MSR57

STUDY OF TIME-COURSE RELATIONSHIP USING MODEL-BASED NETWORK META-ANALYSIS: A LINEAR TIME-COURSE MODEL

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OBJECTIVE

To generate evidence from more than one study with multiple treatments at different follow-up times

BACKGROUND

- Network Meta-Analysis (NMA) is used to generate evidence from more than one study with multiple treatments but lacks efficiency and accuracy when studies report findings at different follow-up times
- NMA can increase the precision of estimates compared with standard pair-wise meta-analysis, but it relies on the consistency assumption that there is no difference between direct and indirect evidence
- For establishing a time-course relationship a parametric functional form was required. Model-based network meta-analysis (MBNMA) which is a general framework for NMA that incorporates parametric models of time-course relationships has been established
- The benefit of this approach compared with NMA is that it allows the inclusion of studies with different follow-up times, and therefore provides the possibility of including clinical trials from earlier in clinical development

RESULTS

- Results of the linear time-course model were examined using the forest plot & prediction plot
- The method generates a network of comparisons across multiple treatments over different time points and the posterior median with 95% credible intervals for the change in efficacy for each treatment versus treatment of interest has been calculated
- The posterior median and 95% credible intervals for treatment B vs A: -0.87 (-2.32, 0.38) whereas for treatment C vs A: -0.74 (-2.08, 0.49), treatment D vs A: -0.64 (-1.95, 0.62), treatment E vs A: -0.59 (-1.90, 0.77)

Figure 1: Network Plot showing the connection of different studies with treatments

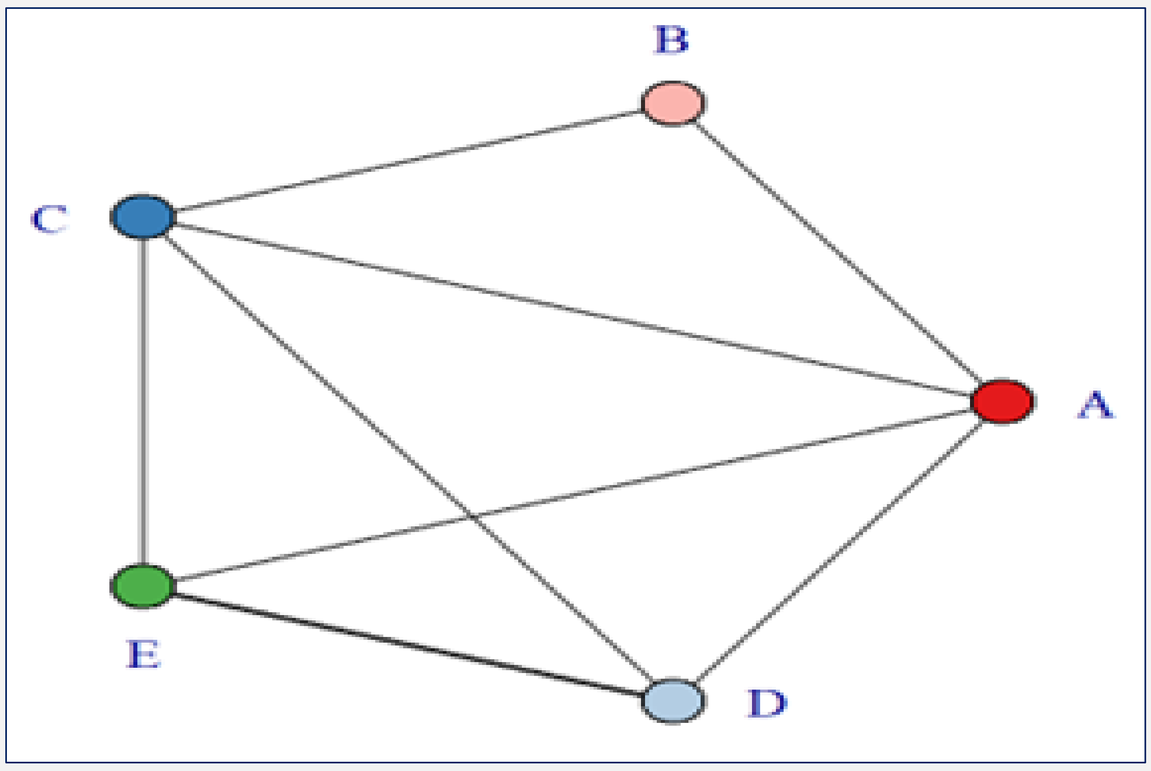
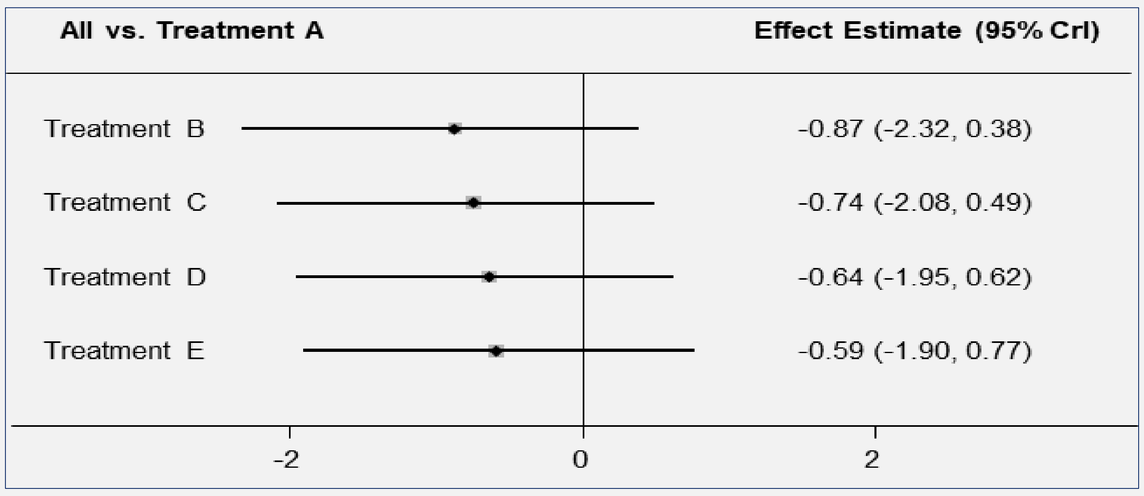


Figure 2 : Forest Plot showing posterior median with CIs for All vs. Treatment A



METHODOLOGY

- MBNMA[1] is a new technique for evidence synthesis that allows the incorporation of a parametric time course in NMA, which enables the inclusion of studies with different follow-up times in a manner that explains heterogeneity/inconsistency
- By pooling relative effects within studies, time-course MBNMA preserves randomization and allows for testing of consistency between direct and indirect evidence in the network, whilst making use of all the available evidence at different time points
- "MBNMAtime" package in R was adopted to perform a meta-analysis of studies with multiple follow-up measurements in order to account for linear time-course relationships with multiple treatment comparisons. The analysis was performed in R v4.2.1
- The package allows a range of different time-course models to be fitted in a Bayesian framework such as Log-linear time-course MBNMA, Piecewise linear time-course MBNMA with a knot at different time points, Emax time-course MBNMA, Emax time-course MBNMA with two parameters, B-spline time-course MBNMA and many more

Figure 3: Time Plot showing the mean response of treatments at different time points

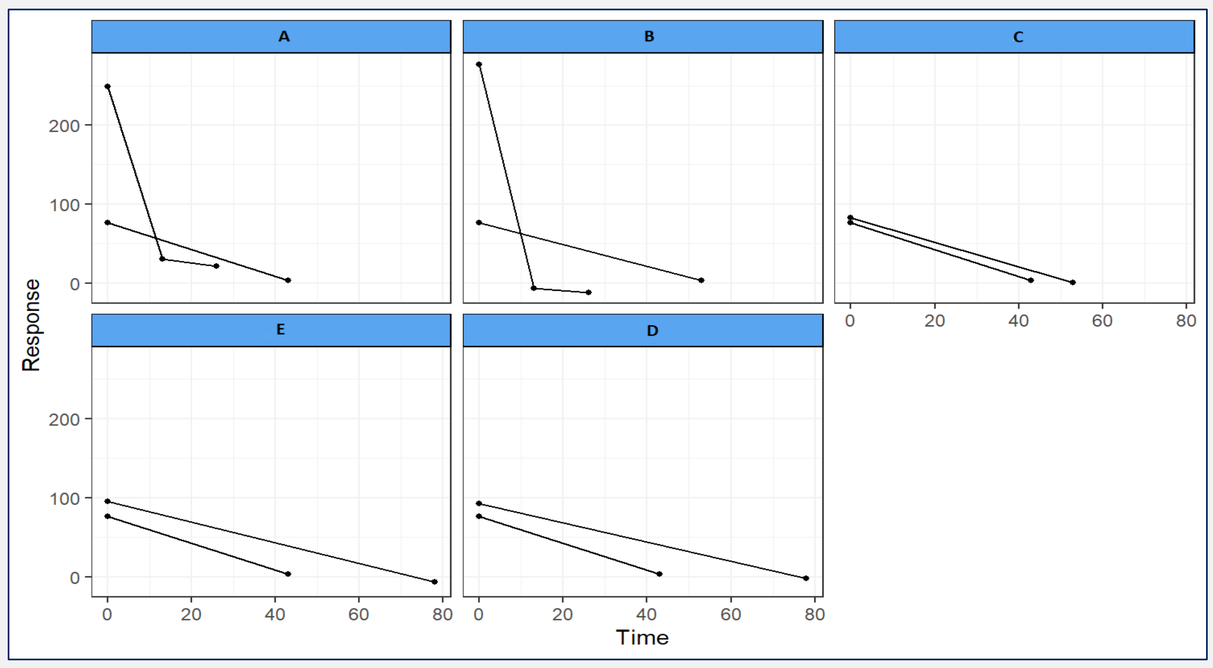
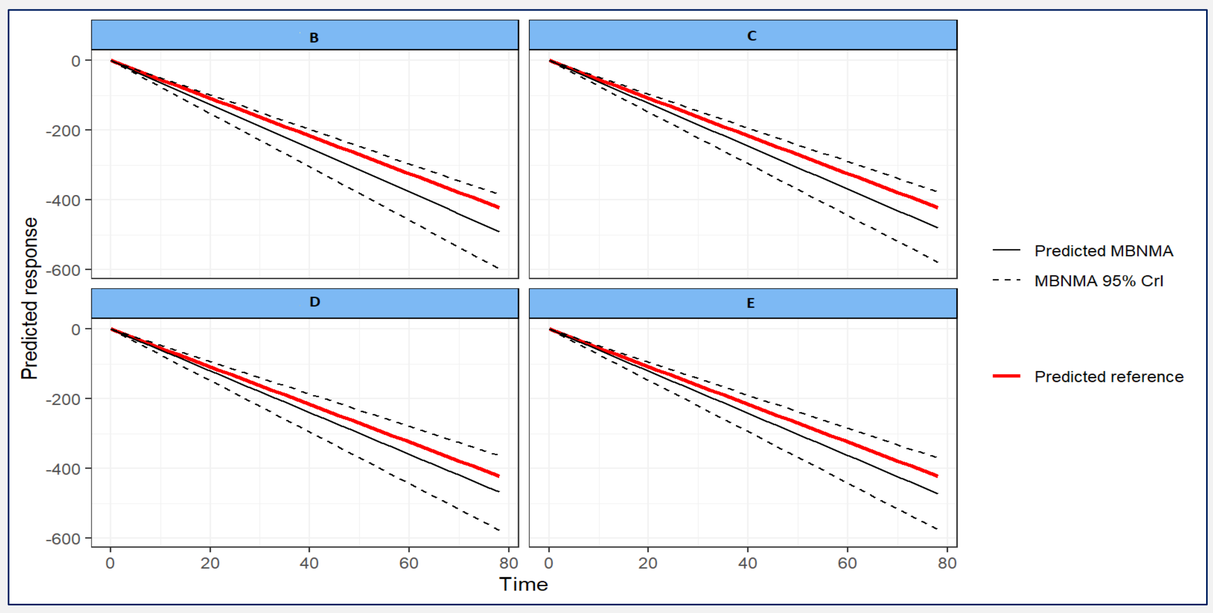


Figure 4: Prediction Plot showing the response of treatments at different time points (Reference = Treatment A)



CONCLUSION

- MBNMA works efficiently and effectively on data sets including multiple treatments at multiple follow-up times and is statistically robust for synthesizing direct and indirect evidence to estimate relative effects- supporting its use in evidence synthesis. The results obtained from the linear time-course MBNMA model suggest that all the relative effects obtained are statistically insignificant
- By demonstrating that time-course can be included in NMA in a statistically robust manner, we hope that this will allow the inclusion of trials from drug development into reimbursement agency decision-making. Doing so can help to bridge the gap in evidence synthesis technique that currently exist between Pharmacometrics and Health Technology Appraisal

Reference
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 Sep;11(5):678-697. DOI: 10.1002/jrsm.1432. Epub 2020 Aug 4. PMID: 32662206.

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