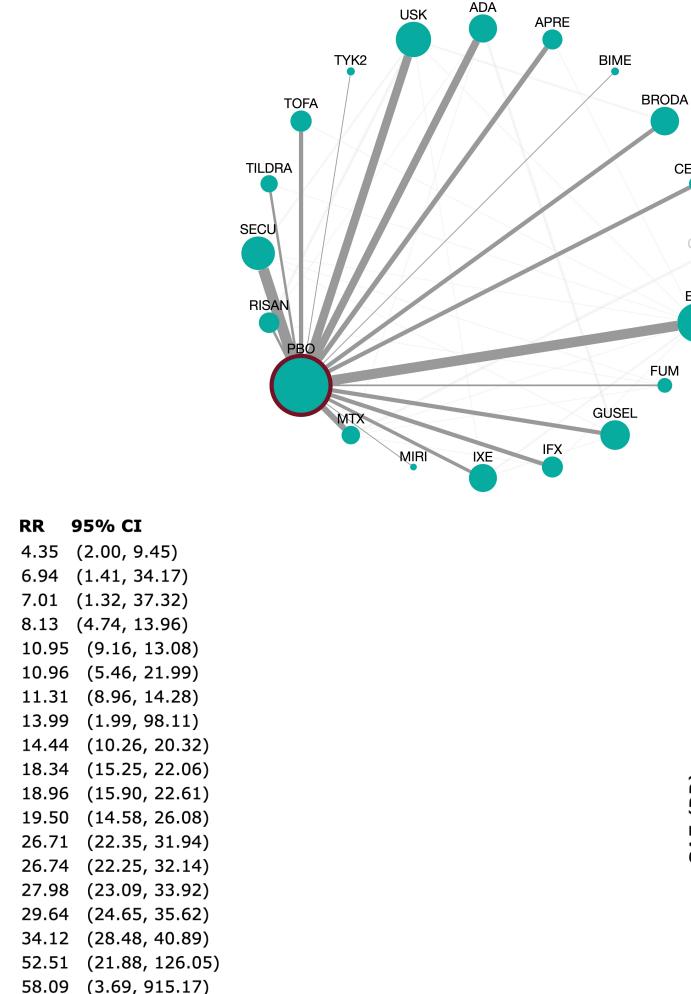
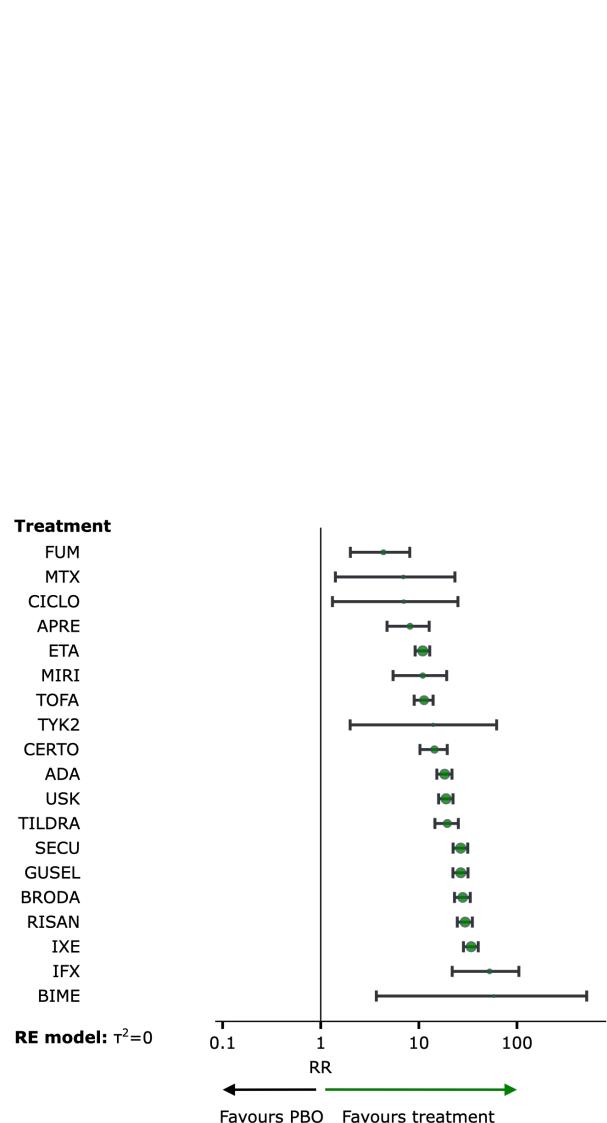
# Examples of outputs: networks



## Examples of outputs: transitivity boxplots



## Examples of outputs: forest plots

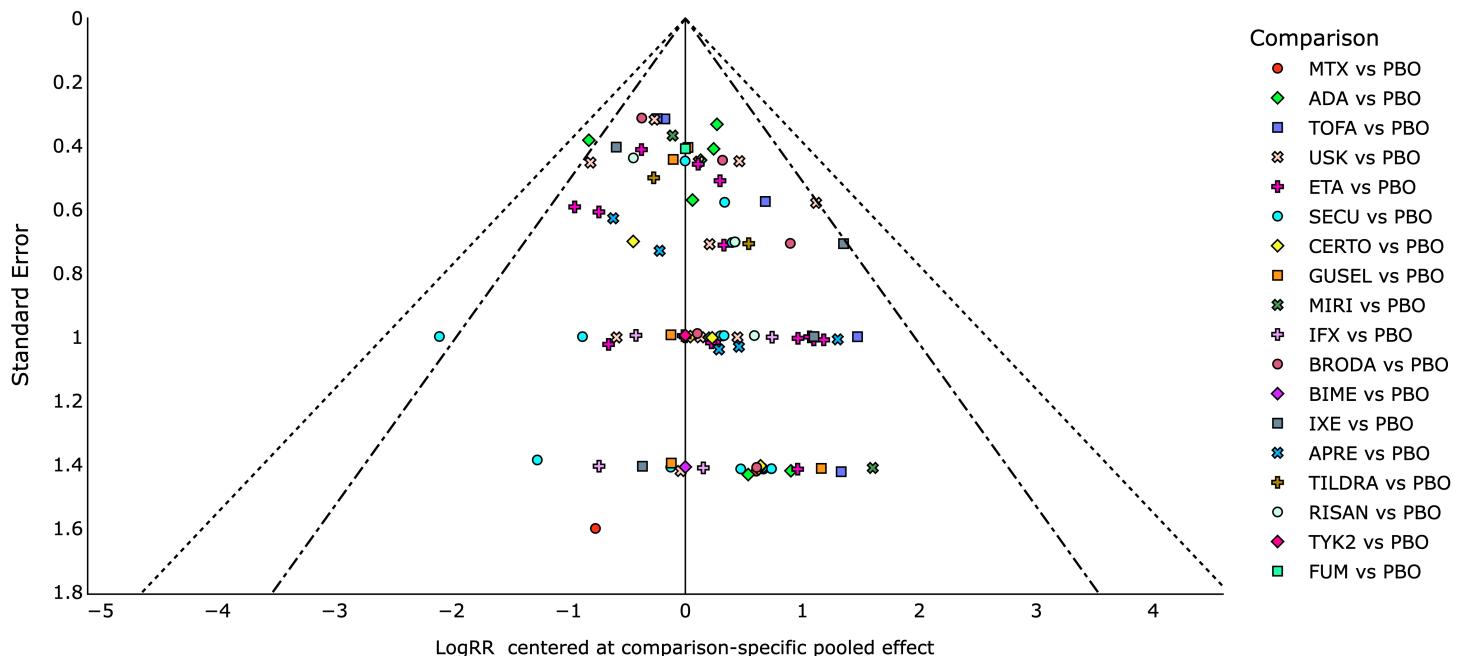


# Examples of outputs: league table

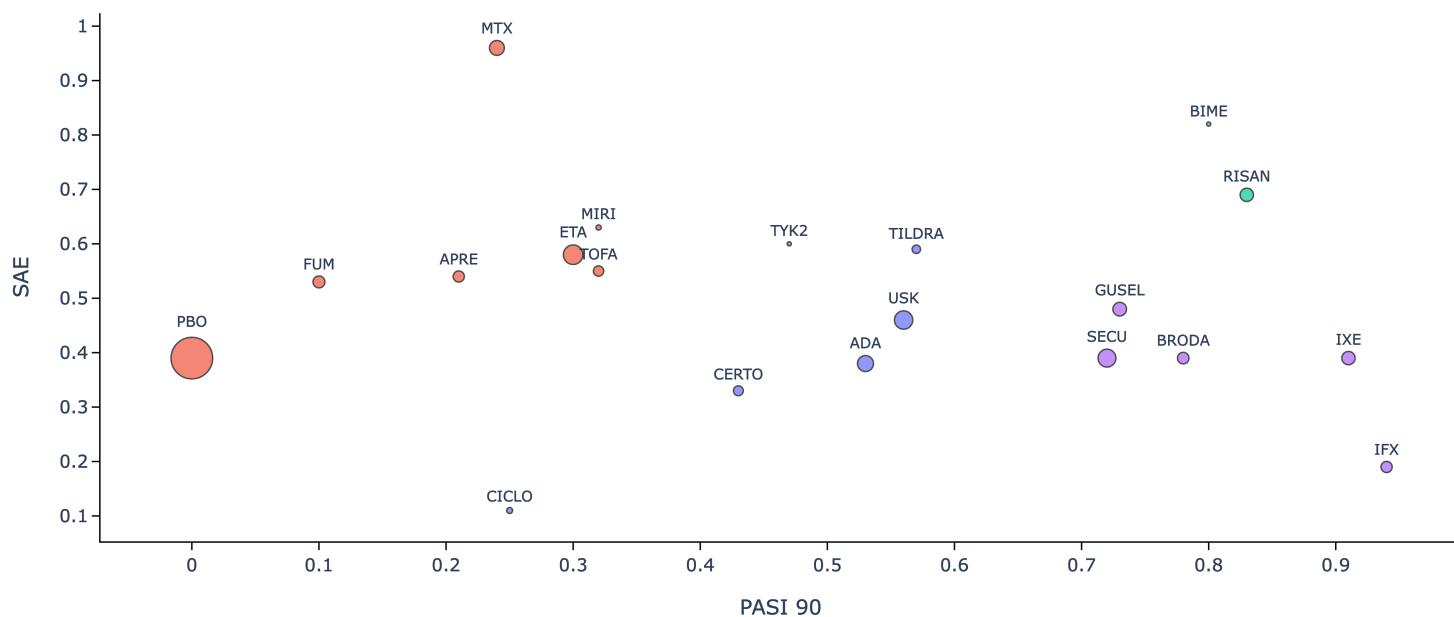
Treatment	IFX	IXE	RISAN	BIME	MIRI	SECU	GUSEL	BRODA	ADA	ETA	PBO
IFX	IFX	1.45 (0.59, 3.53)	2.08 (0.88, 4.96)	0.14 (0.01, 2.35)	2.29 (0.49, 10.61)	1.46 (0.63, 3.39)	0.62 (0.25, 1.55)	0.69 (0.27, 1.79)	0.69 (0.30, 1.62)	0.56 (0.24, 1.27)	1.48 (0.71, 3.10)
IXE	1.54 (0.63, 3.74)	IXE	1.44 (0.74, 2.80)	0.20 (0.01, 3.23)	1.58 (0.38, 6.65)	1.01 (0.53, 1.91)	0.90 (0.51, 1.57)	1.01 (0.46, 2.18)	1.00 (0.55, 1.85)	0.81 (0.46, 1.41)	1.03 (0.62, 1.70)
RISAN	1.77 (0.73, 4.31)	1.15 (1.01, 1.31)	RISAN	0.28 (0.02, 4.62)	0.91 (0.22, 3.75)	0.70 (0.42, 1.18)	1.29 (0.66, 2.54)	1.45 (0.70, 2.99)	1.45 (0.84, 2.49)	1.16 (0.64, 2.09)	1.41 (0.89, 2.21)
BIME	1.11 (0.06, 19.96)	1.70 (0.11, 26.98)	1.96 (0.12, 31.07)	BIME	0.31 (0.01, 6.67)	0.20 (0.01, 3.21)	0.22 (0.01, 3.63)	0.20 (0.01, 3.27)	5.10 (0.32, 82.47)	0.24 (0.02, 3.95)	0.20 (0.01, 3.16)
MIRI	4.79 (1.57, 14.67)	3.11 (1.52, 6.39)	0.37 (0.18, 0.76)	5.30 (0.31, 91.07)	MIRI	0.64 (0.16, 2.59)	1.42 (0.33, 6.04)	1.59 (0.37, 6.91)	1.59 (0.39, 6.49)	1.28 (0.31, 5.18)	0.65 (0.17, 2.48)
SECU	1.97 (0.81, 4.78)	1.28 (1.12, 1.45)	1.11 (1.00, 1.23)	2.17 (0.14, 34.45)	0.41 (0.20, 0.84)	SECU	0.90 (0.46, 1.76)	1.01 (0.50, 2.03)	1.01 (0.58, 1.78)	0.81 (0.47, 1.41)	0.98 (0.65, 1.48)
GUSEL	0.51 (0.21, 1.24)	0.78 (0.72, 0.85)	0.90 (0.79, 1.02)	2.17 (0.14, 34.43)	2.44 (1.19, 5.01)	1.00 (0.88, 1.14)	GUSEL	1.12 (0.50, 2.50)	1.12 (0.63, 1.98)	0.90 (0.48, 1.70)	0.92 (0.53, 1.58)
BRODA	0.53 (0.22, 1.30)	0.82 (0.71, 0.95)	0.94 (0.83, 1.08)	2.08 (0.13, 32.92)	2.55 (1.24, 5.26)	1.05 (0.94, 1.17)	1.05 (0.90, 1.22)	BRODA	1.00 (0.49, 2.05)	1.25 (0.61, 2.54)	1.03 (0.57, 1.87)
ADA	0.35 (0.14, 0.85)	0.54 (0.48, 0.60)	0.62 (0.55, 0.69)	0.32 (0.02, 5.00)	1.67 (0.81, 3.44)	0.69 (0.60, 0.78)	0.69 (0.63, 0.75)	0.66 (0.56, 0.77)	ADA	1.25 (0.71, 2.19)	1.03 (0.68, 1.56)
ETA	0.21 (0.09, 0.51)	0.32 (0.29, 0.36)	0.37 (0.32, 0.43)	5.31 (0.33, 84.05)	1.00 (0.49, 2.05)	0.41 (0.36, 0.47)	0.41 (0.36, 0.47)	2.56 (2.19, 2.99)	1.67 (1.45, 1.94)	ETA	0.83 (0.55, 1.23)
PBO	52.51 (21.88, 126.05)	34.12 (28.48, 40.89)	0.03 (0.03, 0.04)	58.09 (3.69, 915.12)	10.96 (5.46, 21.99)	0.04 (0.03, 0.04)	26.74 (22.25, 32.14)	27.98 (23.09, 33.92)	18.34 (15.25, 22.06)	10.95 (9.16, 13.08)	PBO

# Examples of outputs: consistency and small-study checks

Comparison	direct	indirect	p-value
ADA vs GUSEL	0.678	0.737	0.5124
ADA vs PBO	15.1776	19.7713	0.2054
BRODA vs PBO	31.5189	27.255	0.5679
ETA vs IXE	0.3276	0.3074	0.6193
ETA vs TOFA	0.8968	1.3581	0.0989
IXE vs PBO	39.5201	33.6765	0.6337
IXE vs USK	1.7263	1.8419	0.6201
PBO vs TOFA	0.1125	0.0777	0.1367



# Examples of outputs: ranking



## NMastudio

- is *fully* interactive, flexible web application
- simplifies the whole NMA process and assists in interpretation of findings
  
- Can ease analyses for people with no programming skills
- But also, can ease visualisations for people with programming skills

## Recommendations

- We recommend to follow guidelines provided in the tutorial/online material
- We recommend to use NMastudio following advice from experienced statisticians

## In the near future:

- more options for the graph customisation
- more alerts/warnings in general (e.g. for transitivity/consistency)
- R console to show netmeta errors
- sensitivity analyses (e.g. by RoB, year of publication)
- Option for uploading analyses results and only perform visualisation

❖ **Python package: ‘nmastudio’**  
(under development)



## In a bit further future:

- option for Bayesian NMA analyses (linking NMAsstudio to R + JAGS or Stan)
- permanent link to your project
- .....not restricted to this list!

**Any ideas/suggestions are very welcome, your feedback is important**

please email me at [silvia.metelli@u-paris.fr](mailto:silvia.metelli@u-paris.fr) if you want to get in touch

APP: <https://www.nmastudioapp.com>

TUTORIAL/ DOCUMENTATION: <https://www.nmastudioapp.com/doc>

NEWS/OUTREACH: <https://www.cer-methods.com/>

**THANK YOU!**  
(special thanks to netmeta and CINeMA developers)

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