NMAstudio web-application: A brief tutorial

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Abstract. For a given medical condition, network meta-analysis (NMA) compares multiple available treatments in a network of comparative studies and provides both direct and indirect estimates of the relative treatment effects for all treatments. Despite NMA is increasingly used to inform decision-making, the lack of user-friendly software is still limiting its usage within a restricted community of researchers and end-users. In this tutorial, we describe NMAstudio, a novel user-friendly tool aimed to produce and visualise network meta-analyses in a fully interactive way. NMAstudio enhances visualisation while simplifying the reporting and interpretation of findings. The main feature of NMAstudio is to provide a direct visual connection between a customizable network diagram and the main NMA outputs. The user uploads their data and interacts with the network diagram by clicking one or more nodes-treatments or edges-comparisons. Based on the selection made, tailored outputs and information are displayed. NMAstudio is written in Python and connected to the R package `netmeta` to produce the NMA results. A network of 20 drugs for chronic plaque psoriasis is used as a running example to demonstrate our tool.

1 Introduction

Network meta-analysis (NMA) pools evidence from different studies on multiple treatments to estimate all relative treatment effects and thus, the amount of evidence to be displayed and interpreted can be burdensome, especially when many treatments available. A comprehensive NMA assessment typically involve many graphical outputs, including forest plots for the network estimates, league tables reporting all possible two-by-two treatment comparisons, comparison-adjusted funnel plots, plots displaying ranking of treatments, and many more. However, the available software tools so far still do not provide satisfactory solutions to improve visualisation and screening of such large and complex results.

Towards this end, we have developed NMAstudio, a new interactive web-application to simplify the whole NMA process and enhance visualisation of results. The key feature of NMAstudio is

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that the user can directly interact with a network diagram to produce tailored NMA outputs by clicking one or more nodes-treatments or edges-comparisons. An example is the following: the user clicks on a node in the network graph, say placebo, and in the forest plot section will appear an NMA forest plot of estimates against placebo.

In the form of a tutorial, we will describe into details each step the user should undertake to perform a full NMA appraisal. To fix ideas, the web interface appearance is shown in Figure 1: on the left side of the screen, a network plot is displayed alongside with a dropdown menu for extra network settings; while on the right side of the screen, the user may find seven different tabs. The first tab is used to upload and explore user's data, while each of the subsequent tabs correspond to a key part of an NMA assessment. In the following, we will describe general functionalities of the application, as well as specific functionalities for each of the tabs, i.e. each step of the NMA assessment. Throughout, we will assume the reader is familiar with the basic concepts of evidence synthesis and meta-analysis.

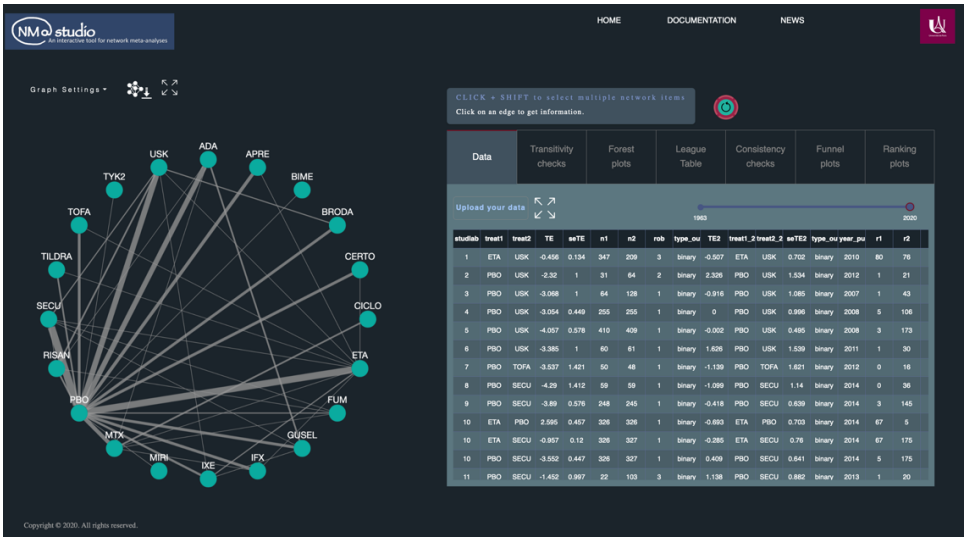

Figure 1 Browser illustration of the NMAstudio web interface.

1 Hosting and demo data

Hosting: NMAstudio is a Python web-application embedded into the Python Dash environment and further connected to the R package netmeta (1) to produce the network meta-analysis estimates. The NMA results are then read into Python where interactive and downloadable visualisations are produced using 'Plotly' modules. The application is open-source and can be freely accessed via any web browser at http://www.nmastudioapp.com, although we recommend to use Firefox or Chrome browsers for optimal deployment. We suggest the reader to follow both the guidelines provided in this tutorial and the full User Guide manual, downloadable from the web documentation page at http://www.nmastudioapp.com/doc. The latter provides additional advice and more detailed descriptions of all the available options for each plot and table of our application.

Demo data: To demonstrate our tool, we use a network of 158 RCTs comparing 20 pharmacological treatments for chronic plaque psoriasis which have been recently evaluated in a Cochrane systematic review (2) (3). Two outcomes are used a measure of efficacy and a measure of safety of treatment.

- **Efficacy**: proportions of participants achieving Psoriasis Area Severity Index ≥ 90 (PASI 90) (RR)
- **Safety**: serious adverse events (SAE) (RR)

This data set is permanently loaded as default data project and we strongly encourage the users to explore and familiarize with NMAstudio through this example before uploading their own data.

2 User data upload

NMAstudio allows two outcomes to be uploaded and analysed simultaneously, however the second outcome is optional and can be dismissed. For each outcome, a choice should be made about the type (continuous or binary) and the desired effect measure, which is to be chosen among mean difference (MD) and standardized mean difference (SMD) for continuous outcomes and odds ratio (OR) or risk ratio (RR) for binary outcomes. To increase flexibility, different data formats are also allowed (long format, wide format and wide inverse-variance format). For instance, if the data are uploaded in long format, they are transformed into contrast-based format as expected by the R package netmeta. Recall that:

Long format: a study contributes as many rows as treatments present in the study. There is a single treatment per row. For long format data, the user should provide the following:

Continuous outcome	**Binary outcome**
• mean *y* (numeric)	• number of events *r* (numeric)
• standard deviation *sd* (numeric)	• sample size *n* (numeric)
• treatment *treat* (string or numeric	• treatment *treat* (string or numeric)

Wide format: one data row per study. There is a single comparison per row, containing summary data for each treatment arm and corresponding standard errors. For wide format data, the user should provide the following:

Continuous outcome	**Binary outcome**
• means in each arm *y1, y2* (numeric)	• number of events in each arm r*1, r2* (numeric)
• standard deviation in each arm *sd1, sd2* (numeric)	• sample size in each arm *n1, n2* (numeric)
• treatment in each arm *treat1, treat2* (string or numeric)	• treatment in each arm *treat1, treat2* (string or numeric)

Wide inverse-variance (iv) format: one data row per study (as wide contrast), but instead of summary data for each treatment, only a comparison-specific estimate, assumed to be gaussian, of the relative treatment effect is available, alongside its standard error. For wide 'iv' format data, the user should provide the following:

Continuous outcome	**Binary outcome**
• means in each arm *y1, y2* (numeric)	• number of events in each treatment arm r*1, r2* (numeric)
• standard deviation in each arm *sd1, sd2* (numeric)	• sample size in each treatment arm *n1, n2* (numeric)
• treatment in each arm *treat1, treat2* (string or numeric)	treatment in each arm *treat1, treat2* (string or numeric)

Further, the user should also provide two additional mandatory variables:

1. **year**: study-level year of publication,
2. **rob**: study-level risk of bias (RoB). RoB takes three possible values (low, medium, high) and should be encoded in the user data file in one of the following ways: {1, 2, 3}, {l, m, h}, {L, M, H}, {low, medium, high} or {LOW, MEDIUM, HIGH}).

Treatment class: Optionally, the user can also provide information about the class of treatment. If such variable is present in the data, there will be an option for colouring nodes of the network by class of treatment. So far, the class variable should take the name of 'treat_class' if data are uploaded in long format and 'treat1_class' and 'treat2_class' in case of contrast format. The variable can either be numeric or string.

Except for treatment class (optional), custom field names are possible for each variable and the user will be prompted to fill a data selection form, as shown in an example in Figure 3. The user should first select the data format and the desired effect size. Based on the selection made, empty cells to be filled with the users' variable names will appear.

Figure 2 Example of a data upload process, with uploaded data in long contrast, and binary outcomes. Note that the "Upload" button is activated only once all data selection cells are filled.

Once the project set-up is completed, all NMA analysis are automatically produced, the data table will be displayed in the 'Data' tab and the corresponding network plot will appear on the left part of the screen (*cnf* Figure 1). By clicking one or multiple nodes and/or edges the user is now ready to:

- explore and filter their data in real time (the full or filtered data table can be expanded and exported in csv via dedicated buttons).
- visualise the evolution of the network over time by using the time slider on the right-top of the data Tab (this particular feature will be discussed in the next section).

- Explore all NMA outputs produced within each of the remaining six tabs and the project.

3 Presentation of the evidence

3.1 Network plot

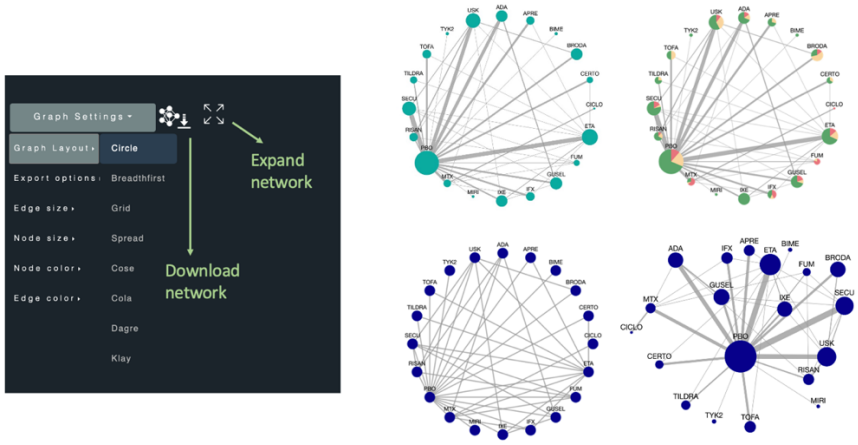

Figure 3 Screenshot of Graph Settings options (left) and network plot, circle layout, for the efficacy outcome PASI 90.

The default network as it appears on the app homepage (*cnf.* Figure 1) has no node size and edge size proportional to the number of studies in that comparison. Node and edge size, as well as other settings and different layouts can be customised by the user using the 'Graph Settings' menu, as shown in Figure 3. We refer the reader to the User Guide documentation for detailed descriptions of all the available layouts. The most appropriate layout is to be chosen according to the data and network information that the user seeks to put more emphasis on. The network can also be expanded via the dedicated icon (see Figure 3) to minimise the risk of overlapping nodes in very large networks. In addition, it is possible to manually adjust the plot by dragging and zooming nodes to resize the network appearance. Note that NMAstudio allows to display both the network relating to the first outcome (default) as well as the second outcome, if present: the network for the second outcome automatically appears upon selection via the dedicated toggle-switches the tabs.

Finally, as mentioned above, the app contains a slider (Data Tab, upper-right side) that the user can drag ahead to show the evolution of the evidence over time. The left marker corresponds to the year when the first trial was conducted (1963 in the psoriasis example reported here), while the right marker is the last year of additional available evidence (2020). The slider contains one

marker for each point in time in which evidence was added. As a simple example, Figure 4 shows how the network of evidence has evolved over three timestamps, 1963, 2010, 2020. Note also that the data table is filtered accordingly in real-time.

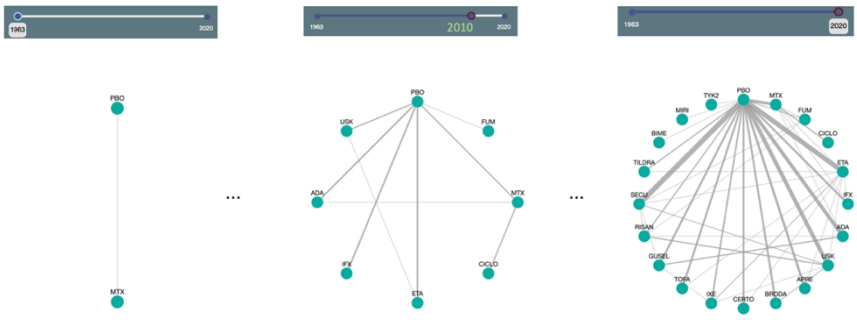

Figure 3 Example of evolution of the network over three different timestamps.

3.2 NMA assessment

Transitivity checks: Transitivity is the core assumption of network meta-analysis that makes the use of indirect evidence valid thus evaluation of its plausibility is fundamental to ensure validity of the whole NMA process. However, transitivity can only be checked graphically by looking at whether important differences in the distribution of the potential effect modifiers exist in the data. More detailed explanation of transitivity can be found elsewhere (4) (5). All the effect modifiers present in the data and suspected to differ in distribution should be checked. In NMAstudio, users can select the effect modifier they wish to investigate in the 'Transitivity' tab. As an example, in Figure 5 we have analysed the distribution of mean age of participants in each trial. The boxplots are fairly similarly distributed across comparisons, suggesting no intransitivity with respect to this variable. Users can highlight some boxplots of interest by clicking on the corresponding comparison-edge(s) in the network plot.

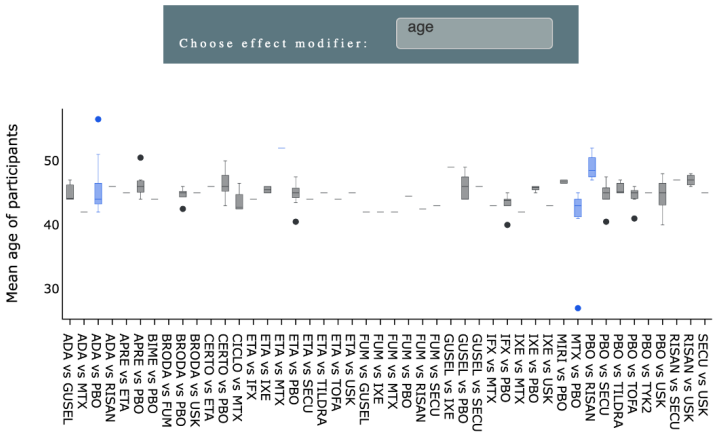

Figure 4 Transitivity boxplots with some comparisons highlighted in blue.

Note: if data are uploaded in long format each effect modifier the value of a variable can differ between treatment arms; for example, the mean age or percentage of women in the treatment arm. In this situation, two variables instead of one variable will be included in the output dataset. The values "1" and "2" are added to the names for these variables, e.g. "mean.age1" and "mean.age2" for the mean age. More info at: https://rdrr.io/cran/netmeta/man/pairwise.html

Forest plots: Three different forest plots are available: (i) forest plots of network estimates for the outcome of interest, (ii) forest plots of pairwise comparisons and (iii) bi-dimensional forest plots containing network estimates of the first outcome on the x-axis and containing network estimates of the second outcome on the y-axis. Figure 6 shows how to produce forest network estimates forest plots for a single outcome or two outcomes together: the reference treatment (placebo here) is selected from the network and the corresponding plots appear in the 'NMA' or 'Bi-dimensional NMA' subtabs in the right part of the homepage. Information about heterogeneity is annotated to the NMA forest plot. The direction of the outcome (beneficial vs. harmful) can also be annotated to the plot. Although not shown here, pairwise forest plots for each direct comparison are also available, upon edge-click.

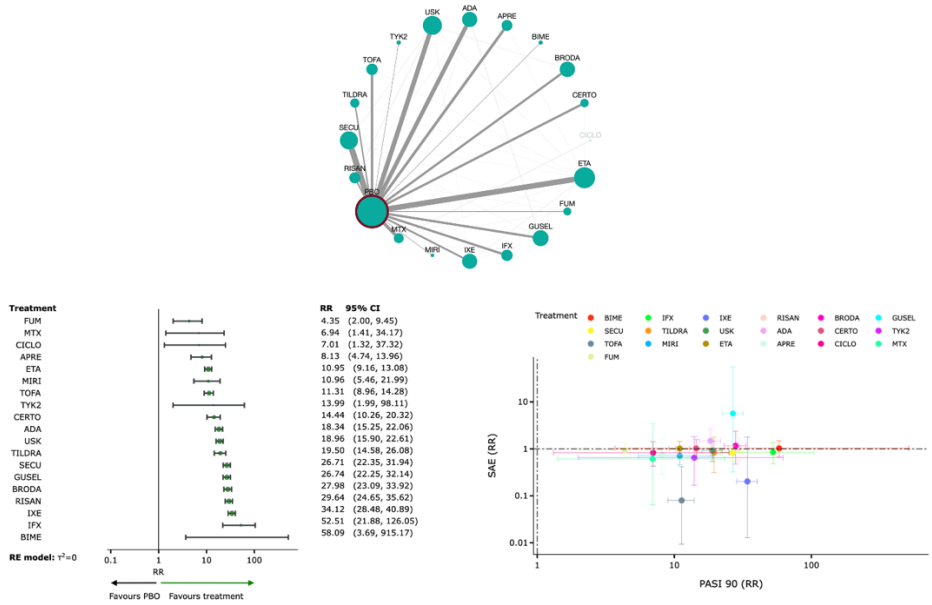

Figure 5 NMA and bi-dimensional forest plots for the efficacy outcome, alongside network plot with selected node as reference treatment for the analyses.

League tables

A league table typically contains all two-by-two estimated treatement effects from a network meta-analysis. NMAstudio allows for the full table to be displayed and saved, as well as a reduced league table containing only treatments selected in the network. The ordering of selection corresponds to the order of appearance of treatments in the table. NMAstudio also allows to colour the table cells according to some criterion of interest. At the moment, two colouring options are available: by the average risk of bias in the comparison, and by the credibility in the full body of evidence from the CINeMA software (Confidence in Network

Meta-Analysis) (8) (9) (10). To assess and summarize the level of concern for each comparison, CINeMA uses four domains of confidence ("high", "moderate", "low", "very low"), which result from an assessment of the confidence in each network meta-analysis estimate in terms of within-trial bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. Some threshold values and evaluation rules need to be decided for carrying out some of the CINeMA steps: these are typically finalised through discussions between researchers and clinicians. After carrying out the CINeMA assessment following the principles above, in Figure 7 we report a table of relative treatment effects for both efficacy and safety, coloured by confidence in the evidence.

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

Figure 7 League table containing RRs for efficacy (lower triangle) and safety (upper triangle) with their 95%CIs derived from network meta-analysis and colored by certainty of evidence assessed for each comparison with CINeMA. Each cell is classified as high (green), moderate (blue), low (yellow) and very-low (red) confidence in the evidence. RRs larger than 1 favour the treatment on the left for the lower triangle and smaller than 1 for the upper triangle.

Note: NMAstudio requires the user to upload the CINeMA report file in its original format, with mandatory columns "Comparison" and "Confidence rating", as shown below.

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
ADA:GUSEL	3	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ADA:PBO	8	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High
ADA:RISAN	1	No concerns	Undetected	No concerns	No concerns	No concerns	No concerns	High

Consistency checks

Inconsistency expresses statistical disagreement of direct and indirect evidence, and can sometimes reflect the presence of intransitivity or heterogeneity in the network. NMAstudio reports results from two statistical tests assessing the presence of inconsistency i.e. local inconsistency in parts of the network and global inconsistency in the whole network (11). An example of both tests produced via NMAstudio is reported in Table 1 and Table 2. Table 1 suggests that no overall inconsistency is present while Table 2 (where we have selected a subset of comparisons clicking edges in the network) suggests that two comparisons, tofacitinib (TOFA) vs. etanercept (ETA) and tofacitinib vs. placebo, have some concerns of intransitivity. Information about the number of studies can be found in the dedicated box (*cnf* Figure 2) when clicking the comparison of interest.

Table 1 Design-by-treatment interaction tests for efficacy and safety, alongside Q statistic and degrees of freedom.

Outcome	Q	df(Q)	p-value
PASI 90	22.9497	27	0.6877
SAE	32.348	26	0.1819

Table 2 Node-splitting local tests for inconsistency in each direct comparison: P-values <0.10 and 0.10<p-values<0.15 flagged as red and yellow respectively.

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

Small-study effects assessments

To evaluate the presence of small-study effects (13) comparison-adjusted funnel plots can be used, as these plots report each study's effect estimates centred at the comparison-specific effect against their reversed standard error and so allow to further investigate the distribution of the effect sizes. An asymmetry in the plot might suggest that larger effects tend to be systematically found in smaller studies. In this case, the effects are suspect to have been inflated for publication (14) (15). An ordering of the treatments is necessary for a meaningful interpretation of this plot, and when this is not possible only the studies compared to the same reference treatment should be included in the plot. At present, NMAstudio allows for the second option only. In our example, we report the funnel plot for efficacy for all active treatments against placebo. The plot is shown in Figure 8 and was produced clicking on the node 'PBO' in the network plot, which was thus used as reference. Here, the funnel plot suggests no evidence of small-study effects as the points are quite well symmetrically distributed around the axis. Available options for further plot customisation are reported in the User Guide.

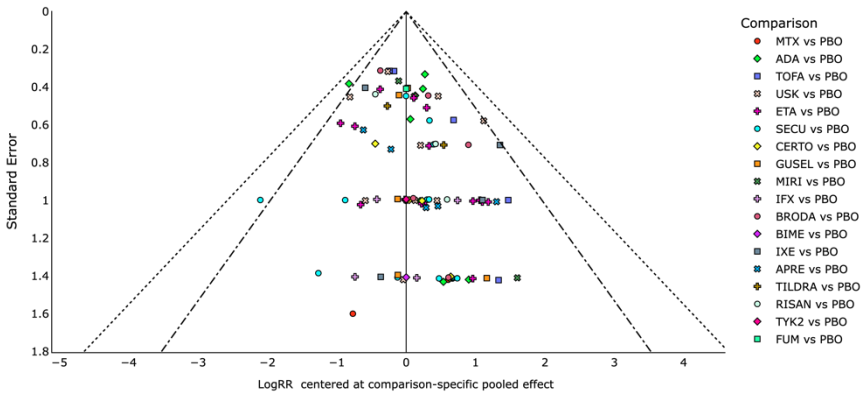

Figure 7 Comparison-adjusted funnel plot for the efficacy outcome, showing logRRs for studies compared to Placebo (PBO). The plot is automatically produced upon clicking on the node 'PBO' in the network plot.

Treatment ranking

After all the previous assessments have been performed, network meta-analyses typically aim to provide a final ranking of treatments, which is one of the most competitive advantages with respect to standard meta-analyses. The most commonly used measures to quantify ranking are the surface under the cumulative ranking curve (SUCRA) for each treatment and its frequent analogue, the P-score (16). NMAstudio uses P-scores to rank treatments as they are provided in netmeta, which performs frequentist inference. As SUCRAs, P-scores range from 0 to 1, and can be interpreted as an average *degree of certainty* for a treatment to be better than the other treatments in the network. NMAstudio provides two different graphical representations of ranking via P-scores: a heatmap of treatments sorted by P-scores, and a scatterplot of P-scores for the two outcomes, if both are present. In the heatmap, treatments are sorted and coloured from best to worse P-score, however when both outcomes are present, the sorting is made according to the first (main) outcome of interest. The scatterplot displays instead P-scores of the first outcome on the x-axis and P-scores for the second outcome on the y-axis. Clearly, optimal treatment(s) should have high values in both outcomes. However, when uncertainty is high, rankings may be not very informative and looking at the relative treatment effects may be clinically more relevant and appropriate (17). Thus, we encourage the users to always evaluate ranking also in light of the uncertainty found in the estimates. In Figure 9, we report the two plots hereby described alongside the fundamental toggle switch to drive the direction of the ranking, i.e. to choose whether the outcomes are beneficial or harmful.

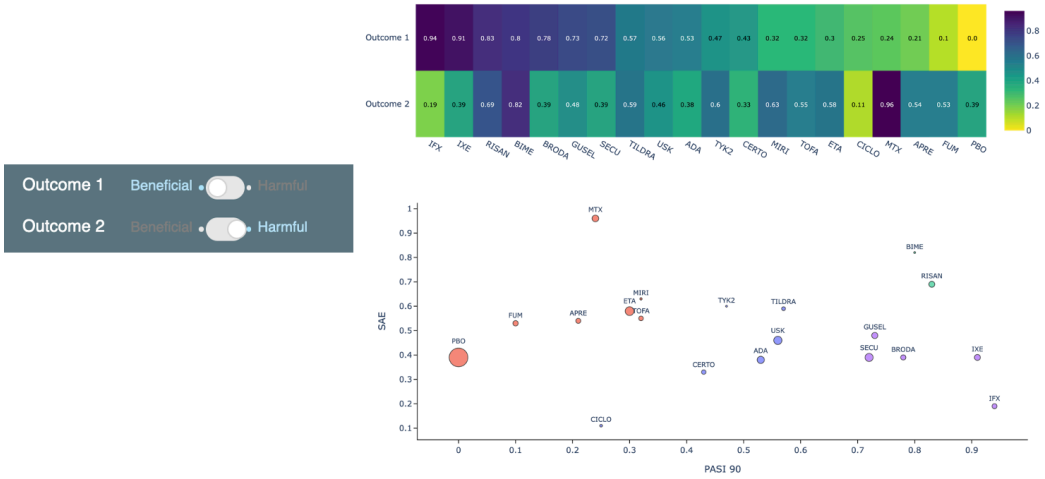

Figure 8 P-scores heatmap and scatter plots for both outcomes In the scatterplot, the size of the bubble is proportional to the number of people randomised in that treatment and each colour correspond to treatments placed in the same cluster (via simple K-means).

4 Short summary

In this tutorial, we have introduced a novel web application, NMAstudio, and presented how it can be used to produce and visualise network meta-analyses through easy “point and click” interactions. NMAstudio is the first web interface in the field of network meta-analysis to provide

full interactivity between the network plot and all the most relevant NMA outputs. Given that navigating through large and complex outputs can be very time-consuming and sometimes confusing, we believe interactivity is an essential feature, especially when having large networks with many treatments. Many options for customise all the graphical displays are available and although not listed in this tutorial, they are all summarised in the software accompanying User Guide. Further updates will soon be available. First, we seek to include Bayesian analyses by connecting Python to R-Jags or the Stan environment. This can enable analysis on a number of settings for which frequentist analysis is not possible or poorly performant. We wish to also allow users to upload directly their results and use the app for visualisation purposes only. To this end, we plan to partner NMAstudio with a corresponding Python package. Finally, we intend to add options for performing sensitivity analyses as well as to strengthen our current system of warnings. Further options in the customisation of the network plot are also foreseen. Examples include, but are not restricted to, colouring of edges by risk of bias and edge size by study precision. All forthcoming and future features are listed in the app at the page http://www.nmastudioapp.com/news. We hope that this resource will prove useful for researchers and end-users undertaking network meta-analyses, especially to those less accustomed to programming languages, and that it will help to communicate meta-analytic data and results more clearly to vast and diverse audience. The full software is open-source and the code is freely available at https://github.com/silviametelli/network-meta-analysis.

References

1. G. Rücker, G. Schwarzer, U. Krahn, and J. König. netmeta: Network Meta-Analysis using Frequentist Methods, 2017. R package version 0.9-5. https://CRAN.R-project.org/package=netmeta.

2. Sbidian E, Chaimani A, Garcia-Doval I, Do G, Hua C, Mazaud C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2017 Dec 22;12:CD011535.

3. Sbidian E, Chaimani A, Garcia-Doval I, Doney L, Dressler C, Hua C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2021 Apr 19;4:CD011535.

4. Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. Res Synth Methods. 2012 Jun;3(2):80–97.

5. Chapter 11: Undertaking network meta-analyses. Cochrane handbook for systematic reviews of interventions, pp. 285-320. Available from: https://training.cochrane.org/handbook/current/chapter-11

6. Fujian Song, Douglas G Altman, Anne-Marie Glenny, and Jonathan J Deeks. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. Bmj, 326(7387):472, 2003.

7. Luo Y, Chaimani A, Furukawa TA, Kataoka Y, Ogawa Y, Cipriani A, et al. Visualizing the evolution of evidence: Cumulative network meta-analyses of new generation antidepressants in the last 40 years. Res Synth Methods. 2021;12(1):74–85.

8. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Giovane CD, Egger M, et al. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. PLOS Med. 2020 Apr 3;17(4):e1003082.

9. Papakonstantinou et al. CINeMA: Software for semiautomated assessment of the confidence in the results of network meta-analysis Campbell Systematic Reviews 2020 16 e1080]

10. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. PLoS One. 2014;9(7):e99682.

11. Veroniki AA, Vasiliadis HS, Higgins JPT, Salanti G. Evaluation of inconsistency in networks of interventions. Int J Epidemiol. 2013 Feb;42(1):332–45.

12. Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. Statist Med. 2010;29(7-8):932-944.

13. Chaimani A, Salanti G. Using network meta-analysis to evaluate the existence of small-study effects in a network of interventions. Res Synth Methods. 2012 Jun;3(2):161–76.

14. Ioannidis JPA. Why Most Discovered True Associations Are Inflated. Epidemiology. 2008 Sep;19(5):640–8.

15. Barbui C, Cipriani A, Brambilla P, Hotopf M. 'Wish bias' in antidepressant drug trials? J Clin Psychopharmacol. 2004 Apr;24(2):126–30.

16. Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. BMC Med Res Methodol. 2015 Jul 31;15(1):58.

17. Salanti G, Nikolakopoulou A, Efthimiou O, Mavridis D, Egger M, White IR. Introducing the treatment hierarchy question in network meta-analysis. Am J Epidemiol. 2021 Nov 23; kwab278.