BUDGET IMPACT ANALYSIS OF MEDICINES: UPDATED SYSTEMATIC REVIEW AND IMPLICATIONS

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KEYWORDS

Budget Impact Analyses; Drugs; Medicines; Systematic Review

ABSTRACT

Introduction: This evaluation determines whether published studies to date meet the key characteristics identified for budget impact analyses (BIA) for medicines, accomplished through a systematic review and assessment against identified key characteristics. Methods: Studies from 2001 to 2015 on "budget impact analysis" with "drug" interventions were assessed, selected based on their titles/abstracts and full texts, with their characteristics checked according to key criteria. Results: Out of 1984 studies, 92 were identified. Of these, 95% were published in Europe and the USA. 2012 saw the largest number of publications (16%) with a decline thereafter. 48% met up to 6 or 7 out of the 9 key characteristics. Only 22% stated no conflict of interest. Conclusion: The results indicate low adherence to the key characteristics that should be considered for BIAs and strong conflict of interest. This is an issue since BIAs can be of fundamental importance in managing the entry of new medicines including reimbursement decisions.

KEYWORDS

Budget Impact Analyses; Drugs; Medicines; Systematic Review; Guidelines
**INTRODUCTION**

Budget Impact Analysis (BIA) is a last step in Health Technology Assessment (HTA), which allows health authorities to know whether a particular new technology is safe, effective, and efficient as well as affordable to the health care system.

Increasingly, BIAs are seen as an important tool in decision-making in the face of the increasing pressure on resources through ageing populations and the continual launch of new premium priced technologies [1,2]. These pressures have increased the requirement among health care professionals and systems to consider all aspects of new medicines as part of their decision-making, including their potential budget impact. This reflects the growing use of horizon scanning and forecasting activities among health authorities, especially for new medicines [1-3]. Consequently in recent years, health authorities and the main HTA institutions have expanded their guidelines to encompass BIAs [4-8]. However, BIA is not a technique that is currently well established in the literature. Few publications appear to meet the established definitions and to date published studies, including reviews, show that a number of published BIAs do not reach the desired quality level, and there are concerns with their findings [4,5,8].

The current study aims to determine whether the publications not carried out by Health Technology Agencies meet the key characteristic for undertaking BIAs for medicines. Subsequently, provide guidance to all key stakeholders based on the findings from the health authority and/or budget holder perspective. This will be achieved through a systematic review of BIA studies, a verification of the characteristics adopted in each study and an analysis of the results according to identified key characteristics. It is not aim of this study to analyze the quality of published BIA studies.

**METHODS**

This systematic review of studies was carried out in accordance with the Cochrane Collaboration Handbook [9] guidelines and has been reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [10]. We did not include BIAs from HTA Agencies as our aim was not to assess the quality of BIAs but whether published BIAs met identified key characteristics given current concerns.

**Eligibility criteria**

Only primary studies with "budget impact analysis" design and a "drug" as a means of intervention were included in this review. Analyses of new medicines were accepted, as well as comparisons of alternative and well-establish therapeutic perspectives. Date and language of the publication were not exclusion criteria.

**Study search**

A systematic bibliographic search of electronic research databases and grey literature was performed in November 2015. This included a search of PubMed, Central (Cochrane), Centre for Reviews and Dissemination (University of York) and Lilacs regional databases using the parameters described in the eligibility criteria. The searches were conducted using strategies developed specifically for each database and the respective MeSH descriptors. An illustration of the search strategy for PubMed, Central (Cochrane) and Lilacs are included in the Appendix (Appendix 1A, 1B, 1C). The years ranged from 2001 until November 2015.
Study selection

Following the search strategies, publications were organized into a program, which excluded duplicates, with each study randomly assigned to at least two independent blind reviewers among the co-authors. The reviewers selected the studies in two reading phases: titles and abstracts (Phase 01) and full text (Phase 02). A third reviewer helped resolve any disagreements. Theoretical studies, analyses performed by Health Technology Evaluation Agencies, dosage comparison studies and comparison of drugs with procedures or devices were excluded.

Data collection and analysis

We used a dedicated electronic form to collect the main characteristics of the publications included in the study. The data were collected in duplicate with each study randomly assigned to at least two independent blind reviewers among the co-authors.

Selection of parameters

According to leading publications, the main characteristics to be considered in any BIA are the adopted perspective, technology comparison scenarios, product and service costs, time horizons, populations of interest, the method of calculation, the evaluation of uncertainties (sensitivity analysis) and model validation. Additionally, the data must be from reliable sources, reflect reality, be reproducible and easy to interpret by health care managers [4-8,11]. In order to evaluate the selected studies, this study considered the following characteristics identified from the literature that BIA studies should meet and contain: features of the health care system in question; the perspective; the population; a scenario analysis; direct costs, time horizons; framework; an uncertainty evaluation, and validation. Two independent blind reviewers used the dedicated electronic form to collect the key characteristics in each of the 92 selected studies.

RESULTS

Out of a total of 1984 publications, 92 were finally included in this systematic review. The breakdown of papers is described in Figure 1.
The publications retrieved were between 2001 and 2015, with more than 70% published in 2010 or later (Figure 2).

**Figure 2 - Evolution of the quantity of BIA studies per year (n=92)**

The origin of the studies by continent and country where consolidated by total (2001 to November 2015) as well as two time periods; i.e. from 2001 to 2009 and from 2010 to November 2015 (Table 1), with most studies published from 2010 onwards.
Table 1 - Origin of the studies by Continent and Country per periods (n=92)

<table>
<thead>
<tr>
<th>Continent</th>
<th>Country (n)</th>
<th>All years*</th>
<th>2001 to 2009</th>
<th>2010 to 2015*</th>
</tr>
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<tr>
<td></td>
<td></td>
<td>Σ n %</td>
<td>Σ n %</td>
<td>Σ n %</td>
</tr>
<tr>
<td>Europe</td>
<td>Spain (13) United Kingdom (11) Italy (8) Belgium (4) Greece (4) France (3) Netherlands (3) Denmark (2) Finland (2) Hungary (2) Germany (1) Ireland (1) Norway (1) Switzerland (1)</td>
<td>56 60,9</td>
<td>12 50,0</td>
<td>44 64,7</td>
</tr>
<tr>
<td>Americas</td>
<td>USA (22) Brazil (4) Canada (3) Chile (1) Colombia (1)</td>
<td>31 33,7</td>
<td>12 50,0</td>
<td>19 27,9</td>
</tr>
<tr>
<td>Asia</td>
<td>Thailand (2) Iran (1)</td>
<td>3 3,3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Africa</td>
<td>South Africa (1)</td>
<td>1 1,1</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Oceania</td>
<td>Australia (1)</td>
<td>1 1,1</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Total</td>
<td></td>
<td>92 100,0</td>
<td>24 100,0</td>
<td>68 100,0</td>
</tr>
</tbody>
</table>

* Until November 2015

The greatest number of BIA studies (four) were performed for infliximab, followed by rosuvastatin, trastuzumab and natalizumab, with three studies each. The main disease area focus of the sourced studies for the systematic review was: (a) antineoplastic and immunomodulator agents - 34%; (b) nervous system diseases - 18%; (c) systemic anti-infection medicines - 16% and (d) cardiovascular system - 9%. Medicines for orphan diseases and diseases of the alimentary tract and metabolism, blood and hematopoietic organs, the respiratory system, perception organs, diseases that require systemic hormonal drugs excluding sexual hormones and insulins, and musculoskeletal system/alimentary tract and metabolic diseases accounted for the remaining studies (23%).

Characteristics of the published studies according to the main characteristic for the formulation of BIAs

**Features of the health care system:** 22 studies (24%) [12,13,15,16,18,19,26,33,35,48,51,54,77,81,83,84,86,88,92,93,100,102] described some type of feature of the health care system in which the analysis was performed. The most reported characteristics were universal health coverage (59%).

**Perspective:** 82 studies (89%) [12-17,19-24,26-68,70-72,77,78,80-85,87-93,95-103] that performed BIA were focused on the budget holder. In all, the perspective of the 92 studies was broken down as follows: the public health system (59%), health insurance companies (24%), paying parties (10%), hospitals (5%), and society (2%).

**Population:** All the studies reported the evaluated population, which was equally divided between the total and the sample population. Estimates of the population size of interest were taken from epidemiological studies (73%) and others (27%).

**Scenario analysis:** At least one type of scenario comparison was reported by 83 of the studies (90%) [12-17,19-63,65-71,73,75-85,89-98,100,102,103]. Bearing in mind that the same study may have made more than one assessment: comparisons involved costs comprised 33%, epidemiologic data 17%, the use of different medicines 16%, and market share 15%. These analyses accounted for 81% of all comparisons. The others included comparisons of standards of the use of technologies (12%) and comparisons of treatments (7%).
**Direct costs:** 62 studies (67%) [12-20,22,24,25,29-31,35,36,38,39,41-45,47,48,50,52-61,64-67,69, 71,72,75,76,79,81-84,89,91-93,95-97,99,100,102,103] reported the analysis of at least one of the costs related to the therapeutic area (i.e. cost of any diagnostics, current interventions, treatment of any adverse events, hospitalization, devices, supplies used, etc.) in addition to the costs of the medicines. The remainder considered only the medicine costs as a direct cost.

**Time horizon:** 67 studies (73%) [12-14,18-20,22-24,26,27,29,30,33,35-50,52-55,57-59,61,63,64,66-72,74-77,80-83,85,89-91,93-96,99,100,102,103] reported a time horizon from 1 to 5 years. 21 studies (23%) reported a time horizon of 3 years. The time horizon cycle used most often in the calculations was one year (68%).

**Method of calculation (framework):** 22 studies (24%) [12,14-16,24,26,27,29,30,33,38-40,42,46,48,50,53,54,88,91,102] reported using some form of good practice guideline with 77% reported using ISPOR guidelines. Calculation methods based on a spreadsheet and a simple decision-making tree (static) were used in 59% of the studies. Simple calculation methods such as future expenditure projection without the use of a transition state model that took disease gravity into account were found in 28% of the studies. More complex calculation methods with the use of a spreadsheet and the Markov-like decision-making tree (dynamic) were employed in 13% of the studies. The BIA calculation method was included in 50% of the studies.

**Uncertainty evaluation:** At least one type of sensitivity analysis was used to evaluate uncertainty in 67 studies (73%) [12-20,24,26-31,33-50,52-57,59,62,63,68,71,73,74,77-83,85,86,89,91-97,100,102,103]. The type of analysis most used was univariate (one way) analysis, employed in 76 of the studies, followed by probabilistic analysis (Monte Carlo) in 9% of the studies and multivariate (Multiway) analysis in 6% of the studies. Considering that the same study may have performed sensitivity analysis for more than one dimension, 34% of the analyses included costs, 22% included epidemiologic data, 15% included market share, 14% included clinic procedures and 8% included the recipient population.

**Validation:** 5 studies (5%) [37,39,40,56,92] reported some type of BIA validation. Face validity, the extent to which the model corresponded to the reality as evaluated by a professional with experience in the problem, was adopted in four studies. Verification of mathematical calculations was reported in one study.

In order to better understand the profile and course of the studies between 2001 and 2015, the number of key characteristics for the production of BIA studies was recorded for each study. This was then recorded against the sum of published BIA studies for that year (Figure 3).
Subsequently, a trend analysis was conducted regarding the key characteristics for producing BAs. The average for each year was calculated by taking the sum of the number of the key characteristics for producing BAs by all studies published in a given year divided by the sum of the studies published in that year (Figure 4).
Two other characteristics were checked: 55% of the analyses reported conflict of interests, 74% reported pharmaceutical company funding and 5% contained no details of conflicts of interest or funding sources. Table 2 contains details of the key characteristics of the studies with and without pharmaceutical company funding.

**Table 2 - Quantity of key characteristics meeting in studies with and without pharmaceutical company funding and conflict of interest (n=51 and 15)**

<table>
<thead>
<tr>
<th>Quantity of key characteristics found in studies</th>
<th>Studies with pharmaceutical company funding AND conflict of interest</th>
<th>Studies without pharmaceutical company funding OR conflict of interest</th>
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<td>$\Sigma n$</td>
<td>$%$</td>
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<td>2</td>
<td>2</td>
<td>3,9</td>
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<td>3</td>
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<td>4</td>
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<td>5</td>
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<td>6</td>
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<td>7</td>
<td>10</td>
<td>19,6</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>5,9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>51</strong></td>
<td><strong>100,0</strong></td>
</tr>
</tbody>
</table>

**DISCUSSION**

The current study sought to better understand the key characteristics of the 92 identified BIAs studies to provide future guidance. 2010 saw the number of studies (12 in all) double in relation to the previous year (Figure 2). The number of published studies remained at approximately this level in the following 5 years. The evolution of number of studies meeting the 9 identified key characteristics showed that 69% met at least 5 of the key characteristics and 53% met 6. In 2010, 6 studies met 7 of the key characteristic. In 2012, the greatest number of analyzed studies (16%), 3 met 8 of the key characteristic, the best result in the study period. In 2014 and 2015, only 1 study per year met 8 of the key characteristic (Figure 3). There was an ascending line in the number of published studies meeting the key characteristics ($y = 0.1142x + 4.3333$) (Figure 4), suggesting that the number of BIAs meeting the key characteristics should
increase in the future. However, the analysis performed from 2010 presented a downward line \((y = -0.083x + 5.8197)\). This is a concern.

Other identified concerns included the fact that BIAs are typically targeted at health authority decision makers; however, only 24% of the studies reported anything about the health systems in question. In addition, only 24% of the analyzed studies reported following a good practice guideline or principle. One third of the sourced studies used only drug costs to make up direct medical costs and only 5% of the studies recorded eight of the nine characteristic for the production of BIAs, and none of the sourced studies recorded all nine. Overall, the lack of sensitivity analysis and validation were some of the main reasons for non-compliance with the main characteristic for BIAs. This low presence of the key characteristic for BIAs has been seen in previous analyses.

Previous systematic reviews of BIAs have made important contributions to the development of BIAs including highlighting concerns. Mauskopf et al [4] (2005) analyzed 10 multi-country studies of disease records, the comparison parameters used, outcomes, study designs and the results obtained. Orlewska et al [5] (2009) analyzed the records of the methods used in 34 multi-country studies and, more recently, Van de Vooren et al [8] (2014) analyzed 17 European BIAs studies concerning the occurrence of other economic evaluations associated with these analyses. Additionally, Garattini et al [6] (2011) analyzed and recorded the characteristic of BIA in 5 multi-country studies in an attempt to clarify the role of this type of evaluation in relation to other modalities of health economic evaluation.

In 2005, Mauskopf et al [4] reported no clear methodological guidelines and that few studies met the BIA definition. However, the belief in the evolution of the theme was clear. In 2009, Orlewska and colleagues [5] confirmed that BIAs studies typically lacked the desired quality. However, positive changes were expected following the establishment of the investigation principles and good practice guidelines as a tool to codify and establish relevant questions as well as enhance the standardization and transparency of future BIAs studies. Frustrating the expectations, a recent review by Van de Vooren and colleagues [8] of European studies published in 2014 stated that BIA was still not a well-established technique and that many studies did not reach an acceptable quality. According to these authors, many of the published studies lack reliable data sources, i.e. estimates from other countries, assumptions from expert panels as well as reliable epidemiological and local cost data, and very often the results were given as costs per patient. These characteristics made it difficult to provide results that are acceptable for the local situation and key decision makers. In this way, what might be considered a differential in relation to other types of economic evaluation ends up being a weakness of many current BIAs studies. These issues can be directly linked to the funding of studies and conflict of interest. Indeed, the funding of BIAs studies by pharmaceutical companies is a recurrent theme. This occurred in 58% of the studies analyzed by Orlewska and colleagues [5] (2009) and 88% of those by van de Vooren and colleagues [8] (2014). In the current study, only 21% of the studies reported not being supported by pharmaceutical companies. A similar low percentage reported a lack of conflict of interest. Of the 92 studies, 51 (55.4%) reported pharmaceutical company funding and conflict of interest with only 12 studies (13.0%) reporting no pharmaceutical company funding or conflict of interest (Table 2). 33.3% of the studies without pharmaceutical company funding or conflict of interest met 7-8 key characteristics for BIA against only 25.5% studies with funding from pharmaceutical companies and conflict of interest.
Studies that do not show acceptable quality, which are funded by companies and present a conflict of interest, may result in an appreciable credibility issue among health authority decision makers. Considering that most BIAs studies have focused on chronic diseases that require high-aggregated value treatments, with appreciable budget investment, this lack of credibility is a significant concern from the health system managers' viewpoint. This would suggest resources currently being spent by companies on the production of BIAs to support reimbursement, funding and utilization decisions for their new technology including new medicines are being wasted. In view of this, we believe that key stakeholders involved in the development of BIAs do not yet fully realize the power of their BIAs for health system management. This includes the use of BIAs to help determine the feasibility of the adoption of a new technology by a health system including preparing potential budgets [104,105,106]. BIA results enable decision-makers to know whether technologies are affordable to the users of a health care system and whether technologies should be adopted or not in all or specified sub-populations in question. Moreover, BIAs may help determine the way health authorities and other key stakeholder groups agree how new medicines or other new technologies should be introduced into health care systems [2,3]. Even in the face of budgetary restraints, healthcare managers have the power to establish strategies that enable the adoption of new health care technologies, either through resource reallocation or disinvestment or even specific strategies such as the gradual establishment of graded clinical protocols geared at different degrees of patients' needs [2,3,107,108]. However for this, health care managers must have guaranteed high quality and a low risk of bias of BIAs. This means encouraging greater independence and quality in their production. We look forward to these developments to enhance the future utility of this important decision making tool.

**CONCLUSION**

Budget Impact Analysis is an important decision-making tool. It enables accurate (re)allocation of financial resources in a given health system, either through the evaluation of new technologies or the re-evaluation of existing technologies. Greater adherence to the key characteristic of good practices for BAIs has been seen in the recent years. However, most BIAs studies currently conducted are still far from an agreed standard of excellence. The results indicate low adherence to the key characteristics for the production of BIAs. Additionally, many studies report conflict of interest and funding from the companies. BIAs have often become part of company marketing strategies and away from the intended goal of providing short and medium term economic consequences of new technologies from a health system perspective. This is a concern as BIAs are of fundamental importance in budget allocation as well as in decisions regarding pricing and utilization of new technologies. Future studies must be strongly committed to high methodological quality and low bias to enhance their use among health authority decision makers.

**KEY POINTS**

*What is already known about the topic?*
- Budget Impact Analyses (BIA) are increasingly seen by health authority personnel as an important decision-making tool enabling improved accuracy in the (re)allocation of financial resources. However, there are concerns with the quality of current BIAs.

*What does the paper add to existing knowledge?*
- A systematic review of all studies up to November 2015 was undertaken to assess whether the publications meet the key characteristics for the production of BIAs for medicines. This
resulted in 92 identified publications meeting the strict criteria for inclusion, the majority (95%) of which were published in Europe or the USA;

- Improvement in adherence to the identified key characteristics for BIA studies has been seen in the recent years. However, adherence to the key characteristic of good practices still remains low. Furthermore, many studies report conflict of interest and industry funding.

**What insights does the paper provide for informing health care-related decision-making?**

- This is a concern and suggests BIAs have increasingly become part of marketing strategies and away from their intended goal of providing, short and medium term economic consequences of technologies to health authority decision makers to help with future budget allocation/investment decisions

- Future researchers as well as commercial organisations must be committed to high methodological quality and low bias levels when conducting future BIAs to enhance their use among health authority decision makers, which should be an intended goal.

**Expert Commentary**

BIAs are increasingly required by health authorities across countries to help with the planning of budgets for new valued premium priced medicines. However, this systematic review demonstrated that there are still concerns with the quality of studies. This was despite publications suggesting that key items and features should be addressed including the health care system in question, the perspective, the anticipated population, direct costs, the time horizons and uncertainty evaluation. This has implications for their usefulness among health authority personnel. The most effective and promising strategies for BIAs in the future is the production of studies strongly committed to a high methodological quality and a low bias to enhance their use among health authority decision makers.

**Five-year Review**

It is envisaged that the quality of BIA studies will increase with increasing consciousness among those that produce them, including pharmaceutical companies, that BIAs are of fundamental importance in budget allocation as well as in decisions regarding the pricing and utilization of new technologies including new premium priced medicines. This will be possible over the next few years with agreement and consolidation of BIA methodologies.

**Acknowledgements and conflicts of interest**

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The authors have no other conflicts of interest to declare.

**REFERENCES**

Papers of special note have been highlighted as:

* of interest

** of special interest


*The study presents a clear structure respecting the key characteristics of BIAs.*


*The study presents a clear structure regarding key characteristics of BIAs.*


*The study presents a clear structure regarding key characteristics of BIAs.*


40 Mori AT, Norheim OF, Robberstad B. Budget Impact Analysis of Using Dihydroartemisinin-Piperaquine to Treat Uncomplicated Malaria in Children in Tanzania. Pharmacoeconomics. 2015. Epub ahead of print online.

**Good study demonstrating change in total budget of drugs and diagnostics versus variation in the cost of the drug analysed.**


*The study presents a clear structure respecting the key characteristics of BIAs.*


*The study presents a clear structure regarding key characteristics of BiAs.*


*The study presents a clear structure respecting the key characteristics of BIAs.*


## APPENDIX

### Appendix 1A - Search strategy: PubMed

<table>
<thead>
<tr>
<th>Connector</th>
<th>Field</th>
<th>Parameter</th>
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<td>AND All fields ((((&quot;pharmaceutical preparations&quot; [Mesh]) OR Pharmaceutical Preparations [Text Word]) OR Drugs [Text Word]) OR Medicines [Text Word])</td>
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### Appendix 1B - Search strategy: LILACS

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<td>AND All fields (((&quot;Pharmaceutical Preparations&quot; OR &quot;Preparaciones Farmacéuticas&quot; OR &quot;Preparações Farmacêuticas&quot;) OR (tw: &quot;drugs&quot; OR &quot;medicines&quot; OR &quot;medicamentos&quot;) OR (VS2.002.001))</td>
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### Appendix 1C - Search strategy: Central (Cochrane)

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