The Relationship Between Financial Impact and the Likelihood of Drug Reimbursement in the Australian Health Care System

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ABSTRACT

- **Objectives:** In this study we estimated the relationship between the financial impact of a new drug on the health care system in Australia and the probability of the drug being recommended for reimbursement by the Pharmaceutical Benefits Advisory Committee (PBAC).
- **Methods:** Data in the PBAC summary database regarding drug-reimbursement decisions made between July 2005 and November 2009 were abstracted. Financial impact was categorized as A$0 or less, greater than A$0 up through A$10 million, and greater than A$10 million per year. Descriptive analysis, logistic analysis, and recursive partitioning decision analysis were used to estimate the relationship between the financial impact of a new drug indication and the probability of its reimbursement. The multivariable analyses controlled for other clinical and economic variables that have been shown to be correlated with the probability of reimbursement, including the cost per quality-adjusted life-year gained.
- **Results:** In all analyses, financial impact was a significant predictor of the probability of reimbursement. For example, in the logistic analysis, the odds ratio of reimbursement for a drug submission with a financial impact greater than A$10 million compared with A$0 or less was 0.12 (95% confidence interval [CI]: 0.03-0.55); the odds ratio of reimbursement for a drug submission with a financial impact greater than A$0 up through A$10 million compared with A$0 or less was 0.16 (95% CI: 0.04-0.60). In the recursive partitioning decision analysis, the first split of the data was for submissions with a positive financial impact compared with those with a negative financial impact.
- **Conclusions:** In Australia, financial impact on the health care system is an important determinant of whether a new drug is recommended for reimbursement, even when cost-effectiveness estimates and other clinical and economic variables are controlled.

INTRODUCTION

- A financial impact analysis for a new drug provides estimates of the new drug's likely impact on a health care decision maker's short- and long-term annual costs.
- Health Technology Assessment (HTA) agencies, including those in Canada, England & Wales, Australia, Germany, France, and the US ask the manufacturer for estimates of the new drug's likely financial impact if it is to be reimbursed.
- The guidelines for financial impact analysis provided by the HTAs are generally less detailed than those for cost-effectiveness analysis. However, PBAC provides very detailed guidelines about how the financial impact should be estimated.
- The reimbursement decisions of HTA agencies generally can be categorized into four types: unrestricted approval, restricted approval, deferral, and not approved for reimbursement.
- Different countries have different rates of each type of decision, with PBAC rejecting a large number of submissions but allowing multiple re-submissions. These re-submissions, which frequently are limited to a subset of the initially requested population and may include a lower price, often result in eventual approval.

OBJECTIVE

- To estimate the relationship between the financial impact of a new drug on the health care system in Australia and the probability of the drug being recommended for reimbursement by the Pharmaceutical Benefits Advisory Committee (PBAC).

METHODS

- **Data Extraction**
  - The data file of decisions by PBAC was created by abstracting data from the PBAC Web site (http://www.health.gov.au/internet/main/publishing.nsf/ Content/public-summary-documents-by-product).
  - Data were taken from decisions made from July 2005 through November 2009.
  - If a product had more than one submission for the same indication, more than one record was created under the same unique identification number. However, if a product had multiple submissions that included a different indication, a new unique identification number was created for that product and indication.
- **Economic Variables**
  - Outcome variable was PBAC's decision to recommend (with or without restrictions) or not to recommend (including defer) a listing,
  - Input variables were incremental cost-effectiveness ratio (cost per QALY), financial impact for each product, population size, clinical evidence presented, disease category, use of a surrogate endpoint, use of a placebo comparator and manufacturer claim for the clinical benefits of the new product.
  - Financial impact was categorized as A$0 or less, greater than A$0 up through A$10 million, and greater than A$10 million per year.
  - Cost per QALY was categorized as greater than A$0 up through A$30,000, greater than A$30,000, and none (less than zero).
- **Statistical Methods**
  - The unit of analysis for all analyses was the unique drug and indication submission after July 2005. Only the first observed submissions of the unique drug and indication combination within our database were included in the univariate and multivariable logistic analyses.
  - Univariate analysis was performed to explore the association between the PBAC recommendation and the variables described above.
    - The association was tested by Pearson's chi-square test.
  - Multivariable logistic regression was performed to evaluate the relationship between recommendation and categorical financial impact, while adjusting for other factors.
    - The probability of category "recommended" was modeled.
    - Variables were included in the model if they showed an association with the recommendation with a *P* value less than or equal to 0.25 were included in the model
    - The predictive accuracy of the model was assessed using the concordance index c, which also is an estimate of the area under the receiver operating characteristic curve (ROC). A model with an area under the ROC of 0.75 or greater is considered to have good predictive accuracy.
    - Wald's method was used to test the parameters and to construct CIs for odds ratios.
  - Recursive partitioning decision tree analysis was performed using the JMP analysis software (SAS, Cary, North Carolina).

RESULTS

Univariate Analysis

- A total of 260 submissions, representing 214 unique drug plus indication combinations and 46 re-submissions during the data abstraction time period, were extracted from the PBAC Website.
- Of the 260 submissions 153 (58.9%) submissions were recommended and 107 (41.1%) submissions were not recommended for listing.
- The univariate association between recommendation and potential predictors is presented in Table 1. Four variables—financial impact, cost per QALY, manufacturer's claim, and placebo comparator—had a highly statistically significant association with the PBAC recommendation (*P* < 0.0001).

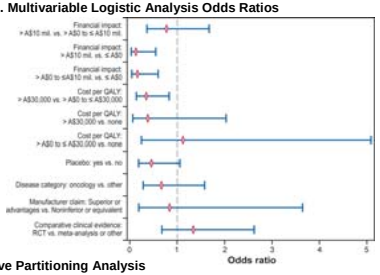
Table 1. Univariate Analyses

	PBAC Recommendation			
	Yes (n = 113)	No (n = 89)	Row Total	*P* Value[a]
Variable[b]	%	%	n	
Financial impact (millions A$)				
> 10	37.1	62.9	62	< 0.0001
> 0 to ≤ 10	53.1	46.9	96	
≤ 0	91.4	8.6	35	
Cost per QALY (thousands A$)				
> 30	26.1	73.9	46	< 0.0001
> 0 to ≤ 30	51.7	48.3	60	
None	72.9	27.1	96	
Population size				
High	46.2	53.8	39	0.3755
Medium	56.5	43.5	46	
Low	59.0	41.0	117	
Manufacturer claim				
Superior and advantages	38.5	61.5	96	< 0.0001
Noninferior or equivalent	71.7	28.3	106	
Comparative clinical evidence				
RCT	51.1	48.9	92	0.2038
Meta-analysis or other	60.0	40.0	110	
Placebo comparator				
Yes	31.4	68.6	51	< 0.0001
No	64.2	35.8	151	
Disease category				
Oncology	41.7	58.3	36	0.0570
Other	59.0	41.0	166	
Surrogate endpoint				
Yes	56.0	44.0	141	0.7867
No	53.9	46.1	52	

Multivariable Logistic Regression

- For the logistic model, the effect of financial impact (*P* = 0.0177) was statistically significant (Figure 1). The predictive accuracy of the logistic model was good (AUC = 0.78). The results indicated that:
  - The odds of recommending a drug submission for listing with a financial impact of greater than A$10 million was 0.12 (95% CI: 0.03-0.55) times the odds of recommending a drug with a financial impact of A$0 or less;
  - the odds of recommending a drug submission for listing with a financial impact of greater than A$0 up through A$10 million was 0.16 (95% CI: 0.04-0.60) times the odds of recommending a drug with a financial impact of A$0 or less.

Figure 1. Multivariable Logistic Analysis Odds Ratios



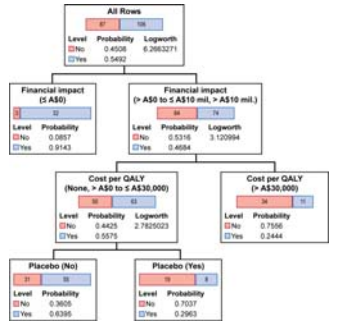
Recursive Partitioning Analysis

- Figure 2 presents the recursive partition decision tree. Besides the variables used in the logistic analyses, we also included population size and surrogate endpoint.
  - Grouping the two financial impact categories, greater than A$0 up through A$10 million and greater than A$10 million into a single category (positive financial impact) and comparing it to A$0 or less (budget neutral or savings), financial impact was the factor used to make the first partition (logworth = 6.3).
  - Cost per QALY (≤A$30,000 or >A$30,000) and placebo were the next predictors selected in the recursive partitioning.

Recursive Partitioning Analysis (continued)

- The results of the recursive partitioning model indicated that the chance of being recommended for reimbursement for drug submissions with:
  - A financial impact at or below A$0 was 91.4%
  - A financial impact greater than zero and a cost per QALY ≤A$30,000 was 64.0%
  - A financial impact greater than zero and a cost per QALY >A$30,000 was 24.4%
  - A financial impact greater than zero, a cost per QALY≤A$30,000 and with placebo used as a comparator (29.6%).
- The area under the ROC curve generated by this recursive partitioning decision tree was equal to 0.76.

Figure 2. Recursive Partitioning Model Results



Limitations

- The major limitation is that, in many cases, the financial impact on the health care system was provided in the public summary document only as an inequality, such as "less than A$10 million." Thus, it was not possible to enter financial impact into the model as a continuous variable. Instead, we created three financial impact categories. This limitation meant that we were not able to develop a point estimate of a financial impact threshold using the recursive partitioning decision analysis technique.

CONCLUSIONS

- Our findings that financial impact on the Australian health care system appears to have a significant impact on reimbursement decisions is consistent with the conclusions of the recent published analyses even when financial impact is not specifically listed as a criterion [1-3].
- The implications of the findings in this paper are that, in Australia, the financial impact to the health care system is an important determinant of whether a new drug is recommended for reimbursement, even when controlling for the impact on reimbursement of cost-effectiveness estimates and other economic and clinical variables.
- Whether this finding is true in other countries is an empirical question that can be resolved only by performing similar analyses in these jurisdictions.

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