MSR127

Generalizability of Trial-Based Economic Evaluations. Methods to Account for Covariates and Impact on Cost-Effectiveness and Value of Information

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Introduction

- Economic evaluations based on randomized clinical trials (RCTs) may lack generalizability if heterogeneity is not accounted for[1].
- We propose a methodological framework to assess the generalizability of cost-effectiveness and value of information (VoI) estimates to the real-world setting in the presence of heterogeneity. Such methods can guide optimal resource allocation and future research decisions.

Methods

- Data from the TASMINH-2 trial[2] were analyzed to estimate the cost-effectiveness of self-management of hypertension vs usual care.
- Covariate selection was based on fitting univariate and multivariate regression models for costs and quality-adjusted life years (QALYs) including all baseline characteristics as covariates. Important covariates from a statistical and clinical perspective were considered in flexible Bayesian generalized linear models (GLMs)[3].
- The generalizability of the results to the target population that consisted of patients with hypertension recruited in real-world evidence (RWE) studies in the UK was explored by averaging over the joint covariate distribution in the target population via numerical integration methods.
- The integration over the joint covariate distribution was performed with 2D Gauss-Kronrod quadrature with a relative tolerance of 10^{-4}.
- Cost-effectiveness results are reported as incremental net monetary benefits (INMBs) estimated at a willingness-to-pay threshold (WTP) of £20,000/QALY as follows:
- $INMB = (QALYS_{int} - QALYs_{comp}) * WTP - (Costs_{int} - Costs_{comp})$

Results

- A GLM assuming lognormal distributions on costs and beta distributions on QALYs fitted separately in each trial arm provided the best fit to the TASMINH2 data.
- Three covariates (baseline EQ-5D, IMD score, chronic kidney disease [CKD]) were identified as important predictors of QALYs and were included in the analysis.
- Patients recruited in RWE studies had lower baseline EQ-5D[4], were slightly more deprived[5] and were more likely to have CKD[6] compared to patients recruited in the TASMINH-2 trial (Table 1).
- Given that two continuous and a binary covariates were included in the analysis, the joint covariate distribution of baseline EQ-5D and IMD score in the two categories defined by CKD was required.
- Mixture distributions were fitted to EQ-5D in both CKD categories (Figure 1) and a mixture distribution and a lognormal distribution to IMD score in the CKD and no CKD categories, respectively (Figure 2). The same types of distributions were assumed in target population, albeit with different parameters.
- At a cost-effectiveness threshold of £20,000/QALY, self-management of hypertension was associated with an INMB of -£351.00 in patients recruited in TASMINH-2. When generalizing the results to patients recruited in RWE studies, the INMB was estimated at -£551.00 (Table 2).
- Population expected value of perfect information (EVPI) for hypertensive patients in the United Kingdom for a 10-year time horizon was estimated at £77million for patients recruited in TASMINH-2 and at £39million for patients recruited in RWE studies.

Table 1: Covariate information for the populations of interest

Covariate	TASMINH-2	Target population*
Baseline EQ-5D, Mean (SD)	0.837 (0.201)	0.764 (0.279)
IMD score, Median (SD)	17.31 (12.94)	18.84 (11.97)
CKD (%)	9.40	13.60

*Based on real-world evidence studies. CKD: chronic kidney disease; IMD: index of multiple deprivation; SD: standard deviation

Figure 1: Baseline EQ-5D for patients with (left) and without (right) chronic kidney disease in TASMINH2: histogram of observed data with fitted density of mixture distributions

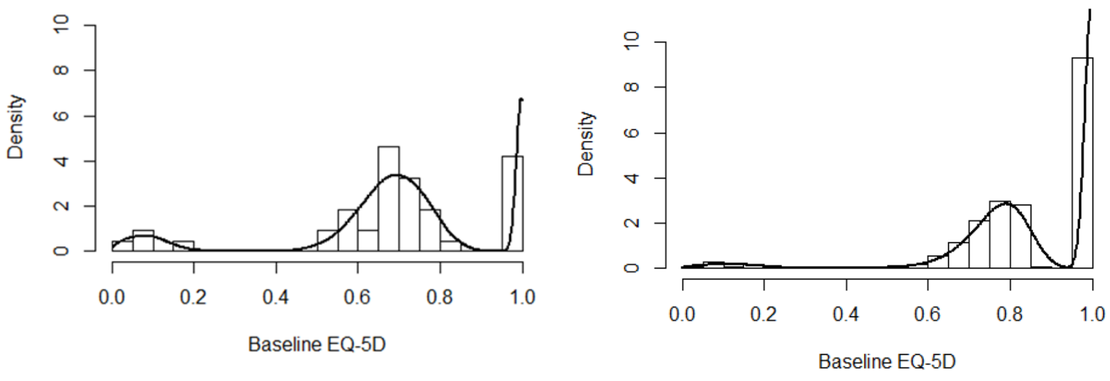

Figure 2: IMD score for patients with (left) and without (right) chronic kidney disease in TASMINH2: histogram of observed data with fitted density of mixture and lognormal distributions

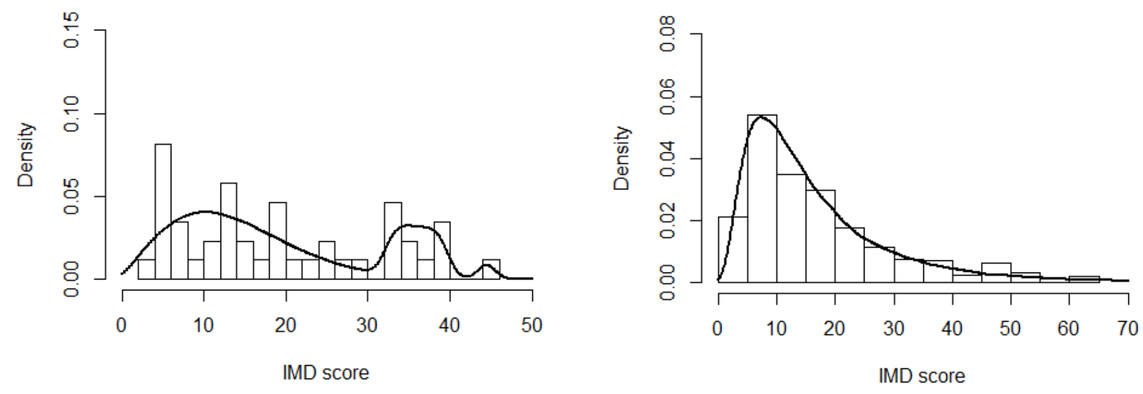

Table 2: Cost-effectiveness results in the populations of interest

Results	TASMINH-2	Target population*
Expected INMB§ (£)	-351.00	-551.00
Probability of being cost-effective§ (%)	16.00	8.40

*Based on real-world evidence studies. § At a cost-effectiveness threshold of £20,000/QALY. INMB, incremental net monetary benefit

Table 3: Value of information results in the populations of interest

Results	TASMINH-2	Target population*
Per person EVPI§ (£)	32.30	16.30
Population EVPI in UK§ (£million)	77.00	39.00

*Based on real-world evidence studies. § At a cost-effectiveness threshold of £20,000/QALY. EVPI, expected value of perfect information

Conclusions

Cost-effectiveness results are less favorable for self-management of hypertension when generalizing RCT findings to patients recruited in RWE studies in the UK. Incorporating RWE can support optimal resource allocation and further research decisions.

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