Factors Associated with the Outcomes of Rapid Reviews Submitted to the NCPE

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Background

- The National Centre for Pharmacoeconomics (NCPE) conducts health technology assessments (HTAs) for all drugs seeking reimbursement in Ireland.
- The first step in the HTA process is the Rapid Review (RR) – a dossier submitted to the NCPE by the marketing authorisation holder. It provides information on the drug, relevant clinical evidence and economic factors.
- Based on the outcome of the RR appraisal, the NCPE can make a number of recommendations to the decision-maker (Figure 1). They will advise if a decision on reimbursement can be made at this time or if further assessment in the form of a full HTA is required.
- Depending on the outcome at RR stage, there may be implications for time-to-market and timelines for patient access to new drugs. As a result, stakeholders are interested in gaining greater insight into factors associated with RR outcomes.[1,2]

Objective

- To explore and evaluate factors associated with the outcomes of RR submissions presented to the NCPE, contributing to the literature in three ways:
  - Use data uniquely available to the NCPE
  - Add explanatory variables not included in previous analyses
  - Use new methods to classify RR outcomes for binomial analysis

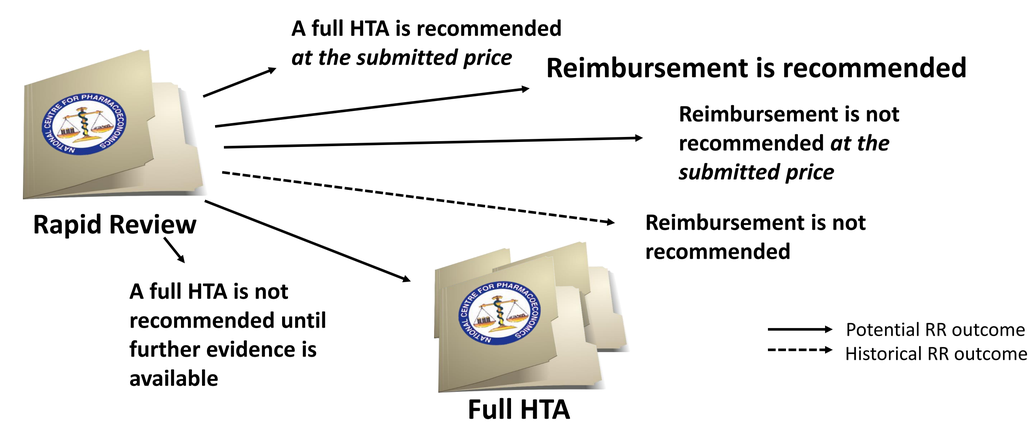


Figure 1 – Overview of Rapid Review Outcomes

Results

Table 2 – Results of multivariate binomial logistic regression model

	'Positive' vs. 'Negative'	
	Marginal Effects at Mean	*Std. Error*
Therapeutic Area (*vs. Other*)		
Oncology (non-haematological)	-0.508***	0.100
Haem-Oncology	-0.401***	0.139
Infectious	0.051	0.137
Neuromuscular	-0.449***	0.100
Endocrine	-0.121	0.140
Immunomodulators	-0.251*	0.134
Company Experience	-0.024**	0.012
Time	-0.063***	0.024
First-in-Class	-0.324***	0.103
Orphan	-0.076	0.110
Pivotal Trial Design (*vs. Active control)*		
Other	-0.284**	0.120
Placebo-controlled	-0.167**	0.078
Single-arm	0.358**	0.161
Pivotal Trial Phase *(vs. Phase III)*		
Phase II	0.134	0.172
Other	0.472**	0.229
QoL *(vs. No Benefit)*		
Not Reported	0.208**	0.093
Positive Benefit	0.339**	0.133
Cost	-0.006***	0.001
Categorical Net BI *(vs. Negative)*		
Neutral	-0.078	0.171
None estimable	-0.582***	0.149
Positive	-0.340**	0.138

N = 335; LR (df) = 189 (21); Adj. pseudo-R^2 = 0.315

*p < 0.10, ** p < 0.05, *** p < 0.01. Terms in bold represent the independent variable name; terms in italics represent the comparator or 'base-case' for categorical variables. BI = Budget Impact; HTA = Health Technology Assessment; QoL = Quality of Life

Methods

- **Database generation:** all RRs commissioned between 2012 and 2018. For each RR, we collected and inputted data on a range of variables (see Figure 2).
- **Analysis:** multivariable model was estimated using binary logistic regression techniques, such that:

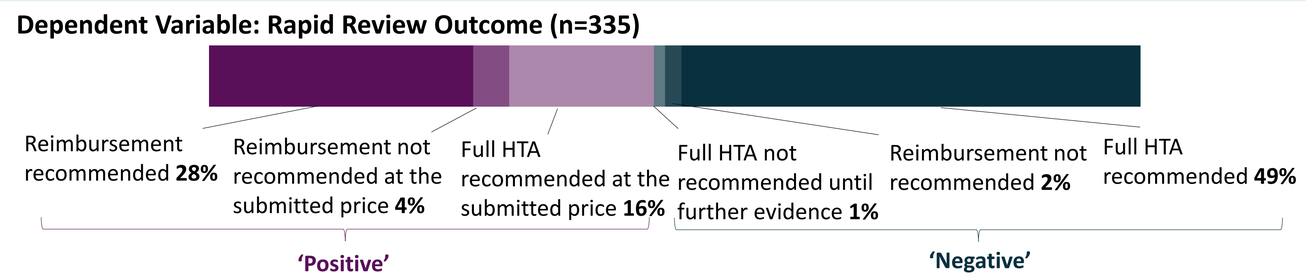
$$RR_i = f\left(X_i^D, X_i^C, X_i^E, \varepsilon_i\right)$$

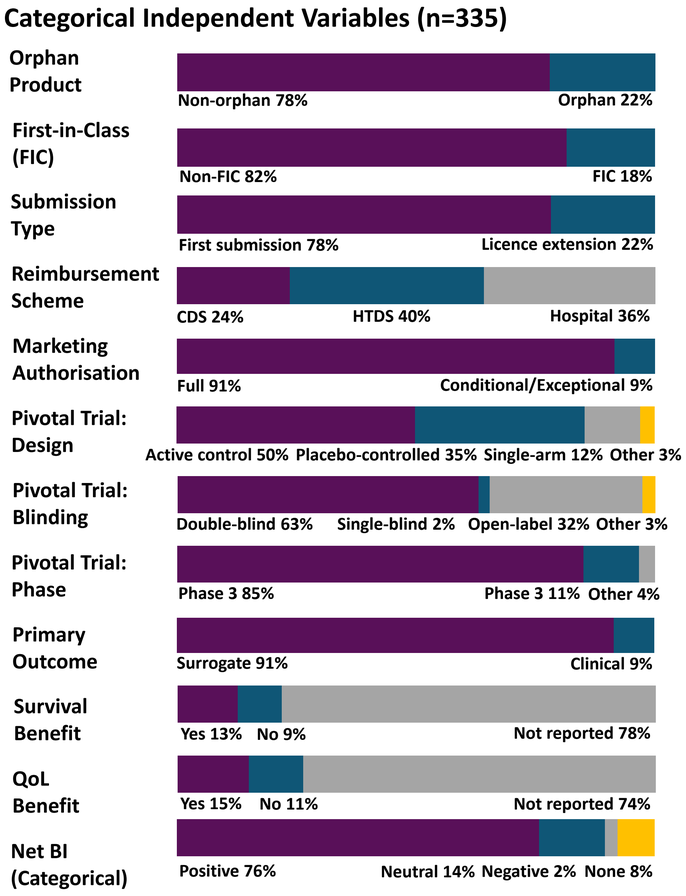
- where RR_i is the RR outcome for submission *i*, X_i^D is a vector for drug-specific factors, X_i^C is a vector for clinical evidence variables and X_i^E is a vector for economic factors. ε_i represents the error term for submission *i.*
- **Dependent variable:** a binary outcome measure indicating 'positive' if a RR received an outcome recommending reimbursement after RR stage, or that reimbursement may be considered after price negotiation.

Software used:
- Data collection – Excel
- Analysis – Stata

Model specification informed by:
- Literature review
- Interview with HTA experts
- Multicollinearity
- Missing data (not random)

Model Assessment
- Likelihood Ratio
- Wald tests
- McFadden's R^2





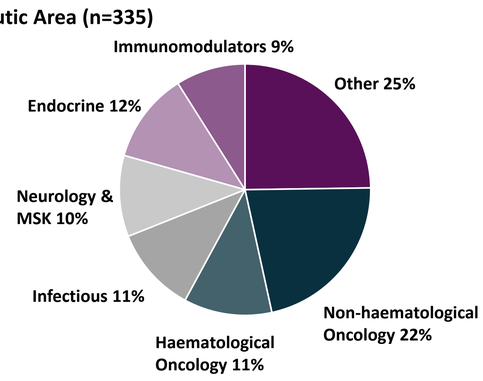


Figure 2 – Descriptive Statistics

Table 1 – Continuous independent variables

	Unit	Mean (SD)	Median	Obs
Company Experience	Sub's	3.98 (4.57)	2	335
Time	Years	3.11 (1.91)	2.99	335
Eligible Population	Patients	16,062 (74,806)	192	280
Cost	€	46,489 (81,422)	16,480	335
Gross BI	€	14,359,130 (21,055,050)	6,400,000	285
Net BI	€	7,744,262 (20,554,550)	1,219,422	202

BI = Budget Impact; Sub's = Submissions

Conclusions

- We present a descriptive analysis of the factors associated with RR outcome for all RR submissions to the NCPE between 2012 and 2018.
- Irish drug costs and measures of net drug budget impact had not been included in prior analyses.[1] We find that drugs with higher costs and positive net drug budget impacts are associated with a lower probability of a 'positive' recommendation.
- Drugs which are designated 'First-in-Class' and those relating to certain therapeutic areas are associated with a lower probability of a 'positive' recommendation. These factors are not explicit decision-making criteria in deciding RR outcomes. The results may be a result of confounding from variables not captured in our model.
- An unexpected finding included the increased probability of a 'positive' recommendation for drugs with single-arm pivotal trials, when compared to those with active comparators. This may be a result of omitted variable bias. Further characterisation of these drug submissions may be useful.
- Our results highlight the complexity of the RR process and outcomes. We emphasize that the relationships we find are descriptive in nature, and are not causal. Further research is needed to characterize other salient factors not accounted for here.

Limitations
- Sample size (ordinal, multinomial)
- Poor sensitivity of certain variables
- Omitted variable bias
- No causality identified

References
1. Murphy A, Redmond S. To HTA or Not to HTA: Identifying the Factors Influencing the Rapid Review Outcome in Ireland. Value in Health 2019;22(4):385-390
2. O'Donnell H, Lamrock F, Tilson L, Barry M. Letter to the Editor 'To HTA or Not to HTA: Identifying the Factors Influencing the Rapid Review Outcome in Ireland. Value in Health. 2019; *Article in Press.*