Predictors for Recommendations of Cancer Drugs in Decision Making: A Systematic Literature Review

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Background and objective

- The cancer burden has risen to 18.1 million new cases and 9.6 million deaths in 2018 globally. [1]
- The high morbidity and mortality of cancer diseases have spurred the rapid process of cancer research and new drug development, especially in recent years.
- The European Medicines Agency approved about 10 new cancer medicines per year from 2012 to 2018 compared to about four new medicines per year from 2001 to 2011. [2]
- In the United States, cancer remained the predominant area of innovation, accounting for an average of 25% of all approvals by the U.S. Food and Drug Administration. [3]
- The rising disease burden and high price of new oncology medicines, combined with uncertainties in clinical and economic evidence, have brought substantial challenges to payers and health technology assessment (HTA) in making decisions on coverage.
- Several countries have taken specific measures to deal with these challenges and provide patients maximum affordable access to oncology care. [4-6]

Example of HTA solutions to increase access to cancer drugs	
Canada	pan-Canadian Oncology Drug Review was established in 2011 to be responsible for the assessment of cancer drugs
United Kingdom	Cancer Drugs Fund was set up in 2011 to improve patient access to new cancer drug
Korea	Two new schemes including a risk-sharing agreement and waiver of pharmacoeconomic data submission were developed to expand the coverage benefit to four severe diseases including cancer

- This review was intended to comprehensively summarize the significant predictors and their relative importance in HTA decisions for cancer drugs.

Method

- A systematic literature review was performed by searching Ovid Medline and Embase from their inception to 2 July 2020.
- The search strategy included but was not limited to the following keywords: “HTA” or “subsidy” or “coverage” or “reimbursement” or “listing” combined with “criteria” or “factor” or “driver” or “preference” and “recommendation” or “appraisal” or “decision-maker” and “cancer”.
- Studies were selected based on the following inclusion and exclusion criteria:

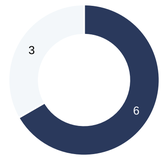
Inclusion and exclusion criteria	
Inclusion criteria	**Exclusion criteria**
1) Studies that investigated HTA reports of cancer drugs 2) Studies that conducted univariable or multivariate analyses 3) Studies that were published in English	1) Studies that investigated the stated preference of decision-makers using quantitative methods

- The data of included studies were extracted by two researchers independently, including the study characteristics, analysis and modelling methods, and modelling results.
- The factors were divided into five categories: 1) disease-related factors, 2) technology-related factors, 3) clinical outcome-related factors, 4) economic outcome-related factors, and 5) other factors.
- The factors were considered as the significant factors for HTA recommendations if their p-values were below the significance level of 0.05 from the univariable or multivariable analysis.
- The unadjusted odds ratios (ORs) for categorical factors were calculated based on the descriptive data (if available) from the included studies.
- The analysis was performed with R software version 4.0.3.

Result

- A total of 9 studies, including 1146 decisions from 6 agencies in 6 different countries (Australia, Belgium, Korea, Canada, France and England), were eligible to be included for review.
- Among the included studies, the number of HTA decisions ranged from 17 to 393 (median=75).
- Most studies (n=6) had no specific restrictions on the type of cancers.

Distribution of decision targets



- From the univariable analysis, improvements in clinical outcomes and cost-effectiveness were found to be the significant predictors for the committees in Belgium, Korea and Canada.

Significant factors identified from univariable analysis *	
Disease related-factor	No factors were identified
Technology related-factor	• Curative technology (+) in Australia • Resubmission status (+) in Australia • Orphan drugs (-) in Belgium
Clinical outcome related-factor	• Improvement in clinical outcomes (+) in Belgium, Korea, Canada • Accepted clinical outcomes (+) in Australia • Active comparators (+) in Australia • Accepted comparators (+) in Australia • Low uncertainty in clinical evidence (+) in Australia • High quality of clinical evidence (+) in Canada • Low number of adverse events (+) in Canada
Economic outcome related-factor	• Cost effectiveness (+) in Australia, Belgium, Korea, Canada • Low budget impact (+) in Australia, Belgium • Low uncertainty in economic evidence (+) in Australia • Application of risk-sharing agreement (+) in Korea

* - represents negative factor; + represents positive factor

- From the multivariable analysis, cost-effectiveness was found to be the strongest positive predictor for the recommendations for the agencies in England, Korea and Canada.

Significant factors identified from univariable analysis *	
Disease related-factor	• Absence of alternatives (-) in Belgium
Technology related-factor	No factors were identified
Clinical outcome related-factor	• Improvement in clinical outcomes (+) in Belgium • Active comparators (+) in Australia • Low uncertainty in clinical evidence (+) in Australia • High quantity of clinical evidence (-) in Belgium
Economic outcome related-factor	• Cost effectiveness (+) in England, Korea, Canada • Application of risk-sharing agreement (+) in Korea

* - represents negative factor; + represents positive factor

- From the univariable analysis, no factors related to characteristics of disease were identified as the significant factors for recommendations among the studied agencies.
- From the multivariable analysis, no factors related to characteristics of technology were identified as the significant factors for recommendations among the studied agencies.

CONCLUSIONS

Despite the different drug reimbursement systems and the socioeconomic situations, cost-effectiveness and/or improvement in clinical outcomes seem to be the most important predictors of recommendations of cancer drugs in the majority of committees. Few factors related to characteristics of disease and technology were found to be significantly associated with decisions among the studied agencies.

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