How is the societal perspective defined in health technology assessment? Guidelines from around the globe

Running title: Societal perspective in health technology assessment guidelines

Tuba Saygın Avşar[1], Xiaozhe Yang[2], Paula Lorgelly[3]

[1] Department of Applied Health Research, University College London, UK, ORCID ID: 0000-0002-4143-3852, correspondence: t.avsar@ucl.ac.uk

[2] Institute of Global Health, UCL

[3] School of Population Health & Department of Economics, University of Auckland, New Zealand

Word count: 5,620

ABSTRACT

Some researchers have argued that the aim of an economic evaluation should be to offer guidance on resource allocation based on the interest of the public from a societal perspective. The application of a societal perspective in health technology assessment (HTA) while common in many published studies is not mandated in most countries, and there is limited discussion on what the societal perspective should encompass. This study aimed to systematically compare and contrast the HTA guidelines in different countries.HTA methods guidelines were identified through international HTA networks, such as ISPOR and GEAR. The respective HTA agencies were grouped into two categories: well-established and newly-developed, based on the establishment date. Data extracted from the guidelines summarised the methodological details in the reference cases, including specifics on the societal perspective. The database search yielded 46 guidelines, and 65% explicitly considered the societal perspective. The maturity of these agencies is reflected in their attitudes towards the societal perspective; the societal perspective is defined in 70% of the guidelines of well-established agencies and only 56% of those of newly-developed agencies. The guidelines from multi-payer healthcare systems are more likely to consider the societal perspective. Although most guidelines from the well-established agencies recommend the inclusion of a societal perspective, the types of costs and consequences that should be included and the recommended approaches to valuing them are variable. The direct costs to family and carers are included in 73% of the societal perspective definitions and non-health outcomes were considered in only 40%. Most HTA guidelines lack clear guidance on what to include under specific perspectives. Considering the recent advancements in economic evaluation methods, it is timely to re-think the role of the societal perspective in HTA guidelines and adopt a more comprehensive perspective to include all costs and consequences of healthcare services.

Keywords: Health technology assessment, societal perspective, economic evaluation

Key points

- Most HTA guidelines are insufficient in providing clear guidance on what to include under different perspectives.
- 70% of guidelines published by well-established agencies and 56% by newly developed agencies explicitly consider the societal perspective, although there are substantial variations in how societal perspective is defined.
- International collaboration is needed to reach a consensus that would help align the evidence base and provide an opportunity for consistency in the definitions of costs and outcomes under the societal perspective.

1. Background

Economic evaluations help guide the allocation of scarce health care resources by comparing the costs and consequences of alternative interventions, practices, and policies. The perspective of an economic evaluation is a key dimension; it can either be that of the patient, the healthcare provider, the healthcare funder, the healthcare system or society. In his seminal paper Torrance [1] argues that "*The appropriate viewpoint depends on the question to be answered … [and] In general, the societal viewpoint is the appropriate one for public policy decision making*" (p.7). Despite this early support for the societal perspective, the healthcare funder or healthcare system perspective often dominates, but as interventions have become more complex, the societal perspective is often promoted as it can identify cost-shifting between sectors and on to patients and their families [2]. Additionally, it is now more widely acknowledged that there are benefits beyond those experienced by patients, particularly to caregivers [3].

A specific definition of the societal perspective is absent from the health economics literature, particularly with respect to the breadth of what should be included [4-6]. In practice, the societal perspective is vague and often applied opportunistically depending on what information is collected and available. Many studies that claim to use a societal perspective seemingly omit relevant outcomes or costs, such that the societal perspective in the published literature often is less comprehensive than it could be. There are also variations in the methods used to measure and value all relevant elements as well as how to report the findings, as highlighted in the systematic review of economic evaluations which adopted a societal perspective.[6].

The second panel on cost-effectiveness in health and medicine recommends reporting two reference case analyses, from the healthcare perspective and the societal perspectives [7]. Recently Walker et al. [8] developed a framework for the economic evaluation of policies with costs and outcomes falling on different sectors and involving different decision-makers. They argue that such a framework would avoid the use of the abstract societal perspective and help conceptualise the societal perspective by defining dimensions that require a trade-off. Additionally, there are other goals that society may wish to achieve when allocating scarce resources, such as equity [9] or sustainability [10].

The use of economic evaluation to inform healthcare decision-making, especially in advanced economies, is well established. Health technology assessment (HTA) guidelines, designed and published by HTA agencies to ensure a consistent and transparent standard of practice, document the methods for economic evaluations which are intended to inform decision-making. There is significant variation in HTA guidelines published in different countries [11], including with respect to the perspective they recommend. Culyer and colleagues found that 34% of all published guidelines recommend the societal perspective, and it is not an official requirement of the reimbursement decisions in most countries [12].

Although some guidelines recommend the societal perspective, the recommended methods for identifying, measuring, and valuing costs and outcomes vary. HTA guidelines from different countries have been reviewed previously with a specific focus on time horizon, costs, outcomes, discounting, sensitivity analysis, equity aspects, and results [13]. However, to the best of our knowledge, an overview with a specific focus on the societal perspective and how it is explicitly defined in HTA guidelines has not been undertaken. This paper compares and contrasts how different HTA agencies consider the societal perspective in their respective guidelines. Such information can contribute to the development of new guidelines and encourage a discussion on an internationally accepted definition of the societal perspective. Additionally, the paper provides a useful resource for informing manufacturers making submissions on how to design their evidence generation strategies to collect relevant data.

2. Methods

Data

Country-specific HTA guidelines were mainly identified through the websites of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and Guide to Economic Analysis Research (GEAR). Additionally, the websites of the Heath Technology Assessment International (HTAi), the International Network of Agencies for Health Technology Assessment (INAHTA) Network of HTA Agencies in the Asia-Pacific (HTAsiaLink), the HTA Network of the Americas (RedETSA) and the International Decision Support Initiative (iDSI) were searched for any additional national guidelines. The search for guidelines was conducted in June 2021 and then updated in February 2022. The websites either included the guidelines or provided the links to the guidelines. The agency websites were checked for more recent versions of the guidelines. The inclusion and exclusion criteria were as follows:

- The most recent guideline published by an agency was included, and previous versions were excluded except to confirm the date an agency was established.
- National guidelines were included; the guidelines that covered a single region of a country were excluded.
- Documents identifying the process of HTA rather than providing technical recommendations on methods were excluded.

Data extracted from each guideline summarised the methodological details in the reference case, including any specifics on the societal perspective in the reference case or its use in supplementary/scenario analyses. The definitions of direct and indirect costs and outcomes employed in this study were adopted from Drummond et al. [14], as summarised in Table 1.

Table 1 Types of costs and outcomes accrued by different stakeholders

Types of costs and outcomes	Definitions	Stakeholders
Direct medical costs	Medical costs (prevention or treatment)	Healthcare system, patients, family and carers
Direct non-medical costs	Transportation and accommodation costs, and other costs	Healthcare system, patients, family and carers
Indirect costs	Productivity costs, and other indirect costs	Patients, family, and carers
Health outcomes	Impacts on life expectancy, quality of life, and other health benefits (e.g., prevention)	Patients, family and carers
Non-health outcomes	Intangible outcomes, such as pain Impacts on education, crime, the environment, and other	Patients, family and carers Patients, family and carers, and other sectors

The guideline search and selection were completed by two authors independently, and the data extraction was undertaken by one author and checked by another. Information on the predominant funding systems of the countries when guidelines were identified were categorised using the Global Health Expenditure Dataset published by the World Health Organisation [15]. Additionally, the guidelines were grouped according to the numbers of payers in the countries based on the published literature [16-25].

Analysis

The evidence from the HTA guidelines was narratively synthesised, and the specifics of each guideline were compared. In order to explore the impact that a country's health system funding mechanism may have on the perspective, comparisons also took this (essentially the source of a countries health budget constraint) into consideration. The predominant funding system was defined by the highest proportion of healthcare expenditure as reported by WHO [15]. This included taxation, social insurance (mandatory contributory health insurance schemes, such as social health insurance), and out-of-pocket (direct out-of-pocket payment by households).

HTA is more institutionalised in advanced economies, with the establishment of HTA in Australia as early as 1990. Therefore, the HTA agencies were grouped into two categories: well-established and newly-developed agencies. A well-established HTA agency was defined as a national institution that was established before 2009, while those that were founded in 2009 or later were defined as newly-developed. Admittedly, this is a rather arbitrary date but it aligns with the publication of the ISPOR Taskforce on transferability across jurisdictions, which could promote the introduction of national

HTA agencies [26]. The establishment dates were obtained from the guidelines or the agency websites. However, if this was not available or the organisation that published the HTA was not founded as an HTA agency (e.g. Slovenia's Health Insurance Institute), this distinction was made based on the earliest guideline available online from the same agency.

3. Results

The ISPOR and GEAR websites listed 43 and 45 guidelines, respectively. Additionally, the iDSI website included the recently developed Indian HTA guidelines. After removing duplicates, 49 guidelines were identified; one guideline from Bhutan was excluded because it only defined the HTA process and did not include any technical guidance, and one guideline from the Catalan was excluded because its coverage is regional. Additionally, the Iranian guidelines were not accessible online. Since the Danish Centre for HTA was closed in 2012, their guidelines were excluded, and instead, the guidelines published by the Danish Medical Agency were included[27].

Overall, 46 guidelines from 51 countries were included (note that some agencies were cross-national, and the number of countries was greater than the number of guidelines), and 16 of these were published by newly-developed agencies (those post-2009). A list of all the guidelines is provided as a supplementary appendix. The selected guidelines, the corresponding countries, along with the publication year of the first and most recent HTA guidelines and the specifics regarding the perspective, are presented in Tables 2 and 3 for well-established and newly-developed agencies, respectively.

The societal perspective in HTA guidelines

The societal perspective features in 30 guidelines (65%). It is explicitly considered in 21 (70%) of the guidelines published by the well-established agencies and in nine (56%) of those published by the newly-developed agencies. The societal perspective is mandated in the reference cases of nine well-established (30%) and four newly-developed (25%) HTA agencies. Additionally, nine guidelines allowed supplementary analyses to be submitted from a perspective broader than healthcare but did not explicitly define this perspective as societal (Supplementary appendix, Table 3). For example, the Japanese guidelines allow productivity costs to be included as an additional analysis with do not mention a societal perspective [55], while Belgium allows "*analyses from a broader perspective*" but does not define this perspective [79].

Among the countries with a funding system that is dominated by taxation 27% recommend the societal perspective in the reference case similar to those with a social insurance-based system (29%). Notably, two out of six countries where the predominant funding method is out-of-pocket payment also recommend the societal perspective in the reference case [28, 29]. The number of payers in the healthcare systems has an impact on HTA agencies' approach the societal perspective. Among the countries with a single-payer healthcare financing system, 56% considered the societal perspective whereas the corresponding figure was 75% in the guidelines from multi-payer healthcare systems.

The societal perspective is most comprehensively defined in the Dutch guidelines, which suggest that "*all relevant societal costs and benefits, irrespective of who bears the costs or to who the*

benefits go, should therefore be taken into account in the evaluation and reporting" [27]. The Cuban guidelines explain that *the social perspective* is appropriate when the decision-maker pursues the public interest (as is the Cuban case) [30].

The Indian [28] and Indonesian [31] HTA agencies request both the societal and healthcare system perspectives in the reference case. The Indian guidelines refers to the multi-payer structure of the healthcare financing to justify the recommendation of presenting the analysis from a healthcare and societal perspective separately. Additionally, 17 agencies recommend [32-38] or allow [39–43, 45, 46, 54, 59, 85] the societal perspective as part of a complementary analysis. For example, Canada's guidelines [33] suggest that "*a societal perspective may be evaluated in a non-reference case analysis that allows for the full consideration of all costs and outcomes associated with the evaluation of the intervention*"(p.31). Similarly, the Irish guidelines [41] recommend undertaking additional analyses in some circumstances, not necessarily from a full societal perspective but including the impacts outside the healthcare system. These circumstances are defined as "*if there are significant costs or savings accruing to departments other than health (for example, the Department of Education). Inclusion of such an analysis must be clearly justified and supported by sufficient evidence*" (p.23).

Many guidelines, however, provide no description of specific circumstances regarding when to use the societal perspective; they only mention the types of costs and outcomes to be included in the analysis, including the German and Philippine guidelines [35, 43]. Therefore, although most agencies acknowledge the importance of the societal perspective, many guidelines either omit it or lack a detailed description of what it should encompass. As an exception, the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines list the costs and outcomes that should be included if an analysis is conducted from a societal perspective, providing some specific examples [33]. Additionally, most of the guidelines that recommend or allow for the societal perspective in an additional analysis do not specify the requirements of such analysis in the way that the reference case was presented. These guidelines do not explicitly recommend including all relevant costs and outcomes under the societal perspective but state that they may be included. For example, the Croatian guidelines state: *"including all cost and benefits outside the health care system, may be presented in addition, if considered relevant for some topics" [42]* (pg.16). Similarly, NICE suggests that "*in exceptional circumstances for medicines, when requested by the Department of Health and Social Care in the remit for the evaluation, the scope will list requirements for adopting a broader perspective on costs*" [40] (pg.39).

Costs to be included under the societal perspective

Table 4 summarises the types of costs and outcomes included within the societal perspective in addition to the healthcare perspective in the guidelines published by the 30 agencies which feature the societal perspective. The agency guidelines recommend submissions include diverse types of costs that are classified differently based on type (e.g. direct costs) or the stakeholder who accrues the cost (e.g. patient). Most guidelines suggest that all direct and indirect medical and non-medical costs and additional costs should be considered under the societal perspective [29, 30, 32-34, 37, 39, 41, 47-50]. Many countries exclude costs to other sectors [28, 31, 35, 40, 43, 50-52]. India's guidelines only mention direct medical and non-medical costs when considering the societal

perspective [28]. The implementation costs are considered only by the German HTA agency, it is suggested this should be estimated in a sensitivity analysis [35]; while the clinical trial costs are only mentioned in the South Korean guidelines, which explicitly state that expenses incurred in the clinical trial itself that are not incurred in the actual treatment process should not be included [53].

The Dutch guidelines offer a detailed description of costs to be included under the societal perspective and require the inclusion of costs for patient and family, such as travel expenses and unpaid work [47]. The Danish, Canadian and Indonesian guidelines also list all the costs to be included from the perspectives of provider, patient, payer, and societal, and provides detailed descriptions [27, 31, 33]. The Danish guidelines recommends including costs of pharmaceuticals, hospital costs, transport costs and time spent by patients and relatives, costs to general practitioners and practicing medical specialists, and municipal costs (home-care, rehabilitation, and disability equipment costs) [27]. According to CADTH [33], under the societal perspective, the costs incurred by the public healthcare payer can include drugs, medical devices, procedures, care at home, informal care and long-term care in nursing homes. The costs to patients can include any out-of-pocket expenses for healthcare, transport, paid caregivers, premiums paid to private insurers, and patients' time spent for travel and treatment. The costs to the government can include social services, affordable housing, and education.

The various HTA guidelines are found to be inconsistent with respect to terminology. For example, the Hungarian HTA guidance [36] defines travel costs as an indirect cost to patients, although they are usually considered direct non-medical costs, which is the definition employed by Drummond et al. [14]. While the Thailand guidelines defines "*time lost while receiving treatment*" as a direct non-medical cost that should be included in the reference case analysis (p.33)[50]. Indirect costs are either not defined or defined as productivity losses in most guidelines (e.g. IQWiG, HIQA [35, 41]) while unpaid work is not considered.

The various guidelines differ on whether to include productivity losses. Most guidelines (n=17) consider productivity costs under the societal perspective, while the Danish guidelines explicitly state that the productivity costs are never to be included [27]. Canada's CADTH states "*time lost from paid and unpaid work by both patients and informal caregivers as a result of illness, treatment, disability, or premature death should be included in an additional non-reference case analysis"* (p.21) [33]. Notably, although India adopts the societal perspective as the reference case in its guidelines, HTAIn exclude productivity loss in their definition of reference case [28]. Conversely, the Finnish and Japanese HTA agencies do not recommend the societal perspective but suggest conducting an additional analysis focusing on productivity costs [54, 55]. The Japanese guidelines state: "*Public healthcare payer's perspective is a standard perspective, but if the introduction of a selected technology has a direct influence on productivity, it is acceptable to perform an analysis that considers the broader costs and counts productivity loss as a cost"* [56] (p. 5).

Apart from the types of costs, some agency guidelines classify costs based on the types of stakeholders. Among the guidelines that explicitly consider the societal perspective, 63% include the costs to other sectors. Australia, Canada, and the Netherlands suggest that the costs incurred by the public healthcare system, private healthcare providers, patients, caregivers, and other social sectors, such as the government, should be considered [32, 33, 47]. For instance, the Dutch

guidelines defines the costs to other sectors as "*costs incurred in sectors outside the healthcare system, for example municipal services, education or voluntary work"* and "*Productivity losses: costs of absenteeism or unproductivity during paid work (presenteeism) and unpaid work*" (p. 28). In addition to these parties, the Canadian guidelines also adopt the costs borne by private insurers. For example, CADTH [33] suggests that "*a standard hospital stay may be covered by the public payer, but an upgrade to a private room may be paid for by the private payer; or if individuals with public drug plan coverage have to pay an annual deductible prior to receiving drug coverage, this deductible may be covered by private payers in cases in which individuals are covered by both private and public plans"* (p. 29). Moreover, England, India, and Norway recommend including a broad list of stakeholders which might incur resource use and costs relating to justice, education, and housing. Of the guidelines that recommend the societal perspective in the reference case, four omit costs to the sectors outside the healthcare system [28, 31, 50-52]. These guidelines do not provide any justification for excluding the costs to other sectors under the societal perspective.

Measuring and valuing productivity costs

Amongst the countries that allow for the inclusion of productivity loss under the societal perspective or as additional analysis, the methods adopted to measure and value productivity loss vary (see Table 55). The Friction Cost Approach (FCA) and Human Capital Approach (HCA) are the primary approaches. The HCA is a means to measure productivity loss in hours worked due to illness, while the FCA suggests that loss occurs only when the society is required to change workers owing to illness and that others could fill the vacancies in the short term [57]. Most countries prefer the HCA, while Canada, Germany, and the Netherlands recommend utilising the FCA to evaluate the costs incurred by productivity loss [29, 34, 35, 37, 46, 49, 52, 58]. The other countries that promoted the use of a societal perspective do not clearly state the specific methods to measure and value productivity costs [30-32, 41, 48, 51, 59, 60]. For example, Australia's guidelines adopt fundamental assumptions, including production made up of replacement workers if the patient is absent for an extended period who would otherwise be out of work [32]. This approach to valuing productivity loss is consistent with the FCA, but this is not clearly stated in the guidelines.

Outcomes to be included under the societal perspective

National HTA guidelines that recommend the inclusion of several types of outcomes and various outcome measures under the societal perspective, are summarised in Table 6 However, there is ambiguity since most guidelines do not explicitly define what outcomes should be included under the societal perspective. The guidelines from Australia, Canada, Ireland, the Netherlands, Scotland, and Taiwan suggest that all health and non-health outcomes to patients, caregivers, community, and dependents should be considered [32, 33, 38, 41, 47, 58]. England, Croatia and Cuba recommend including all health outcomes of patients, family and carers, excluding non-health outcomes [30, 40, 42]. In contrast, the newly-developed agency guidelines generally suggest including the impacts on patients only, except the guidelines from India that promote the

presentation of the impacts on carers as well [28]. The Chinese, Danish, Indonesian, Norwegian, and Portuguese guidelines include non-health outcomes for patients only [27, 29, 31, 51, 52].

The Indian guidelines suggests submissions "*use a measure of health outcome that is broad to capture all socially valued aspects of health*" without naming any specific outcome. Similarly, the Scottish guidelines states that any non-health benefits that have a value to individuals should be noted with no further explanation [38]. Many guidelines (n=12) state that including non-health outcomes is necessary from the societal perspective. However, only the CADTH's guidelines specifically lists the types of non-health benefits, which include the reduction in criminal behaviour and better educational achievements. The Australian PBAC guidelines provide an example of non-health outcomes such as a more convenient form of drug administration to the patient while the Irish HIQA mentions improved education attainment that may be included under the societal perspective [32, 41].

Specific measures of health benefits are referred to in the various guidelines, such as quality-adjusted life years (QALY), disability-adjusted life years (DALY) and life-years gained (LYG) (Table 66). Most countries recommend the use of QALYs while natural units are recommended by seven agencies [30, 36, 39, 42, 48, 60]. Brazil, India and Indonesia also recommend using DALYs [28, 31, 34]. With respect to the non-health benefits, the Australian and Canadian guidelines recommend distinct approaches to evaluate non-health benefits, including conjoint analysis, discrete choice experiments, cost-consequence analysis (CCA), cost-benefit analysis (CBA), time-trade-off and standard gamble, while others do not specify any measures or methods [32, 33].

None of the national guidelines mentioned environmental impacts.

4. Discussion

To the best of our knowledge, this is the first study to explore how the societal perspective has been incorporated into the HTA guidelines of different countries. The study finds notable differences in how HTA agencies approach the societal perspective. Some well-established agencies adopt the societal perspective as the reference case or recommend it to be presented in additional analyses, while other agencies have narrow budget perspectives, which exclude the costs and consequences outwith the healthcare system. The guidelines from agencies based in countries with multi-payer systems are more likely to consider a societal perspective explicitly. There are substantial variations in the definition of the societal perspective in the HTA guidelines regarding the types of costs and outcomes to be included and the recommended methods for measuring and valuing these. The study findings also indicate that most guidelines which recommend or allow the societal perspective actually refer to a perspective that is wider than the healthcare system but not a full societal perspective that covers all the health and cost outcomes to the broader society. The Danish guidelines acknowledged this by defining the recommended perspective as the limited societal perspective.

HTA methodologies are continually evolving, and this is true of the HTA agencies reviewed, each is at a different stage and degree of development. The maturity of a country's guideline is reflected in the attitudes towards the societal perspective. While most guidelines published by well-established HTA agencies (70%) accept the inclusion of a societal perspective even though it might not be the

reference case, among the newly-developed HTA agencies, only nine (56%) guidelines explicitly considered the societal perspective. One of the potential reasons behind the difference in the breadth of perspective between well-established and newly-developed HTA agencies might be a country's limited resources; undertaking an analysis that employs the societal perspective usually requires primary data collection and patient self-reporting, which could increase research costs [61] and introduce heterogeneity in multinational trials that is difficult to address. A limited budget, may mean evidence on the return on investment for payers or the healthcare system is prioritised [62]. Moreover, some employees and contractors of newly-developed HTA agencies may not have the skills, capacity or data to undertake analyses from a societal perspective.

At odds with this is that some high-income countries (e.g. Finland and New Zealand) do not recommend the societal perspective. This may in part be explained by the fact that there are degrees of maturity or it may reflect an explicit choice under a fixed budget. For example, the New Zealand guidelines state, "*If societal costs were included in analyses, this could result in Pharmac considering issues it has no control over*" (p.49). This reflects the opportunity cost of healthcare investment decisions, while it might be acknowledged that healthcare has costs and consequences beyond the health sector, these are not within the scope of the health budget (and specifically for Pharmac, the pharmaceutical budget that they control).

One of the key variations across countries that this study identified was whether productivity costs were included in a societal perspective. In the HTA guidelines included in this study, half allow and over a third (37%) recommend the inclusion of productivity loss in their societal perspective. It is noteworthy that India and Norway suggest the exclusion of productivity loss even though they adopt the societal perspective in the reference case. One reason for neglecting productivity loss might be the difficulties in measuring and valuing productivity loss, particularly given the extent of the informal sector in India. FCA and HCA were the most common methods suggested to valuing productivity loss. Several agencies reviewed in the study recommend FCA since HCA uses unrealistic assumptions and overestimates productivity costs [33]. Nevertheless, the implementation of FCA has been limited as reliable data on country-specific periods of friction are insufficient [11].

Another issue is the inclusion of additional costs such as social care, which are incurred by other sectors, including the community and judiciary systems. Amongst the guidelines that recommend adopting a societal perspective, 37% concur that costs incurred by the other sectors should be excluded. None of the guidelines identified in the review discusses how to measure and value these costs, which might illustrate that most countries encounter difficulties in calculating these. For instance, the Irish HTA agency states, "*the policy-makers in reality could not capture all costs and outcomes within the other sectors"* [41]. One reason for the omission of additional costs in economic evaluations is that the research on approaches to identify, measure and value costs that are outside the healthcare system are lagging behind the improvements in healthcare technologies [62]. The other reason is that the inclusion of costs outside the healthcare system can be seen as double-counting because these effects might already be included in health outcome measures, such as QALYs [2].

With respect to the outcomes, most of the guidelines from the countries with well-established HTA agencies suggest that all health and non-health effects on patients and caregivers should be

considered. Many guidelines only considered the direct health impacts on patients, overlooking the potential outcomes on the health of the other groups such as caregivers [30, 34, 39, 48, 63, 64]. However, under the societal perspective, all health outcomes, including spillover effects, should be considered. The Dutch HTA guidelines set a good example that all direct health effects and non-health effects for patients and carers are considered under the societal perspective [47]. Neglecting these health impacts occurred by others might prevent decision-making authorities from achieving the ultimate objective of optimising social health [65].

Consideration of the non-health effects is also important in scoping the societal perspective. Most HTA guidelines overlook the consequences beyond health. There are 12 countries that recommend including non-health impacts in the economic evaluation from a societal perspective. However, no country clearly defines the types of non-health outcomes to be included in the analysis except Canada [33]. Mastrigt et al. [66] identified some potential challenges of incorporating non-health benefits in economic evaluations, including the difficulties in identifying all types of non-health consequences and exploring the suitable approaches to measure and value these outcomes. Which non-health benefits should be included in the HTA guidelines is a question that warrants further research. Cost-effectiveness analysis utilising a multi-sectorial method has been posited, this includes simultaneous assessment of outcomes in the healthcare system and, for example, in education and justice [67].

The review also finds that none of the HTA guidelines consider the environmental impacts despite the international recognition of the significant impact of health care on the climate crisis [68]. HTA agencies should have a leadership role with respect to exploring how best to consider the environmental impacts of health technologies and services. Some methods to incorporate the environmental impacts in economic evaluations have been proposed [69].

Some of the findings of this study were similar to the findings of the systematic review of the societal perspective in economic evaluations [6]. For example, amongst the economic evaluations claiming to adopt a societal perspective, few (36%) considered intersectoral health and cost outcomes other than the productivity costs; we find that 40% of the guidelines recommending the societal perspective included non-health outcomes. The parallels between the HTA guidelines and economic evaluations regarding the approaches towards the societal perspective is not surprising considering most published economic evaluations follow the HTA guidelines within their jurisdictions.

While this study provided a thorough review of HTA agencies' position and interpretation of the societal perspective, the agency guidelines included were limited to those available online. Additionally, the study followed a practical approach to identify the guidelines from the databases of international HTA networks, instead of conducting a systematic review. Notably, some guidelines are less detailed than desirable. For example, ICERs HTA guidelines [89] refers briefly to scenario analyses using a modified societal perspective, while ICERs more recent Value Assessment Framework [70] dedicates more than a page to a discussion of perspective. It is also important to acknowledge that some guidelines, China and Spain, were recommendations issued by academics rather than national HTA agencies, this however is unlikely to change the results reported, given academics are often involved in the development and review of agency guidelines. Another consideration is that the categorisation of the HTA agencies as well-established and newly-

developed were based on an arbitrarily chosen time point (2009) to enable a comparison based on the maturity of the guidelines and the approaches towards the societal perspective. Furthermore, the types of costs and outcomes were classified based on the definitions of Drummond et al.[14] and Sanders et al. [7] and the number of healthcare payers were identified from the published studies [16-25], and different classifications could lead to different findings.

Beyond the scope of this study, but noteworthy to discuss is the relationship between decision thresholds and perspective. Cost-effectiveness thresholds cannot be separated from the choice of perspective in HTAs. There are limited studies on whether a different threshold should be utilised for analyses undertaken from a wider perspective [70, 71]. Demand-side thresholds rely on willingness to pay (WTP) while supply-side thresholds are estimated based on opportunity costs of disinvesting [72]. It can be argued that under a fixed healthcare budget, adopting a societal perspective instead of health system would require a lower supply-side threshold due to opportunity costs outside the health system while the demand-side threshold would not necessarily change. Thus, HTA agencies in countries with a flexible healthcare budget and/or a demand-side threshold might be more likely to recommend the societal perspective. As discussed in previous studies HTA agencies usually adopt heuristic threshold values [73]. Thailand's HITAP and Canada's CADTH provide an exception, that is HITAP uses a demand-side threshold and recommends the use of societal perspective in the reference case while CADTH used a supply-side threshold and recommends the health system perspective [33, 74]. However, it is not clear if this is the case for all the HTA agencies and other factors may mediate the relationship between perspective and threshold. Since most guidelines do not include a cost-effectiveness threshold, an analysis of the relationship between the type of threshold adopted and the preferred perspective was not possible in this study but is an important area for future research.

5. Conclusion

Despite the substantial methodological advancements in economic evaluations since the inception of HTA agencies in the 1990s, most HTA guidelines are insufficient in providing clear guidance on what to include under different perspectives. It seems timely to reconsider the societal perspective and adopt (or at the very least define) a more comprehensive perspective to include all impacts of healthcare investments.

If national HTA agencies continue to limit the promotion of the societal perspective, there is no incentive for researchers or industry to further the methods nor collect the data that are needed to undertake evaluations from a societal perspective. If this were to happen it could significantly limit our understanding of the impact of health, and health economics' contribution to understanding the social determinants of health [75].

HTA agencies from across the globe have strong links and have recently collaborated to produce an internationally accepted definition of HTA [76]. This is an opportune time for a similar collaboration to explore the definition of the societal perspective. Each agency could still choose to have a different perspective, but a consensus would help align the evidence base and provide an

opportunity for consistency in the definitions of costs and outcomes and an understanding of where the opportunity costs and benefits foregone are experienced.

Culyer [77] has argued in support of this approach to progressing HTA, better informing decision making and ensuring better decisions; he argues *"Only if the societal approach is adopted will decision makers be confronted with a full information set of the costs and consequences of alternative actions; anything less comprehensive will necessarily be subject to omitted variable bias, probably of unknown sign and size, causing either over- or under-investment in new technologies (as well as in old ones)." (pg 33)* We ask, if not now, then when?

Disclosures and declarations

Funding: Tuba Saygın Avşar (TSA)'s time is supported by the National Institute for Health and Care Research ARC North Thames and UCLPartners. The views expressed in this publication are those of the author(s) and not necessarily those of the National Institute for Health and Care Research or UCLPartners.

Conflict of interest: None.

Ethics approval: Not applicable.

Data availability: All the reports in this study are available online.

Author contributions: All authors contributed to the study conception and design. Material preparation, data collection was performed by TSA and Xiaozhe Yang while the analysis was conducted by TSA and Paula Lorgelly (PL). The text was written by TSA and all authors reviewed and approved the manuscript.

Acknowledgements: This paper was presented at the Health Economists' Study Group Winter meeting, Leeds 2022. The authors are grateful to Kara Hansen for her insightful discussion and members of the audience for their suggestions and contributions, the paper has been considerably improved thanks to this societal effort.

References

1. Torrance, G.W., *Measurement of health state utilities for economic appraisal: A review.* Journal of Health Economics, 1986. **5**(1): p. 1-30.
2. Jönsson, B., *Ten arguments for a societal perspective in the economic evaluation of medical innovations*. 2009, Springer. p. 357-359.
3. Al-Janabi, H., A. Manca, and J. Coast, *Predicting carer health effects for use in economic evaluation.* PLoS One, 2017. **12**(9): p. e0184886.
4. Kim, D.D., et al., *Perspective and Costing in Cost-Effectiveness Analysis, 1974–2018.* PharmacoEconomics, 2020. **38**(10): p. 1135-1145.
5. Neumann, P.J., *Costing and Perspective in Published Cost-Effectiveness Analysis.* Medical Care, 2009. **47**(7): p. S28-S32.
6. Drost, R.M., et al., *Conceptualizations of the societal perspective within economic evaluations: a systematic review.* International journal of technology assessment in health care, 2017. **33**(2): p. 251-260.
7. Sanders, G.D., et al., *Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine.* Jama, 2016. **316**(10): p. 1093-1103.
8. Walker, S., et al., *Striving for a societal perspective: a framework for economic evaluations when costs and effects fall on multiple sectors and decision makers.* Applied health economics and health policy, 2019. **17**(5): p. 577-590.
9. Culyer, A.J. and Y. Bombard, *An equity framework for health technology assessments.* Medical Decision Making, 2012. **32**(3): p. 428-441.
10. Nicol, E., *Sustainability in healthcare: efficiency, effectiveness, economics and the environment.* Future Healthc J, 2018. **5**(2): p. 81-81.
11. Sharma, D., et al., *National healthcare economic evaluation guidelines: a cross-country comparison.* PharmacoEconomics-Open, 2021: p. 1-16.
12. Culyer, A., et al., *Rival perspectives in health technology assessment and other economic evaluations for investing in global and national health. Who decides? Who pays?* F1000Research, 2018. **7**.
13. Mathes, T., et al., *Methods of international health technology assessment agencies for economic evaluations-a comparative analysis.* BMC health services research, 2013. **13**(1): p. 1-10.
14. Drummond, M.F., et al., *Methods for the economic evaluation of health care programmes*. 2015: Oxford university press.
15. World Health Organisation, *Global Health Expenditure Database*. 2021.
16. Bichay, N., *Health insurance as a state institution: The effect of single-payer insurance on expenditures in OECD countries.* Social Science & Medicine, 2020. **265**: p. 113454.
17. Kanavos, P., et al., *Latin America Healthcare System Overview. A comparative analysis of fiscal space in healthcare.* London: London School of Economics and Political Science, 2019.
18. World Health Organization, *The Kingdom of Thailand health system review.* 2015.
19. Myint, C.-Y., et al., *A systematic review of the health-financing mechanisms in the Association of Southeast Asian Nations countries and the People's Republic of China: lessons for the move towards universal health coverage.* PloS one, 2019. **14**(6): p. e0217278.
20. Vončina, L. and I. Rubil, *Can people afford to pay for health care? New evidence on financial protection in Croatia.* 2018.
21. Cheng, Q., et al., *Equity of health financing in Indonesia: A 5-year financing incidence analysis (2015–2019).* The Lancet Regional Health-Western Pacific, 2022. **21**: p. 100400.
22. Verma, A.K., M.A. Hassali, and F. Saleem, *Health care financing in Malaysia: A way forward.* Archives of Pharmacy Practice Vol, 2015. **6**(4).
23. Philippines, D.o.H., *The Philippine health system at a glance.* 2008.
24. Nikulina, O. and A. Ratkin. *Current state of financing health care system in Russia: regional aspect*. in *SHS Web of Conferences*. 2020. EDP Sciences.
25. Singapore Ministry of Health. *Healthcare schemes and subsidies*. 2022 [cited 2022; Available from: https://www.moh.gov.sg/cost-financing/healthcare-schemes-subsidies.

26. Drummond, M., et al., *Transferability of economic evaluations across jurisdictions: ISPOR Good Research Practices Task Force report.* Value in health, 2009. **12**(4): p. 409-418.
27. Medicinrådets. *The Danish Medicines Council methods guide for assessing new pharmaceuticals*. 2021; Available from: https://medicinraadet.dk/media/wq0dxny2/the_danish_medicines_council_methods_guide_for_assessing_new_pharmaceuticals_version_1-2_adlegacy.pdf.
28. Health Technology Assessment in India [HTAIn]. *Health Technology Assessment in India: A Manual*. 2018 23.11.2021]; Available from: https://htain.icmr.org.in/images/pdf/htain%20manual.pdf.
29. Gordon, G., et al. *China Guidelines for Pharmacoeconomic Evaluations*. 2020 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/China-Guidelines-for-Pharmacoeconomic-Evaluations-2020.pdf.
30. Ministry of Health (Cuba). *Methodological Guidelines for Health Economic Evaluation*. 2003 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/Methodological-Guidelines-for-Health-Economic-Evaluations-in-Cuba.pdf.
31. Indonesian Health Technology Assessment Committee [InaHTAC]. *Health Technology Assessment Guideline*. 2017 23.11.2021]; Available from: https://adphealth.org/upload/resource/FINAL_HTA_ENG_-1.pdf.
32. Pharmaceutical Benefits Advisory Committee [PBAC]. *Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee: Version 5.0.* . 2016 09.11.2021]; Available from: https://pbac.pbs.gov.au/content/information/files/pbac-guidelines-version-5.pdf.
33. Canadian Agency for Drugs and Technologies in Health [CADTH]. *Guidelines for the economic evaluation of health technologies: Canada*. 2017 09.11.2021]; Available from: https://www.cadth.ca/sites/defaul t/files/pdf/guidelinesfortheeconomicevaluationofhealthtechnologiescanada4thed.pdf.
34. Ministry of Health (Brazil). *Economic Assessment Guideline* 2014 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/Avaliacao_Economica_Brazil2014.pdf.
35. Institute for Quality and Efficiency in Health Care [IQWiG]. *General Methods: Version 6.0.* . 2020 23.11.2021]; Available from: https://www.igwig.de/methoden /general-methodsversion-6-0.pdf
36. HU WO. *Professional healthcare guideline on the methodology of health technology assessment*. 2017 01.12.2021]; Available from: https ://tools.ispor .org/PEgui delin es/sourc e/HTA_Guide line_HUN_eng.pdf.
37. Agencja Oceny Technologii Medycznych (Poland). *Health technology assessment guidelines (version 3.0).* . 2016 01.12.2021]; Available from: https://www2.aotm.gov.pl/wp-conte nt/uploa ds/wytyczne_hta/2016/20161104_HTA_GuidelinesAOTMiT.pdf.
38. Scottish Medicines Consortium. *Guidance to Submitting companies for completion of new product assessment form.* 2021 01.12.2021]; Available from: https://www.scottishmedicines.org.uk/media /4527/20190626-guidance-on-npaf.pdf.
39. Behmane D, L.K., Irs A, Steikunas N. *Baltic guideline for economic evaluation of pharmaceuticals (pharmacoeconomic analysis)*. 2002 01.12.2021]; Available from: https://tools.ispor.org/PEguidelines/source/Baltic-PE-guideline.pdf.
40. National Institute for Health and Care Excellence [NICE]. *NICE health technology evaluations: the manual*. 2022 17.05.2022]; Available from: https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781.
41. Health Information and Quality Authority [HIQA]. *Guidelines for the economic evaluation of health technologies in Ireland: Version 6*. 2020 09.11.2021]; Available from: https://www.higa.ie/sites/default/files/2020-09 /HTAEconomic-Guidelines-2020.pdf.
42. Care, A.f.Q.a.A.i.H. *The Croatian Guideline for Health Technology Assessment Process and Reporting, 1st ed.* . 2011 01.12.2021]; Available from: https://tools.ispor.org/PEguidelines/countrydet.asp?c=41&t=4.
43. Health Technology Assessment Unit. *Philippine HTA methods guide*. 01.12.2021; Available from: https://hta.doh.gov.ph/philippine-hta-methods-guide/.
44. Health Insurance Institute of Slovenia. *Rules on the Classification of Medicinal Products*. 2013 16.01.2022]; Available from: http://www.uradni-list.si/1/content?id=112932.

45. Institute of Technological Evaluation in Health [IETS]. *Manual for the development of economic evaluations in health*. 2014 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/Methodological-Guidelines-for-Health-Economic-Evaluations-in-Cuba.pdf.
46. Walter, E.Z.S. *Guidelines on health economic evaluation, consensus paper.* . 2006 01.12.2021]; Available from: https://tools.ispor.org/PEguidelines/source/Guidelines_Austria.pdf.
47. National Health Care Institute [NHCI]. *Guideline for economic evaluations in healthcare* 2016 23.11.2021]; Available from: https://tools.ispor.org/PEguidelines/source/Netherlands_Guideline_for_economic_evaluations_in_healthcare.pdf.
48. López-Bastida, J., et al., *Spanish recommendations on economic evaluation of health technologies.* The European Journal of Health Economics, 2010. **11**(5): p. 513-520.
49. The Swedish Dental and Pharmaceutical Benefits Agency (TLV). *Amendment to the Swedish Dental and Pharmaceutical Benefits* 2017 16.01.2022]; Available from: https://www.tlv.se/.
50. Ministry of Public Health. *Ministry of Public Health guidelines for health technology assessment in Thailand (2nd ed)*. 2014 01.12.2021]; Available from: https://www.hitap.net/docum ents/168738.
51. Norwegian Medicines Agency [NoMA]. *Guidelines for the submission of documentation for single technology assessment (STA) of pharmaceuticals: version 2.0.* . 2018 23.11.2021]; Available from: https://legemiddelverket.no/Documents/English/Public%20funding%20and%20pricing/Documentation%20for%20STA/Guidelines%2018.10.2021.pdf.
52. Alves da Silva E, G.P.C., Sampaio C, et al. . *Guidelines for economic drug evaluation studies*. 1998; Available from: https://www.infarmed.pt/documents/281/1432055/PCAEC04vering.pdf.
53. Health Insurance Review & Assessment Service (HIRA). *Pharmaceutical Economic Evaluation Guidelines*. 2006 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/Korean_PE_Guidelines_Korean_Version.pdf.
54. Lääkkeiden Hintalautakunta (Finland). *Preparing a health economic evaluation to be attached to the application for reimbursement status and wholesale price for a medicinal product. 2019.* 2019 01.12.2021]; Available from: https://www.hila.fi/content/uploads/2020/01/Instructions_TTS_2019.pdf.
55. Kamae, I., et al., *Health technology assessment in Japan: a work in progress.* Journal of Medical Economics, 2020. **23**(4): p. 317-322.
56. Centre for Outcomes Research and Economic Evaluation for Health [C2H]. *Official Guideline for Cost-Effectiveness Evaluation*. 2019 23.11.2021]; Available from: https://c2h.niph.go.jp/tools/guideline/guideline_en.pdf.
57. Pearce , A., *Productivity Losses and How they are Calculated*. 2016, The Center for Health Economics Research and Valuation (CHERE).
58. Centre for Drug Evaluation. *Guidelines of methodological standards for pharmacoeconomic evaluations in Taiwan.* 2006 01.12.2021]; Available from: https://www.ispor.org/PEgui delin es/sourc e/2006_PEG_EN_2009.pdf.
59. Malaysian Ministry of Health [MMoH]. *Pharmacoeconomic Guideline for Malaysia*. 2019 23.11.2021]; Available from: http://www.pharmacy.gov.my/v2/ms
60. Danish Centre for Health Technology Assessment (DACEHTA). *Health Technology Assessment Handbook*. 2007 01.12.2021]; Available from: http://aaz.hr/resources/pages/57/1.%20HTA%20Handbook%20DACEHTA.pdf.
61. Griffiths, U.K., R. Legood, and C. Pitt, *Comparison of Economic Evaluation Methods Across Low-income, Middle-income and High-income Countries: What are the Differences and Why?* Health economics, 2016. **25**: p. 29-41.
62. Drost, R.M., A.T. Paulus, and S.M. Evers, *Five pillars for societal perspective.* International journal of technology assessment in health care, 2020. **36**(2): p. 72-74.
63. Bobinac, A., et al., *Health effects in significant others: separating family and care-giving effects.* Medical Decision Making, 2011. **31**(2): p. 292-298.
64. Canaway, A., et al., *Close-person spill-overs in end-of-life care: using hierarchical mapping to identify whose outcomes to include in economic evaluations.* Pharmacoeconomics, 2019. **37**(4): p. 573-583.

65. Brouwer, W.B., *The inclusion of spillover effects in economic evaluations: not an optional extra.* Pharmacoeconomics, 2019. **37**(4): p. 451-456.
66. van Mastrigt, G.A., et al., *A qualitative study on the views of experts regarding the incorporation of non-health outcomes into the economic evaluations of public health interventions.* BMC public health, 2015. **15**(1): p. 1-17.
67. Claxton, K., M. Sculpher, and A. Culyer, *Mark versus Luke? Appropriate methods for the evaluation of public health interventions.* 2007.
68. Tennison, I., et al., *Health care's response to climate change: a carbon footprint assessment of the NHS in England.* The Lancet Planetary Health, 2021. **5**(2): p. e84-e92.
69. Marsh, K., et al., *Incorporating environmental outcomes into a health economic model.* International journal of technology assessment in health care, 2016. **32**(6): p. 400-406.
70. Thokala, P., et al., *Cost-effectiveness thresholds: the past, the present and the future.* Pharmacoeconomics, 2018. **36**(5): p. 509-522.
71. Remme, M., M. Martinez-Alvarez, and A. Vassall, *Cost-effectiveness thresholds in global health: taking a multisectoral perspective.* Value in health, 2017. **20**(4): p. 699-704.
72. Pandey, H., M. Paulden, and C. McCabe, *Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability. Edmonton, Canada: Institute of Health Economics (IHE); 2018*. 2021.
73. Sampson, C., et al., *Supply-Side Cost-Effectiveness Thresholds: Questions for Evidence-Based Policy.* Applied Health Economics and Health Policy, 2022. **20**(5): p. 651-667.
74. Teerawattananon, Y., et al., *The use of economic evaluation for guiding the pharmaceutical reimbursement list in Thailand.* Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen, 2014. **108**(7): p. 397-404.
75. Marmot, M., et al., *Closing the gap in a generation: health equity through action on the social determinants of health.* The lancet, 2008. **372**(9650): p. 1661-1669.
76. O'Rourke, B., W. Oortwijn, and T. Schuller, *The new definition of health technology assessment: A milestone in international collaboration.* International journal of technology assessment in health care, 2020. **36**(3): p. 187-190.
77. Culyer, T., *Are there really ten good arguments for a societal perspective in the economic evaluations of medical innovations?"*, in *Portrait of a Health Economist*, A. Culyer and G. Kobelt, Editors. 2014, Institute of Health Economics: Lund. p. 33-38.
78. The Belgian Health Care Knowledge Centre (KCE). *Belgian guidelines for economic evaluations and budget impact analyses: second edition. KCE Reports 183C.* 2012 01.12.2021]; Available from: https://kce.fgov.be/en/belgian-guidelines-for-economic-evaluations-and-budget-impact-analyses-second-edition.
79. State Institute for Drug Control (SKUL). *Procedure for assessing cost-effectiveness analysis* 2016 16.01.2022]; Available from: http://farmakoekonomika.cz/wp-content/uploads/2016/10/DP_CFES_13-10-2016_final.pdf.
80. Ministry of Health (Israel). *Guidelines for the submission of a request to include a pharmaceutical product in the national list of health services—Appendix D: instructions for performing an economic assessment.* 2010 01.12.2021]; Available from: https://tools.ispor.org/PEguidelines/source/Israel-Guidelines-for-submission2010.pdf.
81. Italian Medicines Agency (AIFA). *Guidance to applicants for the submission of pharmacoeconomic analysis within the Pricing and Reimbursement Dossier* 2020 16.01.2022]; Available from: https://www.aifa.gov.it/en/web/guest/home.
82. Pharmaceutical Management Agency (New Zealand). *Prescription for pharmacoeconomic analysis. Methods for cost-utility analysis version 2.2 2015* 2015; Available from: https://www.pharmac.govt.nz/assets/pfpa-2-2.pdf.
83. Ministry of Health (Russia). *Methodological Recommendations for Conducting A Comparative Clinical-Economic Assessment Of A Medicinal Preparation*. 2016 16.01.2022]; Available from: https://rosmedex.ru/wp-content/uploads/2016/12/MR-KE%60I-23.12.2016.pdf.
84. Ministry of Health (Slovak Republic). *Decree on the details of the pharmaco-economic analysis of the medicinal product*. 2011 16.01.2022]; Available from: https://www.zakonypreludi.sk/zz/2011-422.

85. Ministry of Health (South Africa). *Publication of the guidelines for pharmacoeconomic submissions*. 2013 01.12.2021]; Available from: https://tools.ispor.org/PEguidelines/countrydet.asp?c=38&t=4.
86. Taiwan Society for Pharmacoeconomic and Outcomes Research (TaSPOR). *Guidelines of methodological standards for pharmacoeconomic evaluations in Taiwan.* 2006 01.12.2021]; Available from: https://www.ispor.org/PEgui delin es/sourc e/2006_PEG_EN_2009.pdf.
87. Wu, T.-Y., A. Majeed, and K.N. Kuo, *An overview of the healthcare system in Taiwan.* London journal of primary care, 2010. **3**(2): p. 115-119.
88. Institute for Clinical and Economic Review (ICER). *A Guide to ICER's Methods for Health Technology Assessment*. 2020 16.01.2022]; Available from: https://icer.org/wp-content/uploads/2021/01/ICER_HTA_Guide_102720.pdf.
89. Ministry of Health and Population. *Pharmacoeconomic Unit, Central Administration for Pharmaceutical Affairs. Guidelines for reporting pharmacoeconomic evaluations in Egypt. Version 01.* 2013 01.12.2021]; Available from: <http://www.eda.mohp.gov.eg/Files /402Egyptian_Pharmacoeconomic_guidelines.pdf.
90. Haute Autorité de Santé [HAS]. *Choices in methods for economic evaluation. Saint-Denis La Plaine: Department of Economics and Public Health Assessment*. 2012 01.12.2021]; Available from: https://www.has-sante.fr/upload/docs/application/pdf/2012-10/choices_in_methods_for_economic_evaluation.pdf.
91. Common Market of the Southern Cone (MERCOSUR). *Methodological Guidelines for Studies of Economic Evaluation of Health Technologies* 2009 16.01.2022]; Available from: https://www.mercosur.int/.
92. General Health Council. *Guide for Conducting Economic Evaluation Studies for Updating the Basic Table and Catalog of Supplies of the Health Sector in Mexico.* . 2015 16.01.2022]; Available from: https://tools.ispor.org/PEguidelines/source/Mexico_GCEEE_2015.pdf.
93. Agency for Care Effectiveness [ACE]. *Drug Evaluation Methods and Process Guide: Version 1.0*. 2018 23.11.2021]; Available from: https://www.ace-hta.gov.sg/resources/process-methods#health-technology.
94. Swiss Federal Office of Public Health (BAG). *Manual for submitting applications for the assumption of costs for new or disputed benefits* 2009 16.01.2022]; Available from: https://www.bag.admin.ch/bag/de/home.html.

Table 2: Recommended perspectives of the guidelines published by well-established HTA agencies

Country	HTA Agency	Agency established date	Latest guideline	Mandatory	Predominant funding system (% h.care spending)	Single payer	Reference case perspective	Societal perspective considered[+]
Australia [32]	Pharmaceutical Benefits Advisory Committee (PBAC)	1990*	2016	Yes	Taxation (72%)	Yes	Healthcare	Yes
Austria [46]	Institute for Pharmacoeconomic Research	2003	2006	No	Taxation (36%)	No	Not specified	Yes
Baltic (Estonia, Latvia, Lithuania)[39]	Health authorities from Baltic countries	2002	2002	No	S. insurance (58%) Taxation (61%) S. insurance (40%)	No	Healthcare	Yes
Belgium[78]	Healthcare Knowledge Centre (KCE)	2006	2015	Yes	Taxation (39%)	No	Healthcare	No
Canada[33]	Canadian Agency for Drugs and Technologies in Health (CADTH)	1995*	2017	Yes	Taxation (67%)	No	Healthcare	Yes
Croatia[42]	Agency for Quality and Accreditation in Healthcare	2007	2011	Yes	S. insurance (66%)	No	Healthcare	Yes
Czech Republic[79]	State Institute for Drug Control (SUKL)	2007*	2020	No	S. insurance (54%)	Yes	Healthcare	No
Cuba[30]	Ministry of Health	2003	2003	No	Taxation (89%)	No	Societal	Yes
England[40]	National Institute for Health and Care Excellence (NICE)	2005	2022	Yes	Taxation (79%)	Yes	Healthcare	Yes
Germany[35]	The Institute for Quality and Efficiency in Health Care (IQWiG)	2004	2020	Yes	S. insurance (65%)	Yes	Healthcare	Yes
Hungary[36]	National Institute of Pharmacy and Nutrition	2005	2017	Yes	Taxation (47%)	No	Healthcare	Yes
Ireland[41]	Health Information and Quality Authority (HIQA)	2007	2020	Yes	Taxation (74%)	No	Healthcare	Yes
Israel[80]	Pharmaceutical Administration	2002	2010	No	Taxation (41%)	Yes	Healthcare	No
Italy[81]	Italian Medicines Agency	2003	2020	No	Taxation (74%)	Yes	Healthcare	No
Netherlands[47]	National Health Care Institute (NHCI)	2006	2016	Yes	S. insurance (60%)	No	Societal	Yes
New Zealand[82]	Pharmaceutical Management Agency (Pharmac)	1993	2015	Yes	Taxation (73%)	Yes	Healthcare	No
Norway[51]	Norwegian Medicines Agency (NoMA)	2007	2018	Yes	Taxation (86%)	No	Societal	Yes
Philippines[43]	Department of Health, Health Technology Assessment Unit	2000	2020	Yes	Out of pocket (49%)	No	Healthcare	Yes
Portugal[52]	National Authority of Medicines and Health Products (INFARMED)	1998	1998	Yes	Taxation (59%)	No	Societal	Yes
Russia[83]	Ministry of Health	2002*	2016	Yes	Taxation (40%)	Yes	Healthcare	No
Slovenia[44]	Ministry of Health, Health Insurance Institute	2006	2013	Yes	S. insurance (65%)	Yes	Healthcare	No
Scotland[38]	Scottish Medicines Consortium	2001	2021	Yes	Taxation (79%)	Yes	Healthcare	Yes
Slovak Republic[84]	Ministry of Health	2008*	2011	Yes	S. insurance (58%)	No	Not specified	No
South Africa[85]	National Department of Health Pricing Committee	2005	2013	No	Taxation (59%)	No	Healthcare	No
South Korea[53]	Health Insurance Review Agency (HIRA)	2000	2006	Yes	S insurance (43%)	Yes	Societal	Yes
Spain[48]	Study Group	NA	2010	No	Taxation (67%)	Yes	Societal	Yes
Sweden[49]	Dental and Pharmaceutical Benefits Agency (TLV)	2003	2017	Yes	Taxation (85%)	Yes	Societal	Yes
Taiwan[86]	Centre for Drug Evaluation (CDE)	2008*	2014	No	S insurance (100%)[87]	No	Societal	Yes
Thailand[50]	Ministry of Health	2007	2014	Yes	Taxation (65%)	Yes	Societal	Yes
USA[88]	Institute for Clinical and Economic Review (ICER)	2006	2020	No	Taxation (38%)	No	Healthcare	Yes

***Year of the first guideline available online. S. insurance: Social insurance**
[+] Explicitly mentioned the societal perspective and provided a definition albeit limited.

Table 3: Recommended perspectives of the guidelines published by newly-developing HTA agencies

Country	HTA Agency	Agency established date	Latest guideline	Mandatory	Predominant funding system (% h.care spending)	Single payer	Reference case perspective	Societal perspective considered[+]
China[29]	Study Group	NA	2020	No	Out of pocket (35%)	Yes	Societal	Yes
Brazil[34]	Ministry of Health	2009	2014	Yes	Taxation (40%)	No	Healthcare	Yes
Colombia[45]	The Evaluation Institute Technology in Health (IETS)	2012	2014	Yes	Taxation (36%)	Yes	Healthcare	Yes
Denmark[27]	Danish Medicines Council	2017	2021	Yes	Taxation (83%)	Yes	Societal	Yes
Egypt[89]	Egyptian Drug Authority (EDA)	2013*	2013	No	Out of pocket (63%)	No	Not specified	No
Finland[54]	Pharmaceutical Price Committee	2011*	2019	Yes	Taxation (76%)	No	Not specified	No
France[90]	Department of Economics and Public Health Assessment	2012*	2012	Yes	Social insurance (45%)	Yes	Healthcare	No
India[28]	Health Technology Assessment in India (HTAIn)	2016	2018	No	Out of pocket (55%)	No	Societal	Yes
Indonesia[31]	Indonesian Health Technology Assessment Committee (InaHTAC)	2013	2017	No	Taxation (35%)	No	Societal	Yes
Japan[55]	Centre for Outcomes Research and Economic Evaluation for Health (C2H)	2018	2019	Yes	Social insurance (50%)	No	Healthcare	No
Malaysia[59]	Ministry of Health Malaysia	2011*	2019	No	Taxation (52%)	No	Healthcare	Yes
MERCOSUR[91]	MERCOSUR (Argentina, Brazil, Paraguay, Uruguay)	2009*	2009	Yes	Social insurance (37%) Taxation (40%) Out of pocket (42%) Social insurance (36%)	Yes	Healthcare	Yes
Mexico[92]	General Health Council	2015*	2015	Yes	Out of pocket (42%)	Yes	Healthcare	No
Poland[37]	The Agency for Technology Assessment and Tariff System (AOTMIT)	2009	2016	Yes	Social insurance (60%)	No	Healthcare	Yes
Singapore[93]	Agency for Care Effectiveness (ACE)	2015	2018	No	Taxation (42%)	Yes	Healthcare	No
Switzerland[94]	Swiss Federal Office of Public Health (BAG)	2009*	2009	Yes	Social insurance (36%)	Yes	Healthcare	No

*** Year of the first guideline available online. NA: Not appliable**
[+] Explicitly mentioned the societal perspective and provided a definition albeit limited.

Table 4: Summary of the guidelines that explicitly considered the societal perspective

Country	Societal perspective in reference case (R) or additional analysis(A)	Direct medical costs to patients	Direct non-medical costs to patients	Indirect costs to patients	Direct medical costs to family & carers	Direct non-medical costs to family & carers	Indirect costs to family & carers	Costs to other sectors	Health outcomes to patients	Non-health outcomes to patients	Health outcomes to family & carers	Non-health outcomes to family & carers	Environmental impacts	% Within Country
Well-established HTA agencies														
Austria	U	Y	Y	Y	N	N	N	N	Y	N	N	N	N	31%
Australia	A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	85%
Baltic	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
Canada	A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	85%
Croatia	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
Cuba	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	69%
England	A	Y	N	Y	Y	N	Y	N	Y	N	Y	N	N	46%
Germany	A	Y	Y	Y	N	N	Y	N	Y	Y	Y	N	N	54%
Hungary	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
Ireland	A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	85%
Netherlands	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	92%
Norway	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y	N	N	62%
Portugal	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N	N	N	69%
Philippines	A	Y	Y	N	N	N	N	N	Y	N	N	N	N	23%
Scotland	A	Y	N	N	Y	N	N	Y	Y	Y	Y	Y	N	54%
South Korea	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	69%
Spain	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	69%
Sweden	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	69%
Taiwan	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	85%
Thailand	Y	Y	Y	N	N	N	N	N	Y	N	N	N	N	31%
USA	A	Y	Y	Y	Y	Y	Y	N	Y	N	Y	N	N	62%
Newly developing HTA agencies														
Brazil	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
China	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	77%
Colombia	A	Y	U	U	U	U	U	U	Y	U	U	U	N	15%
Denmark	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N	N	N	69%
India	Y	Y	Y	N	N	N	N	N	Y	N	Y	N	N	38%
Indonesia	Y	Y	Y	Y	N	Y	N	N	Y	Y	N	N	N	54%
Malaysia	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
MERCOSUR	A	Y	Y	Y	Y	Y	Y	N	Y	N	N	N	N	54%
Poland	A	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	62%
% Across Countries	43%	100%	87%	83%	73%	67%	73%	63%	100%	40%	37%	20%	0%	

A: Additional analysis, R: Reference Case, Y: Yes, N: No, U: Unclear, % Within Country: % of included items within one country guideline, % Across Countries: % of countries including one item.

Table 55: Recommended methods to measure and value productivity loss under the societal perspective

Country	Measurement and valuation of productivity costs
Austria	Human capital approach
Australia	Not stated
Brazil	Human capital approach
Canada	Friction cost approach
China	Human capital approach
Cuba	Any
England	Not stated
Finland	Not stated
Germany	Friction cost approach
Indonesia	Not stated
Ireland	Not stated
Netherlands	Friction cost approach
Norway	Any
Poland	Human capital approach
Portugal	Human capital approach
Spain	Any
Sweden	Human capital approach
Taiwan	Human capital approach

Table 66: Types and measures of outcomes to be included under the societal perspective

Health outcomes measures	Countries
QALYs preferred	Austria, Australia, Canada, China, Columbia, Denmark, England, Ireland, Netherlands, Norway, Scotland, South Korea, Sweden, Thailand
LYs and QALYs	Poland, Portugal, Taiwan
Natural units and QALYs	Baltic, Cuba, Denmark, Germany, Hungary, Spain, Croatia
LYs, DALYs and QALYs	Brazil, India, Indonesia
QALYs Quality Adjusted Life Years; LYs Life Years; DALYs Disability Adjusted Life Years	