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A Systematic Review of Health Economic Evaluation Studies Using the Patient's Perspective

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ABSTRACT

Background: Patient-centered care has become increasingly important and relevant for informed health care decision making. **Objective:** Our study aimed to perform a systematic review of health economic evaluation studies from the patient's perspective. **Methods:** PubMed, EMBASE, and Cochrane Central databases were searched through May 2014 for cost-effectiveness, cost-utility, and cost-benefit studies using the patient's perspective in their analysis. The reporting quality of the studies was evaluated on the basis of Consolidated Health Economic Evaluation Reporting Standards. **Results:** We identified 30 health economic evaluations using the patient's perspective, of which 7 were conducted in the United States, 9 in Europe, and 14 in Asian or other countries. Seventeen of 23 health conditions evaluated were chronic in nature. Among 12 studies that justified the use of the patient's perspective, patient's financial burden associated with medical treatment was the most commonly cited rationale. A total of 29, 17, and 15 studies examined direct medical, direct nonmedical, and indirect costs,

respectively. Seventeen studies also included societal, governmental or payer's, and/or provider's perspective(s) in their analyses. Based on Consolidated Health Economic Evaluation Reporting Standards, more than 20% of the reporting items in these studies were either partially satisfied or not satisfied. **Conclusions:** There is a paucity of health economic evaluations conducted from the patient's perspective in the literature. For those studies using the patient's perspective, the true patient costs were not fully explored and study reporting quality was not optimal. With the increasing focus on patient-centered outcomes in health policy research, more frequent use of the patient's perspective in economic studies should be advocated.

Keywords: cost-effectiveness analysis, cost-benefit analysis, cost-utility analysis, patient's perspective, systematic review.

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Introduction

With escalating health care costs and more available treatment options, health policy has been driven by the value proposition using the cost-effectiveness framework to determine health interventions that provide the best health outcomes for the resources invested. A health economic evaluation can be conducted from one or more perspectives, such as societal perspective, public-health perspective, health care system perspective, health care payer's perspective, institutional perspective, and/or patient's perspective. A perspective used in a study is based on its research question and restricted to types of costs and outcomes included in the analysis, which are specific to the study stakeholders' interests. In other words, different stakeholders are interested in health care costs and outcomes that are relevant to their interests; thus, study results from different perspectives are different from one another. Commonly, health economic evaluation studies are performed from the perspectives of health care payers or organizations to assess the value of alternative

interventions because they are the direct payers for health care services [1,2]. A typical example is a cost-effectiveness analysis comparing a novel drug to its current standard-of-care treatment, and the study result can be used to make drug-formulary decision for health care plans and/or organizations. In such cases, costs incurred outside of the health plans or organizations, such as patient's out-of-pocket costs, are not accounted for, leaving other stakeholders' interest out of the decision-making process [3]. In fact, a novel drug or an alternative intervention that may appear to be clinically and economically justified from one perspective may not be necessarily the same if analyzed from another perspective.

With the recent movement toward *patient-centered care*, which is broadly defined as "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions" [4], the role of patients in treatment decisions has played an important part in health policy as well as in treatment recommendations from health care providers. For health outcome

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studies using the patient's perspective, outcomes are commonly examined in terms of health-related quality of life, patient preference, and/or the portion of health care costs that patients are responsible for. Specifically, costs from the patient's perspective are typically the expenses that patients pay for medical products or health care services not covered by their health insurance. These costs may include direct medical costs (i.e., costs incurred for medical products and services used to prevent, detect, and treat a disease as well as costs from co-payment, coinsurance, and deductibles), direct nonmedical costs (i.e., costs for nonmedical services that are results of illness or disease such as transportation or travel costs), and indirect costs (i.e., costs that result from potential productivity loss due to morbidity and/or mortality such as work income loss or premature death) [5]. In some countries, patient's out-of-pocket health expenditure can be a significant amount and thus should not be overlooked. According to the World Bank, the out-of-pocket health expenditure in terms of the percentage of private expenditure on health in the United States was 22.3% in 2013, whereas it was significantly higher in Canada (50.1%), the United Kingdom (56.4%), and Australia (57.1%) [6]. Patient's out-of-pocket costs or "patient" costs can be a significant financial burden, particularly in health conditions that are costly to treat and involve high patient costs such as cancer or dental services, in chronic debilitating diseases such as post-traumatic stress syndrome, chronic kidney diseases, chronic obstructive pulmonary disease, and stroke, or in health conditions that need special medical equipment, products, or professional services [7–9].

Considering the growing importance of using the patient's perspective in health economic evaluation, it has been advocated that cost outcomes, just as important as clinical and humanistic outcomes, should also be measured around patients who would actively participate in making their treatment decisions [10,11]. Recent studies found that high patient cost sharing (in forms of co-payment or coinsurance) was associated with treatment disruption such as poor treatment initiation, continuation, and adherence, which, in turn, could affect patient treatment outcomes [12,13]. As such, more high-quality health economic evaluation studies should be available to determine optimal treatment choices for patients. In the current study, we performed a systematic literature review of all cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA) studies of health interventions that used the patient's perspective in their analyses. The essential characteristics of these studies were extracted and compared while the quality of each study was evaluated to identify implications for future research needs.

Methods

A systematic literature search of PUBMED, EMBASE, and Cochrane Central was conducted from the earliest possible date through May 2014 with English language restriction. We combined the search terms "economic evaluation" or "cost effective" or "cost effectiveness analysis" or "cost utility" or "cost utility analysis" or "cost benefit analysis" or "benefit cost analysis" with "patient perspective" or "patient's perspective" to form different combinations of these key words for each individual database. For example, in PUBMED, the search strategy used was ("benefit cost analysis"[All Fields] OR "benefit-cost analysis"[All Fields] OR "cost benefit analysis"[All Fields] OR "cost-benefit analysis" [All Fields]) AND ("patient perspective"[All Fields] OR "patient's perspective"[All Fields]) AND ("0001/01/01"[PDAT]: "2014/05/08"[PDAT]) AND English[lang]. Three investigators (B.W.T., Y.H.B., and Q.A.L.) independently reviewed potentially relevant articles and abstracted the data. Discrepancies were resolved through discussion. The review

process was compliant to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [14].

Articles were then screened in full text if they met the following inclusion criteria: 1) a CEA, CUA, or CBA study and (2) the analysis was conducted from the patient's perspective. We excluded studies that 1) were not related to medical interventions, 2) only examined either cost or efficacy/effectiveness of interventions, or 3) were not original research studies (e.g., reviews, commentaries, and editorials). In each included study, details of the study were extracted and delineated. Specifically, data extracted included items evaluated by Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guideline from the International Society of Pharmacoeconomics and Outcomes Research [15], and common items that the three investigators deemed important to be reviewed. The same investigators performed data extraction and analysis. Study results of analyses conducted from additional perspectives (if any) besides the patient's perspective were also documented and reported for comparison in (see Appendix Table 1 and 2 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2016.05.010>).

Study quality was assessed using the CHEERS guideline by the three investigators independently, with disagreements resolved by discussion. The CHEERS guideline, in the form of a checklist, consists of 24 main items within six main sections that were designed to evaluate an economic study: 1) title and abstract, 2) introduction, 3) methods, 4) results, 5) discussion, and 6) other (i.e., source of funding, conflict of interest) (Table). Each item was rated by the extent of reporting in the following categories: "fully satisfied," "partially satisfied," "not satisfied," or "not applicable," as classified by study investigators for the current review. For each study reviewed, the "not applicable" rating was acceptable for four items in the CHEERS guideline: "measurement of effectiveness," "measurement and valuation of preference-based outcomes," "characterizing uncertainty," and "characterizing heterogeneity." Study quality was scored by the total number of items marked for each rating category (except the "not applicable" category). The quality assessment of each study did not determine inclusion or exclusion of the study because studies meeting the inclusion criteria were included in our study regardless of study quality.

Results

We identified 630 articles from initial literature search of the databases. Upon reviewing abstracts, we retrieved 54 full-text articles after removing studies that were duplicate or irrelevant. A total of 30 studies met the inclusion criteria and were included in the final analysis at the end of the screening process (Fig. 1).

Of the 30 articles included in the review [16–45], 21 were CEAs [16,18–25,27–37,39], 4 were CUAs [17,26,38,40], 4 were CBAs [42–45], and 1 consisted of both CEA and CBA [41]. Among those studies, 7 were conducted in the United States [17,20,23,24,28,44,45], 9 in Europe [16,26,31–34,37,41,43], 7 in Asia [25,27,29,30,35,36,39], 3 in Africa [18,22,38], and 4 in other countries. In terms of health intervention types, 12 studies examined drug therapies and 18 investigated nondrug interventions. A total of 20 studies examined two interventions in their analyses, whereas 7 studies examined three interventions [27,30–33,39,43], 2 studies examined four interventions [23,28], and 1 study examined nine interventions [20]. Most studies selected the patient's perspective in their analysis because of the financial burden of treatment in patients. In addition, several studies reported that high patient costs would have an impact on patient adherence to treatment and utilization of the health care services [16,20,23,24,45]. Other reasons included the increasing importance of patient's concerns in medical decision making [23,37,43] and a need to have information on patient costs available as co-payments maintain upward trends [36].

Table – Study quality of the reviewed studies^{†,‡,§}.

Study characteristics	FS	PS	NS	NA
Title and abstract				
1. Title	23	7	0	0
2. Abstract	18	12	0	0
Introduction				
3. Background and objectives	30	0	0	0
Methods				
4. Target population and subgroup	26	3	1	0
5. Setting and location	30	0	0	0
6. Study perspective	25	5	0	0
7. Comparators	29	1	0	0
8. Time horizon	20	7	3	0
9. Discount rate	9	7	14	0
10. Choice of health outcomes	29	1	0	0
11a. Measurement of effectiveness	15	10	1	4
11b. Measurement of effectiveness	4	0	0	26
12. Measurement and valuation of preference-based outcomes	10	4	0	16
13a. Estimating resources and costs	26	0	0	4
13b. Estimating resources and costs	3	1	0	26
14. Currency, price date, and conversion	20	8	2	0
15. Choice of model	18	6	6	0
16. Assumptions	17	9	4	0
17. Analytical methods	18	10	2	0
Results				
18. Study parameters	20	6	4	0
19. Incremental costs and outcomes	24	6	0	0
20a. Characterizing uncertainty	21	1	4	4
20b. Characterizing uncertainty	2	2	0	26
21. Characterizing heterogeneity	19	0	5	6
Discussion				
22. Study findings, limitations, generalizability, and current knowledge	29	1	0	0
Other				
23. Source of funding	18	5	7	0
24. Conflicts of interest	20	0	10	0

FS, fully satisfied; NA, not applicable; NS, not satisfied; PS, partially satisfied.

* N = 30 for each item evaluated.

† The “NA” rating was acceptable for item numbers 11a, 11b, 12, 13a, 13b, 20a, 20b, and 21.

‡ The mean number of items that considered FS was 19.4; PS was 4.1; NS was 2.3; and NA was 4.1.

More than a half of the studies (n = 17) conducted their economic analyses using the patient's perspective and at least one more perspectives such as societal (n = 5) [21,25,31,40,41], government or payer (n = 5) [28,30,31,34,40], and health care provider, for example, health system, hospital, or clinic (n = 11) [16–19,21–24,27,29,41]. Trial analysis was the most frequently used methodology (n = 16) [20,23,26,27,29–33,36–40,42,44], followed by decision-tree model (n = 5) [16,17,25,28,34] and observational analysis (n = 5) [19,21–23,35,41,45]. For patient costs, all except 1 study accounted for direct medical costs [27], 17 studies included direct nonmedical costs [17,19–22,25–27,29–32,35,39–41,43,45], and 15 studies estimated indirect costs [19,20,23–25,27,29–32,35,39,41,42,45]. No studies accounted for intangible costs (i.e., cost of patient's subjective feelings such as pain, anxiety, and fatigue).

Fourteen studies used US dollar as the currency unit [16,17,19–25,28–30,44,45]. In five studies conducted in other countries, currency units were converted to US dollar at the time of their study [16,19,25,29,30]. Three studies did not report the year in which they obtained the cost for analysis [16,24,39]. The study time frames or horizons adopted in the 30 studies ranged widely from 5 days to 14 years, of which 15 studies were less than 1 year [16,17,19–24,30,33,34,36,39,42], 13 studies were at least 1 year [18,25,26,28,29,31,32,35,37,38,40,41,44], and 2 studies did not mention study

periods [43,45]. A total of 13 studies did not mention the use of discount rate during their economic evaluations [17–20,24,27,28,30,39,42,43]. For those studies that used discount rates, the annual rates ranged from 3% to 3.5% [21,22,25,26,31,32,37,44,45]. Seventeen of the 23 health conditions evaluated were chronic diseases in nature.

CEA results were reported as the average cost-effectiveness ratio in 5 studies [18,27,29,35,39], whereas the incremental cost-effectiveness ratio or the incremental cost-utility ratio was reported in 13 studies [17,19–22,24,26,28,32,33,36,40]. Three of the five CBA studies adopted the willingness-to-pay approach to estimate benefits [42–44]. For eight CEA and CUA studies including other perspectives in addition to the patient's perspective in their analyses, the incremental cost-effectiveness ratios or incremental cost-utility ratios calculated from the patient's perspective were much lower than those calculated from other perspectives in most studies [17,19,21,22,24,28] with the exception of two studies [25,40]. As for methods of examining robustness of study results in the analysis, except four studies [29,31,39,41], all reviewed studies performed sensitivity analyses, bootstrapping methods, and reported 95% confidence intervals around the base-case results. Fifteen studies reported the cost-effectiveness curve and/or the cost-effectiveness plane as part of

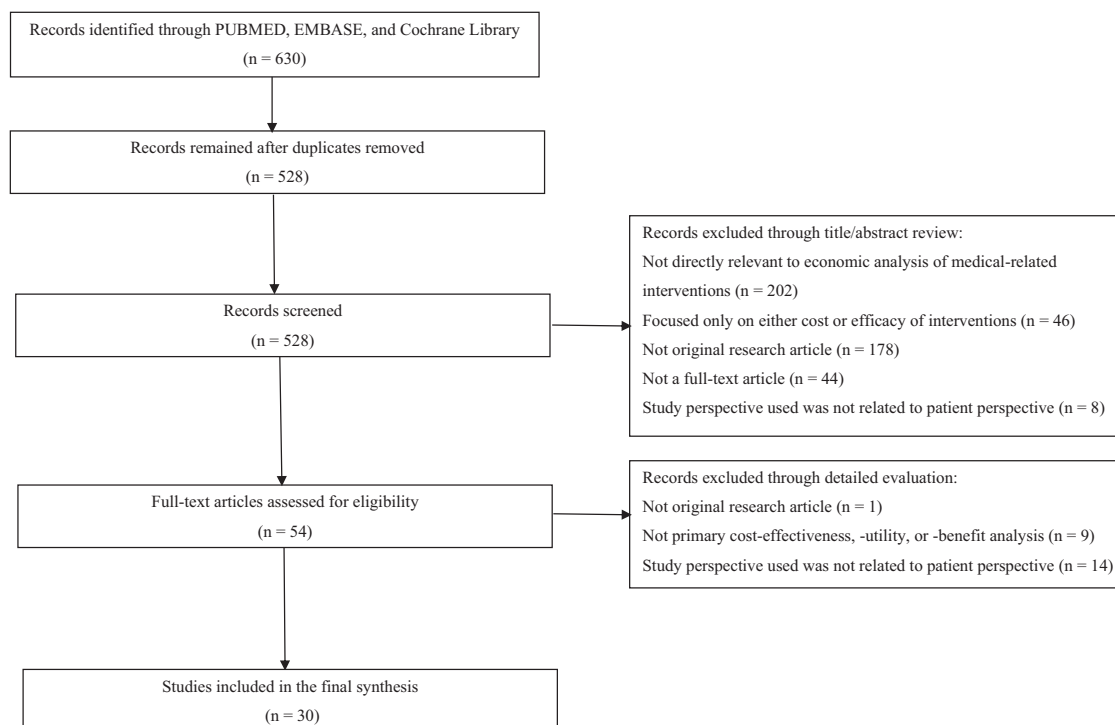


Fig. 1 – The PRISMA flow diagram of the literature search and selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

the results. Of the 30 studies, 8 did not mention or report their funding source if any [16,23,28,35,36,41,42,45], 2 indicated that the authors did not receive any external funding [32,33], and the rest reported receiving funding from different sources (e.g., international organization, national governmental agency, university, and pharmaceutical company). Characteristics and details of the reviewed studies were summarized in (see Appendix Table 1 and 2 in Supplemental Materials found at <http://dx.doi.org/10.1016/j.jval.2016.05.010>).

Quality of these 30 studies was evaluated using the CHEERS guideline. On examining only those items that were rated as “fully satisfied,” “partially satisfied,” and “not satisfied” in these 30 studies, we found that majority (75%) of the checklist items were “fully satisfied,” followed by “partially satisfied” (16%) and “not satisfied” (9%). Overall, for all 24 checklist items evaluated in the guideline, the mean number of items considered as “fully satisfied,” “partially satisfied,” “not satisfied,” and “not applicable” was 19.4, 4.1, 2.3, and 4.1, respectively. Table also presents the details of the study quality ratings.

Discussion

The current analysis is the first systematic review of published health economic evaluation studies conducted from the patient's perspective. With increasing focus on patient-centered care in the current health care reform, patient costs are just as important as clinical and humanistic outcomes, and hence should not be disregarded. Traditionally, health economic evaluation studies were performed to aid medical decisions by health institutions or payers, leaving the patient's perspective out of the equation. Although still fewer in number, health economic evaluations using the patient's perspective in the current literature provided a snapshot of how they are being conducted and also revealed areas that can be improved to assist patients to make better informed decisions. We hope that the current systematic review

may serve as a useful resource on patient-centered health economics for professional patient advocacy organizations such as the National Patient Advocate Foundation, the Patient Advocate Foundation, and the Alliance of Professional Health Advocates [46–48].

The included health economic evaluation studies in our systematic review were different vastly in terms of methods used, types of costs and outcomes measured, and patient populations of interest. For this reason, it was difficult to directly compare results among the studies, let alone the diverse types of interventions the studies examined (e.g., some were drug therapies, whereas others were preventive, diagnostic, or surgical procedures). In addition, most studies were conducted in non-US countries in the context of their specific socioeconomic environments, culture, and health care systems. Overall, direct medical costs were the most common type of cost estimated from the patient's perspective in these studies, followed by direct nonmedical and indirect costs. Nevertheless, to truly estimate patient costs, all relevant costs to the patient, that is, direct medical costs, direct nonmedical costs, and indirect costs, need to be examined fully. Moreover, health care systems vary widely among countries around the world; thus, their cost-sharing structures, that is, percent of patient out-of-pocket expenses, are also broadly different. Consequently, results from studies in other countries should always be interpreted with caution.

There were few published reviews of CEA and CUA studies that briefly discussed patient costs, though from a different angle. Stone et al. [49] examined the cost components in published CUA studies on how the sources for valuation of health care services (i.e., whether costs taken from other published studies or estimated using primary data) were used, what methods were used for estimating costs, and whether the costing methods would change over time regardless of the study perspectives. Different from Stone et al. [49], our review study examined more broadly health economic evaluation studies including CUA, CEA, and CBA studies and specifically those using

the patient's perspective in their analysis. In Tranmer et al.'s [50] review study, the authors reviewed and critiqued published studies that used different methods for measuring patient and caregiver's time and costs due to productivity losses. Although that review offered a good summary of methods measuring indirect costs, our study objectives are completely different from those of the Tranmer et al. [50] study, in which we examined studies that estimated patient costs from all relevant sources not just from the indirect costs.

Study quality is important given the fact that the number of published health economic evaluations will continue to grow; thus, the methods used and results reported should be standardized to facilitate meaningful interpretation and provide a useful means for comparing studies. We assessed quality of the reviewed studies using the CHEERS checklist, a new guideline published by the International Society for Pharmacoeconomics and Outcomes Research in 2013 for evaluating reporting of health economic evaluations, including CEA, CUA, and CBA studies. Overall, none of the reviewed studies was rated "fully satisfied" on all 24 CHEERS checklist items, with an average of 75% of the items being rated "fully satisfied." As an important caveat, it should be noted that the CHEERS checklist is used to examine only the quality of reporting of a health economic evaluation study, not the quality of how the study was conducted.

There are several limitations in the current review that need to be discussed. First, the patient's perspective appeared to be defined differently among the reviewed studies; thus, the types of costs and consequences included were not consistent. Second, methods and sources for valuation of health care services used varied widely among the studies and, as a result, it was difficult to generalize patient costs from these studies. Third, few studies in the review were CUA (i.e., results reported as cost per one additional quality-adjusted life-year gained) or CBA (i.e., results reported as net benefit or benefit-to-cost ratio), so it would not be possible to directly compare results among studies. Fourth, time horizon and funding disclosures were often not reported or were inconsistent among studies; therefore, generalization and biases were difficult to assess. Fifth, manual searching of reference lists of the reviewed articles was not conducted and gray literature was not considered in the current review, so other relevant studies might have been missed. Sixth, similar to other checklists for health economics studies in the literature, an official scoring or grading scheme for study quality was not available with the CHEERS checklist at present [51]; thus, we were able to rate individual items only to the extent of what authors reported in their studies. Last, our systematic review specifically examined health economic evaluations using the patient's perspective, and ideally patient costs should be readily extracted from studies estimating costs using the societal perspective. However, most health economic evaluation studies using the societal perspective do not explicitly or necessarily report patient's direct medical and/or nonmedical costs, but the overall direct medical costs. Looking forward, future research using the patient's perspective should focus particularly on chronic debilitating health conditions (e.g., stroke, post-traumatic stress syndrome, chronic kidney disease, and chronic obstructive pulmonary disease) as well as on disease states involving high patient costs (e.g., cancer, dental services, and end-of-life care). Furthermore, certain patient groups, such as nonexempt employees, elderly, and low-income groups, are especially sensitive to out-of-pocket expenses [52]; therefore, they would potentially benefit the most from economic studies using the patient's perspective.

Conclusions

Currently, there is a paucity of health economic evaluations conducted from the patient's perspective in the literature. For

those studies using the patient's perspective, the true patient costs were not fully explored and study reporting quality was not optimal. With the increasing focus of patient-centered outcomes in health policy research, use of the patient's perspective in economic studies should be advocated.

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Supplemental Materials

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