

Using Bivariate Hierarchical Modelling to Assess the Generalisability by Location of Multinational Trial-Based Cost-Effectiveness Analysis Results

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Abstract

Background: Cost-effectiveness analysis (CEA) in health care is increasingly conducted alongside multicentre and multinational randomised controlled clinical trials (RCTs). Stochastic CEA is designed to account for *between-patient* sampling variability in cost-effectiveness data. In multi-location RCTs however *between-location* variability in cost-effectiveness is to be expected given that countries often differ in factors such as clinical practice, patient case-mix and the unit costs of delivering health care. A failure to acknowledge this feature of the data may lead to misleading conclusions in trial-based economic studies.

Objective: Using data from a recent multinational trial-based CEA, this paper explores the use of Bayesian bivariate hierarchical modelling to handle multinational cost-effectiveness data. This analytical framework explicitly recognises that (i) patient-level costs and outcomes within each country/centre are correlated and (ii) policy-makers are fundamentally country-specific. It is shown that bivariate hierarchical modelling can be used to obtain (a) more appropriate estimates of the population average incremental cost-effectiveness and associated measure of sampling uncertainty compared to standard CEA; and (b) country-level cost-effectiveness estimates which can be used to assess the generalisability by location of the study results, while controlling for *between-counties* differences in *country*-specific and *patients'*-specific characteristics.

Methods: Bayesian bivariate hierarchical modelling and shrinkage estimation.

Results: Standard CEA results displayed a large degree of variability across the 17 countries included in our analysis, producing potentially misleading results. Shrinkage estimation through Bayesian bivariate hierarchical modelling facilitated the appropriate prediction of country-specific cost-effectiveness estimates, while weighting the results based on the level of information available within each country.

Conclusions: Bivariate hierarchical modelling is a promising analytical approach which allows the analyst to obtain trial-wide and country-specific cost-effectiveness estimates. The approach presented in this paper represents a more general framework for the analysis of cost-effectiveness data, which has the potential to (a) explore the generalisability by location cost-effectiveness results; (b) facilitate the synthesis of pre-existing evidence; (c) accommodate prognostic factor adjustment and patient sub-group economic analysis; and (c) explore potential cross-level interactions.
