Revolutionizing Multi-Level Network Meta-Regression: Advancing Analysis with the “multinma” Package

MSR104

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CONCLUSIONS

The **multinma** package offers an advanced approach to meta-analysis by employing Multi-level network meta-regression (MLNMR), and its strength lies in its ability to integrate both Individual Patient Data (IPD) and Aggregate Data (AgD), thereby minimizing aggregation bias and providing population-adjusted treatment effect estimates. This makes it a valuable package for comparative effectiveness research and health technology assessment. Despite some limitations, **multinma** provides researchers with a sophisticated and versatile methodology for robust evidence synthesis across various data types.

INTRODUCTION

- MLNMR extends the IPD network meta-regression to include AgD studies, allowing for a more comprehensive analysis of the evidence and this approach can increase the number of studies included in the NMA, potentially leading to more precise and generalizable findings [1]
- MLNMR uses both IPD and AgD data to increases the accuracy of assessment of the treatment effect [2]
- While fixed-effects models (FEM) yield reliable results in homogeneous conditions, random-effects models (REM) account for heterogeneity by applying prior distributions [3]
- The **multinma** package in R enables efficient implementation of MLNMR analysis using a Bayesian approach for comparative effectiveness research, allowing for the incorporation of prior knowledge and the quantification of uncertainty [4]
- By incorporating covariates as effect modifiers, MLNMR offers a more flexible and potentially more precise approach to modeling treatment effects compared to standard network meta-analysis (NMA) [4]

OBJECTIVE

- To assess the comparative effectiveness of different treatments, with a specific focus on analyzing count and rate data
- To employ an MLNMR approach to synthesize evidence, including both IPD and AgD data

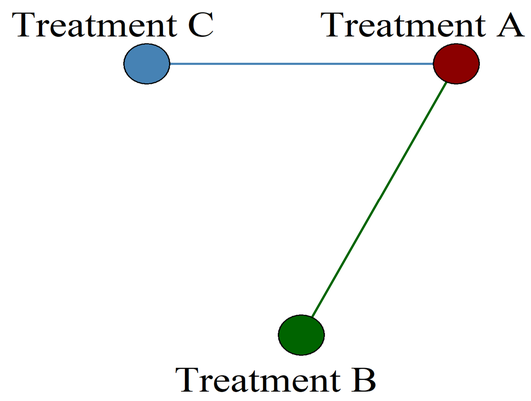
METHODS

- MLNMR was performed in the R software, version 4.4.2, using the **multinma** package
- This analysis comprises two studies: Study 1 with IPD, and Study 2 using AgD data
- Patient-level covariates were scaled and included in the model to account for potential baseline differences between patient groups across the studies
- To assess the treatment effects, FEM and REM were employed
- REM was implemented to account for heterogeneity across the studies. A half-normal prior distribution for heterogeneity was used, with a scale parameter of 2.5 as the base-case scenario
- A sensitivity analysis was performed by varying the scale parameter to 5
- A probit link with binomial likelihood was used to model count outcome and estimate relative risk (RR)
- A log link with a Poisson distribution was used for rate data to calculate the rate ratio (RR)

RESULTS

- Table 1 suggests Treatment C is better than B, showing a lower relative risk (RR < 1 in both FEM and REM). However, Treatment B shows a substantially higher RR compared to A, and Treatment C shows a slightly higher RR compared to A, in both models, indicating a potentially increased risk
- The forest plot for relative risk (Figure 2) indicates that none of the treatment comparisons achieved statistical significance, as evidenced by all credible intervals including the line of no effect. This suggests a lack of clear evidence for a difference between the treatments examined
- REM indicated high uncertainty in RR estimates, with wide credible intervals (CrI) across comparisons, highlighting heterogeneity in treatment effects as shown in Table 1
- Table 2 suggests that Treatment C is associated with a lower rate ratio compared to both Treatment A (statistically significant in FEM) and Treatment B (not statistically significant in either model), suggesting potentially fewer events with Treatment C
- In Figure 2, the forest plot reveals a statistically significant rate ratio for C vs. A, while B vs. A and C vs. B are not significant

Figure 1: Network Geometry of Treatment Comparisons



RESULTS

Figure 2: Forest plot displaying the relative risk estimates and rate ratio

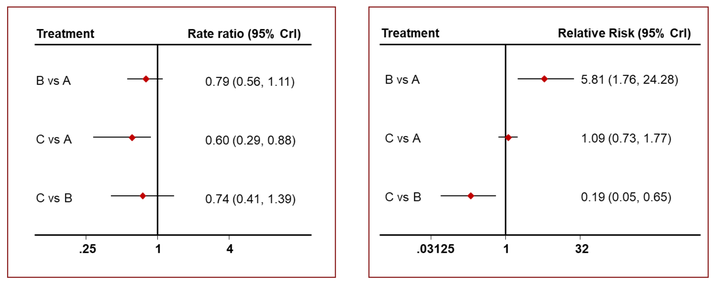


Table 1: Model Statistics for FEM, REM Base case, and REM Sensitivity for count data

Treatment	FEM (Relative Risk)	REM - Base case Relative Risk)	REM – Sensitivity (Relative Risk)
B vs A	5.80 (1.80, 24.30)	5.91 (0.06, 542.31)	5.39 (0.00, 7099.22)
C vs A	1.10 (0.70, 1.80)	1.15 (0.03, 70.48)	0.94 (0.00, 351.27)
C vs B	0.20 (0.00, 0.70)	0.20 (0.00, 58.30)	0.16 (0.00, 7648.14)
DIC	74.31	74.16	74.81

Table 2: Model Statistics for FEM, REM Base case, and REM Sensitivity for rate data

Treatment	FEM (Rate Ratio)	REM - Base case (Rate Ratio)	REM – Sensitivity (Rate Ratio)
B vs A	0.79 (0.56, 1.11)	0.93 (0.62, 1.23)	0.90 (0.62, 1.13)
C vs A	0.60 (0.29, 0.88)	0.49 (0.20, 1.17)	0.58 (0.28, 1.87)
C vs B	0.74 (0.41, 1.39)	0.55 (0.26, 1.09)	0.63 (0.31, 1.07)
DIC	166.94	165.21	172.91

References

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Disclosures

AS, NT, MSM, PB, and SP, the authors declare that they have no conflict of interest

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