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# Assessing the Value of Medicines Beyond Patients' Health Benefit

## A Literature Review on the Concepts and Methods for Pharmaceutical Value Assessments from a Societal Perspective

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# Abstract

**Background**

Formal health technology assessments (HTA) mostly focus on the effectiveness of medicines in terms of producing health benefits. From a societal perspective, it may be questioned whether there are other, broader, relevant dimensions of value.

**Objective**

We provide an overview of the elements of value beyond patients' health benefit that have been included in evaluations of pharmaceuticals to date or that have been discussed in the scientific literature, and the methods that have been proposed to incorporate these into value assessments.

**Method**

We conducted a systematic literature review using MEDLINE through PubMed resource and the Social Science Citation Index (SSCI) through Web of Science portal. Relevant literature included economic evaluations of medicines considering a societal perspective (including reviews of economic evaluations and other empirical work), conceptual frameworks for incorporating broader value dimensions, and commentaries on widening the value scope of HTAs.

**Results**

A total of 180 articles were reviewed, of which 90 (50 percent) were economic evaluations, 26 (14 percent) systematic literature reviews, 25 (14 percent) theoretical studies, and 24 (13 percent) were other empirical studies mostly exploring willingness-to-pay approaches. We found acknowledgements of the limitations of the concepts currently used in value assessments in both the scientific literature as well as gray literature by institutions engaged in health care policy. Despite this, patients' health benefits remain the basis and often the only considered dimension of value in pharmaceutical value assessments. Labor productivity of patients (59 studies, or 33 percent of total reviewed) as well as spillover effects for family members and informal caregivers (42 studies, or 23 percent of total reviewed) were the elements most often discussed or included beyond patients' health benefit in the reviewed literature.

**Conclusion**

A wide range and diversity of value dimensions and beneficiaries of medicines are discussed in the literature. Our review highlights the potential benefits of including additional elements of pharmaceutical value in HTAs. However, more attention needs to be given to the methods used to accommodate a broader value definition in value assessments.



**Keywords:** Health technology assessment, value assessment, pharmaceuticals, societal impact


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# List of abbreviations

| | |
|---|---|
| ASCO | American Society of Clinical Oncology |
| BIA | Budget-impact analysis |
| CBA | Cost-benefit analysis |
| CEA | Cost-effectiveness analysis |
| CUA | Cost-utility analysis |
| CVA | Cost-value analysis |
| DALY | Disability-adjusted life year |
| EFPIA | European Federation of Pharmaceutical Industries and Associations |
| ESMO | European Society for Medical Oncology |
| EUnetHTA | European Network for Health Technology Assessment |
| GVA | Gross value added |
| HrQoL | Health-related quality of life |
| HTA | Health technology assessment |
| ICER | Institute for Clinical and Economic Review |
| MCDA | Multicriteria decision analysis |
| MEDLINE | Medical Literature Analysis and Retrieval System Online |
| n/a | Not applicable |
| NCCN | National Comprehensive Cancer Network |
| OECD | Organization for Economic Cooperation and Development |
| PTO | Person-trade off |
| QALY | Quality-adjusted life year |
| QoL | Quality of life |
| SSCI | Social Science Citation Index |
| WTP | Willingness-to-pay approach |

# 1 Introduction

In many health care systems, value assessments for new medicines take place within the framework of a formal health technology assessment (HTA). In principle, HTA is a systematic evaluation to determine the value of a health technology at different points in time, mainly aiming at informing decision making regarding regulatory approval and reimbursement of health technologies, and at promoting an equitable, efficient, and high-quality health system [1], [2]. The idea of defining drug reimbursement prices according to their perceived value to patients and society is generally referred to as value-based pricing, although notions of what aspects should be included when measuring value differ [3], [4]. When assessing the value of medicines, HTAs mostly focus on effectiveness in terms of producing health gains relating to the patient, as measured by clinical outcomes or health-status indicators.

In recent years, various health care associations, patient groups, researchers, and decision-makers have called for establishing broader value frameworks that consider a variety of value elements. Several HTA bodies are already recommending a societal perspective, i.e., including aspects beyond patients' health benefit, to the evaluation of medicines [5]. Nevertheless, in most cases, the use of broader value elements remains implicit and unsystematic [6].

The objectives of this study were two-fold: to identify and synthesize 1) what value elements beyond patients' health benefit have been used in value assessments of pharmaceuticals to date, and 2) what value elements have not yet been included but have been discussed in different contexts, both in the scientific literature as well as in frameworks developed by institutions engaged in discussions about HTA. We further provide an overview of existing methodological concepts to incorporate some of these value elements into value assessments, including examples of the selection and attempted measurement.

Recent work has proposed different value elements to be considered in HTAs [7], [8], methods to appropriately capture these value elements [9], [10], and empirical work on specific value elements, e.g., value of hope [11]. However, to the best of our knowledge, no previous study has undertaken this kind of comprehensive review of value elements used in pharmaceutical value assessments, including an overview of methods proposed to accommodate a broader value definition.

We have undertaken a systematic literature review to achieve our aims. In the next section, we outline the methods and the analytical framework adopted for the extraction of relevant information from the reviewed publications. This is followed by the results of our literature review. We first provide a detailed synopsis of the various value elements that have been applied or discussed in the recent literature, followed by the methods and approaches that are used or have been proposed to incorporate these elements into value assessments. We end with a discussion of the findings.

# 2 Methods: Literature Review

We searched for peer-reviewed literature using two electronic databases – MEDLINE (Medical Literature Analysis and Retrieval System Online) through PubMed resource and the Social Science Citation Index (SSCI) through Web

of Science portal. First, we accessed MEDLINE, one of the two most comprehensive and commonly used databases for literature searches in medicine and life sciences. Second, in order to ensure coverage of economic and social science journals, we accessed the SSCI database. Both databases were searched using the same search strategy and combination of keywords, which are described in the following section.

The reporting of the applied approach and methods was based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline [12].

## 2.1 Study period and identification of evidence

The study period for inclusion of relevant publications was from January 2010 to August 2019. Our search strategy included English language articles using a combination of keywords divided into main and subcategories. Each keyword from the main category was combined with each keyword from the sub-category at a time, i.e., keywords within a category were connected via the Boolean operator “or”, while the main and sub-category were connected via the operator “and”. We accounted for spellings and selected plural forms, that is, we added an “s” at the end of “value element” and “value dimension” (shown in parenthesis).

Main category keywords

- Health technology assessment
- Value assessment
- Value-based pricing
- Economic evaluation
- Value framework

Sub-category keywords

- Value element(s); value dimension(s); value beyond
- Societal perspective; social perspective; societal value; social value
- Caregiver
- Patient perspective

The determined keywords were translated in search queries for PubMed and SSCI as shown in Annex A. Furthermore, reference lists from the studies selected were screened. In some instances, these include articles that were published prior to 2010.

Finally, we conducted a web-based gray literature search to collect information produced on all levels of government, academics, business, and industry. Similar to the search for peer-reviewed literature, our search strategy included using a combination of keywords (e.g., health technology assessment, value assessment, value framework, etc.) as well as sources selected for their relevance, including key agencies such as the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) and a network of organizations such as the European Network for Health Technology Assessment (EUnetHTA). The relevant gray literature identified through this exercise is shown in Annex B.

## 2.2 Study selection and data extraction

We selected articles according to a three-stage process: During the first stage, after removing duplicates, we screened for abstracts using predetermined selection criteria. This included the publications being one of the following:

(1) economic evaluation of drugs considering a societal perspective including reviews of economic evaluations and other empirical work, or
(2) conceptual framework for including broader value dimensions, or
(3) commentaries and editorials on the need to broaden the value scope of HTAs.

During the second stage, we retrieved articles for all abstracts meeting the eligibility criteria. In addition, relevant studies identified from reference screening and gray literature were incorporated. Finally, in the third stage, we reviewed these articles including gray literature in full, removed articles which on reading did not meet the eligibility criteria, and extracted the relevant data from the final publications included in the review. Duplicate reviewers were used in abstract screening for relevance, and in full-text screening only if unsure about relevance and/or inclusion.

To facilitate the extraction of relevant information from the included articles, we developed an analytical framework by reviewing existing frameworks and relevant evidence from the peer-reviewed and gray literature. Our analytical framework for the full-text analysis and data extraction consisted of five main components: (1) type of study, (2) methods or approach, (3) value dimensions and elements, (4) disease or therapeutic area, and (5) country.

Each of the main components had several different sub-components and is described in more detail in the following:

**Type of study**

The first component considers the type of article. Here articles were classified as theoretical or conceptual, empirical analysis, (systematic) literature review, opinion or perspective pieces, and conference or policy forum summaries. This component reflects whether articles present economic evaluations of medicines in practice, explore modeling approaches, or provide a literature review of the ongoing debate.

**Methods or approach**

This component is associated with the evaluation methods and techniques used. In terms of the analytical methods applied, the respective approach differs based on the outcome and measurement, the perspective adopted, and whether the approaches commensurate or not. These range from commonly used approaches such as cost-effectiveness analysis, cost-benefit analysis, and cost-utility analysis to less frequently used approaches such as stated preference approach or person trade-off approach. This component reflects whether one or more methods emerge as the favored analytic techniques for economic evaluation in health care. It further explores which additional methods were implemented in cases where broader elements of value were incorporated into the evaluation.

**Value dimensions and value elements**

This component relates to the types of outcomes measured or discussed in terms of benefits associated with a medicine. That is, it classifies outcomes into value elements beyond health measures of patients, including paid and unpaid work, changes to out-of-pocket payments, value of hope, scientific spillovers, equity and fairness, and aspects of caregiver burden.

**Disease area or therapeutic area**

This component relates to the types of disease or therapeutic area under consideration in an article. It captures the relative severity and, in some cases, the affected population (e.g., pediatric, or adult patients), and whether there is a clustered effect around assessments with broader value dimensions for certain diseases.

**Country**

Regarding the country of study, articles were classified according to the explicitly mentioned country or the institutional location of the first author (if the study did not focus on a specific country). This component provides descriptive information on the potential concentration of publications in specific countries.

We extensively examined the third component relating to value dimensions and value elements. Because of one of our objectives to identify and analyze the use of or relevant discussion on broader value elements, we extracted the most detailed information from the included articles on this aspect.

# 3 Results

In total, 1,169 potentially eligible peer-reviewed article listings were identified in the electronic databases; of these, 192 articles were identified as potentially useful and abstracts were read in full. A total of 139 articles met the eligibility criteria, and an additional 41 articles were identified as relevant through reference screening or as gray literature, summing up to 180 articles (Figure 1). All the publications included in the review were organized by author(s) name, publication year, and the extracted relevant data as shown in Annex B.

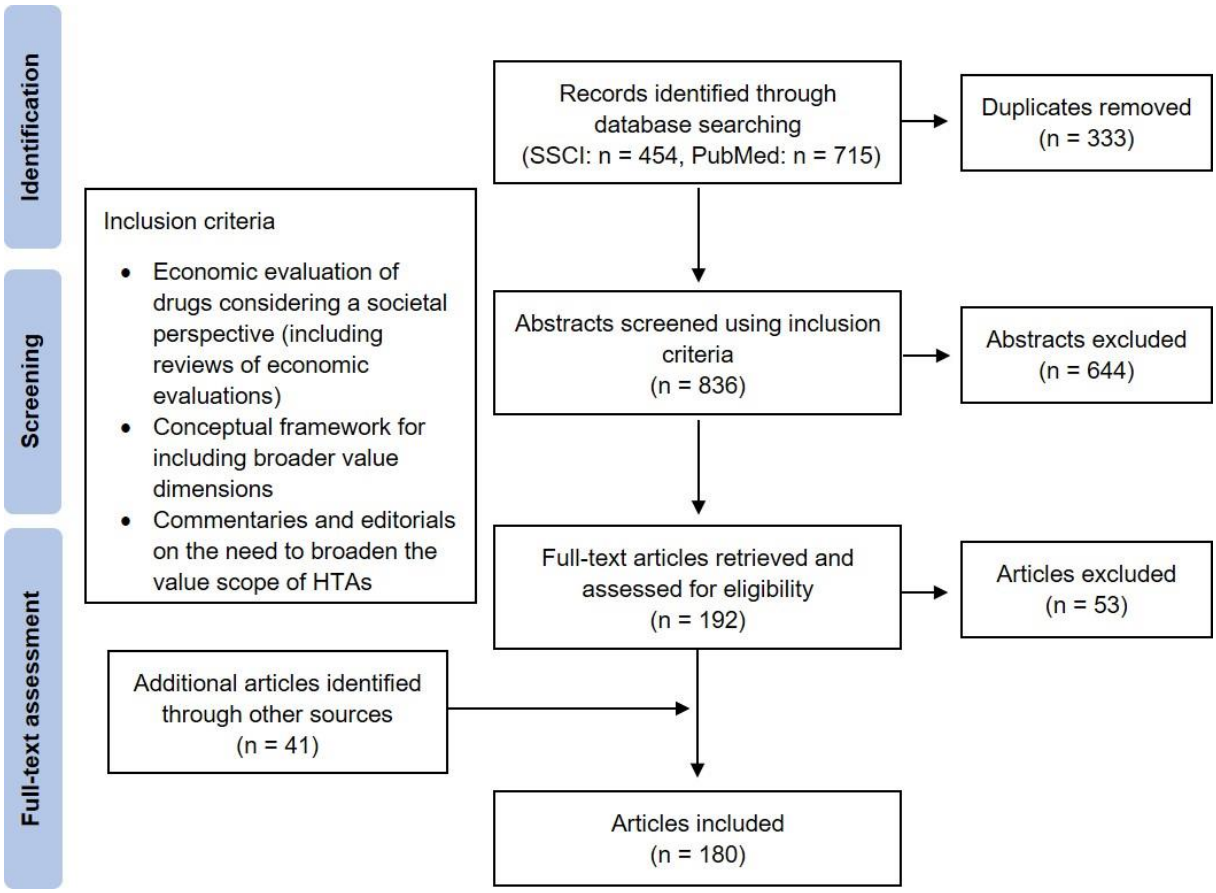


Figure 1: Flow diagram of literature screening and identification process

Table 1: Characteristics of the included articles

| Characteristic | | All articles | | Economic evaluations | |
|---|---|---|---|---|---|
| | | n | % | n | % |
| Number of articles | | 180 | 100.0% | 90 | 100.0% |
| Year of publication | Before 2010 | 6 | 3.3% | 0 | 0.0% |
| | 2010 (January) to 2019 (August) | 174 | 96,7% | 91 | 100.0% |
| Type of article | Economic evaluation | 90 | 50.0% | 90 | 100.0% |
| | Systematic review | 26 | 14.4% | n/a | n/a |
| | Theoretical or conceptual | 25 | 13.9% | n/a | n/a |
| | Other empirical analysis | 24 | 13.3% | n/a | n/a |
| | Opinion or perspective | 13 | 7.2% | n/a | n/a |
| | Conference or policy forum summary | 2 | 1.1% | n/a | n/a |
| Therapeutic area, medical specialty, or health technology (if applicable) | n/a | 67 | 37.2% | 1 | 1.1% |
| | Vaccination | 32 | 17.8% | 29 | 32.2% |
| | Oncology | 24 | 13.3% | 13 | 14.4% |
| | Infectious disease | 9 | 5.0% | 9 | 10.0% |
| | Neurology | 9 | 5.0% | 8 | 8.9% |
| | Mental health | 7 | 3.9% | 4 | 4.4% |
| | Cardiology | 6 | 3.3% | 6 | 6.7% |
| | Rheumatology | 6 | 3.3% | 5 | 5.6% |
| | Pediatrics | 4 | 2.2% | 2 | 2.2% |
| | Pulmonology | 4 | 2.2% | 4 | 4.4% |
| | Immunology | 3 | 1.7% | 3 | 3.3% |
| | Gastroenterology | 2 | 1.1% | 2 | 2.2% |
| | Hematology | 2 | 1.1% | 2 | 2.2% |
| | Dermatology | 1 | 0.6% | 1 | 1.1% |
| | Diagnostics | 1 | 0.6% | 0 | 0.0% |
| | Endocrinology | 1 | 0.6% | 1 | 1.1% |
| | Obstetrics | 1 | 0.6% | 0 | 0.0% |
| | Smoking cessation | 1 | 0.6% | 0 | 0.0% |
| Study country (if applicable) | n/a | 77 | 42.8% | 5 | 5.6% |
| | Netherlands | 12 | 6.7% | 12 | 13.3% |
| | Multiple countries | 12 | 6.7% | 7 | 7.8% |
| | USA | 9 | 5.0% | 8 | 8.9% |
| | Canada | 8 | 4.4% | 6 | 6.7% |
| | Japan | 8 | 4.4% | 8 | 8.9% |
| | Germany | 6 | 3.3% | 6 | 6.7% |
| | Thailand | 6 | 3.3% | 6 | 6.7% |
| | United Kingdom | 5 | 2.8% | 3 | 3.3% |
| | Sweden | 4 | 2.2% | 1 | 1.1% |
| | Australia | 3 | 1.7% | 0 | 0.0% |

| | | | | |
|---|---|---|---|---|
| China | 3 | 1.7% | 3 | 3.3% |
| India | 3 | 1.7% | 3 | 3.3% |
| Taiwan | 3 | 1.7% | 3 | 3.3% |
| Greece | 2 | 1.1% | 2 | 2.2% |
| Italy | 2 | 1.1% | 2 | 2.2% |
| Korea | 2 | 1.1% | 2 | 2.2% |
| Norway | 2 | 1.1% | 2 | 2.2% |
| Belgium | 1 | 0.6% | 1 | 1.1% |
| Brazil | 1 | 0.6% | 1 | 1.1% |
| Colombia | 1 | 0.6% | 1 | 1.1% |
| France | 1 | 0.6% | 1 | 1.1% |
| Ghana | 1 | 0.6% | 0 | 0.0% |
| Iran | 1 | 0.6% | 1 | 1.1% |
| Jordan | 1 | 0.6% | 1 | 1.1% |
| Mexico | 1 | 0.6% | 1 | 1.1% |
| Pakistan | 1 | 0.6% | 0 | 0.0% |
| Poland | 1 | 0.6% | 1 | 1.1% |
| Singapore | 1 | 0.6% | 1 | 1.1% |
| Spain | 1 | 0.6% | 1 | 1.1% |
| Switzerland | 1 | 0.6% | 1 | 1.1% |

## 3.1 Article characteristics

A summary of the characteristics of all included articles is shown in Table 1. The articles meeting the inclusion criteria were published from 2002 to 2019. Only six publications (three percent) were published before 2010. The year 2018 had the highest number of publications included (30 articles, 17 percent).

Of the final 180 publications reviewed, 90 articles (50 percent) were economic evaluations; 26 (14 percent) were systematic literature reviews; 25 (14 percent) were theoretical studies that explored modeling issues and multicriteria decision analysis (MCDA) implementation; 24 (13 percent) were other empirical analyses (mostly willingness-to-pay approaches); 13 (seven percent) were opinion pieces and perspective articles discussing the broader elements of value in HTAs; and two (one percent) were conference or policy forum summaries.

Eighty-four (47 percent) of all included publications referred to cost-effectiveness (CEA) and/or cost-utility analysis (CUA) and of the 90 economic evaluations, 79 (88 percent) used one of the two or both methods (Figure 2). Sixty-seven (37 percent) publications did not focus on a specific therapeutic area. Among those that did, cancer was the most studied disease area with 24 studies (13 percent) and vaccines were the most studied health technology with 32 studies (18 percent). Seventy-seven articles (43 percent) did not explicitly focus on a specific country's population. A wide range of countries were covered in those that did, including a larger pool of low to middle income countries (see listed countries in Table 1).

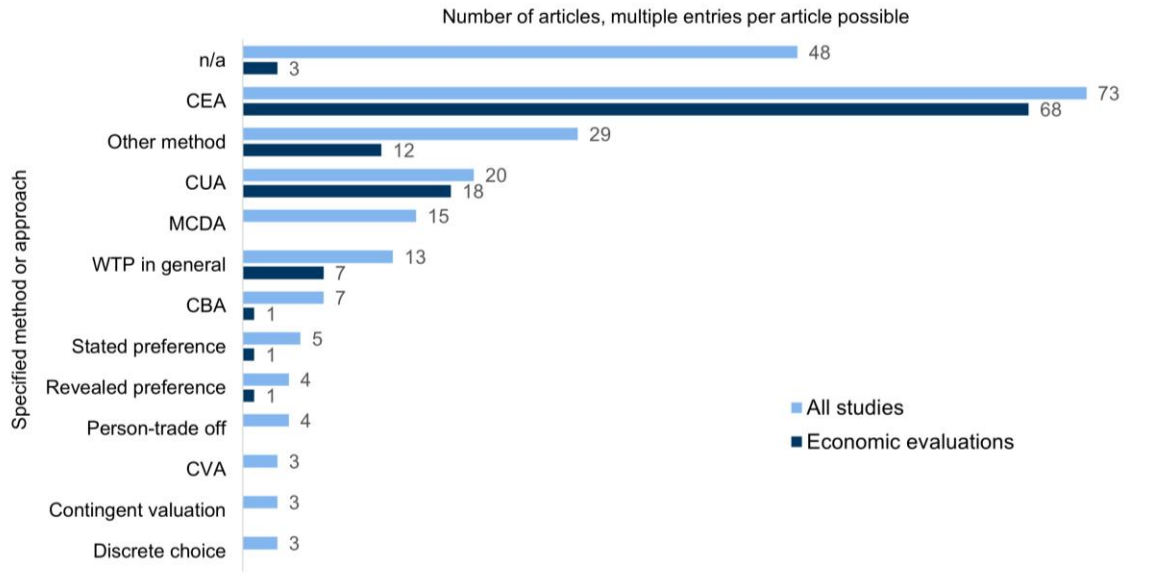


Figure 2: Specified method or approach used in the included articles

## 3.2 Value elements

Our findings show that the majority (62 articles, 69 percent) of economic evaluations used patients' health benefit in terms of quality adjusted life years (QALYs) to measure the benefits associated with a health care technology. Additionally, 18 economic evaluations (20 percent) did not include QALYs but made use of at least one other health measure or clinical outcome. In subsequent sections, we focus on and describe elements of pharmaceutical value that go beyond those patient health benefits.

Figure 3 summarizes the broader value elements found in our literature review by category of beneficiary, i.e., patients, their family and caregivers, or society at large, and by value dimension, i.e., health, economic, or other benefits. The value elements reflect the perspective of the relevant beneficiary and the dimension of benefit achieved. For example, if the perspective is that of a patient, then the focus may have been survival or quality of life within health benefits or productivity gains within economic benefits. The attributes of these value elements and the way in which they were covered in the included publications will be discussed in turn, beginning with health as the first dimension of benefit discussed.

### 3.2.1 Health benefits of caregivers and family members

Our review shows that almost one quarter (42 articles) of all included studies mentioned some form of spillover effects for family members and informal caregivers. A total of five studies included health benefits of caregivers in terms of QALYs [13]–[17]. Other health measures were mentioned as well: One Japanese study found that Alzheimer's disease caregivers are in a particularly vulnerable position, risking their own mental and physical well-being to provide the best care with the resources available to them [18]. Another recent study explored the inclusion and impact of informal care in CUAs and found that the majority of Alzheimer disease studies included some costs or health effects of informal caregiving [19]. Lin and colleagues [16] expanded on this previous study and found that family/informal caregiver spillover health impacts (using caregiver QALYs) were incorporated less often into CUAs compared to spillover costs.

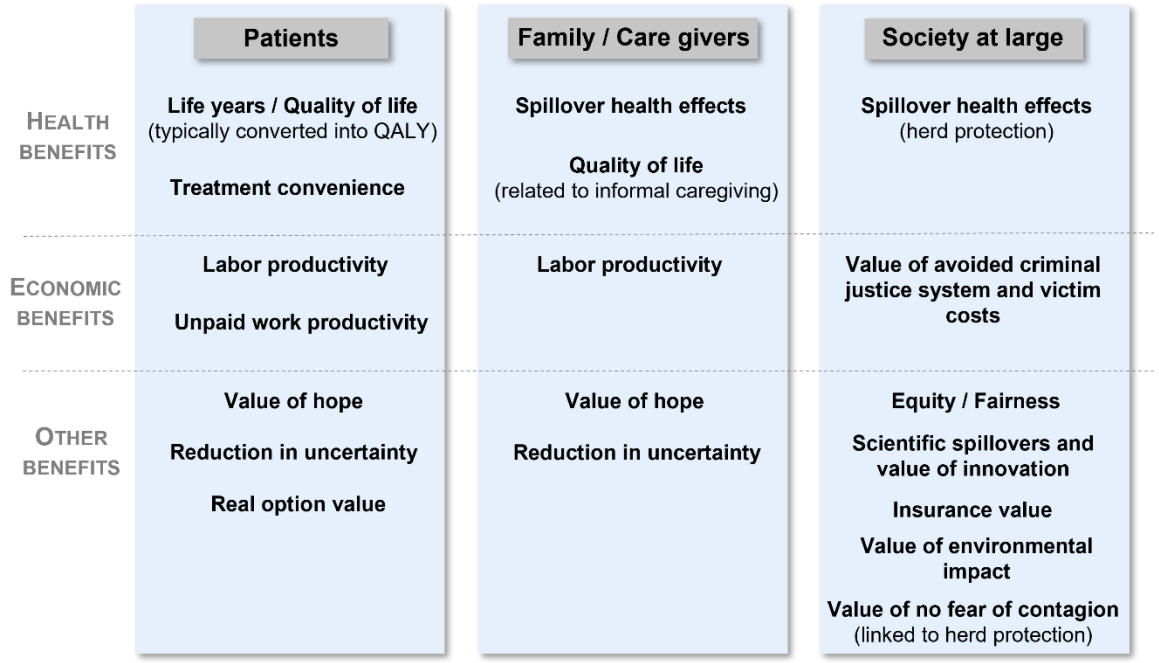


Figure 3: Value elements by category of beneficiary and value dimension

### 3.2.2 Herd protection / Value of no fear of contagion

Three articles (two percent of all included studies) on vaccination had broached the issue of herd protection or consider reduced infection and/or incidence rates in their modelling [20]–[22]. Additionally, one article suggested the value of no fear of contagion associated with infectious diseases as a an additional element of value and logically linked it to the herd protection effect [7]. We did not find any empirical studies investigating or including fear of contagion. The fear of contagion might have gained momentum following the COVID-19 pandemic, however in our review of literature latest from 2019, this dimension has not been considered in too many articles.

### 3.2.3 Labor productivity of patients

Fifty-nine of all included studies (33 percent) mentioned labor productivity of patients and half (forty-six) of the reviewed economic evaluation studies included this element as an indirect cost. Productivity loss was defined generally as a loss of or reduction in time spent on paid work or employment [23]–[26]. However, the descriptions vary widely in extent and comprehensiveness. Several of the economic evaluation studies that reported health related productivity costs did not elaborate on how these were measured or valued e.g., [27]–[31]. Most often lost productivity was measured in terms of the loss of income or foregone earnings using a human capital approach to valuing productivity losses in which it is assumed that labor earnings reflect productive capacity. Additionally, presenteeism or working with limitations were infrequently considered in these studies. Kigozi and colleagues [32] reviewed cost of illness studies and demonstrated that reduced productivity (through presenteeism) was rarely included.

### 3.2.4 Unpaid work productivity of patients

Overall, we found mentions of unpaid work productivity as a relevant element of pharmaceutical value in nine (five percent) of the reviewed articles. Unpaid work is generally defined as a productive activity performed without monetary remuneration that could be replaced by hiring a service, e.g., cleaning, cooking, childcare, and informal care. Only four of the economic evaluations (four percent of the included articles of this type) included unpaid work in their analyses [25], [33]–[35]. This corresponds with the results of an earlier systematic literature review of unpaid work in applied economic evaluations of treatments for rheumatoid arthritis [36] that was part of our study sample, and indicates that unpaid work is still seldomly included, independent of the therapeutic area.

Although unpaid work productivity could be valued using wages plus fringe benefits matched to a specific occupational category, recent studies have valued unpaid work using a contingent valuation approach or proxy good approach (similar to a replacement cost approach) using gross value added (GVA) [34], [37].

### 3.2.5 Labor productivity of caregivers and family members

Our review shows that caregiver burden in terms of labor productivity loss of family members and other caregivers was mentioned in 16 (nine percent) of all included articles and included in almost a fifth (17 percent, 15 articles) of the economic evaluations. The application of this value element centered around pediatric illnesses and the impact of vaccinations, [20], [21], [38]–[42] or diseases such as Alzheimer's [13], [16], [18], [43], [44]. While some studies explicitly defined productivity loss of a caregiver as caregiver's lost time or income in the societal costs [18], [42], [45]–[47], other studies provided no details on either the measurement of productivity costs or the valuation and mentioned loss in terms of opportunity costs or loss of free time [27], [48].

### 3.2.6 Value of avoided criminal justice system and victim costs

Three reviewed articles (two percent) discussed that treatment related declines in criminal activities have a positive externality that extend beyond the health care system and bring large economic and social benefits that outweigh the economic costs associated with the treatment [49]–[51]. A key benefit associated with substance abuse or psychotic disorder treatment is reduction in crime. One way to measure social and economic gain is to value avoided criminal justice system costs (e.g., arrest or time spent in jail) and avoided victim costs (e.g., material or physical damage or spending in anticipation of a crime) [52]. These values are likely to be quantitatively meaningful, especially in treatment of substance abuse and psychotic disorders.

### 3.2.7 Value of hope

Some papers suggested, especially in end of life situations or in life threatening conditions, that patients sometimes appear to make risky treatment decisions and prefer options with greater uncertainty that come with a chance of increased long term survival [7], [53]. In the literature reviewed, this is discussed in five studies (three percent) and referred to as the "value of hope" [11]. Our review suggests that patients are likely to place a higher value on technologies that provide opportunities for a cure or a "chance of durable or tail-of-the-curve survival" [54], especially for certain types of rare diseases (e.g., spinal muscular atrophy among pediatric population) that have a significant impact on patient morbidity or mortality [54] or an increased willingness as a society to trade-off health of other individuals to make a special case for rare disease drugs [55]. Calculating the value of hope could be especially crucial for therapies with uncertain effects that may face challenges with current HTA principles and practices. Our review identifies Lakdawalla and colleagues [11] as providing the only study to quantify the value of hope among cancer patients. Their study investigated whether cancer patients preferred "sure bets" or "hopeful

gambles" [11] in the treatment of cancer. They show estimates that cancer patients are willing to pay at least $35,000 USD for each 1-year increase in the standard deviation of survival [11].

### 3.2.8 Reduction in uncertainty due to new diagnostic

Physicians routinely encounter diagnostic uncertainty in practice. The value of diagnostics for a disease is an element commonly included in value assessments, especially when only data on intermediate clinical or health-state values is available. Two studies in our review (one percent) discussed this element [7], [56]. In these articles, this element typically was described as an improvement in diagnostic tests that could eliminate or reduce diagnostic errors, facilitate the use of better treatment options and decision-making, and the over or underuse of health care resources.

### 3.2.9 Real option value

The concept of options is primarily used in finance where an investor can buy "call options" to purchase the right to buy an asset at an agreed price in future. In our review, six articles (three percent) raised real option value as a value element, which refers to the investments in current health care technologies that extend life and provides patients with a "call option" for better treatment in the future. The evidence suggests that patients perceive option value from treatment as getting one treatment that offers a longer expected survival and increases the likelihood of benefiting from a better treatment in the future [57]. In other words, to enjoy future benefits, patients may prefer increased survival relative to improved health-related utility as Philipson and colleagues [58] reported with zidovudine (AZT) treatment in HIV. Sanchez and colleagues [59] also suggest that the option value of innovative therapies from future medical innovation amounts to 0.76 life-years among chronic myeloid leukemia treatment. This option value is estimated to be worth $63,000 USD, equivalent to nine percent of the average survival gains from existing treatments [59]. This increases to 25 percent in the case of breast cancer [60].

### 3.2.10 Equity and fairness

Overall, equity and fairness was considered in 19 articles (eleven percent) of the reviewed 180 articles. Our review suggests that there is a preference for putting greater weight to health gains accrued by children, those severely ill, and the socioeconomically disadvantaged [61]. Asaria and colleagues [62] discuss the distributional cost-effectiveness analysis as a framework for incorporating equity as an element of value into value assessments. They discuss equity constraint analysis that measures the sacrificed efficiency to meet an equity goal and equity weighting analysis that requires specific equity weights that are used to compare how a policy affects both equity and efficiency [62]. Boujaoude and colleagues [63] describe how equity considerations are currently being incorporated within CEA of rotavirus vaccination and highlight the components of equity that have been used in studies in low and middle income countries. Our review indicates that further developments in methodology would be necessary in this area before equity-weighted QALY maximization could become the norm in economic value assessments. However, even with such developments it is still necessary to accept the simplifying assumptions which are typically necessary in equity-weighted QALY maximization.

### 3.2.11 Scientific spillovers and value of innovation

Scientific spillover was included in six (three percent) of the reviewed publications as an element of value. Scientific spillover is defined as a knowledge spillover whereby one innovation can lead to the development of similar or better technology [64]. Sweeney and Goss [64] suggest that market approval of a new therapy leads to additional research, accumulation of knowledge, and benefits over time, even if the clinical properties of the therapy do not change. Similarly, the value contribution of innovative drug doesn't end with the patent, the value that generics and biosimilars create is attributable to the original innovation [65]. The empirical implications or advantages and disadvantages of the benefits of scientific spillovers are however an area of future research and currently not well understood.

### 3.2.12 Insurance value

Our review shows that three studies (two percent) mention the value of changes in the variance of physical and financial risk associated with a pharmaceutical or health technology [66]–[68]. In other words, by incorporating the insurance value of a drug into value assessments and as a result, providing consumers with access to better medical technology may reduce risk more efficiently than providing them with health insurance. Two of the reviewed articles showed a new methodological development labelled extended cost-effectiveness analysis [67], [68]. It values financial risk protection and distributional consequences in developing countries when government finances a health intervention (e.g., public finance for rotavirus vaccination) irrespective of who receives it. Results from these studies show that the associated gains of public insurance to cover an intervention include health gains, reduced household expenditures, "herd immunity" from increased uptake in vaccinations, and improved equity [67], [68].

### 3.2.13 Value of environmental impact

Our review indicates that health policymakers in countries such as Sweden and England are taking note of environmental impacts when assessing new health technologies [69]. One article did consider the value of environmental impact. However, the evidence base is insufficient to accurately measure technologies' impact on the environment and traditional methods such as CUA may not be suitable for such broader concerns [69]. The empirical implications of augmenting value assessments with environmental impacts remain a fertile area for the future, however methods such as CBA and MCDA (see chapter 3.3) could be potential methods for evaluating health and environmental outcomes [69].

## 3.3 Methods to incorporate broader value dimensions into HTA

Most of the reviewed literature discusses elements of value beyond patients' health benefit, however, the discussion on the methods to accommodate a broader value definition in pharmaceutical value assessments is relatively sparse. The main challenge here is to quantify, value, and aggregate multiple value elements into one measure, whereby the different measures of value would be converted into a common currency. Several methods have been proposed in the literature to accommodate multiple elements within one value assessment (Brazier & Tsuchiya, 2015; Sussex et al., 2013; Wildman & Wildman, 2019). The methods presented here have in common that they do not refer to one specific value element but rather propose comprehensive approaches to include various additional elements within and beyond health. Each method offers its own advantages which will be detailed below. Further, each method is suitable depending on the objective of the value assessment.Cost-benefit analysis

### 3.3.1 Cost-benefit analysis

Cost-benefit analysis (CBA) is a well-established approach in many areas of applied economics, but not commonly used to inform health care decision-making [10], [70], [71]. CBA attempts to value both benefits and costs in the same monetary unit.

Conventional CBA is based on values revealed in market transactions, however, the administered pricing for certain values (e.g., well-being) is completely uninformative [70]. Techniques which attempt to value nonmarket elements are described in Brazier and Tsuchiya [9]. The money-equivalent value of overall benefit is generally defined by the individuals' hypothetical willingness to pay for a health outcome. A common technique to determine this willingness to pay for nonmarket benefits is to use stated preference questions in surveys. Individuals are either asked how much they would be willing to pay for a specific change in outcome (contingent valuation) or asked to rank or choose among different options (best-worst scaling, discrete choice experiments). Reviews of recent studies using best-worst scaling and discrete choice experiments to investigate patient preferences in health care can be found in Cheung and colleagues (2016) and Kleij and colleagues (2017) [72], [73]. The rationale behind proposing this approach is the assumption that in stating their willingness to pay for a certain health outcome, individuals implicitly consider all relevant value elements inherent to this outcome.

However, a drawback of this welfarist approach, i.e., assessing *individual* willingness to pay, is that benefits that accrue to other stakeholders (family, society, etc.) may be neglected since these are not considered in the individual's willingness to pay. Also, willingness to pay for the same benefit crucially depends on personal income and other characteristics, questioning the generalizability of the results [9]. An alternative, non-welfarist, approach is therefore to assess public opinion on how much should be spent on certain treatments or health care policies. Since this is not about touching individual pockets, distributional concerns are not an issue [9].

If the assumptions necessary for its use are accepted, CBA can allow the comparison of health interventions to other policies and thus facilitates the assessment of allocative efficiency across different public sector budgets [9], [10].

### 3.3.2 Weighted QALYs / Cost-value analysis

Another approach that is suggested in the literature is to refine existing measures, mainly being applied to the QALY, through equity weighting [10]. The aim of weighting is to account for other aspects such as severity of the disease or age of the patient in assigning value to a QALY.

A similar approach, called cost-value analysis (CVA), according to Nord (2015) replaces "estimates of aggregate personal value in terms of unweighted QALYs with estimates of overall societal value" [74].

Mostly, QALYs are weighted based on a graded willingness to pay. Techniques for assessing willingness to pay for a QALY are basically the same as for any other outcome. Most frequently used are stated preference questions in surveys (e.g., based on contingent valuation or discrete choice experiments).

Nord (2015) further suggests transforming utilities based on the results of person-trade off studies, which have gained increasing popularity. The idea behind this approach is to replace utilities in conventional QALY calculations measured at a 0 to 1 scale by societal values that are compressed towards the upper end of this scale, implying a decreasing marginal value of increases in individual utility. As basis for the transformation, he proposes to use functional relationships between individual utilities and societal values. These, in turn, can be determined by using person-trade off studies, where survey participants are confronted with treatment scenarios for different patient groups and are asked to judge at what ratio between the absolute number of treated patients they consider both treatment programs equally worth [74]. It is important to note that CVA or weighted QALYs are helpful approaches to inform efficient resource allocation, less so however in providing the basis for determining the value of a single treatment in monetary terms.

### 3.3.3 Multicriteria decision analysis

A third approach that is gaining currency as a way of capturing broader value elements in evaluations of pharmaceuticals is multicriteria decision analysis (MCDA) [10], [75]–[78]. MCDA combines several criteria, possibly from the perspective of different stakeholders. MCDA requires an explicit rating of the importance of each value element considered. However, slightly altered versions of MCDA without scoring and weighting of criteria but with a clearer focus on deliberation, referred to as “partial MCDA”, have also been suggested [79].

The most common way of aggregating different value elements in MCDA is using additive models. Each value element is rated with a numerical score (based on an element-specific scale), which in turn is given a relative weight according to the importance of the element. All weighted scores are then summed up to yield one aggregate measure. A comprehensive overview of this value measurement model as well as alternative methods are described in Thokala and colleagues [78] and Thokala and Duenas [80].

Techniques to balance benefits and costs in MCDA once the aggregate benefit score has been established are discussed in Phelps and Madhavan [81], Thokala and colleagues [78] and in the ISPOR Task Force Report on Good Practices in MCDA [71]. The obvious approach would be to divide the multicriteria scores by its costs, akin to calculating the ratio of costs per health benefit in cost-effectiveness analyses. Other techniques have been discussed in the ISPOR Task Force Report on Good Practices in MCDA [78]. Still, the common denominator among all these techniques is that the different elements are measured in the original unit they are reported in.

While MCDA still requires that all elements included are measurable, it differs from CBA by not requiring the conversion of all value elements into monetary units. This method can be appropriate when comparing different treatment options. Costs per rating score of each option inform about their relative efficiency. In order to inform decisions regarding value-based pricing, however, Wildman and Wildman (2019) suggest a mixed-methods approach in which elements of both CBA and MCDA are combined. This allows for both health and other elements to be combined into a single measure while at the same time to be valued in a common, monetary unit. This approach further helps to overcome a drawback of CBA, that is, the implicit aggregation of all value elements into a single value, which makes it impossible to assess how the overall benefit is related to individual aspects (e.g., health vs. other aspects) [75].

Comprehensive reviews of health economic analyses using MCDA in its various forms and covering a broad range of therapeutic areas can be found in Adunlin and colleagues [82] and Wahlster and colleagues [83].

# 4 Discussion

Our review of the existing literature shows that both the research community as well as institutions engaged in health care policy acknowledge the limitations of the concepts currently used in value assessments and accentuate the need for considering broader elements when assessing the value of medicines (this is especially relevant given the COVID-19 pandemic). This is reflected in the high number of value frameworks that have been published in recent years to facilitate decision-making based on a broader concept of value.

In conclusion, measuring patients’ health benefit in terms of QALYs, remains the basis for most economic value assessments of medicines, although some of their underlying assumptions have been brought into question [84]–[88]. Further, notions of what represents the most relevant value elements beyond health differ. Most value frameworks list changes in productivity of both patients and caregivers, as one or even the most relevant value element. However, the incorporation of information related to productivity has important ethical and moral

dimensions, most research agrees on the importance of fairness or equity concerns, although these are not value elements *on top* of health but rather aspects that need to be considered when determining the *relative* value of different treatments. Family and spillover effects have gained momentum, especially in disease areas such as Alzheimer and pediatric illnesses. Other, less obvious elements have not yet found their way into the bulk of value frameworks, but are mentioned sporadically (e.g., value of hope, or insurance value).

This disagreement over the relevance and the relative newness of some of these elements is also reflected in empirical work. Many value elements have been discussed in theoretical or conceptual studies discussing value frameworks but are rarely empirically applied. This is likely expected as many value elements are hard to define and measure, and their use in formal analysis would need to be justified [89].

A noteworthy exception is productivity, which is the element most economic evaluations refer to when they use the term societal perspective. Still, although all studies of that type in our sample declare taking a societal perspective, almost half of them did not include productivity outcomes in the analysis. Further, there is a lack of consensus on how to value productivity, and no standardized approach has yet been established. We also acknowledge that measuring productivity with other patient benefits (e.g., through QALYs) could suffer from the issue of double counting. However, the current evidence on this issue is considered neither decisive nor conclusive [90]. Nevertheless, some suggest that the impact of double counting is negligible [91]. Finally, the ethics surrounding the use of individualized wages (in some instances) has been questioned as this approach (bottom-up approach) leads to the identification of patients with lower incomes, and a preference for treating patients with higher incomes [92].

For most other value elements discussed in the literature and the various value frameworks, methods for incorporating them are still rudimentary. Unlike productivity, other novel elements are less sizable, making it relatively more challenging to measure them. Incorporating these elements into economic evaluations or in other formal assessments as part of HTA processes depends in large part on the success of, or failure of, measurement in practice; as well as on the judgements about the relevance or irrelevance of each element [93]. Also, the implications of broader value elements on pricing or reimbursement decisions are unclear. Given that the societal perspective is used sparingly, that the process of value-based pricing is relatively complex, and that there is flexibility in interpreting value, the current situation seems likely to lead to a price negotiating process that is rather unstructured or to a process which can be seen as a “new narrative to justify prices of new medicines” [3], [94]. In this context, the discussion of drug prices [95] and profits [96], as well as their absence from much of the literature on value of medicines, are worth mentioning. We also note that a formal analysis alone is typically not sufficient for determining allocation or prioritization of existing resources [97].

We acknowledge some additional aspects that are discussed in the literature with respect to assessing the value of medicines but are not covered in this review. For example, some question if certain aspects of drug administration are adequately captured by standard quality of life measures [98]. Oral administration of cancer drugs for example avoids the inconvenience of infusions, infusion-related infections, and the need for additional administration visits, therefore representing an additional element of value [99], [100]. Also, beyond the need for broader value dimensions, some argue that there is also the need for a broader view in terms of time [8], [74]. Especially for curative treatments, one-time investments generate a lifelong return. A longer-term view may further be relevant when the value of a drug is compared to its cost, which is currently the case in HTA guidelines, which recommend use of a lifetime horizon [8]. We also acknowledge that a societal perspective could vary from country to country (or sometimes within country with regional authorities) and countries would decide which elements should be included in their preferred perspective. Nevertheless, we have identified elements that are useful to the evaluations and HTA processes.

Finally, we highlight a potential limitation. We used a limited set of databases for our search of value assessments using a societal perspective. As a result, although care was taken to include all relevant studies, we could have missed some studies or articles that considered use of broader value elements in value assessments (e.g., use of Embase or EconLit). Nevertheless, the included databases spanned the social sciences, health economics, medical, and life sciences disciplines and therefore provide a comprehensive overview of the literature. And we made every attempt to cover the additional studies from the reference list of the selected articles and comprehensively scan the gray literature.



# 5 Conclusion

Value assessments typically compare benefits using health gain in terms of QALYs or life years (LYs) gained. However, beyond health benefits of the patient, our review shows that there are additional elements that reflect value but are not typically captured in applied value assessments which mostly presented themselves in the form of economic evaluations. These elements range from common but unsystematically used elements such as labor productivity and spillover effects to more novel and typically not considered elements such as value of hope and real option value. Reasons for only limited inclusion of these elements range from lack of data, a general lack of acceptance, difficulty in measuring these elements, or the currently available approaches are limited in nature. Nevertheless, given the significance of these broader value elements, more attention needs to be given in value assessments to the methods used to accommodate a broader definition of value and there is a need to use these value elements in a more explicit manner in value assessments from a societal perspective.

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# Annex

Annex A: Keyword translation in search queries for PubMed and SSCI

**Query Translation PubMed**

((((((((((((VALUE ELEMENTS[Text Word]) OR VALUE ELEMENT[Text Word]) OR VALUE DIMENSION[Text Word]) OR VALUE DIMENSIONS[TEXT WORD]) OR SOCIAL VALUE[Text Word]) OR SOCIETAL VALUE[Text Word]) OR SOCIETAL PERSPECTIVE[Text Word]) OR SOCIAL PERSPECTIVE[Text Word]) OR CAREGIVER[Text Word]) OR VALUE BEYOND[Text Word]) OR PATIENT PERSPECTIVE[TEXT WORD]))) AND (((((HEALTH TECHNOLOGY ASSESSMENT[Text Word]) OR VALUE ASSESSMENT[Text Word]) OR VALUE-BASED PRICING [Text Word]) OR ECONOMIC EVALUATION [Text Word]) OR VALUE FRAMEWORK [TEXT WORD]) Filters: English, Publication date from 2010/01/01 to 2019/08/01

**Query Translation SSCI**

(TS=(("health technology assessment" OR "value assessment" OR "value-based pricing" OR "economic evaluation" OR “value framework”) AND ("social perspective" OR "social value" OR "societal perspective" OR "societal value" OR "value beyond" OR "value element*" OR "value dimension*" OR "caregiver" OR “patient perspective”))) AND LANGUAGE: (English)

Indexes=SSCI Timespan=2010-2019

Annex B: Gray literature from key agencies identified as relevant

| Agency or organization | Title | Summary | Link |
|---|---|---|---|
| Organization for Economic Cooperation and Development (OECD) | Health Technologies and Decision Making | The conclusions presented in this report drew on analysis of a survey of how health technologies are integrated into health systems. Although the report focusses on broader issues such as decision-making at the national, regional and hospital levels and how aspects health care systems facilitate or impede the implementation of decisions, our review focused on how evidence (particularly HTA-based evidence) is produced and used in decision making. | https://read.oecd-ilibrary.org/science-and-technology/health-technologies-and-decision-making_9789264016224-en#page1 |
| Medicines Australia | Value of Medicines | This report discusses the current HTA systems and how policy makers need to take a comprehensive approach to fully recognize the broader societal impact of medicines to ensure that medicines policies suit the needs and expectations of all Australians. | https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2011/02/MA_OccPaper4_ValueOfMedicines.pdf |
| European Network for Health Technology Assessment (EUnetHTA) | HTA Core Model Version 3.0 | HTA Core Model is a methodological framework for collaborative production and sharing of HTA information. The main aim of the HTA Core Model is to enable international collaboration in producing HTA information and efficient sharing of the results so that redundant overlapping work in different countries and regions can be avoided. It consists of three main components: the *ontology* contains an extensive list of generic questions that can be asked in an HTA; a *methodological guidance* to help researchers find answers to questions identified in the ontology; and a *common reporting structure* that provides standard format for the output of HTA projects. | https://www.eunethta.eu/hta-core-model/ |
| National Comprehensive Cancer Network (NCCN) | Evidence Blocks | The National Comprehensive Cancer Network Evidence Blocks (NEB) represents average values from an expert panel in a matrix assessing treatment efficacy, safety, quality and consistency of evidence, and affordability; scores are based on clinical trials and expert panel consensus and range from 1 to 5, with 1 being least favorable and 5 being most favorable. | https://www.nccn.org/evidenceblocks/ |
| European Society for Medical Oncology (ESMO) | ESMO Magnitude of Clinical Benefit Scale | The scale is a standardized, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies | https://www.esmo.org/Guidelines/ESMO-MCBS |
| Institute for Clinical and Economic Review (ICER) | ICER Value Assessment Framework | The ICER value framework describes the conceptual framework and set of associated methods that guide the development of ICER evidence reports. The purpose of the value framework is to support evidence reports that forms the basis for broader stakeholder and public engagement to establish sustainable access to high-value care for all patients. | https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-2/ |

| Agency or organization | Title | Summary | Link |
|---|---|---|---|
| American Society of Clinical Oncology (ASCO) | ASCO Value Framework (AVF) | The ASCO Value Framework (AVF) compares 2 regimens that have been studied in a prospective randomized clinical trial by generating a net health benefit score and comparing the drug acquisition cost of each regimen. | DOI: 10.1200/JCO.2015.61.6706 Journal of Clinical Oncology 33, no. 23 (August 10, 2015) 2563-2577 |
| BIOTECanada | The Canadian Rare Disease Therapies Landscape: Bridging Opportunity to Reality | This report presents the context related to orphan diseases and drugs and propose core principles to help guide the development of drugs for rare diseases (DRD) initiatives. The paper then explores five elements that need to be included in a comprehensive approach to DRDs, namely: (1) research; (2) regulatory environment and intellectual property; (3) health technology assessment (HTA); (4) reimbursement; and (5) health system adoption. Our focus was on the HTA element where the recommendation was that standard HTA approach is not suitable for drugs for very rare conditions. | http://www.biotech.ca/wp-content/uploads/2016/03/white_paper_mar_2.pdf |
| European Federation of Pharmaceutical Industries and Associations (EFPIA) | Working Together with Patient Groups | This report underlines the rationale for interactions between the pharmaceutical industry and patient organizations, suggest the principles on which these interactions should be based, outline the points of collaboration through the life cycle of a medicine, discuss some of the challenges and potential solutions to interact as well as providing a list of resources to support meaningful/appropriate collaboration. | https://www.efpia.eu/media/412524/working-together-with-patient-groups-23102017.pdf |

Annex C: Overview of all included articles and extracted data

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Addario et al., 2018 [101] | Opinion or perspective | n/a | side effects, survival, clinical outcome (any), severity of disease symptoms, out-of-pocket payments, transportation, patient participation, caregiver (any) | Cancer | n/a | USA |
| Adunlin et al., 2015 [82] | Systematic review | MCDA | n/a | n/a | n/a | USA |
| Akutagawa et al., 2017 [102] | Economic evaluation | Cost-outcome description | QALY | Hepatitis C | Japan | Japan |
| Al-Janabi et al., 2011 [103] | Opinion or perspective | n/a | QALY, caregiver (any) | n/a | n/a | United Kingdom |
| Angelis & Kanavos, 2017 [104] | Theoretical or conceptual | MCDA | QALY, other health measure, survival, clinical outcome (any), paid work, out-of-pocket payments, transportation, patient other, caregiver (any), innovation, scientific spillovers, burden of disease, unmet need, safety profile, patient convenience, public health, direct costs | n/a | n/a | United Kingdom |
| Angelis et al., 2018 [6] | Systematic review | n/a | other health measure, survival, clinical outcome (any), paid work, innovation, equity/fairness, disease severity, unmet medical need, safety | n/a | France, Germany, England, Sweden, Italy, Netherlands, Poland, Spain | United Kingdom |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| | | | considerations, public health, productivity loss, efficiency | | | |
| Aponte-González et al., 2013 [27] | Economic evaluation | CEA | DALY, paid work, out-of-pocket payments, transportation, home care costs, patient other, caregiver (any), opportunity cost of time spent for patient and caregiver, compensation for disability days charged to insurance | Human papillomavirus | Colombia | Colombia |
| Armstrong & Mullins, 2017 [105] | Opinion or perspective | n/a | HrQoL, toxicity, out-of-pocket payments, transportation, convenience of treatment, personal values (life priorities), external values (relating to someone else) | n/a | n/a | USA |
| Asaria et al., 2016 [62] | Economic evaluation | CEA | QALE, equity/fairness, health metric on population level: quality-adjusted life expectancy (QALE) | Bowel cancer screening | n/a | United Kingdom |
| Banna et al., 2010 [99] | Opinion or perspective | n/a | convenience of treatment | Cancer | n/a | Italy |
| Berende et al., 2018 [106] | Economic evaluation | CEA | QALY, paid work, out-of-pocket payments, transportation | Lyme disease | Netherlands | Netherlands |
| Boujaoude et al., 2018 [63] | Systematic review | CEA | other health measure, comorbidities, severity of illness, paid work, out-of-pocket payments, patient other, caregiver (any), equity/fairness, | Rotavirus | low- and middle-income countries | Italy |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| | | | persons dependent on patient, protection against financial risks | | | |
| Brazier et al., 2014 [107] | Other empirical analysis | n/a | QALY | Mental health | n/a | United Kingdom |
| Bruijning-Verhagen et al., 2018 [20] | Economic evaluation | CEA, risk-benefit analysis | QALY, survival, out-of-pocket payments, non-health related costs, transportation, caregiver (any), productivity caregiver, herd protection | Rotavirus | Netherlands | Netherlands |
| Canaway et al., 2019 [108] | Other empirical analysis | qualitative in-depth interviews, hierarchical network mapping | caregiver (any), close-person spillovers | n/a | n/a | United Kingdom |
| Carlos et al., 2016 [23] | Economic evaluation | CUA | QALY, paid work | Hepatitis A | Mexico | Mexico |
| Caro et al., 2019 [109] | Opinion or perspective | n/a | QALY | n/a | n/a | United Kingdom |
| Cartwright et al., 2014 [110] | Other empirical analysis | n/a | survival | Cancer | n/a | USA |
| Cheung et al., 2016 [72] | Systematic review | n/a | n/a | n/a | n/a | Netherlands |
| Chim et al., 2017 [111] | Other empirical analysis | population survey | equity/fairness | n/a | Australia | Australia |
| Chua et al., 2018 [112] | Economic evaluation | CEA | QALY, survival | Neuroendocrine tumors | Canada | USA |
| Connolly & Simoens, 2011 [113] | Economic evaluation | cost-minimization analysis | paid work, caregiver (any), opportunity cost of nursing time (not clear formal/informal) | Primary immunodeficiency | Belgium | Switzerland |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Constenla, 2015a [48] | Systematic review | health investment life course approach | paid work, equity/fairness, impact on education, human capital accumulation, economic growth | Malaria | Ghana | USA |
| Constenla, 2015b [114] | Economic evaluation | CEA | DALY, survival, out-of-pocket payments, caregiver (any), productivity caregiver | Pneumococcal diseases | Ecuador, Honduras, Paraguay | USA |
| Cookson et al., 2017 [115] | Theoretical or conceptual | n/a | equity/fairness | n/a | n/a | United Kingdom |
| A. Culyer et al., 2018 [116] | Opinion or perspective | n/a | patient preferences | n/a | n/a | United Kingdom |
| Damm et al., 2017 [117] | Economic evaluation | CEA | QALY, paid work | Human papillomavirus | Germany | Germany |
| de Groof et al., 2019 [118] | Economic evaluation | CEA | QALY | Crohn's disease | Netherlands, United Kingdom | Netherlands |
| de Soárez et al., 2015 [45] | Economic evaluation | CEA | survival, paid work, transportation, caregiver (any), productivity caregiver | Pneumococcal diseases | Brazil | Brazil |
| Devlin & Sussex, 2011 [76] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | United Kingdom |
| Dolk et al., 2016 [21] | Economic evaluation | CUA | QALY, paid work, out-of-pocket payments, transportation, caregiver (any), productivity caregiver, herd protection effects | Influenza | Germany | Netherlands |
| Drost et al., 2017 [119] | Systematic review | n/a | n/a | n/a | n/a | Netherlands |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Drummond et al., 2013 [120] | Theoretical or conceptual | CEA, WTP, Contingent valuation, Discrete choice | QALY, side effects, clinical outcome (any), out-of-pocket payments, patient participation, caregiver (any), social value judgements | n/a | n/a | United Kingdom |
| Ersek et al., 2017 [121] | Theoretical or conceptual | n/a | disease progression, toxicity, survival, clinical outcome (any), out-of-pocket payments, patient participation, patient preferences | Cancer | n/a | USA |
| Essers et al., 2010 [122] | Economic evaluation | CEA | QALY, paid work | Breast cancer | Netherlands | Netherlands |
| European Commission & Directorate-General for Competition, 2019 [123] | Opinion or perspective | n/a | innovation | n/a | n/a | Belgium |
| Eveleigh et al., 2014 [124] | Economic evaluation | CUA | QALY, paid work | Depression | Netherlands | Netherlands |
| Fazel et al., 2014 [49] | Other empirical analysis | n/a | risk of violent crime | Psychatric disorders | Sweden | United Kingdom |
| Finch et al., 2019 [24] | Economic evaluation | CEA | QALY, paid work, caregiver (any) | COPD | Netherlands | Netherlands |
| Fragoulakis et al., 2012 [125] | Economic evaluation | cost-minimization analysis | paid work, transportation | Anemia | Greece | Greece |
| Gandjour & Chernyak, 2011 [126] | Opinion or perspective | n/a | n/a | n/a | n/a | Germany |
| Garau et al., 2015) [127] | Other empirical analysis | semi-structured interviews | paid work, unpaid work, equity/fairness, wealth, economic | n/a | Australia, France, Germany, Italy, Poland, South Korea, | United Kingdom |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| | | | growth, effect on other industry sectors than healthcare | | Sweden, United Kingdom | |
| L. Garrison et al., 2016 [57] | Theoretical or conceptual | n/a | real option value | n/a | n/a | USA |
| L. P. Garrison & Austin, 2007 [56] | Theoretical or conceptual | n/a | n/a | n/a | n/a | USA |
| L. P. Garrison et al., 2018 [128] | Theoretical or conceptual | n/a | n/a | n/a | n/a | USA |
| Gershon et al., 2019 [129] | Economic evaluation | CEA | QALY | Breast cancer | Sub-Saharan Africa | Israel |
| Getsios et al., 2012 [13] | Economic evaluation | CEA | QALY, caregiver (any), QALY caregiver, caregiver time | Alzheimer's disease | United Kingdom | USA |
| Goetghebeur & Cellier, 2018 [130] | Conference or policy forum summary | MCDA | patient perspective | n/a | n/a | Canada |
| Goetghebeur et al., 2010 [131] | Other empirical analysis | MCDA | clinical outcome (any), convenience of the treatment, equity/fairness, public health interest | Turner syndrome | Canada | Canada |
| Gomez et al., 2016 [132] | Economic evaluation | CEA | DALY, survival, out-of-pocket payments | Tuberculosis | South Africa, Brazil, Bangladesh, Tanzania | Netherlands /United Kingdom |
| Goodrich et al., 2012 [14] | Systematic review | n/a | caregiver (any), caregiver health status, QALY caregiver, carer-specific measures, carer's free time | n/a | n/a | United Kingdom |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Graham et al., 2016 [133] | Economic evaluation | CUA | QALY, paid work | Chronic spontaneous urticaria | United Kingdom | USA |
| Griffiths et al., 2013 [28] | Economic evaluation | CEA | DALY, paid work, out-of-pocket payments | Influenza | low- and middle-income countries | United Kingdom |
| Gupta et al., 2015 [18] | Economic evaluation | n/a | other health measure, caregiver (any), productivity caregiver | Alzheimer's disease | Japan | USA |
| Hayajneh et al., 2018 [134] | Economic evaluation | CEA | QALY, paid work | Hepatitis A | Jordan | Jordan |
| Hermans et al., 2018 [33] | Economic evaluation | CUA | QALY, paid work, unpaid work | Knee osteoarthritis | n/a | Netherlands |
| Higgins et al., 2014 [98] | Systematic review | n/a | convenience of the treatment | n/a | n/a | United Kingdom |
| Himmler et al., 2019 [34] | Economic evaluation | CEA | HAQ score, paid work, unpaid work, economic spillover | Psoriatic arthritis | Germany | Germany |
| Hoefman et al., 2013 [135] | Systematic review | n/a | caregiver (any) | n/a | n/a | Netherlands |
| Holko et al., 2018 [35] | Economic evaluation | CEA | QALY, paid work, unpaid work, transportation, special diet | Crohn's Disease | Poland | Poland |
| Hoogendoorn et al., 2013 [136] | Economic evaluation | CEA | QALY, paid work, out-of-pocket payments, transportation | COPD | Germany | Netherlands |
| Hoshi et al., 2012 [137] | Economic evaluation | CEA | caregiver (any), productivity caregiver | Pneumococcal diseases | Japan | Japan |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Hoshi et al., 2017b [38] | Economic evaluation | CEA | QALY, caregiver (any), productivity caregiver | Infant rotavirus | Japan | Japan |
| Hoshi et al., 2017a [138] | Economic evaluation | n/a | n/a | Herpes Zoster, Post-Herpetic Neuralgia | Japan | Japan |
| Hoshi et al., 2018 [139] | Economic evaluation | n/a | n/a | Pertussis | Japan | Japan |
| Hung & Chen, 2011 [140] | Economic evaluation | n/a | n/a | Hepatitis B | Taiwan | Taiwan |
| Hutton et al., 2010 [141] | Economic evaluation | CEA | QALY | Hepatitis B | China | USA |
| Ishiguro et al., 2010 [142] | Economic evaluation | CEA | opportunity costs linked with investments in different branches of an economy, productivity losses for the healthcare sector | Breast cancer | Japan | Japan |
| Jacobs et al., 2018 [143] | Economic evaluation | CEA, WTP | QALY, survival, clinical outcome (any), paid work, caregiver (any) | Atrial fibrillation | Netherlands | Netherlands |
| Jan, 2014 [144] | Systematic review | CBA, cost-consequence analysis | equity, community values | n/a | n/a | Australia |
| Jiménez et al., 2015 [145] | Economic evaluation | CEA, WTP | QALY, HrQoL, clinical outcome (any), paid work | Human papillomavirus | Norway | Norway |
| Jiménez et al., 2014 [146] | Economic evaluation | CEA, WTP | QALY, HrQoL, clinical outcome (any), paid work | Human papillomavirus | Norway | Norway |
| Jönsson et al., 2019 [147] | Systematic review | n/a | hope, real option value, innovation, scientific spillovers | n/a | Europe | Sweden |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Jönsson et al., 2009 [148] | Opinion or perspective | n/a | n/a | n/a | n/a | Sweden |
| Kang et al., 2013 [39] | Economic evaluation | CEA | clinical outcome (any), transportation, caregiver (any), productivity caregiver | Rotavirus | Korea | Korea |
| Kapol et al., 2016 [149] | Economic evaluation | CEA | QALY, clinical outcome (any), transportation, food expenditure | Hepatitis C | Thailand | Thailand |
| Kenworthy et al., 2017 [52] | Economic evaluation | CEA, WTP | QALY, clinical outcome (any), criminal justice system and victim costs | Opioid use disorder | n/a | United Kingdom |
| Keshavarz et al., 2016 [150] | Economic evaluation | CEA, CUA, WTP | QALY, survival, clinical outcome (any) | Hepatitis B | Iran | Iran |
| Khowaja et al., 2017 [151] | Other empirical analysis | qualitative analysis of focus groups | out-of-pocket payments, transportation | Pre-eclampsia | Pakistan | Canada |
| Kigozi et al., 2017 [32] | Systematic review | CEA, CBA, CUA | paid work, productivity as a production factor | n/a | n/a | United Kingdom |
| Kleij et al., 2017 [73] | Systematic review | n/a | n/a | n/a | n/a | Germany |
| Knies et al., 2010 [152] | Systematic review | Other | paid work | n/a | n/a | Netherlands |
| Koopmanschap et al., 2008 [153] | Systematic review | n/a | caregiver (any) | n/a | n/a | Netherlands |
| Kotirum et al., 2017 [154] | Economic evaluation | CEA, CUA, BIA | QALY, survival, clinical outcome (any), transportation, accommodation, caregiver (any) | Haemophilus influenzae type b | Thailand | Australia |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Krol & Brouwer, 2015 [36] | Systematic review | Other | paid work, unpaid work | Rheumatoid arthritis | n/a | Netherlands |
| Krol et al., 2012 [155] | Other empirical analysis | randomized trial / survey | paid work | n/a | n/a | Netherlands |
| Krol et al., 2016 [156] | Systematic review | Other | paid work, unpaid work | n/a | n/a | Netherlands |
| Krol et al., 2015 [19] | Systematic review | n/a | QALY, caregiver (any) | Multiple diseases | n/a | Netherlands |
| Kuhlmann & von der Schulenburg, 2017 [157] | Economic evaluation | CEA | QALY, paid work, out-of-pocket payments | Pneumococcal diseases | Germany | Germany |
| Lachaine, Mathurin, Barakat, & Couban, 2015 [158] | Economic evaluation | CEA | QALY, paid work | Acute promyelocytic leukemia | Canada | Canada |
| Lachaine, Mathurin, Barakat, & Schuh, 2015 [159] | Economic evaluation | CEA | QALY, paid work | Acute promyelocytic leukemia | Canada | Canada |
| Lachaine et al., 2014 [160] | Economic evaluation | CUA | QALY, paid work | Bipolar disorder | Canada | Canada |
| Lachaine et al., 2016 [46] | Economic evaluation | CEA | QALY, caregiver (any), productivity caregiver | ADHD | Canada | Canada |
| D. Lakdawalla et al., 2017 [66] | Theoretical or conceptual | n/a | insurance value | n/a | n/a | USA |
| D. Lakdawalla et al., 2018 [7] | Theoretical or conceptual | n/a | QALY, paid work, out-of-pocket payments, hope, real option value, scientific spillovers, insurance value, equity/fairness, fear of contagion | n/a | n/a | USA |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| D. Lakdawalla et al., 2012 [11] | Other empirical analysis | n/a | survival, hope | Cancer | n/a | USA |
| Lavelle et al., 2019 [15] | Systematic review | CEA | QALY, caregiver (any), QALY caregiver, productivity caregiver, out-of-pocket costs related to child's health condition | Childhood Illness in general | n/a | USA |
| Leelahavarong et al., 2010 [29] | Economic evaluation | CEA, CUA, BIA | QALY, paid work, transportation | Thalassemia | Thailand | Thailand |
| Levy et al., 2013 [161] | Economic evaluation | CEA | QALY | Myelodysplastic syndromes | Canada | Canada |
| Lin et al., 2019 [16] | Systematic review | Other | QALY, DALY, caregiver (any) | Alzheimer's disease | n/a | USA |
| Lindgren & Jönsson, 2012 [65] | Economic evaluation | CEA | QALY, survival, paid work, value of statistically saved life, caregiver (any), long-lasting benefit of a drug after patent expiration, consumption, and economic production | Cardiovascular disease | Sweden | Sweden |
| Lipton et al., 2018 [162] | Economic evaluation | Value Based Price | migraine frequency, paid work | Migraine | USA | USA |
| Lorenzoni et al., 2017 [163] | Economic evaluation | cost-consequence analysis | clinical outcome (any), paid work | Diabetes | Italy | Italy |
| Luyten et al., 2019 [164] | Other empirical analysis | Discrete choice | social value judgements | Vaccination in general | United Kingdom | Belgium |
| Maniadakis et al., 2013 [165] | Economic evaluation | CEA | QALY, relapse, adverse drug reactions, paid work | Depressive disorders | Greece | Greece |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Marsh, Ganz, et al., 2016 [69] | Theoretical or conceptual | n/a | environmental impact | n/a | n/a | United Kingdom |
| Marsh et al., 2012 [77] | Theoretical or conceptual | CEA, CBA, CUA, CVA, MCDA | n/a | n/a | n/a | United Kingdom |
| Marsh, IJzerman, et al., 2016 [71] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | United Kingdom |
| Messali et al., 2013 [166] | Economic evaluation | CEA | QALY, caregiver (any), caregiver time | Brain tumor (glioblastoma) | USA | USA |
| Morishima et al., 2013 [167] | Economic evaluation | CEA | QALY, out-of-pocket payments | Asthma | Japan | Japan |
| Nord & Johansen, 2015 [168] | Systematic review | n/a | equity/fairness | n/a | n/a | Norway |
| Nord, 2018 [169] | Theoretical or conceptual | CVA, WTP | n/a | n/a | n/a | Norway |
| Nord, 2015 [74] | Theoretical or conceptual | CVA, WTP, Person-trade off | QALY, equity/fairness | n/a | n/a | Norway |
| Nord & Johansen, 2014 [170] | Systematic review | WTP, Stated preference, Revealed preference | QALY, equity/fairness | n/a | n/a | Norway |
| Norman et al., 2013 [171] | Other empirical analysis | Stated preference methods | QALY, equity/fairness | n/a | Australia | Australia |
| Nuijten & Mittendorf, 2010 [172] | Economic evaluation | CEA | relapse, paid work, out-of-pocket payments, transportation | Relapsing remitting multiple sclerosis | Germany | Netherlands |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| O'Neill & Twelves, 2002 [100] | Theoretical or conceptual | n/a | convenience of the treatment | Cancer | n/a | United Kingdom |
| Olofsson et al., 2016 [173] | Other empirical analysis | Contingent valuation | equity/fairness | Cancer | Sweden | Sweden |
| Paris & Belloni, 2013 [3] | Systematic review | n/a | n/a | n/a | n/a | France |
| Park et al., 2018 [25] | Economic evaluation | CBA, WTP, Stated preference, Revealed preference | QALY, paid work, unpaid work | Human papillomavirus | United Kingdom | Hong Kong |
| Persson, 2012 [174] | Theoretical or conceptual | n/a | QALY, severity of disease | n/a | Sweden | Sweden |
| Petrou, 2014 [175] | Systematic review | Stated preference, Revealed preference | QALY, equity/fairness | n/a | n/a | United Kingdom |
| Petrou et al., 2013 [176] | Other empirical analysis | Person-trade off | QALY, equity/fairness | n/a | United Kingdom | United Kingdom |
| Pfeil et al., 2012 [43] | Economic evaluation | CUA, BIA | QALY, caregiver (any), caregiver time | Alzheimer's disease | Switzerland | Switzerland |
| Phelps & Madhavan, 2017 [81] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | USA |
| Philipson, Kamal-Bahl, et al., 2017 [8] | Opinion or perspective | n/a | n/a | n/a | n/a | USA |
| Philipson, Thornton Snider, et al., 2017 [177] | Economic evaluation | Other | QALY, caregiver (any), caregiver utility loss, use of special services for persistent disability, producer surplus | Childhood vaccination in general | USA | USA |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Prinja, Bahuguna, et al., 2017 [178] | Economic evaluation | CEA | QALY, survival, out-of-pocket payments, costs to school medical staff, costs for communication campaign | Human papillomavirus | India | India |
| Prinja, Kaur, et al., 2017 [179] | Economic evaluation | CEA | QALY, survival, out-of-pocket payments, transportation | Multiple myeloma | India | India |
| Qin et al., 2018 [180] | Economic evaluation | CEA | QALY, out-of-pocket payments | Advanced hepatocellular carcinoma | China | China |
| Ramos et al., 2017 [26] | Economic evaluation | CEA | QALY, hospitalizations, adverse events, paid work, out-of-pocket payments, transportation, caregiver (any) | Heart failure | Netherlands | Netherlands |
| Rasiel et al., 2005 [53] | Other empirical analysis | n/a | hope | n/a | n/a | USA |
| Reed et al., 2019 [70] | Conference or policy forum summary | CBA, MCDA | BADI | n/a | n/a | USA |
| Rezansoff et al., 2017 [51] | Other empirical analysis | n/a | violent behavior | Schizophrenia | Canada | Canada /USA |
| (Richardson & Schlander, 2019 [181] | Opinion or perspective | n/a | equity/fairness | n/a | n/a | Australia |
| Richardson et al., 2014 [182] | Other empirical analysis | Person-trade off, new method similar to PTO | n/a | n/a | Australia | Australia |
| Richardson et al., 2017 [183] | Other empirical analysis | Person-trade off, new method similar to PTO | equity/fairness | n/a | n/a | Australia |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Rotter et al., 2012 [184] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | USA |
| Ruggeri et al., 2013 [185] | Economic evaluation | CEA | QALY, paid work | Allergic rhinitis | Italy | Italy |
| Sanchez et al., 2012 [59] | Other empirical analysis | n/a | real option value | Chronic myeloid leukemia | n/a | USA |
| Saokaew et al., 2019 [40] | Economic evaluation | CUA, BIA | QALY, survival, cost of meals, transportation, caregiver (any), productivity caregiver including paid and unpaid work | Rotavirus | Thailand | Thailand |
| Schawo et al., 2015 [186] | Economic evaluation | CEA | QALY, caregiver (any), QoL of caregiver, education costs | ADHD | Netherlands | Netherlands |
| Shafrin et al., 2017 [54] | Other empirical analysis | n/a | hope | n/a | n/a | USA |
| Shaker & Greenhawt, 2018 [187] | Economic evaluation | CEA | QALY, other health measure | Peanut allergy | USA | USA |
| Shearer et al., 2017 [188] | Opinion or perspective | n/a | paid work | n/a | n/a | United Kingdom |
| Shih et al., 2012 [189] | Economic evaluation | CEA, CUA | QALY, survival | Breast cancer | Singapore | Singapore |
| Sohn et al., 2010 [41] | Economic evaluation | CEA | survival, transportation, caregiver (any), productivity caregiver | Pneumococcal diseases | Korea | South Korea |
| Somers et al., 2019 [190] | Other empirical analysis | Discrete choice, nominal group technique | treatment attributes, contextual issues | Cancer | n/a | United Kingdom |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Spijker-Huiges et al., 2014 [30] | Economic evaluation | CEA | other health measure, clinical outcome (any), paid work | Radiculopathy | n/a | Netherlands |
| Sribhutorn et al., 2018 [31] | Economic evaluation | CEA | QALY, paid work, additional food cost, transportation, caregiver (any), productivity caregiver, caregiver income loss | Influenza in acute coronary syndromes patients | Thailand | Thailand |
| Sussex et al., 2013 [10] | Theoretical or conceptual | CBA, WTP, Stated preference, Revealed preference, MCDA | n/a | n/a | n/a | United Kingdom |
| Sussman et al., 2018 [191] | Economic evaluation | CEA | QALY, paid work | Migraine | USA | USA |
| Sweeney & Goss, 2015 [64] | Other empirical analysis | n/a | innovation | Cancer | n/a | USA |
| Tantai et al., 2014 [192] | Economic evaluation | CUA | QALY, survival, paid work, transportation, time loss due to treatment, cost of food | Hepatitis B | Thailand | Thailand |
| Ter Wee et al., 2017 [193] | Economic evaluation | CUA | QALY, paid work, out-of-pocket payments, transportation | Rheumatoid arthritis | Netherlands | Netherlands |
| Thibault et al., 2015 [44] | Economic evaluation | CUA | QALY, caregiver (any) | Alzheimer's disease | USA | Canada |
| Thokala & Duenas, 2012 [80] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | United Kingdom |
| Thokala et al., 2016 [78] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | United Kingdom |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Thornton Snider et al., 2017 [60] | Other empirical analysis | Other | real option value | Melanoma | USA | USA |
| Thornton Snider et al., 2012 [194] | Economic evaluation | CEA | QALY, real option value | n/a | n/a | USA |
| Tilford & Payakachat, 2015 [195] | Opinion or perspective | n/a | caregiver (any), family spillover effects | n/a | n/a | USA |
| Tran-Duy et al., 2018 [196] | Economic evaluation | CEA, WTP | QALY, paid work | Rheumatoid arthritis | Netherlands | Netherlands |
| van Hulst et al., 2018 [197] | Economic evaluation | CEA | n/a | Atrial fibrillation | Netherlands | Netherlands |
| van Lier et al., 2018 [198] | Systematic review | Other | paid work, unpaid work, out-of-pocket payments, transportation, health care cost, future related and unrelated cost, insurance value, intervention cost, value added tax | n/a | Europe | Netherlands |
| van Nooten et al., 2012 [199] | Theoretical or conceptual | n/a | innovation | n/a | n/a | United Kingdom |
| Vennera et al., 2016 [200] | Economic evaluation | CEA | exacerbations, paid work | Asthma | Spain | Spain |
| Verbooy et al., 2018 [37] | Other empirical analysis | WTP, Contingent valuation | unpaid work, leisure time | n/a | n/a | Netherlands |
| Verguet et al., 2015 [68] | Economic evaluation | CEA | survival, out-of-pocket payments, insurance value, financial risk | Tuberculosis | India | USA |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| | | | protection, distributional consequences | | | |
| Verguet et al., 2013 [67] | Economic evaluation | CEA | survival, out-of-pocket payments, insurance value, equity/fairness, financial risk protection, distributional consequences | Rotavirus | India, Ethiopia | USA |
| Wahlster et al., 2015 [83] | Systematic review | MCDA | n/a | n/a | n/a | Germany |
| Weinstein et al., 2003 [201] | Theoretical or conceptual | MCDA | n/a | n/a | n/a | USA |
| Westendorp et al., 2018 [202] | Economic evaluation | CEA, CUA | QALY, mRS scale, paid work, out-of-pocket payments | Stroke | Netherlands | Netherlands |
| Whittington et al., 2019 [203] | Economic evaluation | CEA, CUA | QALY, survival, paid work | Rheumatoid arthritis | USA | USA |
| Wildman & Wildman, 2019 [75] | Theoretical or conceptual | CBA, mixed-method approach | n/a | n/a | n/a | United Kingdom |
| Wilson et al., 2012 [204] | Economic evaluation | CEA, CUA | QALY, survival, paid work | Cardiovascular disease | Belgium, Spain, Portugal, Italy | Belgium |
| Wu et al., 2013 [42] | Economic evaluation | CEA | survival, paid work, transportation, caregiver (any), productivity caregiver | Pneumococcal diseases | Taiwan | Taiwan |
| Wu et al., 2012 [22] | Economic evaluation | CEA | paid work, caregiver (any), productivity caregiver, herd effect | Pneumococcal diseases | Taiwan | Taiwan |

| Author(s), Year | Type of article | Methods or approach | Value elements | Disease or therapeutic area | Study country | First author affiliation |
|---|---|---|---|---|---|---|
| Xu et al., 2018 [47] | Economic evaluation | CEA | QALY, survival, caregiver (any), productivity caregiver, caregiver time loss, caregiver lost alternative compensation | Cancer | USA | USA |
| Yamin et al., 2016 [17] | Economic evaluation | CEA | QALY, out-of-pocket payments, transportation, caregiver (any), QALY caregiver, costs for childcare | Rotavirus | France | Israel /USA |
| Yin et al., 2012 [205] | Economic evaluation | CEA | n/a | Encephalitis | China | China |

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