Association of NCPE Submission Outcomes in Ireland with Additional Benefit Rating in Germany

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BACKGROUND

Health Technology Assessments (HTAs) help in prioritising access to new therapies and maintain the viability of the publicly funded health care systems (1). Prior to conducting HTAs, some countries like Germany and Ireland conduct a preliminary assessment. Germany's preliminary assessment is conducted by Institute for Quality and Efficiency in Health Care (IQWiG) and assesses the additional clinical benefit of a medicine and gives a clinical benefit rating on a scale from 0 (lesser benefit) to 5 (major benefit). Ireland's preliminary assessment is the Rapid Review (RR) conducted by the National Centre for Pharmacoeconomics (NCPE). The purpose of the RR is to determine whether a full HTA is required or not and to support price negotiations in cases where a HTA can be avoided. Many studies have investigated the additional benefit ratings in Germany with submission outcomes in other countries, but this study is the first study to investigate the association between these preliminary assessments in Germany and in Ireland.

OBJECTIVE

Given that the same clinical data is used in both preliminary assessments in Germany and Ireland (based on regulatory applications to the European Medicines Agency), we investigated the association between the RR in Ireland and Additonal benefit rating in Germany.

METHODS

All RRs (except medical devices and vaccines) submitted to the NCPE between 2015 to 2020 were extracted from the NCPE archive into a database. The year of the RR being commenced, the drug's ICD-10 category, the reimbursement scheme category, and the orphan and first-class status were recorded in the database for each RR. The outcome of each RR was recorded as HTA recommended or HTA not recommended. HTA Recommended included all such drugs with HTA recommended and HTA recommended at submitted price as RR outcome (2). HTA not recommended included all such drugs with HTA not recommended and HTA not recommended at submitted price as RR outcome (2). To populate the database for Germany's additional benefit ratings, the publicly available source i.e., Gemeinsamer Bundesausschuss (G-BA), IQWiG and AMNOG-MONITOR were used to create matched pairs of RR outcomes and Additional Benefit ratings in the dataset. Care was taken to match drugs based on the same indication. To test the association between RR outcome in Ireland and Additional Benefit rating in Germany Pearson's chi square test was used. A Cramer's V test was used further to establish the effect size or level of association between the two variables.

The Hypothesis for the analysis was as follows: -

H_0: There is no statistically significant association between RR Outcomes in Ireland with that of Additional Benefit rating in Germany

H_a: There is a statistically significant association between RR Outcomes in Ireland with that of Additional Benefit rating in Germany

Decision Rule: P-value less than 0.05 significance level, accept the H_a

RESULTS

There were 217 matched pairs (both RR and additional benefit rating). Figure 1 shows that of the 217 matched pairs, 57% had no additional benefit while 17% had a considerable additional benefit (Fig. 1). Of the matched pairs (n= 156) that received an additional benefit rating of lesser benefit, no benefit and not quantifiable benefit, 41%, 55% and 22% were oncology, first-in-class and orphan drugs respectively (see Table 1). Corresponding figures for the matched pairs (n=61) that received an additional benefit rating of considerable, minor or major were 54%, 77% and 20% respectively. Overall, 19% of the matched pairs were not recommended for an HTA and the remaining were recommended for an HTA. The recommendation for a HTA varied according to the additional benefit rating. Specifically, 100% of the matched pairs with a lesser and major benefit rating were recommended for a HTA, while 74%-96% of the matched pairs with other benefit ratings were recommended for a HTA (see Figure 2). RR outcome and Additional Benefit ratings were correlated (p = 0.027, chi-square test, Cramer's *V* = 0.241), showing statistically significant association, p < 0.05 (Table 2). Therefore, the alternative hypothesis is accepted.

Discussion

The results showed only a moderate level of association. Some of the explanations for this could be that budget impact analysis is importantly factored in the RR dossier in Ireland but not in Germany. Another explanation could be that the objectives of preliminary assessments are different in the two countries wherein a RR determines whether a HTA is required or not while additional benefit rating determines the pricing and reimbursement of a drug in Germany. There are also different approaches to assessing orphan drugs in Ireland and Germany. Effectiveness of the drug with regards to its comparator is another important feature in Germany but not in Ireland.

Conclusion

Our study showed that preliminary assessments in Ireland and Germany are moderately associated despite the fact that same clinical data is used.

Future Work

Future research will focus on investigating the causality of the association between RR outcome and additional benefit rating as previous research in other countries have found that cancer and orphan drugs are driving the association (3-5).

Figure 1: Proportion of matched pairs by Additional Benefit Rating

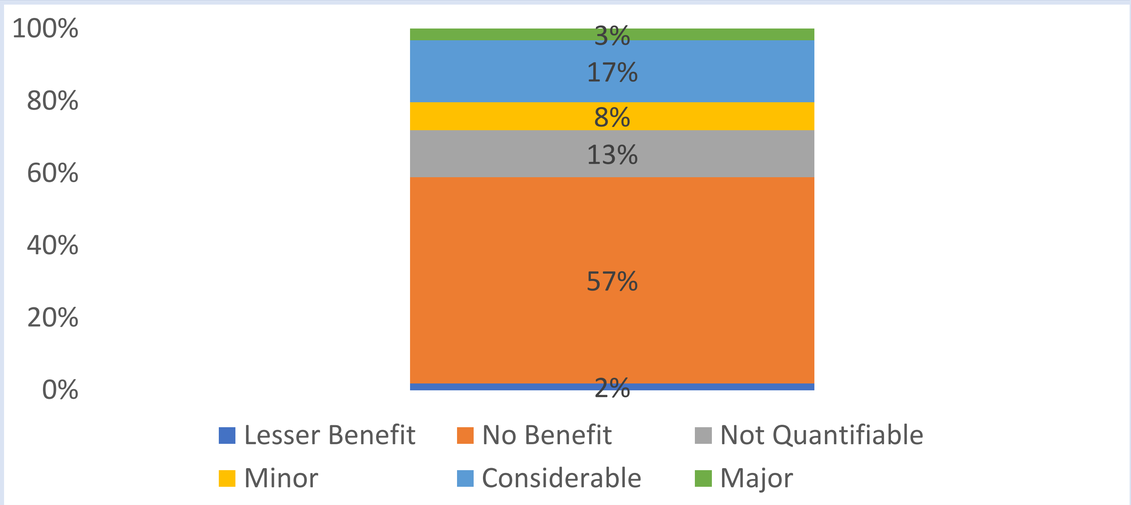

Table 1: Proportion of Additional Benefit Ratings vs ICD-10 category, drug scheme, first-in-class, orphan status

	Additional Benefit Rating (Lesser, No Benefit, Not Quantifiable) (n=156)	Additional Benefit Rating (Considerable, Minor, Major) (n=61)
Neoplasms	41%	54%
Circulatory	5%	3%
Endocrine	12%	7%
Respiratory	4%	0%
Nervous	8%	5%
Other areas	31%	31%
First in class	55%	77%
Orphan drug	22%	20%
Year 2015	14%	14%
Year 2016	18%	18%
Year 2017	22%	22%
Year 2018	16%	16%
Year 2019	17%	17%
Year 2020	13%	13%
GMS	13%	8%
Hospital	40%	38%
High-Tech	46%	54%

Figure 2: NCPE Rapid Review outcome vs GBA Additional Benefit Rating

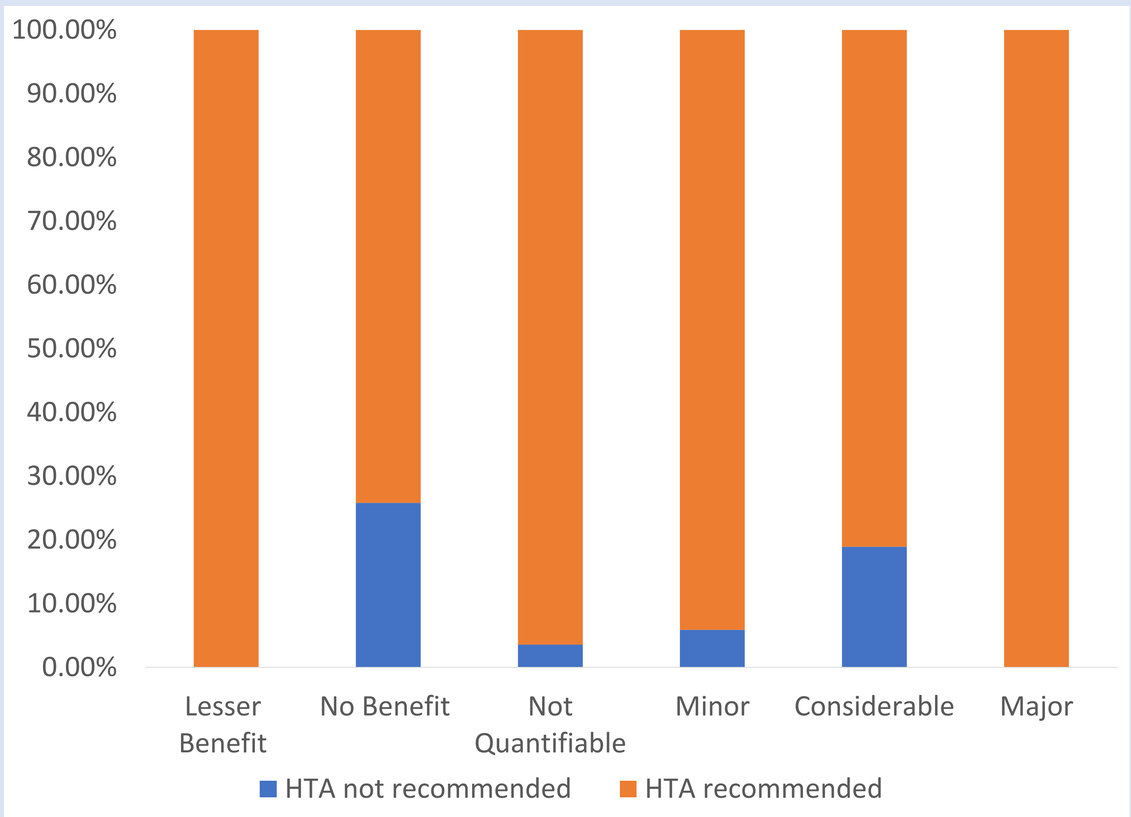

Table 2: Chi-Square Analysis of RR submission outcomes (Ireland) vs Additional Benefit Rating (Germany)

Chi-Square Test	Value	df	Asymp. Sig. (2 Sided)	Symmetric Measures		Value	Approximate Significance
Pearson's Chi Square	12.597[a]	5	0.027	Nominal by Nominal	Phi	0.241	0.027
Likelihood Ratio	16.611	5	0.005		Cramer's V	0.241	0.027
N of Valid Cases	217			N of Valid Cases		217	

Note: N= 217, a. 4 cells (33.3%) have expected count less than 5. The minimum expected count is .76

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