

International survey of methods used in health technology assessment (HTA): does practice meet the principles proposed for good research?

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Objective: To describe research methods used internationally in health technology assessment (HTA) and health-care reimbursement policies; compare the survey findings on research methods and processes to published HTA principles; and discuss important issues/trends reported by HTA bodies related to current research methods and applications of the HTA process.

Methods: Representatives from HTA bodies worldwide were recruited to complete an online survey consisting of 47 items within four topics: (1) organizational information and process, (2) primary HTA methodologies and importance of attributes, (3) HTA application and dissemination, and (4) quality of HTA, including key issues. Results were presented as a comparison of current HTA practices and research methods to published HTA principles.

Results: The survey was completed by 30 respondents representing 16 countries in five major regions, Australia (n = 3), Canada (n = 2), Europe (n = 17), Latin America (n = 2), and the United States (n = 6). The most common methodologies used were systematic review, meta-analysis, and economic modeling. The most common attributes evaluated were effectiveness (more commonly than efficacy), cost-effectiveness, safety, and quality of life. The attributes assessed, relative importance of the attributes, and conformance with HTA principles varied by region/country. Key issues and trends facing HTA bodies included standardizing methods for economic evaluations and grading of evidence, lack of evidence, and data availability for emerging technologies.

Conclusion: This is the first international survey to specifically assess the state of HTA research methods. Future efforts should expand the respondent sample to include more emerging markets and update the results of this survey to specifically address additional aspects of research methods in HTA.

Keywords: survey, technology assessment, payers, research methods, reimbursement

Introduction

Health technology assessment (HTA) increasingly plays an important role in informing reimbursement and pricing decisions and providing clinical guidance on the use of medical technologies across the world. In addition to safety and efficacy information, health economic and outcomes research data are also receiving expanded attention in these assessments in many countries, due to payers seeking better value for money spent on treatments. HTA is now commonly viewed as a tool to assist evidence-based health-care decisions. It has had various definitions over the years and across countries, but as defined herein, it is the systematic evaluation of a medical or health technology for evidence of its safety, efficacy, effectiveness, cost, cost-effectiveness, and ethical and legal implications, both in absolute terms and in comparison with other competing technologies.¹

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Several groups have developed or recommended good practices for the conduct of HTA.²⁻⁵ However, little is known about actual adherence to such recommended principles within HTA organizations. This paper attempts to address this gap by retrofitting the results of an international survey of HTA organizations and reimbursement bodies regarding HTA research practices, methodologies, and key issues to 15 HTA principles proposed in a recent publication for assessing HTA activities that involve allocation of resources (Table 1).²

Specifically, the objectives of this paper are to (1) describe research methods used internationally in health technology

assessment (HTA) and health-care reimbursement policies, (2) compare the survey findings on research methods and processes to published HTA principles, and (3) discuss important issues/trends reported by HTA bodies related to current research methods and applications of the HTA process.

Methods

An online survey was developed consisting of 47 items within four topics related to (1) organizational information and process, (2) primary HTA methodologies and importance of attributes, (3) HTA application and dissemination,

Table 1 Brief summary of 15 health technology assessment (HTA) principles proposed by Drummond et al²

Principle	Description	Survey items in appendix used to address the principle
1. The goal and scope of the HTA should be explicit and relevant to its use	The HTA process should involve multidisciplinary stakeholders and a clear definition of the questions to be addressed by the assessment	9, 10, 15
2. The HTA should be an unbiased and transparent exercise	Optimally, the HTA process is transparent and conducted independently of the group responsible for payment/reimbursement	37, 46, 47
3. The HTA should include all relevant technologies	All relevant technologies should be considered in order to avoid inaccuracy and distortion of the assessment and allocation of resources	9, 17, 18, 19
4. A clear system for setting priorities for HTA should exist	It is important to understand how technologies are selected and prioritized in order to determine the potential bias associated with situations where only select technologies are evaluated	10, 11, 16
5. The HTA should incorporate appropriate methods for assessing costs and benefits	Appropriate guidelines and systematic approaches to evidence synthesis and analysis during an HTA review is important, particularly when more complex statistical and methodological techniques are used to address gaps in the available data for a technology	12, 13, 20, 21, 22, 23,
6. HTAs should consider a wide range of evidence and outcomes	In order to ensure that multiple stakeholder views (ie, clinical, economic, societal) are accounted for in the assessment, it is important to consider a wide range of evidence and outcomes	14, 16, 26
7. A full societal perspective should be considered when undertaking HTAs	Utilizing narrowly defined perspectives for HTA may distort clinical decision-making and policy regarding new technologies	24, 27
8. HTAs should explicitly characterize uncertainty surrounding estimates	It is essential to use sensitivity analyses to understand the robustness of cost-effectiveness results and to describe the uncertainty surrounding results explicitly	28
9. HTAs should consider and address issues of generalizability and transferability	The generalizability and transferability of data in HTAs is increasingly relevant as health care becomes more globalized	15, 25, 30
10. Those conducting HTAs should actively engage all key stakeholder groups	Key stakeholders should be actively engaged by those conducting HTAs in order to understand stakeholder perspectives at various stages of the HTA process	6, 7, 8, 40, 41, 42, 43
11. Those undertaking HTAs should actively seek all available data	All relevant data, both confidential (such as provided by industry sponsors) and publicly available, should be sought when conducting the HTA	30
12. The implementation of HTA findings needs to be monitored	The outcome of HTA decisions may indicate whether the HTA exercise is in fact useful	35
13. HTAs should be conducted in a timely manner	While the timing of HTAs is important, long-term data are generally unavailable when a new technology is approved; a growing trend appears to allow conditional reimbursement until adequate data are available for thorough assessment	31
14. HTA findings need to be communicated appropriately to different decision-makers	HTA results should be specifically tailored to various users of the information, such as physicians, specialists, and health economists	34, 39
15. The link between HTA findings and decision-making processes needs to be transparent and clearly defined	It is important to separate the assessment itself from the actual decision-making in order to avoid issues of equity	10, 29, 36, 37

and (4) quality of HTA, including key issues. For research methodology questions, responses were organized by type of technology – namely, drugs, medical devices, other technologies (eg, surgical or medical procedures, administrative system) – as well as whether the intervention was emerging (not yet available), new, established, or widespread/declining. Item development was based on comprehensive review of the literature for HTA research methods, review of previous HTA survey items/questionnaires identified in the literature or provided by various members of the special interest group, iterative item development and revision with twelve working group members, and online pilot testing with four to five persons (contacts provided by working group members) that then resulted in the survey content being refined and the length of the final survey being shortened. The complete survey with details on each question and response options is available at http://www.ispor.org/sigs/HTA_EBR/HTASurvey.asp. Time to complete the survey was approximately 35–45 minutes, and respondents were instructed to print out the survey before responding in order to have time to ask colleagues about certain areas or questions.

Seventy-one HTA and/or reimbursement bodies from 27 countries were targeted for inclusion in the survey. Respondents from targeted countries were recruited from internal HTA contact lists residing at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), as well as contacts available through working group members in various countries. Respondents were not paid and provided their contact information at the conclusion of the survey if additional follow-up was needed. Efforts were made to target key individuals within the organizations who would be knowledgeable and senior enough to provide insight to the survey questions. Working group members were assigned individual contacts to follow-up via electronic mail and telephone calls.

The survey data were analyzed and presented in this paper as a retrofit with the 15 HTA principles (Table 1) proposed by Drummond et al,² with the addition of key trends and issues in HTA methodology, application, and process. Our survey was developed in tandem with the principles, thus we retrofitted our data to fit the various categories as applicable, as our survey was designed to be broader than the principles and focus on research methods. The survey items are listed in the appendix to this paper.

Key findings

The survey was completed by 30 respondents from a mix of regions/countries: Australia (n = 3; 10%), Canada (n = 2; 6%), Europe (n = 17; 57%), Latin America (n = 2; 6%), and the

United States (n = 6; 20%) (Table 2). The types of agencies/organizations responding were categorized as HTA only (58%), reimbursement only (7%), both HTA and reimbursement (17%), and other (17%; eg, third-party payers and pharmacy benefit managers [PBMs]). In spite of the variety of and number of payers, respondents from the US were limited and reflected primarily a government payer or independent

Table 2 Survey respondents by country and health technology assessment (HTA) organization

Country	Organization
Argentina	Instituto de Effectividad Clinicay (IECS)/Institute for Clinical Effectiveness and Health Policy
Australia	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S); Medical Services Advisory Committee (MSAC); Adelaide Health Technology Assessments (AHTA)
Austria	Ludwig Boltzmann Institut Health Technology Assessment (LBI-HTA)
Brazil	Department to de Ciência e Tecnologia (DECIT) Coordenação Geral de Avaliação de Tecnologias em Saúde (CGATS) – Ministry of Health
Canada	The Canadian Agency for Drugs and Technologies in Health (CADTH); Institute of Health Economics
Denmark	Danish Centre for Health Technology Assessment (DACEHTA)
France	Haute Autorité de Santé (HAS); Committee for Evaluation and Diffusion of Innovative Technologies (CEDIT)
Germany	Institute for Quality and Efficiency in Health Care (IQWiG)
Hungary	Research Centre for Health Economics and Health Technology Assessment, Corvinus University of Budapest, Unit of Health Economics and Health Technology Assessment (HunHTA)
Italy	Regione Veneto
Portugal	National Authority of Medicines and Health Products (INFARMED)
Spain	Osteba, HTA unit. Health Department, Basque Country; Agency for Health Technology Assessment; Andalusian Agency for Health care Technology Assessment; Galician Health Technology Assessment Agency
Sweden	Center for Medical Technology Assessment (CMT), Linköping University; The Swedish Council on Health Technology Assessment (SBU); Läkemedelsförmånsnämnden (LFN) Pharmaceutical Benefits Board
Switzerland	Swiss Federal Office Of Public Health – Medical Technologies Unit
The Netherlands	The Health Care Insurance Board (CVZ)
USA	ECRI Institute (Economic Cycle Research Institute), Institute for Clinical and Economic Review (ICER), Evidence-Based Practice Center – EBPC (Independent HTA bodies); Centers for Medicare and Medicaid Services (CMS); Caremark Rx – CMX (pharmacy benefit manager); Premera Blue Cross (managed care organization)

HTA perspective (collaborative nonprofit or academic consultancy), though the survey was also completed by a large managed care organization (MCO) and a PBM.

Structure of HTA programs

Principle 1. The goal and scope of the HTA should be explicit and relevant to its use

This principle suggests the HTA process should ideally include development of a detailed scoping document with involvement of multidisciplinary stakeholders in clearly defining the questions to be addressed by the HTA and its link to decision-making on the use of the technology. While our survey did not specifically collect information on development of a scoping document by respondents, it did assess the goal and scope of the HTA. In our survey, the role of HTA reported by respondents was primarily for coverage and reimbursement decisions (80%), clinical guidance (70%), and pricing decisions (33%). While a vast majority of respondents employed HTA for coverage and reimbursement decisions (80%) and clinical guidance (70%), only 43% and 48% explicitly included costs and cost-effectiveness evaluations as part of the assessment for drugs and medical devices, respectively.

Principle 2. The HTA should be an unbiased and transparent exercise

The optimal HTA process is conducted independently of the group that will decide on payment or reimbursement, while the HTA process and basis on which decisions are made should be transparent. In our survey, only 17% of respondents indicated a combined HTA and reimbursement role. The majority of funding for HTA came from the government for most respondents (63%); however, the HTA work itself was likely to be partially outsourced. Among the survey respondents, HTA work was performed by either in-house staff (30%), academia (37%), or a combination of in-house HTA staff and outsourcing to independent professional consultants (63%). Among our respondents, 27% always involved stakeholders (primarily manufacturers of the health technologies) in the health technology assessment, 27% sometimes involved stakeholders, and 57% gave stakeholders a chance to review a draft version of the assessment before the report was finalized. Methods and results of the assessments were made available to the public by 80% of respondents. A majority (90%) of the respondents made these reports freely available, while 7% charged a fee for the reports. The survey did not specifically ask whether complete versus partial results were made available to the public.

Principle 3. The HTA should include all relevant technologies

Including all relevant technologies in HTA is important to avoid distorting the assessment and allocation of resources. However, our survey indicates that selection of technologies for assessment and relevant comparators vary. Eight percent of all respondents focused only on drugs in their HTAs (the vast majority addressed drugs, devices, and other technologies as well). All US organizations responding to the survey assessed drugs, whereas 82% of European respondents assessed drugs. Medical devices were assessed by more respondents in Europe than the US (94% vs 76%). When selecting technologies for assessment, the primary criteria for respondents (reported by over 50% for drugs and other technologies, and over 60% for medical devices) were the perceived impact on patient outcomes, the prevalence of the associated medical condition, and the potential cost of the technology. Regarding the evolutionary stage of the technologies assessed, respondents mainly assessed new technologies, with 77% of respondents assessing new drugs and 87% assessing new medical devices; for established or widespread technologies, 47% of respondents assessed drugs and 67% assessed medical devices. Emerging technologies were assessed slightly less than established/widespread technologies (37% and 47% for drugs and medical devices, respectively), and technologies with declining use in practice were rarely assessed by respondents (less than 14% across all technologies). Selection of the comparator(s) was driven by the authoritative bodies for about 50% of the respondents, while both client requests and reasonable comparators selected by the group conducting the HTA were other common approaches. In addition to placebo, the most used or prescribed other health technologies were selected as comparators for more than 50% of respondents.

Principle 4. A clear system for setting priorities for HTA should exist

Understanding how technologies are selected and prioritized for assessment is crucial to determining the potential bias associated with situations where only select technologies are evaluated. Our survey indicated that more than half of all respondents reported potential cost and perceived impact on patient outcomes were the main criteria for selecting health technologies (regardless of whether drug, device, or other technology). Prevalence of a medical condition was also an important factor in selection for an assessment, with approximately half of the respondents requiring an evaluation of the burden of disease in the population specific to the market in

which the technology was being assessed (~53% for drug, 63% for medical devices, and 47% for other technologies). The evolutionary stage of the technology seemed to drive priorities, as new technologies were the most likely to be assessed (75% across technologies) followed by established/widely used technologies (55% across technologies), and emerging (not yet available) technologies (42% across technologies).

Methods of HTA

Principle 5. HTA should incorporate appropriate methods for assessing costs and benefits

This principle seeks to emphasize the role of guidelines and systematic approaches to evidence synthesis and analysis during an HTA review. More complex statistical and methodological techniques are used to address gaps in the available data for a technology (eg, lack of a head-to-head study with a key comparator). We found the starting point and primary methodology used for synthesis of evidence was either systematic review or meta-analysis (>50% across technologies). In addition, we found that meta-analyses (38% of respondents) and comparative analyses (34%) were the most common methodologies being used for drug therapies. For medical devices, post-marketing surveillance (38%) was also a common method, along with meta-analyses (45%) and comparative analyses (36%). Table 3 provides a summary of the most common methods used by region for drugs and medical devices. Figure 1 summarizes the overall frequency of various methods employed for HTA of drugs and medical devices. For bodies that consider cost or cost-effectiveness information, the most common analyses were cost-effectiveness (>75% for drugs and medical devices), with the primary methodology being decision models ($\geq 70\%$ for drugs and medical devices, and 57% for other technologies). Common end points included cost/life-year saved, cost/event avoided, and cost/quality-adjusted life year (QALY). However, cost-effectiveness information was only evaluated for conformance with economic evaluation or pharmacoeconomic guidelines by 47% of respondents for drugs and 33% for medical devices. For the most part, European agencies had clearly defined national guidelines they followed, while US agencies were less organized, with only one (of six total) respondent stating the Academy of Managed Care Pharmacy format as a guideline was followed.

Principle 6. HTAs should consider a wide range of evidence and outcomes

Including a wide range of evidence and outcomes (such as clinical, economic, and societal) ensures that multiple

Table 3 Most common methodologies used in health technology assessment (HTA)

Country	Clinical trial	Epi and observational analyses	Cost and economic analyses	Comparative analyses	Post-marketing surveillance	Modeling	Expert opinion	Group judgment	Systematic review	Meta-analyses
Argentina			DM	DM		DM			DM	DM
Australia	M		M	M		D	D		D	D
Austria		D	D	D		M	DM	M	DM	Σ
Brazil	DM								DM	DM
Canada		DM	DM	DM		DM	DM	DM	DM	DM
Denmark	DM		DM	DM		DM			DM	DM
France*	M	M	M	M	M		M		M	DM
Germany	DM		DM	DM		DM			DM	
Hungary	DM	D	D			DM	D		D	
Italy	D	M	DM	M	DM	DM	M	M	DM	DM
Netherlands	DM	DM	DM	DM			M	DM		
Portugal**	D	D	D	D	D	D	D	DM	D	D
United States	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
Spain	DM	DM	DM	DM	M		M	D	DM	DM
Sweden	DM	D	DM	DM	D	DM	DM		DM	DM
Switzerland						DM			DM	

Notes: *France did not report methodologies for drugs other than emerging drugs; **Portugal did not report methodologies for medical devices; empty boxes mean the country respondent did not check/select the methodology.
Abbreviations: D, drugs; M, medical devices.

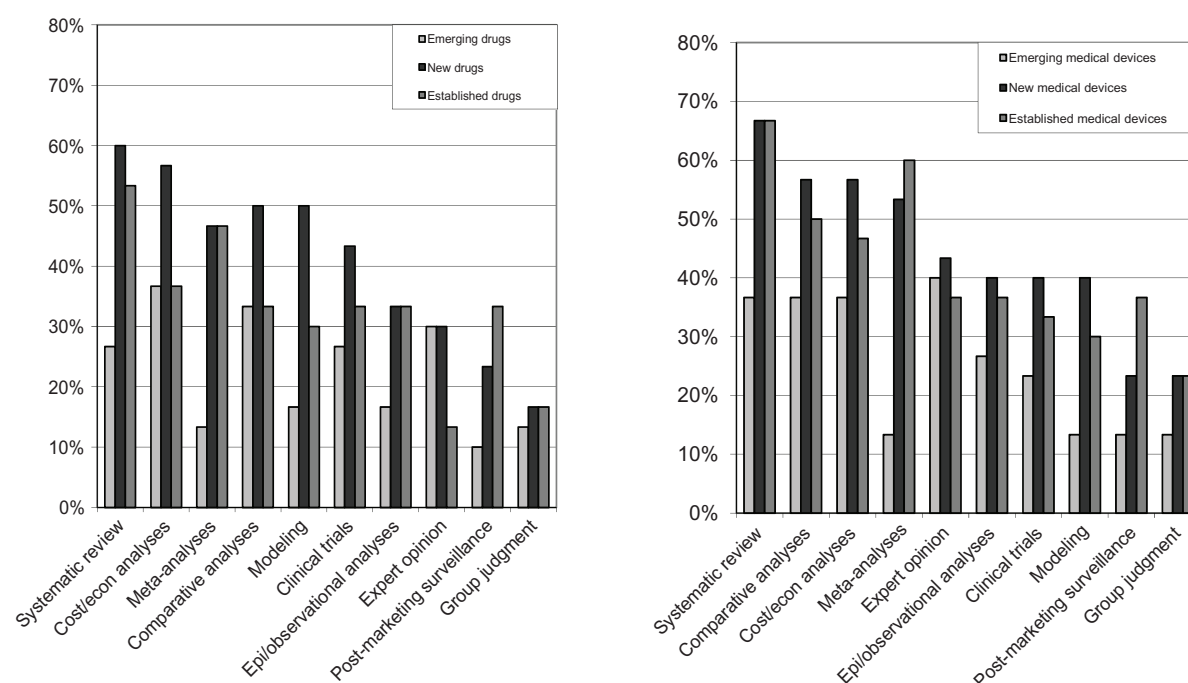


Figure 1 Comparison of assessment methodologies for drugs and medical devices (all respondents).

Note: Proportion of respondents reporting use of methodology.

stakeholder views are included in the review process. Although randomized clinical trials are needed to establish efficacy and achieve regulatory approval, our survey indicates that the most common attributes assessed in HTA processes are effectiveness, safety, costs, and cost-effectiveness across technologies and evolutionary stages. Figure 2 presents the relative importance of the attributes assessed, and shows

the attributes are not weighted equally. While cost and cost-effectiveness are commonly assessed as part of HTA review, effectiveness was rated as the most important attribute, with approximately 80% of respondents rating it highly important for both drugs and medical devices, followed by safety (>70% for drugs and medical devices, >50% for other technologies). Differences by region were also noted among

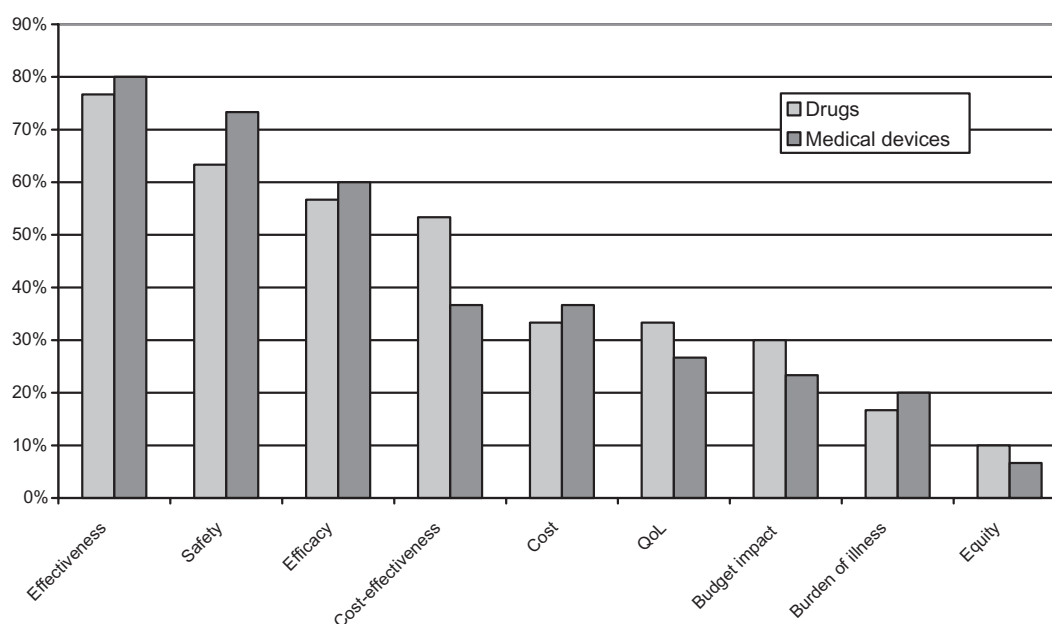


Figure 2 Relative importance of attributes evaluated for drugs and medical devices (all respondents).

Note: Proportion of respondents reporting attribute as "high" importance.

the attributes assessed and their relative importance. While all regions were highly focused on clinical effectiveness and safety, the US respondents, who largely represented government payers or independent HTA bodies in our survey, more frequently evaluated quality-of-life (QoL) information when compared to European respondents, who more frequently assessed cost-effectiveness data. While somewhat surprising for US payers, our sample of respondents reflected more a Center for Medicare and Medicaid Services (CMS) perspective, where coverage decisions are not made on cost. Even among the managed care respondents, they reported including data on QoL in their assessments with moderate frequency.

Principle 7. A full societal perspective should be considered when undertaking HTAs

There is some concern that selection of narrowly defined perspectives for HTA may distort clinical decision-making and policy regarding new technologies. Our survey indicated that at least half of the respondents used a societal perspective regardless of technology, followed by ~35% using primarily a third-party payer perspective. Differences by region were significant. Europe uses a societal perspective (67% across technologies), while the US is more oriented to third-party payers and other perspectives (22% and 33%, respectively). While the societal perspective was most commonly reported, the use of cost per QALY end points was generally not mandatory.

Principle 8. HTAs should explicitly characterize uncertainty surrounding estimates

The use of sensitivity analyses are considered essential to understanding the robustness of HTA findings and conclusions. Quantification of the uncertainty surrounding the estimates may be achieved through one-way, multiway, and probabilistic sensitivity analyses. Our survey specifically focused the question on characterizing uncertainty around cost-effectiveness estimates. Only about half of our survey respondents that included cost-effectiveness as one of the assessed HTA components required mandatory estimation of uncertainty (using confidence intervals) around the cost-effectiveness estimates for both drug and medical device evaluations. Countries reporting mandatory estimates of uncertainty included Denmark, France, Germany, Hungary, the Netherlands, Portugal, and Sweden.

Principle 9. HTAs should consider and address issues of generalizability and transferability

Given the international nature of our survey, the issues of generalizability and transferability of HTA findings, and

specifically cost-effectiveness data, were of particular focus. All respondents considered foreign HTA evaluations in their own process in some way. European agencies were more specific about the organizations they considered, while US HTA agencies were open to any with good methodologies. More than half of the respondents required an understanding of the burden/epidemiology specific to the market in which the technology was being assessed. Furthermore, international data (eg, from multinational trials) may be accepted in some countries, while country-specific or regional/province data is required by other countries. In general, international patient utilities and QoL data are accepted (about 50% across technologies). However, resource-utilization data was split between international data being permitted versus requiring country-specific data (about 30% each, across technologies). Not surprisingly, data on unit costs or price weights was more often required to be country-specific (about 50% for drugs and medical devices). Table 4 provides an overview of the use of international versus country-specific data for approximately 70% of survey respondents who answered this question.

Processes for conducting HTA

Principle 10. Those conducting HTAs should actively engage all key stakeholder groups

To understand all key stakeholders at various stages of the HTA process, it is important to recognize that HTA is primarily initiated by government bodies (80%); however, in the US,

Table 4 Generalizability and transferability of international data as inputs to economic analysis

Country	Patient utility/ quality of life data	Resource- utilization data	Unit cost/ price weight data
Austria	International	Country	Country
Denmark	International	Country	Country
France	–	Country*	Country*
Germany	Country	International	Country
Hungary	Country	Country	Country
Italy	International	International	Not applicable
Netherlands	International	Country	Country
Portugal	International	Country	Country
Spain	International*	–	–
Sweden	International	International	Country
Switzerland	International	International	International
USA	International	International	Not applicable
Canada	International	Other	Other
Australia	International	Country	Country
Argentina	International	International	Country
Brazil	Other	Other	Other

Notes: *Half of respondents for that country answered the question; responses were consistent within countries.

it is initiated by government and HTA agencies with equal frequency. With regard to funding, HTAs are also almost entirely government funded, followed by mostly government with some private contributions (~30%). However, in the US, HTAs are frequently privately funded. The issue of funding seems to play out in the stakeholder involvement. For example, our survey indicated that stakeholders are often (57%) given a chance to review a draft version of the assessment before the report is finalized, a process most frequent in the US (67%). However, approximately half of respondents do not involve stakeholders in the assessment itself. With regard to the final decisions, more than half of the respondents (57%) reported that stakeholders are never involved; in these cases, there is an appeals process in place if stakeholders do not agree with the final decision.

Principle 11. Those undertaking HTAs should actively seek all available data

This principle supports the use of proprietary/confidential data from industry sponsors, as well as use of publicly available data. While this specific question was not directly posed in our survey, we do know that certain agencies accept confidential information as part of the submission, and often these analyses reflect patient-level data analysis as part of the modeling exercises. We are also aware that the CMS will accept confidential data; however, they cannot use it in decision-making unless it is made publicly available.⁶⁻⁷ Given the responses to our stakeholder questions in the survey, we found that it was more frequent than not that the industry sponsor was in some way involved in the assessment, indicating a certain level of collaboration.

Principle 12. The implementation of HTA findings needs to be monitored

The outcome of HTA decisions may indicate whether the HTA exercise is in fact useful. Eighty-six percent of respondents indicated that the organization making the decision on coverage or reimbursement at least partially relied on the conclusions of the assessment. However, only 28% repeat or update the assessment at regular intervals, indicating that prospective tracking of the outcome of the decisions being made generally do not happen on a widespread basis.

Use in decision-making

Principle 13. HTA should be timely

Timing of the HTA is important; however, long-term and effectiveness data are generally not available when a new technology is approved. Conditional reimbursement was

not directly addressed in the survey, as to whether thorough assessment is delayed until adequate data are available. However, timely reassessment appears to be more popular in the US, where at least half of respondents reported performing annual reassessments, while the majority of European respondents do not require mandatory reassessment at any specific regular interval.

Principle 14. HTA findings need to be communicated appropriately to different decision-makers

This principle suggests that the HTA results should be tailored to various users of the information. Our survey indicated that the backgrounds of users of HTA information do indeed vary and include physicians/specialists and health economists as the most common technical backgrounds (73% and 57%, respectively). Interestingly, pharmacists were more common users of the assessments among our respondents in the US than Europe (83% vs 41%). The most common modes of communication for HTA findings were the agency's or government's website (83%), followed by peer-reviewed journals (57%). Our survey respondents that represented European reimbursement agencies indicated that HTA reports they had received were considered excellent in all but one case, while US responses indicated that the quality of reports was either "poor" or "fair" approximately half of the time.

Principle 15. The link between HTA findings and decision-making processes needs to be transparent and clearly defined

This principle describes the separation of the assessment itself from the actual decision-making to avoid equity issues. One such issue is the use of a specific threshold of cost-effectiveness above which the technology would not be funded. Though the use of an explicit threshold appears to the most transparent approach, it may not account for other variables (eg, lack of alternative treatments in advanced cancers where CE thresholds often exceed the generally acceptable limits, or lack of robust data in appropriate population with appropriate comparator). Our survey indicated this was indeed the case, with at least 60% of respondents indicating that specific thresholds were not used to determine whether a technology was cost-effective. To support transparency in decision-making, 90% of survey respondents indicated that the HTA report itself was free and that the methods and results of the assessments were made available to the public almost 90% of the time in Europe and about two-thirds of the time in the US. The survey also suggests that the conclusion of the

assessment is only partially relied upon by the organizations making decisions (>80% of respondents indicated partial reliance on HTA conclusions; 7% of respondents indicated complete reliance).

Key issues and trends for HTA bodies

In conducting the survey, one goal was to understand better the issues and trends facing HTA with regard to research methods. We asked respondents in an open-ended format what the key issues, trends, or topics their agencies or organizations were facing with regard to methodologies used for HTA. A summary of key themes is shown by country in Table 5. The key concerns appear to be linked to the stage of evolution of HTA in the various countries. Common themes included meta-analysis methods for indirect comparisons. Lack of data upon which to base the assessments was also a key challenge. The US entities described a lack of good data from solid, peer-reviewed literature to use as inputs in meta-analyses and analytic framework modeling. European agencies frequently mentioned standardization of methodology and a lack of evidence for emerging technologies. Countries with well-established HTA programs indicated that timeliness and reassessment strategy was of key concern.

Features of the process, application and use of HTA

Beyond research methods, the survey also included questions related to the process and application of HTA. Given the heterogeneity among regions surveyed, we synthesized results for the European respondents (56% of survey respondents and 69% of countries represented), as they generally had more mature HTA processes and systems in place. Figure 3 provides an overview of the characteristics of HTA from the European respondents, technical backgrounds of those making decisions based on the HTA report, use of the findings, methods of dissemination, and stakeholder involvement. Of interest is that the conduct of the HTA is most frequently outsourced or provided by academia in Europe, while the reader of the HTA report and decision-maker is most frequently a physician/specialist.

Discussion

Our survey represents the first published data focusing specifically on HTA research methods gathered directly from representatives within these bodies. It is also the first attempt using prospective survey data to compare conformity of research methods with the 15 HTA principles published by Drummond et al in 2008.² Previously published studies focused on

Table 5 Key methodology trends and issues facing health technology assessment (HTA) bodies

Country/region	Key trends and issues
Argentina	Burden of disease, microsimulation methods
Australia	Timeliness, rapid review methodologies, prioritizing topics for review; lack of evidence for some new and emerging technologies; small patient groups; increasing the use of economic analysis; assessment of diagnostic tests and use of linked evidence; surrogate outcome validity; validity of combined end points; assessment of public health programs
Austria	Need for observational studies/real-life data (monitoring, registries, etc); development of "acceptable" thresholds and methods for resource allocation
Brazil	Establishment and validation of methodology guidelines for economic evaluation and systematic reviews
Canada	Increased consistency in economic evaluations and reviews leading to recommendations; disease management, class review methods; standards for rapid HTA
Denmark	Lack of good studies/data as inputs to the assessments
France	Early assessment of technologies with mechanism for conditional coverage, lack of evidence for emerging technologies
Germany	Development/use of methodologies for health economic evaluations
Italy	HTA moving as a priority to regional health-care agendas
Portugal	Selection of comparators, identification and quantification of costs, uncertainty analysis
Sweden	Link between theory and practice in HTA, uniform analyses for comparative purposes, assessment of diagnostics, timeliness, selection of topics/comparators
Spain	Transparency, rigor, quality assessments, collaboration with other HTA agencies nationally and internationally, improved methods, training of new researchers
Switzerland	Horizon scanning, implementation of regular reassessments
The Netherlands	Selection of comparators/study populations, model structure, and assumptions
USA	CMS: incorporating coverage with evidence development into the technology-assessment process MCO: biggest limitation is lack of solid published, peer-reviewed clinical evidence as inputs to the evaluation process PBM: new technologies' differentiation, especially biotech Independent HTAs: – speaking the language of policy-makers; managing the volume of literature when epidemiology and observational studies are included

(Continued)

Table 5 (Continued)

Country/region	Key trends and issues
	<ul style="list-style-type: none"> – grading bodies of evidence, indirect versus direct meta-analysis, applicability of trials versus potential for bias/confounding in observational studies – we believe that, while HTA is still an immature science, convergence around techniques to grade available evidence will help the field enormously. One challenge that remains, however, is access to good data; advances in meta-analysis and analytic framework modeling are only as good as the input data used, and for all categories with the possible exception of drugs, there is simply not enough good comparative data available

Notes: Summary of text responses to open-ended question: “What are the key issues, trends, or topics your agency or organization is facing with regard to methodologies used for HTA?” Hungary did not respond to this question.

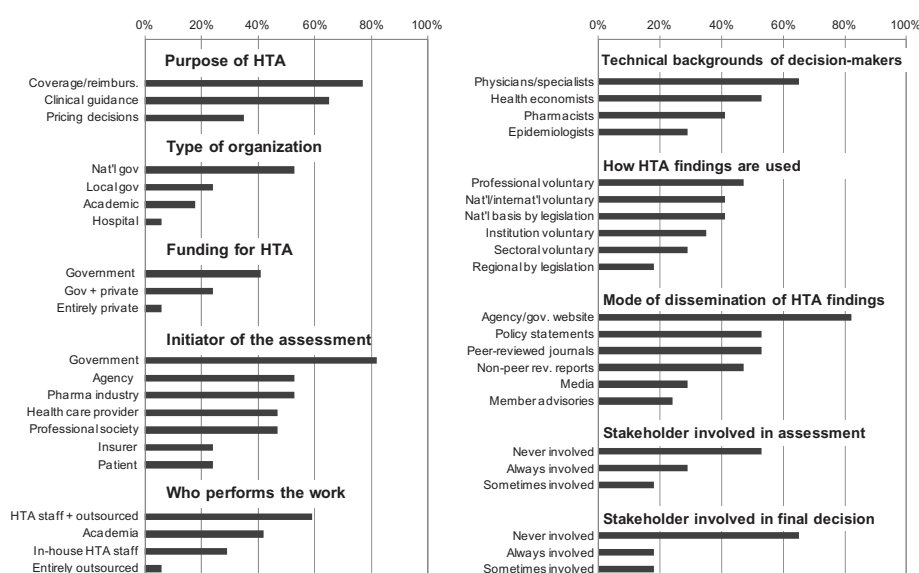
either Europe or the US,^{1,8–12} and more recent HTA surveys have focused on structural characteristics, regional drivers of decision-making, and transferability of HTA to other regions rather than on specific research methods employed.^{13–15} Neumann and colleagues (from the 15 HTA principles group) used a literature-review approach to assess conformity with these HTA principles.¹⁰ While their review provides some insight into conformity with the principles, it was limited by the availability of published data, some of which was more than 10 years old. Results presented in this paper reflect a recent snapshot of HTA research methods and processes.

While none of the countries responding appeared to be meeting all of the recommended HTA principles, the

survey results indicate that there are different approaches and priorities between the various countries surveyed and even within countries when different payers are involved. The finding that in most cases the HTA reports are only partially relied upon in decision-making raises interesting questions about what this indicates related to usefulness of the HTA and the consequences. Perhaps it simply reflects unwillingness by decision-makers to give too much power to HTA agencies, given that the coverage decisions can be politically charged and other aspects have to be considered such as situations with orphan drugs, rare diseases, or children.

The primary limitation with this international survey was the response rate of 25% (30 out of 121 contacts within 71 organizations). Even with direct contact by email and phone calls, we achieved limited or no response from some countries or payers within countries. For instance, representatives of the National Institute for Clinical Excellence did not directly respond to the survey, but rather referred us to their website, and hence this established organization was not represented in our survey results. In addition, some respondents did not complete the entire survey.

In the US, there was significant resistance to providing the type of detail requested about research methods and priorities within the assessments. Nevertheless, there was a diverse representation to reflect the different perspectives within the US, including three independent HTA bodies, a government payer (CMS), a large MCO, and a PBM. Findings within the US were particularly surprising, and suggested that QoL assessment was more frequently assessed and considered of

**Figure 3** Organization, application, and use of health technology assessment (HTA) (European respondents).

higher importance than in Europe (where cost-effectiveness seemed more important). Even MCO and PBM respondents ranked QoL as of medium importance, when it has been generally perceived in the US that MCOs do not value QoL end points in their decision-making. However, a recent survey of 46 US managed care decision-makers appeared to confirm our findings.¹¹ Payers reported that the QoL supplemental information provided in the Academy of Managed Care Pharmacy dossiers is considered one of the more useful sections: 62% reported that the patient reported outcomes/QoL section was useful, compared to 81% for systematic reviews/meta-analyses, 62% for pharmacoeconomic studies, 42% retrospective/observational safety/adverse events studies, 42% persistence/adherence studies, 38% prospective observational cohort studies, 19% patient registries, 19% patient-preference studies, 15% indirect comparisons of clinical benefit, and 12% predictive-risk models.

Another limitation was the presentation of the international survey data as a retrofit to the HTA principles. Not all questions were designed to address each principle, as we were developing our survey as the principles were being released, and so we gathered additional information on the specific research methods used in HTA beyond what was specified in the principles. Future research could be conducted to specifically assess conformity with each of the HTA principles from the outset. In addition, expansion of the respondent base in key emerging markets, such as the Asia-Pacific region, would be valuable and of interest for future reports.

In conclusion, the use of research methods and conformity to published HTA principles varied significantly by country and payer. Despite our relatively small sample, the results suggest that HTA, using evidence-based medicine, will continue to be a rapidly evolving area and in need of standardized research methods and principles to guide assessment and decision-making around drug therapies, medical devices, and emerging technologies. A process for information sharing among HTA bodies may be needed to achieve this standardization in research methods. Future research would be useful to update and expand the results of this survey to address specifically additional aspects of the HTA principles and changes in research methods applied.

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References

1. Perry S, Thamer M. Health technology assessment: decentralized and fragmented in the US compared to other countries. *Health Policy*. 1997;42(3):269–290.
2. Drummond MF, Schwartz JS, Jonsson B, et al. Key principles for the improved conduct of health technology assessments for resource allocation decisions. *Int J Technol Assess Health Care*. 2008;24(3): 244–258.
3. European Federation of Pharmaceutical Industries and Associations (EFPIA). *The Use of Health Technology Assessments (HTA) to Evaluate Medicines: Key Principles*. Brussels: EFPIA; 2005.
4. Emanuel EJ, Fuchs VR, Garber AM. Essential elements of a technology and outcomes assessment initiative. *JAMA*. 2007;298(11): 1323–1325.
5. Hutton J, Trueman P, Henshall C. Coverage with evidence development: an examination of conceptual and policy issues. *Int J Technol Assess Health Care*. 2007;23(4):425–432.
6. Kolber M. Opacity and cost effectiveness analysis in Medicare coverage decisions: health policy encounters administrative law. *Food Drug Law J*. 2009;64(3):515–530.
7. Neumann PJ, Rosen AB, Weinstein MC. Medicare and cost-effectiveness analysis. *N Engl J Med*. 2005;353(14):1516–1522.
8. Perry S. Technology assessment in health care: the US perspective. *Health Policy*. 1998;9(3):17–24.
9. Graf von der Schulenburg JM, editor. *The Influence of Economic Evaluation Studies on Health Care Decision-Making: A European Survey*. Amsterdam: IOS Press; 2000.

10. Neumann PJ, Drummond MF, Jonssen B, et al. Applying key principles for improved health technology assessment: an analysis of 14 HTA organizations. *Value Health*. 2009;12(7):A250.
11. Beeman D, Tam I, Moore JA. *An Evaluation of AMCP Format v 3.0: Managed Care Customer Perspectives*. Presented at the Academy of Managed Care Pharmacy's 23rd Annual Meeting and Showcase; April 27–29, 2011; Minneapolis, MN.
12. Leung MY, Halpern MT, West ND. Pharmaceutical technology assessment: perspectives from payers. *J Manag Care Pharm*. 2012; 18(3):256–264.
13. Moharra M, Kubesch N, Estrada MD, projected al. *Survey Report on HTA Organizations*. Barcelona: Catalan Agency for Health Technology Assessment and Research; 2008.
14. Ackermann J, Toumi M. *What Are the Key Drivers for Changing HTA Decisions? Example of Alzheimer's Disease Treatment in Germany, France, and UK*. Presented at the ISPOR 14th Annual European Congress; November 5–8, 2011; Madrid, Spain.
15. Pichon-Riviere A, Augustovski F, García Martí S, Sullivan SD, Drummond M. Transferability of health technology assessment reports in Latin America: an exploratory survey of researchers and decision makers. *Int J Technol Assess Health Care*. 2012;28(2):180–186.

Appendix

ISPOR HTA Working Group Research Methods Survey Items

1. Organization name:
2. Country:
3. Is the organization a reimbursement agency, HTA body, both, other?
4. How would you classify this organization? (national, local, professional society, industry, academic/not-for-profit, hospital, private insurer/managed care, other)
5. What is the purpose of HTA in your organization? (check all that apply: coverage or reimbursement decisions, support of pricing decisions, support of clinical guidance, other)
6. Who funds the health technology assessment? (entirely government funded, mainly government funded with some private contribution, entirely privately funded, mainly privately funded with some government contribution, other)
7. Who initiates the health technology assessment? (check all that apply: HTA agency, government, pharma industry, healthcare provider, professional society, insurer, patient, other)
8. Where is the assessment work performed? (check all that apply: entirely in-house HTA staff, combined HTA entity staff and outsourced professionals, entirely outsourced, academia, other)
9. What types of technologies are assessed? (check all that apply)
 - a. Drugs (additional categories: pharmaceuticals, biological, vaccines)
 - b. Medical devices
 - c. Other technologies (additional categories: medical/surgical procedure, organization/administrative system, support system, other)
10. How are the technologies selected for assessment? (for drugs, medical devices, and other technologies, check all that apply)
 - a. Perceived impact on patient outcomes
 - b. Potential cost of the technology
 - c. Prevalence of a medical condition
 - d. Assessment feasibility (eg, available data, funding, staff)
 - e. Any new technology
 - f. Selected new technology
 - g. Technology identified by external stakeholders
 - h. Perceived interest by public, academia, health professional, and/or commercial interest
 - i. Other
11. At what evolutionary stage of a technology is it likely to be assessed? (for drugs, medical devices, and other technologies, check all that apply)
 - a. Emerging technology
 - b. New technology
 - c. Established or widespread practice
 - d. Declining use in practice
 - e. Other
12. What are the different assessment methodologies used? (for drugs, medical devices, and other technologies, check all that apply)
 - a. Clinical trials
 - b. Epidemiological and other observational analyses
 - c. Cost or economic analyses
 - d. Comparative analyses
 - e. Post-marketing surveillance
 - f. Modeling
 - g. Expert opinion
 - h. Group judgment
 - i. Benchmark-testing
 - j. Systematic review
 - k. Meta-analysis
 - l. Other
13. What is the primary methodology for synthesis of evidence used? (for drugs, medical devices, and other technologies)
 - a. Only systematic review
 - b. Only meta-analysis
 - c. Both systematic review and meta-analysis
 - d. Other
14. What attributes are evaluated in the assessments? (for drugs, medical devices, and other technologies, check all that apply)
 - a. Efficacy
 - b. Effectiveness
 - c. Safety
 - d. Costs
 - e. Cost-effectiveness
 - f. Quality of life
 - g. Budget impact
 - h. Equity
 - i. Burden of illness
 - j. Other

15. Does the HTA assessment require an evaluation of the burden of disease in the population specific to the market in which the technology is being assessed? (for drugs, medical devices, and other technologies)
 - a. N/A
 - b. Yes
 - c. No
 - d. Depends on the technology being assessed, please explain
16. What is the relative importance of the attributes evaluated in the assessment? (for drugs, medical devices, and other technologies by high, medium, low, n/a)
 - a. Efficacy
 - b. Effectiveness
 - c. Safety
 - d. Costs
 - e. Cost-effectiveness
 - f. Quality of life
 - g. Budget impact
 - h. Equity
 - i. Burden of illness
17. Who chooses the comparator? (for drugs, medical devices, and other technologies)
 - a. Pharmaceutical/medical technology company
 - b. Authoritative body (eg, reimbursement/HTA agency, private insurer, etc)
 - c. Other, specify
18. To what kind of comparator do you compare the technology being assessed? (for drugs, medical devices, and other technologies)
 - a. Placebo only
 - b. Other health technologies
 - c. Placebo and other health technologies
19. How is the comparator chosen? (for drugs, medical devices, and other technologies, check all that apply)
 - a. Most used or prescribed technology
 - b. Cheapest listed technology
 - c. Last listed technology
 - d. Other, specify
20. If cost or cost-effectiveness information is considered, what methods of evaluation are allowed? (for drugs, medical devices, and other technologies)
 - a. N/A
 - b. Clinical trial based economic evaluations
 - c. Cost-effectiveness decision models
 - d. Economic analyses using observational databases
 - e. Other, specify
21. If cost or cost-effectiveness information is considered, what types of analyses are allowed? (for drugs, medical devices, and other technologies)
 - a. N/A
 - b. Cost analysis
 - c. Cost-effectiveness analysis
 - d. Cost-consequence analysis
 - e. Cost minimization analysis
 - f. Budget impact analysis
 - g. Other, specify
22. If cost-effectiveness information is considered, is it evaluated for conformance with any economic evaluation or pharmacoeconomic guidelines? (for drugs, medical devices, and other technologies)
 - a. N/A
 - b. Yes
 - c. No
23. If so, please state the name of the guidelines used for:
 - a. Drugs
 - b. Medical devices
 - c. Other technologies
24. If cost-effectiveness information is considered, what kind of perspective must be used for the cost-effectiveness assessment? (for drugs, medical devices, and other technologies, check all that apply)
 - a. N/A
 - b. Societal
 - c. Third party payer
 - d. Other, specify
25. Is international data (eg, from multinational trials) on patient utilities, for instance, accepted in your country or do they require data specific to the country for the following items? (for drugs, medical devices, and other technologies)
 - a. Patient utilities/QoL (N/A, international data accepted, country-specific data required, other, specify)
 - b. Resource utilization data (N/A, international data accepted, country-specific data required, other, specify)
 - c. Unit cost or price weight data (N/A, international data accepted, country-specific data required, other, specify)
26. If cost-effectiveness information is considered, which endpoints are allowed? (for drugs, medical devices, and other technologies)
 - a. N/A
 - b. Cost per life year
 - c. Cost per event avoided (eg, hospitalization averted)

- d. Cost per quality adjusted life year saved
 - e. Net monetary benefit/net health benefit
 - f. Other, specify
27. If cost-effectiveness information is considered, are cost per QALY endpoints mandatory? (for drugs, medical devices, and other technologies)
- a. N/A
 - b. Yes
 - c. No
28. If cost-effectiveness information is considered, is estimation of uncertainty (eg, confidence intervals) around the cost-effectiveness estimate mandatory? (for drugs, medical devices, and other technologies)
- a. N/A
 - b. Yes
 - c. No
29. If cost-effectiveness information is considered, are thresholds used to determine whether technology is cost-effective? (for drugs, medical devices, and other technologies)
- a. N/A
 - b. Yes (specify threshold levels)
 - c. No
30. Do you also consider HTA evaluations conducted by other organizations or countries?
- a. N/A
 - b. Yes (specify these organizations/countries)
 - c. No
31. Do you repeat the assessment in regular intervals including after the marketing of the product?
- a. N/A
 - b. Yes (specify these intervals and/or what is the element triggering a reassessment)
 - c. No
32. Who has the responsibility to make the final decision on reimbursement?
- a. Your organization
 - b. Different organizations/individual (list)
33. What are the technical backgrounds of the members involved with making the decision? (check all that apply)
- a. Physicians/specialists
 - b. Pharmacists
 - c. Epidemiologists
 - d. Health economists
 - e. Other, specify
34. Does the organization making the decision rely on the conclusions of the assessment?
- a. Yes, completely
 - b. Yes, partially
 - c. No, they make their own decision
 - d. Other, specify
35. How are the HTA findings used?
- a. Reports are used on a national/international basis (ie, voluntarily adopted nationally or even internationally)
 - b. Reports are used on a national basis by legislation (ie, adopted nationally by legislation)
 - c. Reports are used on a regional basis by legislation (ie, adopted regionally by legislation)
 - d. Reports are used on a sectoral basis (ie, voluntarily adopted sectorally)
 - e. Reports are used on a professional basis (voluntarily adopted professionally)
 - f. Reports are used on an institutional entity basis (ie, voluntarily adopted by institutions)
 - g. Other, specify
36. Are methods and results of the assessment made available to the public? (yes, no, other-specify)
37. If yes, is there a fee associated with obtaining the HTA report? (yes, no)
38. What is the mode of dissemination of HTA findings? (check all that apply)
- a. Policy statements
 - b. Peer-reviewed journals
 - c. Non-peer reviewed journals
 - d. Member advisories
 - e. Media
 - f. Clearinghouse
 - g. Agency's or government internet website
 - h. N/A (ie, no dissemination)
 - i. Other, specify
39. Are stakeholders given a chance to review a draft version of the assessment before the report is finalized? (yes, no, other, specify)
40. Are stakeholders involved in the assessment? (yes, always/yes sometimes/no, never)
41. Are stakeholders involved in the final decision? (N/A, yes, always/yes, sometimes/no, never)
42. Is there an appeals process in place if stakeholders are not in agreement with the decision? (N/A, yes, no)

43. How would you describe the state of the methods used in the field of health technology assessment? (mature (established/valid/reliable), not mature (need further development and validation, other-specify)
44. If cost effectiveness information is not considered, what are the reasons for doing so?
45. If the organization is a reimbursement body – how would you rate the quality of HTA reports received? (please respond only if your organization is a reimbursement agency) (for drugs, medical devices, and other technology: N/A, excellent, very good, good, fair, poor)
46. What are the key issues, trends, or topics your agency or organization is facing with regard to methodologies used for HTA?
47. We would appreciate if you could provide your name and contact information in case we need to contact you again for clarification or updates

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