# rnmamod: An R Package for Conducting Bayesian Network Meta-analysis with Missing Participants

*by Loukia M. Spineli, Chrysostomos Kalyvas, and Katerina Papadimitropoulou*

**Abstract** A plethora of R packages exists for performing network meta-analysis, which has significantly enhanced the popularity of this evidence synthesis methodology. The available R packages facilitate the implementation of the majority of the proposed statistical models to conduct and evaluate network meta-analysis, providing necessary results that conform to the PRISMA-NMA statement. The rnmamod package is a novel contribution to performing aggregate data network meta-analysis using Bayesian methods, as it enables the proper handling of missing participant data in all models, even if a handful of the included studies report this information. Rnmamod is the first R package to offer a rich, user-friendly visualisation toolkit that turns a "parameter-dense" output of network meta-analysis into a collecction of comprehensive graphs. The package further facilitates a thorough appraisal and interpretation of the results, allows the cross-comparison of different models and streamlines the preparation of manuscripts for journal submission.

## Introduction

Evidence-based medicine forms the backbone of informed decisions for the benefit of the patients, arising from a meticulous and judicious use of the available evidence. This concept incorporates clinical experience and patient values on the basis of the most up-to-date and reliable scientific evidence(Sackett et al. 1996). However, the medical community is daily confronted with vast amount of clinical evidence to keep pace with, which poses challenges to the optimal practice of evidence-based medicine (Lee 2022). Systematic reviews with pairwise meta-analysis summarise the evidence of a pair of interventions, providing fragmented evidence that does not serve the clinical needs of treatment recommendations based on a plethora of available options. Moreover, evidence regarding the comparability of different interventions at the trial level is also fragmented, as it is impractical to compare all intervention options for a particular condition in signle trial. These limitations led to the development and subsequent establishment of network meta-analysis (NMA), also known as multiple treatment comparison — a new generation evidence synthesis tool (Salanti 2012). Network meta-analysis is the extension of pairwise meta-analysis, collating all relevant evidence for a specific condition, patient population, and intervention options. The purpose is to provide coherent evidence for all possible intervention comparisons, and allow the ranking of the investigated interventions from the most to the least effective for a given outcome (Caldwell 2014). Indirect evidence (obtained from different sets of trials sharing a common investigated intervention/comparator) plays a central role in the development and prominence of NMA.

Since the introduction of indirect evidence and early development of the relevant methodology (Higgins and Whitehead 1996; Bucher et al. 1997), the NMA framework has undergone substantial progress conceptually and methodologically. The fast-pace publications of relevant the patients, arising from a meticulous and judicious use of the available evidence, while taking into account clinical experience and patient values (Sackett et al. 1996). However, the medical community is confronted daily with a vast amount of clinical evidence to keep pace with, challenging the optimal practice of evidence-based medicine (Lee 2022). Systematic reviews with pairwise meta-analysis summarise evidence of pairs of interventions, providing fragmented evidence that fails to meet broader clinical needs on deciding treatment recommendation amongst a plethora of available options. Moreover, evidence regarding the comparability of different interventions at the trial level is also fragmented, as it is impractical to compare all intervention options for a particular condition in a single trial. These limitations led to the development and subsequent establishment of network meta-analysis (NMA), also known as multiple treatment comparison–a new generation evidence synthesis tool (Salanti 2012). Network meta-analysis extends the concept of pairwise meta-analysis to collate all relevant pieces of evidence for a specific condition, patient population, and intervention options. Its purpose is to provide comprehensive evidence for all possible intervention comparisons, enabling the ranking of the investigated interventions from the most to the least effective option for a specific outcome (Caldwell 2014). Indirect evidence (obtained from different sets of trials sharing a common comparator) plays a central role in the development and prominence of NMA.

Most methodological studies on and systematic reviews with NMA have implemented Bayesian methods (Efthimiou et al. 2016; Petropoulou et al. 2017). The advantages of the Bayesian framework

(e.g., flexible modeling, allowance of uncertainty in all model parameters, incorporation of external relevant information and facilitation of probabilistic statements) (Sutton and Abrams 2001), in conjunction with the dominance of the BUGS software (Lunn et al. 2009) during the springtime of the NMA framework, may have contributed to the rising popularity of Bayesian NMA. The numerous R packages on Bayesian NMA also demonstrate the acclaim of Bayesian methods from the evidence synthesis community (Dewey and Viechtbauer 2023). The rest of the section pertains to R packages on Bayesian NMA published in the **CRAN Task View 'Meta-Analysis'** (Dewey and Viechtbauer 2023) that feature a wide methodological and reporting scope: **bnma** (Seo and Schmid 2022), CRANpkg{gemtc} (van Valkenhoef and Kuiper 2021), **pcnetmeta** (Lin et al. 2017), and **rnmamod** (Spineli 2022) (a recent novel contribution).

The R packages **bnma** (Seo and Schmid 2022), **gemtc** (van Valkenhoef and Kuiper 2021), and **pcnetmeta** (Lin et al. 2017) conduct hierarchical NMA using Markov chain Monte Carlo (MCMC) methods through the **JAGS** program (Plummer 2003). However, they differ in their methodological and reporting scope: **bnma** (Seo and Schmid 2022) and **gemtc** (van Valkenhoef and Kuiper 2021) have a greater common basis on methods and outputs than **pcnetmeta** (Lin et al. 2017). This may be ascribed to using the contrast-based modeling approach (trial-specific relative effects, such as log odds ratio (OR), are pooled across the trials), which is the established approach to meta-analysis, whilst **pcnetmeta** (Lin et al. 2017) considers the arm-based modeling approach (arm-specific results, such as log odds, are pooled across the trials), which deviates from the standard meta-analysis practice (Dias and Ades 2016) and is less widespread.

Currently, the package **pcnetmeta** (Lin et al. 2017) does not contain any function to conduct inconsistency evaluation and meta-regression, is limited only to rankograms in terms of hierarchy measures (Salanti et al. 2022), and considers only the trace plots as a visual diagnostic tool. On the contrary, **bnma** (Seo and Schmid 2022) and **gemtc** (van Valkenhoef and Kuiper 2021) offer at least one method for inconsistency evaluation, allow conducting meta-regression, and consider a wider variety of hierarchy measures and diagnostic tools. However, all three R packages provide a small-sized toolkit with functions regarding the presentation of the relative treatment effects: a league table for one outcome that appears only in the console, and a forest-plot or table on the relative treatment effects of all comparisons with the selected intervention. Moreover, they rely more on the function `print()` (the results appear in the console) than visualisation, and present the results mostly in isolation, restricting the ability to gain further insights into the performance of different NMA models (for instance, assuming consistency versus inconsistency).

Due to the complexity and the wide scope of NMA, the researchers are faced with a large volume of results, necessary to understand the evidence base, assess the underlying assumptions, and evaluate the quality of the estimated parameters (model diagnostics) in order to properly answer the investigated research questions. The aforementioned R packages have limited functionalities concerning the presentation of the NMA results, hindering thorough scrutiny, and critical appraisal, necessary for the transparency of conclusions delivered to the end-users of systematic reviews with multiple interventions. Furthermore, undue reliance on the console limits the usability of the results as the R users have to resort to tabulation, afflicting comprehension, especially, when analysing large intervention networks that are naturally associated with an immense amount of results. Alternatively, the R users have to create the functions to obtain the necessary visualisations, a time-consuming process, depending on the R user experience, whilst time and energy could have been put into appraising the results. The R package **rnmamod** (Spineli 2022), published recently in the Comprehensive R Archive Network (available at `https://CRAN.R-project.org/package=rnmamod`), aspires to fill this technical gap by offering a rich, user-friendly visualisation toolkit that turns an inherently dense output of NMA into several coherent graphs. Originally, the **rnmamod** package was inspired by the absence of R packages that properly account for (aggregate) missing participants in the models underlying the NMA framework (e.g., core model, inconsistency assessment, and meta-regression).

The present article introduces the R package **rnmamod** that performs Bayesian hierarchical NMA in JAGS through the R package **R2jags** (Su and Masanao Yajima 2021), while modeling missing participants using one-stage pattern-mixture models (Little 1993). The visualisation toolkit of the package has been developed using the R package **ggplot2** (Wickham 2016) to benefit from the flexibility offered in creating and customising quality graphs. The article has the following structure. Section 2 provides an overview of the pattern-mixture models for aggregate binary and continuous outcome data in NMA. Section 3 delineates the architecture of **rnmamod**, and section 4 exemplifies the several functions of the package using examples from published systematic reviews with NMA. Finally, Section 5 concludes with a discussion on the limitations and future developments of the package.

## Pattern-mixture models for aggregate binary and continuous outcomes

We briefly introduce the pattern-mixture model, originally proposed by Little (Little 1993), and extend it to a summary binary and continuous outcome in the evidence synthesis framework. The pattern-mixture model distinguishes the participants to those completing and those leaving the assigned intervention arm prematurely for several reasons. The former are called *completers* and the latter *missing participants*. There is information only on the outcome of the completers for remaining to the assigned intervention until trial completion. If missing participants are not followed-up after leaving the trial, which is usually the case, their outcome can only be hypothesised with some uncertainty; hence, we can determine a distribution of possible values to describe the hypothetical outcome of missing participants in the assigned intervention. Ideally, this distribution should be elicited using an expert opinion for the investigated outcome and interventions (White et al. 2007). Then, the weighted average of the observed and hypothesised outcomes, using the proportion of completers and missing participants as the corresponding weights, yields the *true* outcome for all randomised participants receiving the investigated intervention. This corresponds to the intention-to-treat analysis, and it is of particular interest to investigate the impact to the treatment effect of different scenarios about the distribution of hypothetical outcome values for the missing participants. This sensitivity analysis is at the core of the literature on handling missing data properly (White et al. 2007; *Missing Data in Randomised Controlled Trials: A Practical Guide.* 2007; *The Prevention and Treatment of Missing Data in Clinical Trials Panel on Handling Missing Data in Clinical Trials.* 2010).

Consider a set of $N$ trials collected using a systematic review process. These trials investigate different sets of two or more carefully-selected interventions for a specific target population and clinical condition. We extract information on the number randomised, the number of completers and missing participants, and the measured outcome from each arm of every trial. The pattern-mixture framework models completers and missing participants simultaneously, maintaining the randomised sample, as follows:

$$\theta_{ik} = \theta^c_{ik} \times (1 - q_{ik}) + \theta^m_{ik} \times q_{ik}$$

where $\theta_{ik}$ is the true outcome in arm $k$ of trial $i$, $\theta^c_{ik}$ and $\theta^m_{ik}$ are the outcomes among the completers and missing participants, respectively (the superscripts $c$ and $m$ stand for completers and missing), and $q_{ik}$ is the proportion of missing participants. It holds that

$$\begin{aligned}
\theta_{ik} &= P(I_{ikj} = 1 | M_{ikj} = 1 \cup M_{ikj} = 0) \\
\theta^c_{ik} &= P(I_{ikj} = 1 | M_{ikj} = 0) \\
\theta^m_{ik} &= P(I_{ikj} = 1 | M_{ikj} = 1)
\end{aligned}$$

for a binary outcome, and

$$\begin{aligned}
\theta_{ik} &= E(Y_{ikj} | M_{ikj} = 1 \cup M_{ikj} = 0) \\
\theta^c_{ik} &= E(Y_{ikj} | M_{ikj} = 0) \\
\theta^m_{ik} &= E(Y_{ikj} | M_{ikj} = 1)
\end{aligned}$$

for a continuous outcome, with $I_{ikj}$ and $M_{ikj}$ being dummy variables referring to whether a participant $j$ experienced the outcome or left the trial prematurely, respectively, and $Y_{ikj}$ referring to the continuous outcome of participant $j$.

### Informative missingness parameters

It has been suggested in the relevant published literature to replace the missingness parameter $\theta^m_{ik}$ with the following parameters to measure the informative missingness as a function of the outcome in completers and missing participants (White, Higgins, and Wood 2008; Mavridis et al. 2015; Turner et al. 2015):

$$\phi_{ik} = logit(\theta^m_{ik}) - logit(\theta^c_{ik})$$

the informative missingness odds ratio (IMOR) in the logarithmic scale for binary outcomes (White, Higgins, and Wood 2008; Turner et al. 2015), and

$$\psi_{ik} = \theta^m_{ik} - \theta^c_{ik}$$

the informative missingness difference of means (IMDoM) for continuous outcomes (Mavridis et

al. 2015). Other informative missingness parameters that have been suggested for binary outcomes are the response probability ratio (Magder 2003; Turner et al. 2015) defined as the ratio of the probability of completing the trial given the outcome being experienced to the probability of completing the trial given the outcome not being experienced,

$$\omega_{ik} = \frac{P(M_{ikj} = 0|I_{ikj} = 1)}{P(M_{ikj} = 0|I_{ikj} = 0)}$$

and the success probability ratio (Akl et al. 2013; Turner et al. 2015) as the ratio of the probability of experiencing the outcome given the missing participants to the probability of experiencing the outcome given the completers,

$$\rho_{ik} = \frac{\theta^m_{ik}}{\theta^c_{ik}} = \frac{P(I_{ikj} = 1|M_{ikj} = 1)}{P(I_{ikj} = 1|M_{ikj} = 0)}.$$

Finally, the informative missingness ratio of means (IMRoM) has also been suggested for the continuous outcomes (Mavridis et al. 2015) defined as the mean outcome given the missing participants to the mean outcome given the completers,

$$\zeta_{ik} = \frac{\theta^m_{ik}}{\theta^c_{ik}} = \frac{E(Y_{ikj}|M_{ikj} = 1)}{E(Y_{ikj}|M_{ikj} = 0)}.$$

The response probability ratio (Magder 2003; Turner et al. 2015) aligns better with a selection model that distinguishes the participants based on their outcome and then further distinguishes between those completing and those leaving the assigned intervention prematurely (Little 1995). The success probability ratio (Akl et al. 2013; Turner et al. 2015) is more likely to be used with the risk ratio for also being a ratio of risks. The IMRoM is intuitively related to the ratio of means (Mavridis et al. 2015). Finally, IMOR and IMDoM are more likely to be used in conjunction to the OR and the mean difference (MD) and standardised mean difference, respectively. In this article, we will consider only the IMOR and IMDoM due to their intuitive relation to the aforementioned effect measures which are also the most frequently used in published systematic reviews and relevant methodological literature (Friedrich, Adhikari, and Beyene 2008; Nikolakopoulou et al. 2014; Bakbergenuly, Hoaglin, and Kulinskaya 2019).

The informative missingness parameters IMDoM and IMOR in the logarithmic scale (log IMOR) take values in $\mathbb{R}$ with zero implying the missing at random assumption (ignorable missingness) and non-zero values indicating the missing not at random assumption (non-ignorable missingness). Essentially, the informative missingness parameters quantify departures from the missing at random assumption. Since these parameters are unknown, the analysts can consider one of the following situations:

- assign a fixed value, which corresponds to imputation (Higgins, White, and Wood 2008; Turner et al. 2015; Spineli 2019),
- assume a distribution with suggested parameter values and proceed with a two-stage approach to synthesise the trials using their adjusted treatment effects and variances for missing participants obtained through the Taylor series approximation in the first stage (White, Higgins, and Wood 2008; Mavridis et al. 2015), or
- use the Bayesian framework to estimate their posterior distribution via an one-stage approach to synthesise the trials (Turner et al. 2015; Spineli 2019; Spineli, Kalyvas, and Papadimitropoulou 2021).

Typically, a normal distribution is assigned on both informative missingness parameters (Higgins, White, and Wood 2008; White, Higgins, and Wood 2008; Mavridis et al. 2015; Turner et al. 2015; Spineli 2019; Spineli, Kalyvas, and Papadimitropoulou 2021). In the Bayesian framework, the analysts assign a prior normal distribution on these parameters and can determine the mean and variance of the normal distribution to be common across the trials and intervention arms, specific to the interventions or trials, as well as identical, hierarchical or independent (Turner et al. 2015; Spineli 2019; Spineli, Kalyvas, and Papadimitropoulou 2021). Table **??** presents the different structural specifications of log IMOR, IMDoM and log IMRoM. The **rnmamod** package allows the user to apply all structural specifications for log IMOR, IMDoM and log IMRoM.

## The architecture of rnmamod

### Functions on data preparation and model implementation

The `run_model()` function has a central role in the architecture of the **rnmamod** package. It is the function of conducting the core NMA model and related analyses to assess the underlying assumptions of NMA. It also comprises the object of most functions to create the necessary visualisations. Initially, `run_model()` calls the `data_preparation()` function to prepare the dataset in the proper format to fit the model in JAGS. The dataset is provided in the one-study-per-row format, typical for codes written in the BUGS language. Then `run_model()` bundles the dataset and the necessary parameters (they have been processed through the `missingness_param_prior()`, `heterogeneity_param_prior()`, and `baseline_model()` functions) to conduct NMA through the `prepare_model()` function. The `prepare_model()` function contains the code in BUGS language to conduct a hierarchical one-stage NMA, as published by the NICE Decision Support Unit in a series of tutorial papers on evidence synthesis methods for decision-making (Dias et al. 2013). The `missingness_param_prior()` and `heterogeneity_param_prior()` functions process the hyperparameters of the selected prior distribution for the informative missingness parameter and the between-study heterogeneity parameter, respectively, to be read by JAGS. The `baseline_model()` function is relevant only in the case of a binary outcome. It processes the baseline risk defined by the user or the default option before conducting NMA.

Subsequent analyses associated with the underlying assumptions of NMA are performed by specially devised functions that inherit most arguments from `run_model()`. Therefore, careful specification of the arguments in `run_model()` is essential for the contingent functions to yield sensible results and ensure meaningful comparison with the NMA results. These functions refer to the local and global consistency evaluation (`run_nodesplit()` and `run_ume()`), network meta-regression (`run_metareg()`), multiple pairwise meta-analyses (`run_series_meta()`) and sensitivity analysis to different missingness scenarios (`run_sensitivity()`) when the number of missing participants has been extracted for all study-arms. The functions `run_nodesplit()` and `run_ume()` call the `prepare_nodesplit()` and `prepare_ume()` functions, respectively, to fit the node-splitting and the unrelated mean effects models in JAGS. The function `improved_ume()` is also called to ensure a proper accommodation of the multi-arm trials in the unrelated mean effects model. In line with `run_model()`, network meta-regression, multiple pairwise meta-analyses, and sensitivity analysis are fitted in JAGS through the `prepare_model()` function. All model-related functions can be passed as an object to the `mcmc_diagnostics()` function to generate the diagnostic plots and measures for the monitored model parameters.

Figure 1 illustrates the network of the functions developed to prepare the data and conduct NMA and related analyses. Nodes and links refer to functions and the synergy of two functions. The node's size indicates the usability of the corresponding function. For instance, `run_model()` is an over-represented node for having a dual role in the network: it is an object to most functions (e.g., `run_nodesplit()` and `mcmc_diagnostics()`) and depends on other functions to operate (e.g., `data_preparation()` and `prepare_model()`). The node's colour indicates the operationality of the function: most functions perform model implementation (green nodes), followed by functions that contain the BUGS code (blue nodes) or process the dataset and prepare specific arguments (purple nodes) for the corresponding model. The `baseline_model()` function contains all three operationalities, whilst `mcmc_diagnostics()` offers only a set with MCMC diagnostics.

### The visualisation toolkit

Figure 2 presents the network of visualisation-related functions alongside `run_model()` and several model-related functions. The functions associated with summarising and presenting the results have a common structure: `run_model()` and the model-related function of interest are passed as objects into the corresponding arguments. Hence, `run_model()` comprises the backbone of the network and forms the largest node (Figure 2). The visualisation-related functions are distinguished into the *stand-alone* and the *platform* functions. The stand-alone functions are immediately related to generating the relevant graphs. For instance, `forestplot_metareg()`, and `interval_panel_ume()` constitute stand-alone functions and return only the intended graph using `run_model()` together with `run_metareg()` and `run_ume()`, respectively, as objects in their arguments. Other stand-alone functions depend on a single function to operate; for example, `rankosucra_plot()` and `kld_plot()` use only the `run_model()` and `robustness_index()`, respectively, in their arguments. The platform functions host the stand-alone functions and generate complementary tables and further graphs. They are easy to spot in Figure 2, as they are named after the related model, with the *plot* affixed at the end: `nodesplit_plot()`, `ume_plot()`, `metareg_plot()`, and `series_meta_plot()`. For instance, `metareg_plot()` calls `scatterplot_sucra()`

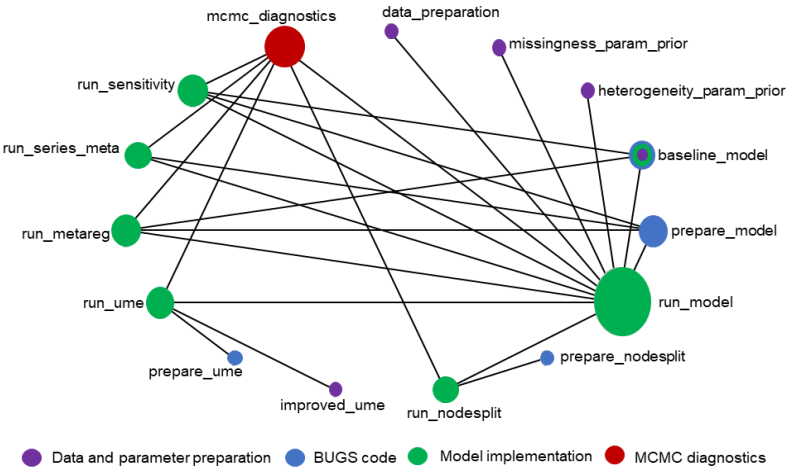


**Figure 1:** Network of functions for data preparation and model implementation

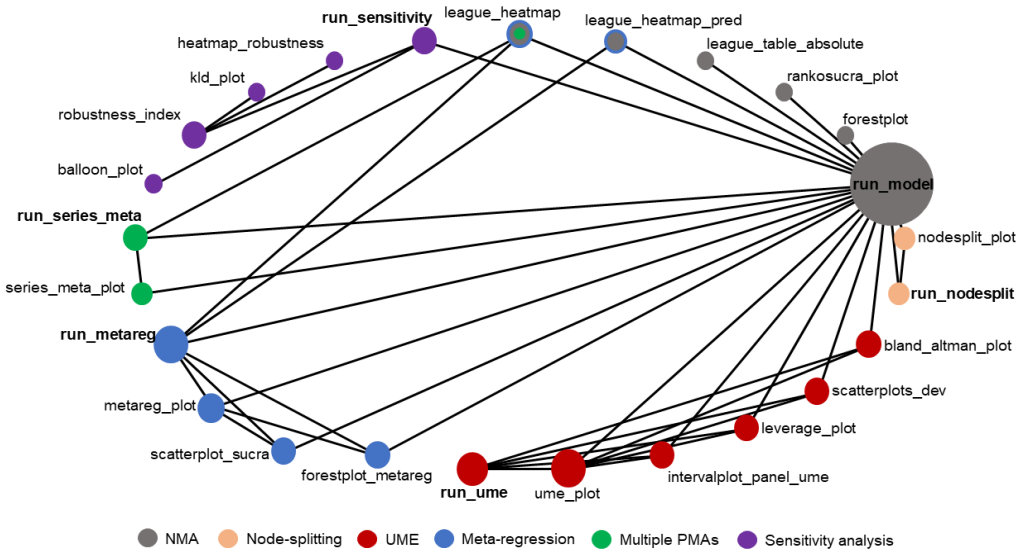


**Figure 2:** Network of functions for summarising and presenting the analysis results

and `forestplot_sucra()` to return the corresponding intended graphs and prints tables in the console where the effect estimates and predictions from NMA are juxtaposed with those from network meta-regression. Every analysis has an individualised visualisation toolkit, indicated by the functions sharing the same colour node (Figure 2). Only network meta-regression (blue nodes) and conducting separate pairwise meta-analyses (green nodes) share a few stand-alone functions with NMA (grey nodes), namely, `league_heatmap()` and `league_heatmap_pred()`.

## A gallery of tooltips examples

## Summary

We have displayed various tooltips that are available in the package **ToOoOlTiPs**.

## References


Akl, Elie A, Bradley C Johnston, Pablo Alonso-Coello, Ignacio Neumann, Shanil Ebrahim, Matthias Briel, Deborah J Cook, and Gordon H Guyatt. 2013. "Addressing Dichotomous Data for Participants Excluded from Trial Analysis: A Guide for Systematic Reviewers." *PLoS One* 8 (2): e57132. https://doi.org/10.1371/journal.pone.0057132.

Bakbergenuly, Ilyas, David C Hoaglin, and Elena Kulinskaya. 2019. "Pitfalls of Using the Risk Ratio in Meta-Analysis." *Res Synth Methods* 10 (3): 398–419. https://doi.org/10.1002/jrsm.1347.

Bucher, H C, G H Guyatt, L E Griffith, and S D Walter. 1997. "The Results of Direct and Indirect Treatment Comparisons in Meta-Analysis of Randomized Controlled Trials." *J Clin Epidemiol* 50 (6): 683–91. https://doi.org/10.1016/s0895-4356(97)00049-8.

Caldwell, Deborah M. 2014. "An Overview of Conducting Systematic Reviews with Network Meta-Analysis." *Syst Rev* 3: 109. https://doi.org/10.1186/2046-4053-3-109.

Dewey, Michael, and Wolfgang Viechtbauer. 2023. *CRAN Task View: Meta-Analysis*. https://CRAN.R-project.org/view=MetaAnalysis.

Dias, Sofia, and A E Ades. 2016. "Absolute or Relative Effects? Arm-Based Synthesis of Trial Data." *Res Synth Methods* 7 (1): 23–28. https://doi.org/10.1002/jrsm.1184.

Dias, Sofia, Alexander J Sutton, A E Ades, and N J Welton. 2013. "Evidence Synthesis for Decision Making 2: A Generalized Linear Modeling Framework for Pairwise and Network Meta-Analysis of Randomized Controlled Trials." *Med Decis Making* 33 (5): 607–17.

Efthimiou, Orestis, Thomas P. A. Debray, Gert van Valkenhoef, Sven Trelle, Klea Panayidou, Karel G. M. Moons, Johannes B. Reitsma, Aijing Shang, Georgia Salanti, and GetReal Methods Review Group. 2016. "GetReal in Network Meta-Analysis: A Review of the Methodology." *Res Synth Methods* 7 (3): 236–63. https://doi.org/10.1002/jrsm.1195.

Friedrich, Jan O, Neill K J Adhikari, and Joseph Beyene. 2008. "The Ratio of Means Method as an Alternative to Mean Differences for Analyzing Continuous Outcome Variables in Meta-Analysis: A Simulation Study." *BMC Med Res Methodol* 8: 32. https://doi.org/10.1186/1471-2288-8-32.

Higgins, Julian P T, Ian R White, and Angela M Wood. 2008. "Imputation Methods for Missing Outcome Data in Meta-Analysis of Clinical Trials." *Clin Trials* 5 (3): 225–39. https://doi.org/10.1177/1740774508091600.

Higgins, Julian P T, and Anne Whitehead. 1996. "Borrowing Strength from External Trials in a Meta-Analysis." *Stat Med* 15 (24): 2733–49.

Lee, Andrew. 2022. "The Development of Network Meta-Analysis." *J R Soc Med* 115 (8): 313–21. https://doi.org/10.1177/01410768221113196.

Lin, Lifeng, Jing Zhang, James S. Hodges, and Haitao Chu. 2017. "Performing Arm-Based Network Meta-Analysis in R with the pcnetmeta Package." *Journal of Statistical Software* 80 (5): 1–25. https://doi.org/10.18637/jss.v080.i05.

Little, RJA. 1993. "Pattern-Mixture Models Formultivariate Incomplete Data." *J Am Stat Assoc* 88 (421): 125–34. https://doi.org/doi.org/10.2307/2290705.

———. 1995. "Modeling the Drop-Out Mechanism in Repeated-Measures Studies." *J Am Stat Assoc* 90 (431): 1112–21. https://doi.org/10.2307/2291350.

Lunn, David, David Spiegelhalter, Andrew Thomas, and Nicky Best. 2009. "The BUGS Project: Evolution, Critique and Future Directions." *Stat Med* 28 (25): 3049–67. https://doi.org/10.1002/sim.3680.

Magder, Laurence S. 2003. "Simple Approaches to Assess the Possible Impact of Missing Outcome Information on Estimates of Risk Ratios, Odds Ratios, and Risk Differences." *Control Clin Trials* 24 (4): 411–21. https://doi.org/10.1016/s0197-2456(03)00021-7.

Mavridis, Dimitris, Ian R White, Julian P T Higgins, Andrea Cipriani, and Georgia Salanti. 2015. "Allowing for Uncertainty Due to Missing Continuous Outcome Data in Pairwise and Network Meta-Analysis." *Stat Med* 34 (5): 721–41. https://doi.org/10.1002/sim.6365.

*Missing Data in Randomised Controlled Trials: A Practical Guide.* 2007. Health Technology Assessment Methodology Programme: Birmingham. https://researchonline.lshtm.ac.uk/id/eprint/4018500.

Nikolakopoulou, Adriani, Anna Chaimani, Areti Angeliki Veroniki, Haris S Vasiliadis, Christopher H Schmid, and Georgia Salanti. 2014. "Characteristics of Networks of Interventions: A Description of a Database of 186 Published Networks." *PLoS One* 9 (1): e86754. https://doi.org/10.1371/journal.pone.0086754.

Petropoulou, Maria, Adriani Nikolakopoulou, Areti-Angeliki Veroniki, Patricia Rios, Afshin Vafaei, Wasifa Zarin, Myrsini Giannatsi, et al. 2017. "Bibliographic Study Showed Improving Statistical Methodology of Network Meta-Analyses Published Between 1999 and 2015." *J Clin Epidemiol* 82: 20–28. https://doi.org/10.1016/j.jclinepi.2016.11.002.

Plummer, Martyn. 2003. *JAGS: A Program for Analysis of Bayesian Graphical Models Using Gibbs Sampling*. Edited by Kurt Hornik, Friedrich Leisch, and Achim Zeileis. Technische Universität Wien, Vienna, Austria. https://www.R-project.org/conferences/DSC-2003/Proceedings/Plummer.pdf.

Sackett, David L, William M Rosenberg, J A Gray, R B Haynes, and W S Richardson. 1996. "Evidence

Based Medicine: What It Is and What It Isn't." *BMJ* 312 (7023): 71–72. https://doi.org/10.1136/bmj.312.7023.71.

Salanti, Georgia. 2012. "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* 3 (2): 80–97. https://doi.org/10.1002/jrsm.1037.

Salanti, Georgia, Adriani Nikolakopoulou, Orestis Efthimiou, Dimitris Mavridis, Matthias Egger, and Ian R White. 2022. "Introducing the Treatment Hierarchy Question in Network Meta-Analysis." *Am J Epidemiol* 191 (5): 930–38. https://doi.org/10.1093/aje/kwab278.

Seo, Michael, and Christopher Schmid. 2022. *Bnma: Bayesian Network Meta-Analysis Using 'JAGS'*. https://CRAN.R-project.org/package=bnma.

Spineli, Loukia M. 2019. "An Empirical Comparison of Bayesian Modelling Strategies for Missing Binary Outcome Data in Network Meta-Analysis." *BMC Med Res Methodol* 19 (1): 86. https://doi.org/10.1186/s12874-019-0731-y.

———. 2022. *Rnmamod: Bayesian Network Meta-Analysis with Missing Participants*. https://CRAN.R-project.org/package=rnmamod.

Spineli, Loukia M, Chrysostomos Kalyvas, and Katerina Papadimitropoulou. 2021. "Continuous(ly) Missing Outcome Data in Network Meta-Analysis: A One-Stage Pattern-Mixture Model Approach." *Stat Methods Med Res* 30 (4): 958–75. https://doi.org/10.1177/0962280220983544.

Su, Yu-Sung, and Masanao Yajima. 2021. *R2jags: Using r to Run 'JAGS'*. https://CRAN.R-project.org/package=R2jags.

Sutton, Alex J, and Keith R Abrams. 2001. "Bayesian Methods in Meta-Analysis and Evidence Synthesis." *Stat Methods Med Res* 10 (4): 277–303. https://doi.org/10.1177/096228020101000404.

*The Prevention and Treatment of Missing Data in Clinical Trials Panel on Handling Missing Data in Clinical Trials.* 2010. Division of Behavioral; Social Sciences; Education, Washington, DC: The National Academies Press. www.nap.edu.

Turner, N. L., S. Dias, A. E. Ades, and N. J. Welton. 2015. "A Bayesian Framework to Account for Uncertainty Due to Missing Binary Outcome Data in Pairwise Meta-Analysis." *Stat Med* 34 (12): 2062–80. https://doi.org/10.1002/sim.6475.

van Valkenhoef, Gert, and Joel Kuiper. 2021. *Gemtc: Network Meta-Analysis Using Bayesian Methods*. https://CRAN.R-project.org/package=gemtc.

White, Ian R, James Carpenter, Stephen Evans, and Sara Schroter. 2007. "Eliciting and Using Expert Opinions about Dropout Bias in Randomized Controlled Trials." *Clin Trials* 4 (2): 125–39. https://doi.org/10.1177/1740774507077849.

White, Ian R, Julian P T Higgins, and Angela M Wood. 2008. "Allowing for Uncertainty Due to Missing Data in Meta-Analysis—Part 1: Two-Stage Methods." *Stat Med* 27 (5): 711–27. https://doi.org/10.1002/sim.3008.

Wickham, Hadley. 2016. *Ggplot2: Elegant Graphics for Data Analysis*. Springer-Verlag New York. https://ggplot2.tidyverse.org.

*Loukia M. Spineli*
*Midwifery Research and Education Unit*
*Hannover Medical School*
*Carl-Neuber-Strasse 1, 30625, Hannover, Germany*
https://www.github.com/LoukiaSpin
*ORCiD: 0000-0001-9515-582X*
Spineli.Loukia@mh-hannover.de

*Chrysostomos Kalyvas*
*Biostatistics and Research Decision Sciences*
*MSD Europe Inc., Brussels, Belgium*
https://www.github.com/ckalyvas
*ORCiD: 0000-0003-0606-4518*
chrysostomos.kalyvas@merck.com

*Katerina Papadimitropoulou*
*Health Economics and Market Access*
*Amaris Consulting, Lyon, France*
https://www.github.com/Katerina-Pap
*ORCiD: 0000-0002-5732-4044*
katerina.papadimitropoulou@gmail.com