

**Mixed Treatment Comparisons using Aggregate- and Individual-Patient Level Data: An Efficient use of Evidence for Cost-Effectiveness Modelling**

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Objectivos (Objectives): It is desirable to use all relevant sources of evidence to estimate effectiveness for use in a cost-effectiveness (CE) analysis. Meta-analysis can be utilised to synthesise pair-wise comparisons of the same interventions. Mixed treatment comparisons (MTC) extends this framework allowing the simultaneous statistical synthesis of information on more than two interventions. A proportion of this evidence, though, might be available at the individual participant level (IPD). This paper describes existing MTC evidence synthesis methodology for CE assessment, and develops a series of novel statistical models aimed to fully exploit the existing data, regardless of whether available at aggregate - (e.g. study) or at the individual participant level.

Metodologia (Methodology): Bayesian statistical evidence synthesis models to estimate effectiveness parameters from multiple interventions were developed. Within a binary outcome framework, proposed models allow for the synthesis of IPD within a MTC framework and also for the simultaneous analysis of IPD and aggregate data, together with study and individual level covariates. Model extensions were performed to assess assumptions over the treatment-effect covariate interactions (i.e. exchangeable and independence associations). We are not aware of these models being described or implemented previously.

Resultados (Results): The effectiveness of home safety education and the provision of safety equipment (i.e. possession of functioning smoke alarm devices, binary outcome – Yes/No) for the prevention of childhood injuries in the household was used as a motivating example. This case study included 20 trials (evidence from 11 available at the summary level and 9 available as IPD), summing up to approximately 11,500 participants. Seven implementation strategies were defined and a structured network of evidence was constructed. Comparisons of the newly developed synthesis models results against the simple case of MTC using summary data were performed. As expected, irrespective of the evidence format used, all synthesis models which do not consider information on covariate(s) show similar results, i.e. more intensive interventions (providing education, equipment (with fitting) and home inspection) were more effective (OR vs usual care of 4.5 (95% credible interval: 1.4 to 14.8)). Evidence relating to the binary covariate ‘household parent status’ (i.e. two or single parent household) was considered as a potential treatment-effect modifier. By extending our models to consider this covariate we accounted for potential ecological bias and study-level confounding, often found when synthesizing evidence at the aggregate level. Results of synthesizing IPD evidence using information on a covariate show a clear improvement in accuracy over estimated treatment-covariate interaction terms when compared to the results obtained from synthesizing summary evidence.

Conclusões (Conclusions): Including evidence at individual participant level in the MTC synthesis is advisable when exploring participant level covariates; even when IPD are only available for a fraction of the studies forming the evidence base. Our findings show that it will produce intervention effect estimates of higher accuracy which may be valuable for estimating subgroup effects or adjusting for inconsistency.