Validation of a Mixed Model for Repeated Measures Approach to Including Trials with Varying Follow-up in Indirect Treatment Comparisons of Long-Term Outcomes

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Introduction

- Indirect treatment comparison (ITC) methods are required to assess the relative efficacy between treatments when no head-to-head clinical trials are available.
- However, trials will frequently include a combination of different follow-up lengths, making it challenging to perform long-term comparisons, particularly when the outcome of interest is some summary of the entire longitudinal response (eg, area under the curve).

Objective

To validate a mixed model for repeated measures (MMRM) approach to include trials with various follow-up times in meta-analyses of long-term outcomes.



Reference

Pedder H, Boucher M, Dias S, Bennetts M, Welton NJ (2020) Performance of modelbased network meta-analysis (MBNMA) of time-course relationships: A simulation study. Res Synth Methods 11 (5): 678-697.

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- This study adapts model-based network meta-analysis (MBNMA) models to the single arm situation.¹ The proposed approach uses a multivariate normal
- likelihood with unstructured variance covariance matrix which assumes that missing timepoints are missing at random and can be considered similar to an aggregate version of MMRM.
- An estimate of the correlation on marginal logit responders are included in the multivariate normal likelihood on logit probabilities with correlation between timepoints assumed to be equal for both treatments of interest.
- The MMRM approach is compared to a simpler approach assuming no correlation across timepoints (equivalent to independent meta-analyses).
- Models are conducted within a Bayesian framework using aggregate level inputs.

Timepoint	MMRM	No correlation	True Value
1	0.83 (0.17)	0.75 (0.25)	1
2	1.36 (0.11)	1.23 (0.25)	1.5
3	1.66 (0.2)	1.61 (0.44)	2
4	2.52 (0.32)	2.56 (0.41)	3
5	2.92 (0.98)	2.22 (1.28)	4
6	6.01 (1.61)	6.8 (2.53)	4.5
7	4.38 (1.39)	4.47 (1.57)	5
8	6.09 (2.33)	3.78 (3.64)	7

Disclosures

S. Walsh is an employee of EVERSANA[®]; **T. Disher** is an employee of EVERSANA[®]

Funding

This study was supported by EVERSANA®

Methods

Table 1. Comparison of MMRM and No correlation model of mean value

- timepoints.
- time differ.

MSR100

Results

• If there are many timepoints with missing data, applying an MMRM approach can lead to significant improvements in the estimation of effects and their precision.

 In situations where final models are combined in random effect meta-analysis, the MMRM approach would allow for a more reliable estimate of between trial heterogeneity than is otherwise possible.

• With those benefits considered, if the difference between the full set of timepoints and the observed is large neither approach has much effect on the estimates at later

• The MMRM approach can be challenging to implement computationally and in settings where the distance between timepoint measurements or their correlation over

Conclusions

Applying an MMRM approach may be valuable in situations where unanchored comparisons conducted at earlier timepoints are forced to use limited trials at later timepoints due to a lack of long-term data or study design characteristics (eg cross-over).

