Exploring the Impact of Data Availability on Time-Course Model-Based Network Meta-Analysis

MSR114

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Background and Objectives

- Network meta-analysis (NMA) synthesizes evidence from clinical trials by combining direct and indirect comparisons across a connected network.
- Standard NMA focuses on a single timepoint per trial, even as studies increasingly report outcomes at multiple timepoints.
- Time-course model-based NMA (MBNMA) has been proposed to enhance standard NMA by incorporating longitudinal data, enabling the use of all available evidence.[1]
- This approach can help mitigate the heterogeneity and inconsistency that may arise when comparing trials which assess outcomes at different timepoints and may provide deeper insights into pharmacological benefits such as time to onset of action or prolonged treatment effects.
- The objective of this work is to add to the existing literature validating this method[2] to develop a more robust understanding of the applicability and potential challenges of time-course MBNMA by exploring the impact of limited data availability.

Methods

- Individual patient-level data for a binary event outcome were simulated across three treatments and placebo using predefined response curves based on cubic basis functions. Events were sampled with random noise, bounded between 0 and 1, and converted to the logit scale with estimated standard errors.
- Using simulated data, time-course MBNMA was applied with R package MBNMAtime[1] to describe the temporal relationship between treatment and a binary event outcome. A time-course model was fit using natural cubic splines with 3 evenly spaced knots.
- Scenarios involving common data availability issues were analyzed for their impact on outcome measures (**Figure 1**).
  - Scenarios considered three 24-week placebo-controlled trials each assessing a different investigational agent at two week intervals. Missing data were applied to only one trial in the network (ie, trial 1), which assessed treatment A versus placebo.

Figure 1: Data availability for trial 1 in each scenario

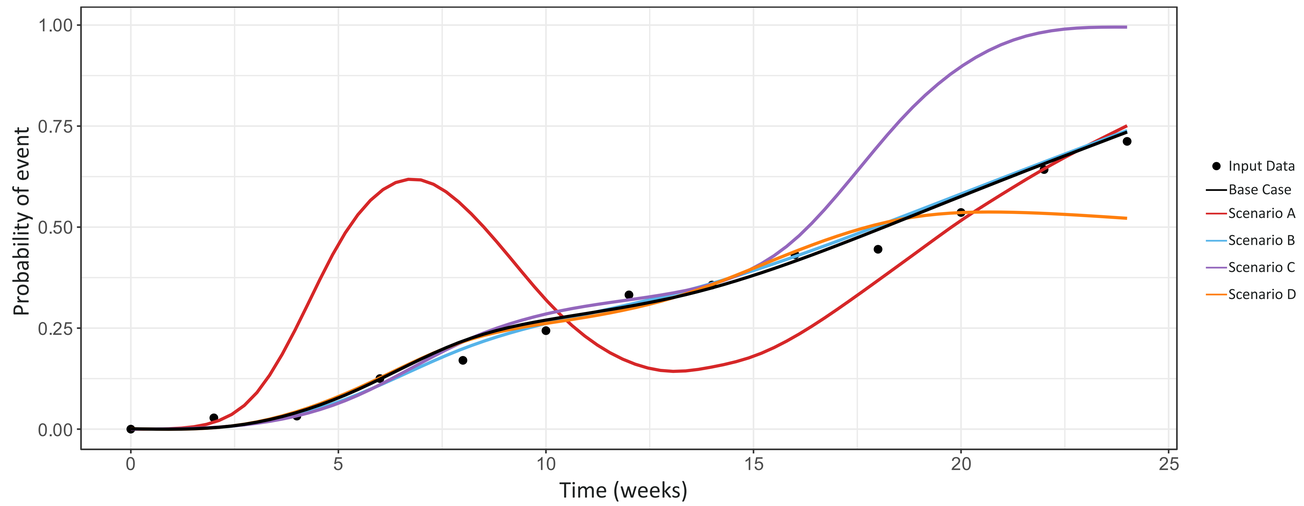
Scenario	Time (weeks)											
	2	4	6	8	10	12	14	16	18	20	22	24
Base Case	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Scenario A	✓	X	X	X	X	X	X	X	X	X	✓	✓
Scenario B	✓	X	X	✓	✓	X	✓	✓	X	X	✓	✓
Scenario C	✓	✓	✓	✓	✓	✓	✓	✓	X	X	X	X
Scenario D	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	X

Data available ✓ Data missing X

Results

- Varying levels of data availability influenced the outcomes observed across scenarios.
- Overall, results suggest that when data are missing at numerous sequential timepoints, this method may be inappropriate as results are largely driven by the selected interpolation approach. Furthermore, results indicate that this method may be ill-suited for extrapolating past the final reported timepoint.
- Results for treatments which were not directly impacted by missing data remained consistent across scenarios.

Figure 2: Response of treatment A over time in each scenario



Scenario A

- In Scenario A, data were missing at multiple sequential timepoints throughout the middle of trial **(Figure 1)**.
- Model results varied substantially from both the input data and the base case scenario, where data were available at all timepoints **(Figure 2)**.

Scenario B

- In Scenario B, data were missing intermittently throughout the trial **(Figure 1)**.
- Model results were closely aligned with both the input data and the base case scenario **(Figure 2)**.

Scenarios C and D

- In Scenarios C and D, data were missing at timepoints near the end of the trial **(Figure 1)**.
- Model results were unable to accurately extrapolate beyond the last included timepoint **(Figure 2)**.

Conclusion

Time-course MBNMA provides a framework for integrating data at multiple timepoints, facilitating a more nuanced evaluation of treatment effects within a network. This method may be most valuable for scenarios with a large amount of data available, or intermittent missing data, provided that data are available for the final timepoints of interest.

Abbreviations MBNMA = model-based network meta-analysis; NMA = network meta-analysis.

References

1. Pedder H, Dias S, Bennetts M, Boucher M, Welton NJ (2019). "Modelling time-course relationships with multiple treatments: Model-based network meta-analysis for continuous summary outcomes." Research Synthesis Methods, 10(2), 267-286.
2. Pedder H, Boucher M, Dias S, Bennetts M, Welton NJ. Performance of model-based network meta-analysis (MBNMA) of time-course relationships: A simulation study. Res Synth Methods. 2020;11(5):678-697.

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