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

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Abstract The development of several R packages for conducting network meta-analysis has enhanced the popularity of this evidence synthesis tool. The available R packages facilitate the implementation of most models to conduct and evaluate network meta-analysis and provide the necessary results, conforming to the PRISMA-NMA statement. The rnmamod package is a novel contribution to conducting aggregate network meta-analysis using Bayesian methods, as it allows addressing missing participants properly in all models, even if a handful of the included studies report this information. Importantly, 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 several comprehensive graphs. Furthermore, the package functions on various models allow processing their output to create visualisations tailored to the user preferences. Therefore, rnmamod aids the thorough appraisal and interpretation of the results, the cross-comparison of different models and the manuscript preparation for journal submission.

Introduction

Evidence-based medicine is the backbone of informed decisions for the benefit of the patients, stemming from a meticulous and judicious use of the available evidence, while taking into account also the clinical experience and patient values (Sackett et al. 1996). However, the medical community is faced daily with several intervention options and dosages, challenging the optimal practice of evidence-based medicine (Lee 2022). Systematic reviews with pairwise meta-analysis summarise the evidence of pairs of interventions, providing fragmented evidence that does not serve the clinical needs. Moreover, evidence in the comparability of different interventions at the trial level is also fragmented, as it is not feasible to compare all intervention options for a condition in one trial. These limitations led to the development and later establishment of network meta-analysis (NMA), also known as multiple treatment comparison, a new generation evidence synthesis tool (Salanti 2012). Network meta-analysis is an extension of pairwise meta-analysis for collecting all relevant pieces of evidence for a specific condition, patient population, and intervention options to provide coherent evidence for all possible intervention comparisons, and allow ordering the investigated interventions from the best to worst 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.

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 methodological articles and systematic reviews with NMA attest to the increasing popularity of NMA in the wide medical and evidence synthesis community (Efthimiou et al. 2016; Petropoulou et al. 2017). Needless to say that the availability of statistical analysis software is the driving force to the advances and wide dissemination of NMA. A review of the methodology and software for NMA (Efthimiou et al. 2016) listed several statistical software tools used to promote NMA, with the **R** software (R Core Team 2022) being the most popular to develop and compare methods for NMA, followed by **Stata** (StataCorp 2021) and **SAS** software (SAS Institute 2020).

In the last decade, there has been a raise in the R packages for NMA with various functionalities (Dewey and Viechtbauer 2022). These packages can be categorised by, among others, the analysis framework (frequentist or Bayesian), the assumed distribution of the input data (exact distribution, known as one-stage approach, or normality approximation, known as two-stage approach), the modeling approach (contrast-based or arm-based), the scope breadth (conduct NMA and assess heterogeneity and inconsistency or address part of the NMA framework), the outcome structure (aggregate, individual patient data or mixture of both), and the outcome data type (binary, continuous, multinomial, and so on). Most packages fall into many categories. For instance, **gemtc** (van Valkenhoef and Kuiper 2021), probably the most popular R package for Bayesian NMA, allows both for one-stage and two-stage approaches using contrast-based modeling, has a wide scope, and deals with aggregate outcome data of many types. **netmeta** (Rücker et al. 2022) is currently the only R package developed exclusively for NMA in the frequentist framework based on the graph theory (Ruecker

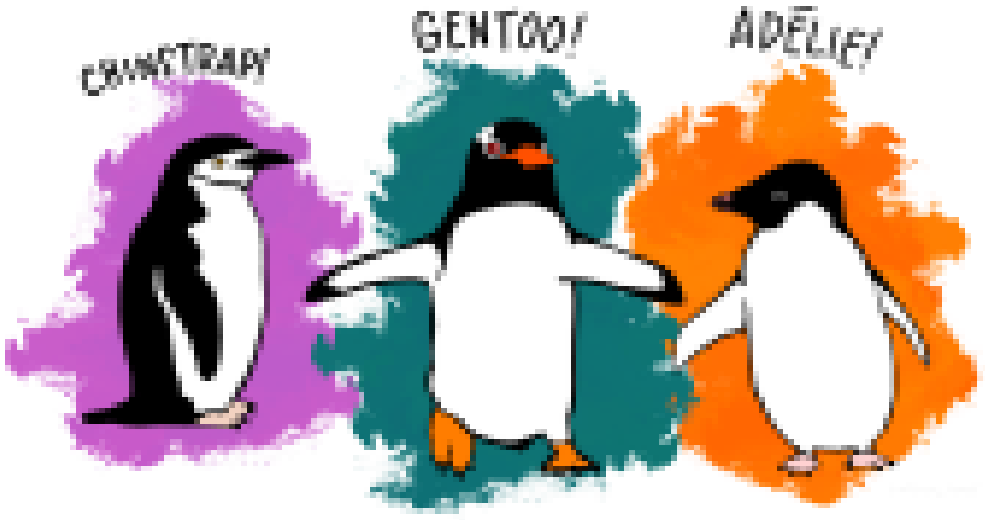

Figure 1: Artwork by allison_horst

2012), allows only for a two-approach approach (contrast-based modeling), has also a wide scope, and accommodates binary, rates, and continuous aggregate outcome data. On the other side, R packages, such as **nmathresh** (Phillippo et al. 2018), **nmaplateplot** (Z. Wang et al. 2021), and **nmarank** (Nikolakopoulou, Schwarzer, and Papakonstantinou 2021) do not perform NMA, but use the NMA results (obtained using other R packages or statistical software tools) as an input to provide, for instance, decision-invariant bias-adjustment thresholds and intervals (**nmathresh**), various league tables in heatplot style with all intervention comparisons (**nmaplateplot**), or an intervention hierarchy approach tailored to the research question (**nmarank**).

- Mention why rnmamod is needed.

Background

Some packages on interactive graphics include **plotly** (Sievert 2020) that interfaces with Javascript for web-based interactive graphics, **crosstalk** (Cheng and Sievert 2021) that specializes cross-linking elements across individual graphics. The recent R Journal paper **tsibbletalk** (E. Wang and Cook 2021) provides a good example of including interactive graphics into an article for the journal. It has both a set of linked plots, and also an animated gif example, illustrating linking between time series plots and feature summaries.

Customizing tooltip design with ToOoOlTiPs

ToOoOlTiPs is a packages for customizing tooltips in interactive graphics, it features these possibilities.

A gallery of tooltips examples

The **palmerpenguins** data (Horst, Hill, and Gorman 2020) features three penguin species which has a lovely illustration by Alison Horst in Figure 1.

Table 1 prints at the first few rows of the `penguins` data:

Figure 2 shows an plot of the penguins data, made using the **ggplot2** package.

```
penguins %>%
  ggplot(aes(x = bill_depth_mm, y = bill_length_mm,
             color = species)) +
  geom_point()
```

Table 1: A basic table

species	island	bill_length_mm	bill_depth_mm	flipper_length_mm	body_mass_g	sex	year
Adelie	Torgersen	39.1	18.7	181	3750	male	2007
Adelie	Torgersen	39.5	17.4	186	3800	female	2007
Adelie	Torgersen	40.3	18.0	195	3250	female	2007
Adelie	Torgersen	NA	NA	NA	NA	NA	2007
Adelie	Torgersen	36.7	19.3	193	3450	female	2007
Adelie	Torgersen	39.3	20.6	190	3650	male	2007

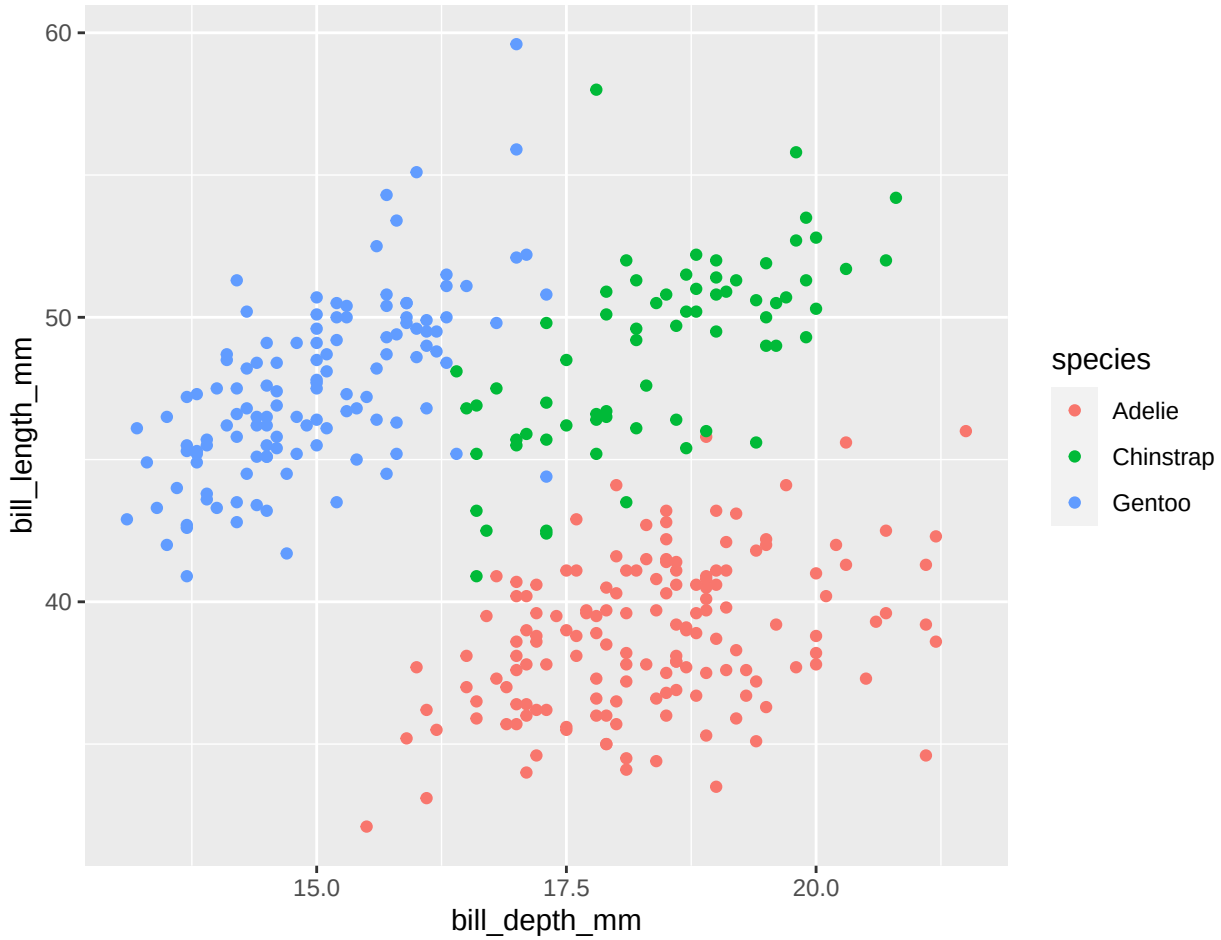

Figure 2: A basic non-interactive plot made with the ggplot2 package on palmer penguin data. Three species of penguins are plotted with bill depth on the x-axis and bill length on the y-axis. Visit the online article to access the interactive version made with the plotly package.

Summary

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

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