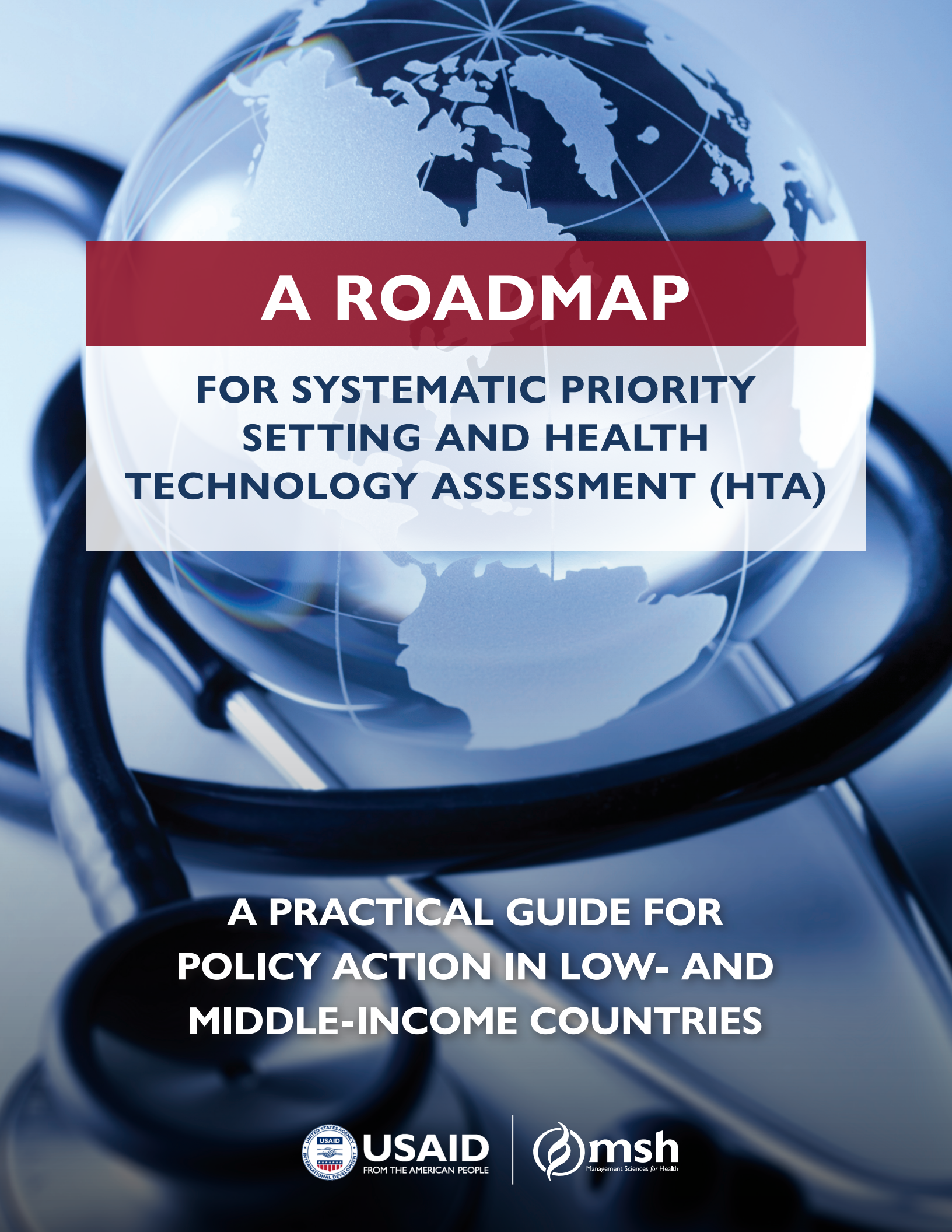

A ROADMAP

FOR SYSTEMATIC PRIORITY SETTING AND HEALTH TECHNOLOGY ASSESSMENT (HTA)

A PRACTICAL GUIDE FOR POLICY ACTION IN LOW- AND MIDDLE-INCOME COUNTRIES

USAID FROM THE AMERICAN PEOPLE | msh Management Sciences for Health

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CONTENTS

ABSTRACT

All health systems face the challenge of managing and allocating limited resources for health. "A Roadmap for Systematic Priority Setting and Health Technology Assessment (HTA)" advocates the use of health technology assessment (HTA) in low- and middle-income countries (LMICs) to determine the value of a health technology (e.g., a drug, medical device, diagnostic test, medical procedure) at different points in its lifecycle. The purpose is to inform decision making to promote an efficient, equitable, and high-quality health system.

We structured this document using an adapted stages model of policy processes, including agenda setting, policy formulation, adoption/implementation, and impact evaluation. However, health-related policy making is not always a straightforward process, and overlapping and non-linearity of these stages may occur. This structure will help implementing partners navigate the political process of institutionalizing HTA.

This document aims to go beyond listing capacity building needs and cross-country, cross-comparing HTA. The introduction illustrates the need for explicit priority setting to achieve universal health coverage (UHC), presents general definitions relevant for priority setting and HTA, and summarizes the history and evolution of HTA in different settings.

In Chapter 2, we explore the policy process for successfully implementing HTA. We present a variety of policy analysis tools for partners in seizing or creating windows of opportunity for HTA policy action. These instruments also help characterize the content, context, and processes conducive to high-quality HTA and the involvement of stakeholders throughout the formulation and implementation stages of the intervention.

The policy formulation and adoption/implementation stages (Chapters 3 and 4) inform when, why, and how best (pragmatically) to incorporate HTA into existing health systems. We present some principles of best practice for HTA, address common methodological considerations, offer practical solutions to address these challenges, and indicate some useful capacity-building approaches for both HTA doers and users.

The impact evaluation stage in Chapter 5 discusses potential frameworks for monitoring and evaluating the impact of HTA implementation. We highlight the importance of measuring HTA's overall impact to secure its long-term political support and funding.

Lastly, we present conclusions and recommendations and discuss the policy implications for LMICs. This is particularly addressed to the US Agency for International Development Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program, led by Management Sciences for Health and its partners. We also present next steps for proof-testing the proposed framework for HTA institutionalization in LMICs.

In developing this document, we conducted a systematic literature review of approaches to HTA implementation and institutionalization in LMICs. We tested our main assumptions and refined our findings through multiple rounds of additional input and feedback from HTA global experts and LMIC stakeholders. Further refinement through in-person workshops is planned for 2020 and 2021.

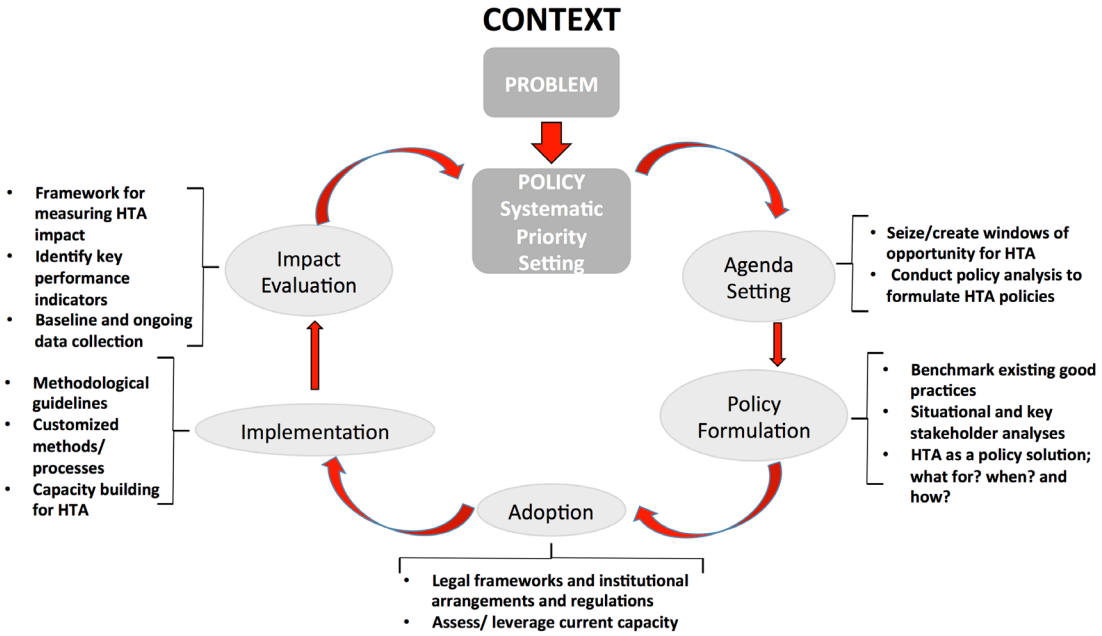
Health care resource-allocation decisions are complex and involve the assessment and appraisal of the best available evidence, keeping in mind societal values and other contextual considerations. The global momentum for HTA presents a window of opportunity for advancing the HTA agenda in LMICs; however, neither HTA reports nor the results of economic models or cost-effectiveness analyses should be used blindly in decision making.

DEVELOPING A ROADMAP FOR HTA POLICY

All health systems face the challenge of managing and distributing limited resources to meet their population's health needs. "A Roadmap for Systematic Priority Setting and Health Technology Assessment (HTA)" advocates the context-sensitive use of health technology assessment (HTA) in low- and middle-income countries (LMICs), which is a multidisciplinary process that uses explicit methods to determine the value of a health technology (e.g., a drug, medical device, diagnostic test, medical procedure) at different points in its lifecycle. The purpose is to inform decision making to promote an efficient, equitable, and high-quality health system.

We adapted the stages (heuristic) model of the policy process [1] to characterize the basic elements of dynamic policy making for HTA (figure 1). The roadmap is accordingly structured around the four main stages of this process: agenda setting, policy formulation, adoption/implementation, and impact evaluation. Because health-related policy making is not always a straightforward process, some stages may overlap, or non-linearity of these stages may occur. The heuristic approach we follow is expected to be applicable with certain degrees of variation to both democratic and more authoritarian regimes.

Figure 1: A framework for institutionalizing HTA



Source: Developed by the authors

There is global momentum for using HTA to advance sustainable universal health coverage (UHC), presenting an opportunity for policy action in LMICs. Our roadmap goes beyond a description of capacity-building needs and a comparison of HTA institutions, methods, and processes in different settings. Its overall goal is to provide implementing partners in LMICs with resourceful tools for leveraging that opportunity to advance HTA use.

In **Chapter 1**, the need for explicit priority setting to achieve UHC is presented, and general definitions of priority setting and HTA-associated concepts are provided. The introduction also features the history and evolution of explicit priority setting and HTA in different settings.

In **Chapter 2**, the importance of the policy process (political economy) for successfully implementing HTA policies is explored. We describe the potential usefulness of Kingdon's policy streams model for seizing or creating windows of opportunity for HTA policy action. We also elaborate the Gilson and Walt policy triangle (content, context, process) and stakeholder analyses that could be used to advance explicit priority setting and HTA to the stages of policy formulation and adoption/implementation.

Policy formulation is described in **Chapter 3**. It includes the features of situational, legal frameworks, institutional arrangements, and regulatory landscape analyses to inform when, why, and how best to incorporate HTA within existing health systems. We also provide insights on best practices for HTA beyond the features of comparative safety, efficacy, effectiveness, and cost-effectiveness as stakeholder perceptions and engagement, transparency, communication, ethical, social, cultural, legal, organizational, and environmental aspects, as well as wider implications for the patient, relatives, caregivers, and the population and equity considerations are also relevant.

Chapter 4 covers HTA adoption/implementation, considers methodological guidelines and reference case development, the need to customize processes and methods, and the implications of using cost-effectiveness thresholds in isolation in LMICs without considering other relevant factors. We also discuss HTA best practice and argue that capacity building should first assess, and then leverage existing capacities. The aim here is to close the HTA knowledge gaps among doers and users.

The last stage of the policy process, impact evaluation, is considered in **Chapter 5**. We outline various monitoring and evaluation frameworks for HTA implementation and identify performance indicators, measuring baseline performance, and scaling data collection processes. This chapter also stresses the importance of early measurement of HTA's overall impact from to secure political support and funding.

The **final chapter** presents conclusions, policy implications, and next steps for proof-testing the proposed framework to further institutionalize HTA in LMICs.

In preparing this document, we conducted a systematic literature review to gather evidence on approaches for implementation and institutionalization of HTA in LMICs. The first round of searches was limited to articles published in English, French, and Spanish as of December 2019; we identified additional records through other sources until April 15, 2020. In total, the database searches identified 18,599 records, of which 11,559 were eligible for abstract review and 1,597 for full-text review. The first qualitative synthesis for this roadmap included 262 articles (Annex 1). Following data refinement, preliminary test of the main assumptions of the roadmap, and additional input from HTA global experts and LMIC stakeholders, we identified an additional 42 documents. A total of 304 articles were included in the qualitative synthesis (Annex 2).

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CHAPTER 1

INTRODUCTION

According to the World Health Organization (WHO), the critical output of the principles of universal health coverage (UHC) is that all people and communities can use the health services they need, in sufficient quality to be effective, while ensuring that users of these services are not exposed to financial hardship [1]. UHC has become one of the ultimate goals of the Sustainable Development Goals as it not only provides financial protection to the population but also ensures access to essential quality health services [2]. Health systems around the world are advancing UHC at variable speeds due to resource concerns, political dynamics, and other competing challenges.

As countries move toward achieving UHC, there is an increasing need to ensure the effective management and allocation of finite resources as the demand for health care services grows. However, in many countries—particularly low- and middle-income countries (LMICs)—priority setting for health typically consists of an ad hoc process that lacks transparency and is not capable of addressing and dealing with the competing interests of governments, donors, and other stakeholders [3].

Achieving financially sustainable and granting effective UHC represents a major challenge, particularly among resource-constrained settings that lack the ability to mobilize additional domestic funding for health and have limited capacity to efficiently allocate available resources and a limited tradition of engaging relevant stakeholders throughout the priority-setting process. Therefore, setting priorities in an explicit manner is critical and costs, quality of health care, and explicit consideration of those who will be affected by decisions need to be balanced throughout this dynamic process [4].

The history and evolution of health technology assessment (HTA) matter for those interested in advancing systematic and more transparent processes to inform resource allocation decisions in different settings. Therefore, this chapter summarizes experiences from high-income countries (HICs) that have successfully institutionalized HTA and reports on the current status of priority setting and HTA in different regions around the globe, with a special focus on LMICs. This chapter also presents past and current global endeavors for HTA.

1.1 IMPORTANT CONCEPTS

Priority setting can be defined as a discussion aimed at consensus building, even as a contested process of political nature [5]. It involves making choices based on a ranking that utilizes systematic rules for the distribution of limited health care resources among competing priorities [6]. As WHO recommends, countries seeking UHC should be accountable to the populations they serve [7]; hence, priority setting should be explicit and ensure that those making the decisions are known and accountable and that they use clear rules and robust methods for assessing health technologies transparently, inclusively, and independently [8].

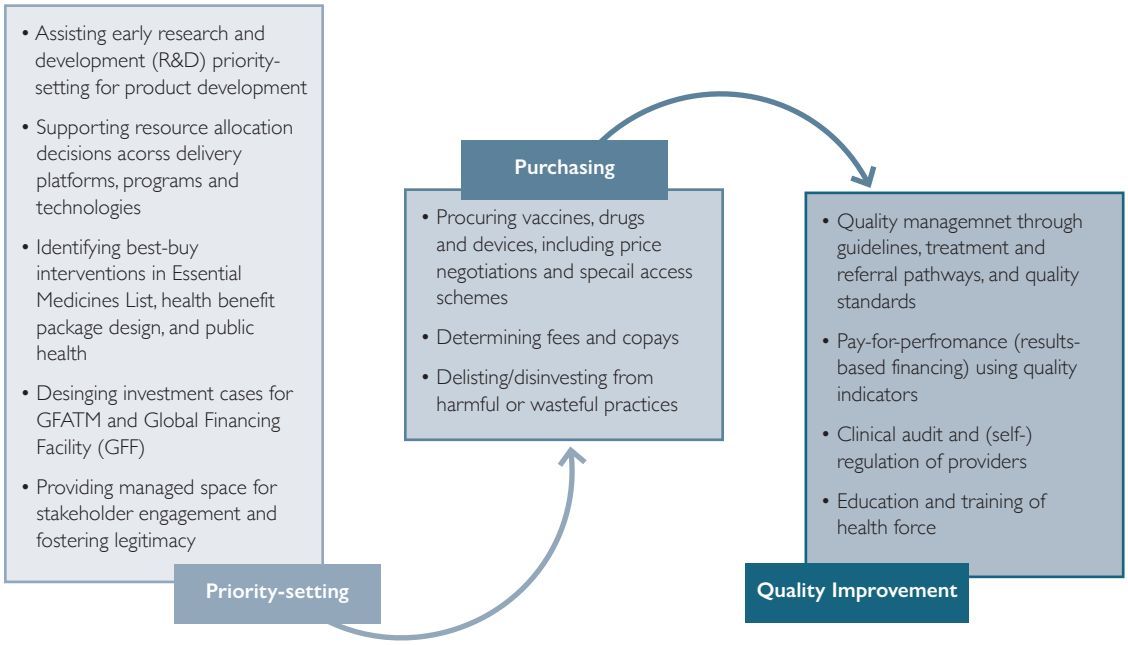
Successful priority setting is a desirable goal for decision makers, but there is no agreed definition of successful priority setting [9]. Different disciplines offer their own perspective, defining successful priority setting through values such as efficiency, equity, or justice, and priority setting can be based on health economics, policy approaches, or evidence-based medicine [9]. Priority-setting frameworks can help decision makers throughout the process, but priority setting involves the adjudication between many values, and people will disagree about which values should dominate. When relevant values conflict, decision makers must develop context-sensitive agreements to achieve their priority-setting goals [9].

According to an international joint task group convened in 2019 by the International Network of Agencies for Health Technology Assessment (INAHTA), Health Technology Assessment international (HTAi), and other organizations, HTA is defined as "a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an efficient, equitable and high-quality health system" [10].

According to a recent publication [11], HTA could have several applications for informing decision making, ranging from informing priority setting to purchasing and quality improvement (figure 2). Nonetheless, the scope of this roadmap is narrower, focusing mainly to support LMICs to establish systematic priority setting for resource allocation decisions (across delivery platforms, programs, and technologies). Resource allocation decisions could pertain to identifying best-buy investments for essential medicines lists, designing health benefit packages and identifying the best-buy of public health interventions, and designing investment cases for donors in different disease areas.

In all cases, the HTA process provides managed space for stakeholder engagement and fostering legitimacy. With adaptations, the scope of application of this roadmap could also be expanded to inform purchasing and quality improvement decisions.

Figure 2. HTA: Several applications for informing decision making



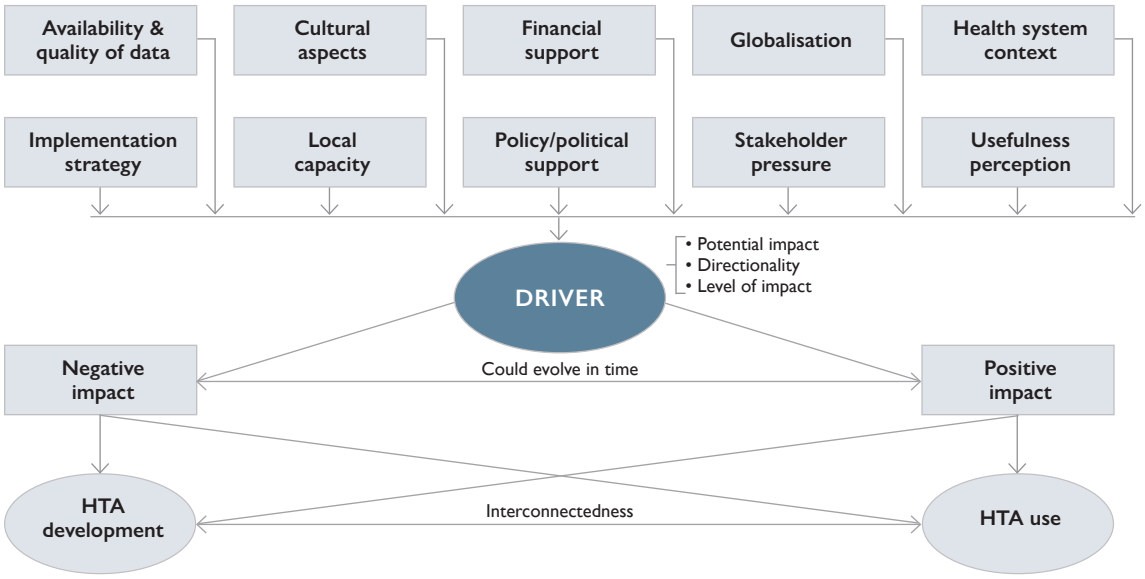
Source: O'Brien et al., 2019 [12]

1.2 CATALYSTS FOR HTA ADOPTION

The practical reasons for any country to adopt and institutionalize HTA vary. They include a need for evidence-based and resource allocation decision making support; improving credibility, accountability, and transparency of the decision making process itself; and interest in providing better-quality health services [13–17]. Initiation models for HTA could be top-down (distilled from political interest); bottom-up (driven by academic/research interest), or both (converging) [17]. HTA driven by political forces generally has a shorter time to initiation than HTA initiated by academia [13, 14, 17].

Figure 3 illustrates the potential drivers of HTA development and use, such as availability and quality of data, having/lacking an implementation strategy, cultural aspects, local capacity, financial support, policy/political support, globalization, stakeholder pressure, health system context, and usefulness [18].

Figure 3. Emergent drivers for the development and use of HTA



Source: Castro et al., 2016 [18]

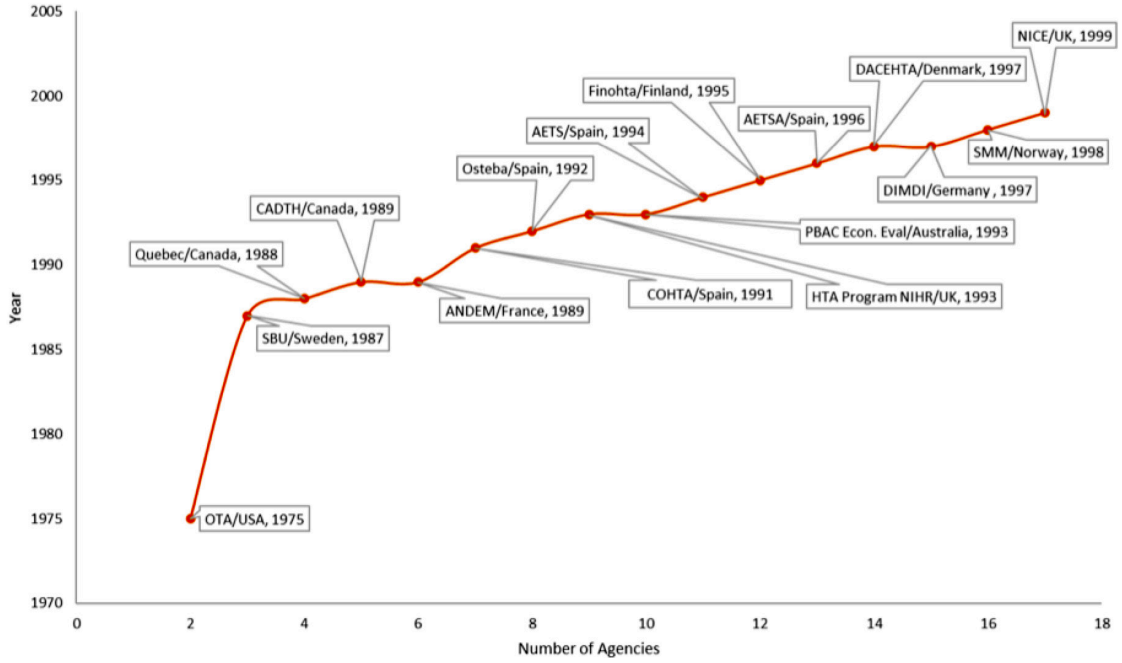
During the 1960s and 1970s, Organization for Economic Cooperation and Development (OECD) countries started realizing the challenges of providing quality health care within the resources available. Health expenditures were rising, while the demand for new and innovative technologies continued to increase [13, 16, 19–21]. However, the incremental health benefits did not match the increased expenditure on and diffusion of these medical technologies [16, 20, 21]. This led to a series of reforms in Western European countries, Canada, Australia, and the United States, which began in the mid-1970s and lasted to the 1990s.

Advances in science also increased data on system performance and produced higher-quality scientific evidence [21]. During this time, Dr. Archie Cochrane published his book on safety, efficacy, and effectiveness, which laid the foundation for evidence-based medicine, a fundamental component of HTA [19]. All of these factors may have played a role in HTA initiation in HICs.

1.3 GENESIS AND HISTORY OF HTA

The first technology assessment institution, although not exclusively health related, was the Office of Technology Assessment (OTA), established in the US public sector in 1972 to inform the US Congress of the advantages and disadvantages of newly developed technologies that started assessing health programs in 1975 [19] and became attractive to other Western countries that were similarly dealing with imperfect and asymmetric information to make decisions. From the mid-1970s to late 1990s, Austria, Australia, Denmark, France, Germany, the United Kingdom, the Netherlands, and Sweden created similar institutions [13–17, 19–22] (figure 4).

Figure 4. Timeline of establishment of first set of HTA agencies



Source: Developed by the authors

In the pioneering countries before 2000, the foundations of HTA as a policy solution had already been established over several years (indicating the incremental nature of the policy process). The governments already had institutional structures, an engaged academia, and a science-oriented community of other stakeholders in place that were geared toward research and evidence generation and use. In many cases, the top-down interest of politicians and policy makers merged with existing academic interests, leading to a converging mode of HTA initiation [13, 14, 16, 17, 21, 22].

1.4 THE EVOLVING LANDSCAPE OF HTA IN DIFFERENT SETTINGS

Almost all HICs and OECD members have implemented HTA methods and processes within their health systems. Recent examples of HTA agencies in the developing world have emerged in Latin America, North Africa, Eurasia, Central and Eastern Europe, and Asia [13, 14]. According to INAHTA, 51 HTA member agencies support health-system decision making, affecting more than 1 billion people in 32 countries around the globe; however, the total number of HTA-producing organizations beyond INAHTA affiliates is much higher [15].

1.4.1 CENTRAL AND EASTERN EUROPE

As the European Union (EU) gained momentum, HTA became a topic for coordination and harmonization in member states [13]. In 1988, the EU formulated the transparency directive, stating that pricing of health care services and technologies needed to be done in a transparent, systematic, and verifiable manner [13, 23]. As Central and Eastern European countries have joined the EU, they became bound by European Commission regulations, including the transparency directive. For nearly three decades, the EU has invested in HTA research, coordination, collaboration, and capacity-building activities for its member states. This has produced the EUR-ASSESS, HTA-EUROPE, European Collaboration on HTA (ECHTA), and the European Network for HTA (EUnetHTA) [13]. All of these measures were critical in strengthening the capacities of existing members and in promoting and scaling up HTA in the next wave of countries in Central and Eastern Europe to join the EU.

Central and Eastern European countries that are now part of the EU or being considered for accession have seen higher, albeit varying, degrees of success in the scale up and institutionalization of HTA. Many have adopted pragmatic models for HTA implementation and utilization, in which countries benchmark and transfer HTA results from other jurisdictions for use in their own decision making—an approach with subsequent transferability limitations. These include **Hungary**, **Poland**, and **Slovakia**, which have legal and institutional frameworks that require HTA to be used for determining pricing and reimbursement of health care technologies [24–27]. Between 2011 and 2015, EU members such as **Croatia, Bulgaria, Lithuania,** and **Romania** introduced HTA [27–34]. Other countries, such as **Serbia**, have not had EU-sustained incentives or support to scale up HTA more rapidly [35–37].

Ukraine established its HTA Department under the State Expert Center, a state enterprise of the Ministry of Health (MoH), in January 2019 after continuous support from the US Agency for International Development (USAID). **Turkey**, now being considered for EU membership, established three state-level HTA authorities, albeit with different levels of coordination, limited guidelines, methodology harmonization, and number of HTA reports developed. However, only one of these three authorities is still in operation. Nonetheless, given the incentive to join the EU, both Turkey and Ukraine are investing in building their own capacities for HTA through academic programs and continued support and, in the case of Ukraine, from USAID and the Safe, Affordable and Effective Medicines for Ukrainians (SAFEMed) program [38, 39].

1.4.2 LATIN AMERICA

As HTA began to take a foothold in HICs, the Pan American Health Organization (PAHO) initiated a technology development unit in the 1980s and supported regional workshops on the subject going into the late 1990s [13, 40]. This development, in addition to Latin American countries' engagement in broader health sector reforms in the 1990s, fueled interest in using HTA [13, 40]. This interest coincided with the World Bank's agenda of promoting the concept of minimum benefits packages of health care to support countries' explicit priority setting [40].

Beginning in 2000, PAHO designated HTA as an essential public health function, and some academic institutions in the region began HTA studies. PAHO also started helping countries think about their potential HTA strategies, train experts, and promote international collaboration. [13, 40]. By the mid-2000s, Argentina, Brazil, Chile, and Mexico had developed agencies and strategies focused on HTA institutionalization [13, 40].

The role of RedETSA (HTA Network of the Americas), established by PAHO in 2011 and aimed at promoting regional collaboration, has been important. PAHO championed the first regional resolution on implementing HTA among member states in 2012, which created political momentum for WHO's World Health Assembly Resolution 67.23 on HTA in 2014 that further emphasized the use of HTA globally. Over the past decades, the Inter-American Development Bank (IADB) has published several influential documents and supported many Latin American countries to introduce more systematic and transparent processes for setting priorities and to update publicly funded benefit packages.

- **Mexico.** Mexico has a long history of HTA after one of its policy champions was engaged with OTA when it was established in the United States in the early 1970s. Since the 1980s, several research and academic institutions have developed HTA reports and evaluations on the use of health technologies in Mexico [37]. In 2004, Mexico established the National Center for Technological Excellence in Health (CENETEC) as its national HTA agency [41].
- **Chile.** Chile set up a department for HTA within the MoH in 1997 that used principles of evidence-based medicine to develop a national benefits package [40, 42]. In 2013, it set up a national commission

that created a proposal for an independent HTA agency [42]. Nevertheless, Chile's use of HTA has been intermittent over the last decade.

- **Argentina.** The Institute of Clinical Effectiveness and Health Policy (IECS), an independent not-for-profit HTA agency, was established in Argentina in 2002 [43]. Since its establishment, IECS has been supporting capacity building throughout Latin America and developing HTA reports that have informed decision making in Argentina and neighboring countries.
- **Brazil.** In 2003, the National Health Surveillance Agency (ANVISA) established an organizational unit for HTA that operated for more than a decade. Brazil started developing a strategy for HTA in 2006 and created a commission for HTA, which was the precursor to the current agency, the National Commission for Technologies Incorporation to the Unified Health System (CONITEC). CONITEC was established in 2011 to advise the MoH on decisions related to adoption, disinvestment, or changes in the use of health technologies as well as on the development or update of clinical protocols or therapeutic guidelines [44].
- **Colombia.** Colombia also set up a national HTA agency, the Institute of Technology Assessment (IETS), in 2012 with technical and financial support from the IADB and UK's National Institute for Health and Care Excellence (NICE) International [14]. IETS is in charge of informing the Colombian government on the value of technologies to be listed or delisted from the publicly financed benefits package. The institution is also in charge of developing, adapting, and endorsing clinical protocols and clinical guidelines. In recent years, there has been a growing interest in using HTA principles to inform centralized negotiations and risk-sharing agreements [14].
- **Others.** Countries like Uruguay, Costa Rica, Peru, and Ecuador have also introduced at various levels of development the principles and methods of HTA to inform benefits package design and coverage within their national health insurance payers. However, in many parts of Central America and the Caribbean (other than Costa Rica), the level of HTA implementation is still limited.

The implementation of HTA has had varying degrees of success in terms of rigor and linkage to decision making in Latin America. While guidelines for HTA and/or economic evaluations exist in most countries, the lack of local data combined with low methodological rigor limit the quality of HTA reports in some of these settings. Although evolving, countries often still use reports from other jurisdictions, including those from Europe, to determine recommendations on inclusion or exclusion of health technologies on reimbursement lists [45]. As is the case with the Central and Eastern European countries, pragmatic HTA models (benchmarking and transferring assessment results from other contexts) are still being used in many places; however, unlike the Central and Eastern European countries, the use of such pragmatic approaches is not explicitly stated in country legislation.

In recent decades, different countries within this region have passed reforms or endorsed legislation enshrining health as a human or fundamental right; this has empowered citizens to challenge their health systems via judicial claims (i.e., *acciones de tutela, recursos de amparo, medidas de proteccion*) in terms of coverage and reimbursement for treatments that were not considered as part of publicly funded benefit packages and not initially budgeted for [14, 44]. The lack of robust methods to conduct and appraise HTA and a limited tradition of transparency that leads to coverage denials further add to this issue.

1.4.3 ASIA

A handful of countries in Asia have implemented HTA or the principles of HTA; however, the literature did not indicate long-term engagement of regional agencies such as WHO or the Asian Development Bank on

priority setting or HTA. However, recent efforts led by the Bill & Melinda Gates Foundation; Wellcome Trust; UK Department for International Development (DFID); HTAi; and other donor-funded platforms, such as the International Decision Support Initiative (iDSI) and the Government of Japan-United Nations Development Program-backed Access and Delivery Partnership, have strengthened local capacity and promoted HTA in the region.

HTAsiaLink, a network of HTA agencies in Asia, was established in 2011 to strengthen individual and institutional HTA capacity, reduce duplication and optimize resources, and share HTA-related lessons among members. The network has also initiated several joint research projects, raised awareness of the importance of HTA within the region and beyond, and gained global recognition while establishing relationships with other global networks [46].

- **Malaysia.** The Malaysian Health Technology Assessment Section (MaHTAS) was established in 1995 under the MoH to help ensure that its facilities use safe, effective, and cost-effective health technology. This is done through full and mini-HTA reports and information briefs and, more recently, through horizon-scanning of emerging health technologies and development and implementation of national evidence-based clinical practice guidelines (after 2001) [47]. Malaysia's HTA program has begun playing a more significant role in health technology policy formulation and decision making, which is anticipated to grow [48].
- **South Korea.** HTA was adopted as a national policy in the late 1990s in South Korea, where the Health Insurance Review and Assessment Service determines the benefits package using HTA processes. In 2009, the National Evidence Based Healthcare Collaborating Agency (NECA) was spun off as an independent HTA and horizon-scanning agency [49].
- **Thailand.** Funded by the government, Thailand has one of strongest and most influential HTA programs in the region. The Health Intervention and Technology Program (HITAP) is a semi-autonomous research unit under Thailand's Ministry of Public Health. It was established in 2007 to appraise a wide range of health technologies and programs, including pharmaceuticals, medical devices, health interventions, individual and community health promotion, disease prevention, and social health policy, to inform Thai policy decisions. In 2013, HITAP established an international unit, drawing on its local and international experiences to work at the global level with overseas development aid international organizations, nonprofit organizations, and other governments to build capacity for HTA. HITAP is one of the founding members of iDSI along with UK's NICE now defunct international division [46].
- **China.** Since the 1980s, China's HTA development has evolved through various stages before being integrated into existing health care policies. Tangible efforts for HTA could be traced back to the early 1990s [50]. The first exploration of HTA consisted of research support from an academic center, but without any regulatory functions. The establishment of the HTA division at the China National Health Development Research Center (CNHDRC), a government-led health research body, in 2008 laid the foundation by establishing HTA frameworks and processes. It is responsible for promoting, developing, implementing, and monitoring HTA. The China HTA network, comprising 34 universities, hospitals and providers, research centers, and industry associations and societies, incorporates industry expertise in developing HTA methodologies. In 2018, China launched the National Center for Medicine and Health Technology Assessment under the CNHDRC, with iDSI as a core partner.
- **Others.** India, Indonesia, Iran, Kazakhstan, Pakistan, and the Philippines are recent entrants into the HTA arena over the last five years as they scale up their UHC programs to support the design of benefits packages. These countries are all working on implementation roadmaps for scaling up HTA; however, capacity gaps in terms of quality of assessments, transparency of processes, and linkage to decision making

remain a challenge [51]. In addition to support from iDSI, UNICEF (Philippines), WHO, the World Bank, and USAID, all governments have committed their own funding to support national HTA committees.

1.4.4 MIDDLE EAST AND NORTH AFRICA

Implementation of HTA is still in an early stage with some heterogeneity in the Middle East and North Africa (MENA); nonetheless, different international meetings over the past years have increased the interest of donors, policy makers, and implementing partners in advancing systematic priority-setting policies in the region, such as the WHO East Mediterranean Regional Office- and HTAi-led initiatives in Tunisia 2013 and Egypt in 2014. In addition, the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) has held high-visibility meetings and is supporting the development of HTA research skills in the United Arab Emirates and neighboring countries through a certificate in evidence-based research [52].

Reimbursement systems in the region still rely heavily on external reference pricing used as a cost-minimization tool that benchmarks against the lowest list prices in reference countries [53]. Nonetheless, regulators are realizing the need to transition to value-based assessment systems to give patients access to different health technologies through more efficient and fair pricing, especially for expensive lifesaving products [54]. As a result, more local regulators are changing legislation and policies to incorporate HTA. For example, in **Egypt** and **Lebanon**, authorities recommended that drug developers submit an economic analysis (e.g., budget impact) to inform negotiations with manufacturers. Currently, these requests are focused mostly on expensive innovative products; for example, the King Hussein Cancer Centre in **Jordan** uses HTA to evaluate the costs and benefits of costly cancer treatments.

Tunisia established the Tunisian Authority of Assessment and Accreditation in Healthcare (INEAS) in 2012, which recently released its methods manual and is the only MENA representative at INAHTA [54, 55]. **Egypt** and **Saudi Arabia** have included the development of HTA agencies in their 2030 health care vision goals.

MENA health policy experts expect that HTA advances over the next 10 years will include capacity building through graduate and postgraduate programs, enhanced institutionalization, HTA scope expanding from pharmaceuticals to non-pharmaceutical technologies, and HTA methods moving beyond cost-effectiveness and explicit thresholds by applying multiple criteria decision analysis frameworks and increased international collaboration [56].

1.4.5 SUB-SAHARAN AFRICA

Unlike other regions where organizations such as the EU and PAHO have played critical roles in harmonizing HTA efforts or where donors and funders, including DFID, USAID, and the development banks, have supported work in the field, such support does not seem to exist yet in sub-Saharan Africa. This provides an opportunity for policy entrepreneurs and international partners to introduce and promote HTA scale up for sustainable UHC in Africa.

Although the African Union has not been engaged in issues of priority setting and HTA, countries such as South Africa, Ghana, Tanzania, and Ethiopia have initiated HTA activities.

- **South Africa.** South Africa is a member of the iDSI initiative and has hosted national and regional workshops to promote HTA with local partners such as PRICELESS/University of Witwatersrand and Clinton Health Access Initiative (CHAI) [57]. It has also supported the costing of a national HTA agency. The Department of Health in South Africa is creating a national HTA strategy as it scales up its national health insurance scheme and HTA's function will increase [57].

- **Ethiopia.** Ethiopia is implementing a widescale community-based health insurance scheme and is preparing to launch a social health insurance scheme. To meet its increasing need for HTA, the Health Economics and Financing Analysis (HEFA) team was established within the Finance Resource Mobilization Department under the MoH. The HEFA team has benefited from technical support provided by the Universities of Bergen and Harvard through the Disease Control Priorities-Ethiopia (DCP-E) project funded by the Gates Foundation [58, 59].
- **Tanzania.** With support from iDSI and Access Delivery Partnership [60], Tanzania has established an HTA committee and revised its national essential medicines list and standard treatment guidelines using HTA principles [61].
- **Ghana.** Ghana has benefited from the long-term engagement with HTA implementing partners (initially NICE International and more recently the Global Health and Development Group [GHD] at Imperial College) to scale up its national health insurance system [62]. In more recent years, GHD, as a core partner of iDSI, has provided technical capacity-building support in collaboration with the Norwegian Institute of Public Health and HTAi [57]. Ghana recently concluded an economic evaluation for hypertension management and in 2018 held regional meeting on setting priorities fairly, co-organized by iDSI and HTAi [62].
- **Kenya.** In Kenya, iDSI, UKAID, and the Global Fund have initiated the design of a health benefits package and activities to improve the efficient use of resources for HIV programs [63]. HTA is supported under iDSI with HITAP as the lead institution and also supported by the Royal Thai government.

1.5 PAST AND CURRENT GLOBAL ENDEAVORS FOR HTA

In terms of the history of HTA agencies, it is worth noticing that globalization and international regulations have an impact on the introduction and subsequent operations of these type of bodies. Below we cite some past and present global endeavours that have been influential for HTA establishment in different settings.

Although the **WHO** Europe regional office in 1984 urged that "…all member states should have established a formal mechanism to systematically assess the appropriate use of health technologies," reiterated at the 2007 World Health Assembly (WHA60.29 on Health Technologies) [64], many countries, even in Europe, struggled to establish more systematic and data-driven priority-setting processes during the early years of implementation. This could also be the case for many LMICs as they advance on establishing their own HTA processes and mechanisms.

In 2014, WHO recognized that "the efficient use of resources is a crucial factor in the sustainability of health systems' performance… as they move towards universal health coverage," and urged all member states to establish national systems for HTA assessment and use it as a means of achieving UHC (WHA67.23) [65]. This statement was further reaffirmed by the UN General Assembly (Resolution A/74/2) of October 2019 as part of the political declaration of the high-level meeting on UHC advocating for strengthening Member States' capacity on health intervention and technology assessment to achieve evidence-based decisions at all levels [66]. The need for cost containment and the above-mentioned statements have been pivotal drivers for HTA adoption in many LMICs.

Recently (December 2019), the **Global Fund to Fight AIDS, Tuberculosis and Malaria** issued its Market Shaping Strategy Mid-Term Review Position Paper on piloting a cost-effectiveness analysis for selected health products and interventions. This document advocates for more efficient and effective collaboration with Unitaid-Global Drug Facility (GDF) and/or the Global Alliance for Vaccines and Immunization (GAVI). "The fact that much

of what the Global Fund finances has not been assessed for cost-effectiveness implies that impact can be further maximized" [67]. Therefore, in the case of those LMICs that fund most of their programs and services through international assistance, there is an opportunity to use HTA principles to improve allocative and technical efficiency.

Development partners, the private sector, and civil societies have also played an influential role in enabling and supporting HTA agencies. **The International Society for Technology Assessment in Health Care**, established in 1984 [68], and its successor, **HTAi**, in 2003 have shaped the landscape of international collaboration in HTA. As national programs were established, in 1993, **INAHTA** was created to support communication and cooperation at the agency level. ISPOR was established in 1995 with the goal of serving as a catalyst to advance the science and practice of health economics and outcomes research and has substantially influenced HTA methods and processes development globally.

It is also worth mentioning that in 2004, the European Commission and Council of Ministers targeted HTA as a political priority, leading to the establishment of **EUnetHTA** in 2009, aimed at supporting collaboration among European HTA organizations. Nevertheless, their work on methods and international collaboration mechanisms (i.e., the development of the EUnetHTA Core Model for HTA) have helped advance HTA beyond the EU borders.

iDSI, a global network working to achieve UHC and the health Sustainable Development Goal 3, was launched in 2013 to support LMICs to make better decisions about how much public money to spend on health care and how to make that money go further. Most of iDSI's work has been funded by the Bill & Melinda Gates Foundation, DFID, and the Rockefeller Foundation and focused on Asian and African countries. The iDSI Secretariat sits at the Center for Global Development.

Other development partners have long provided technical assistance to countries for their HTA capacity building and development, including the World Bank's early HTA involvements in China in 1997 and 1998 and more recently CNHDRC co-led with iDSI; USAID's work conducting a landscape study of informal and formal HTA processes and evaluating the HTA-regulatory interactions; and direct support of governments in HTA capacity building globally, including Afghanistan [69], South Africa [70], Ukraine [39], and Indonesia [71], through various projects (e.g., SPS, SIAPS, GHSC, SAFEMed), including the MSH-managed Joint Learning Network (JLN) and its related products.

HTAi has established an Interest Group on HTA in developing countries, and recent EU projects on HTA (i.e., AdHopHTA, ADVANCE-HTA, MedTechHTA, INTEGRATE-HTA) have engaged LMIC partners to make sure that the tools they develop are also relevant for these settings [72–75]. Additional sources developed by international partners aimed at informing HTA institutionalization include "Priority-Setting in Health, Building institutions for smarter public spending" published by the Center for Global Development in 2012 [76]; iDSI's Toolkit for HTA published in 2018 [77]; a the recent publication by Norheim et al., "Global Health Priority-Setting-Beyond Cost-Effectiveness" [11].

External drivers like globalization and regional and international collaboration could be considered as relevant for HTA institutionalization, but other domestic factors seem equally important for subsequent institutional transformation of these type of bodies. HTA institutions seem particularly vulnerable to political decision making. Many examples, including the disappearance of the OTA in the US in the early 1990s; the transformation of the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) into CADTH in 2006; and the changing remits, governance, and activities of institutions like NICE in the UK, ANVISA in Brazil, the German Agency of Health Technology Assessment (DAHTA) and the German Institute of Medical Documentation and Information (DIMDI) in Germany, and IETS in Colombia, may back this statement.

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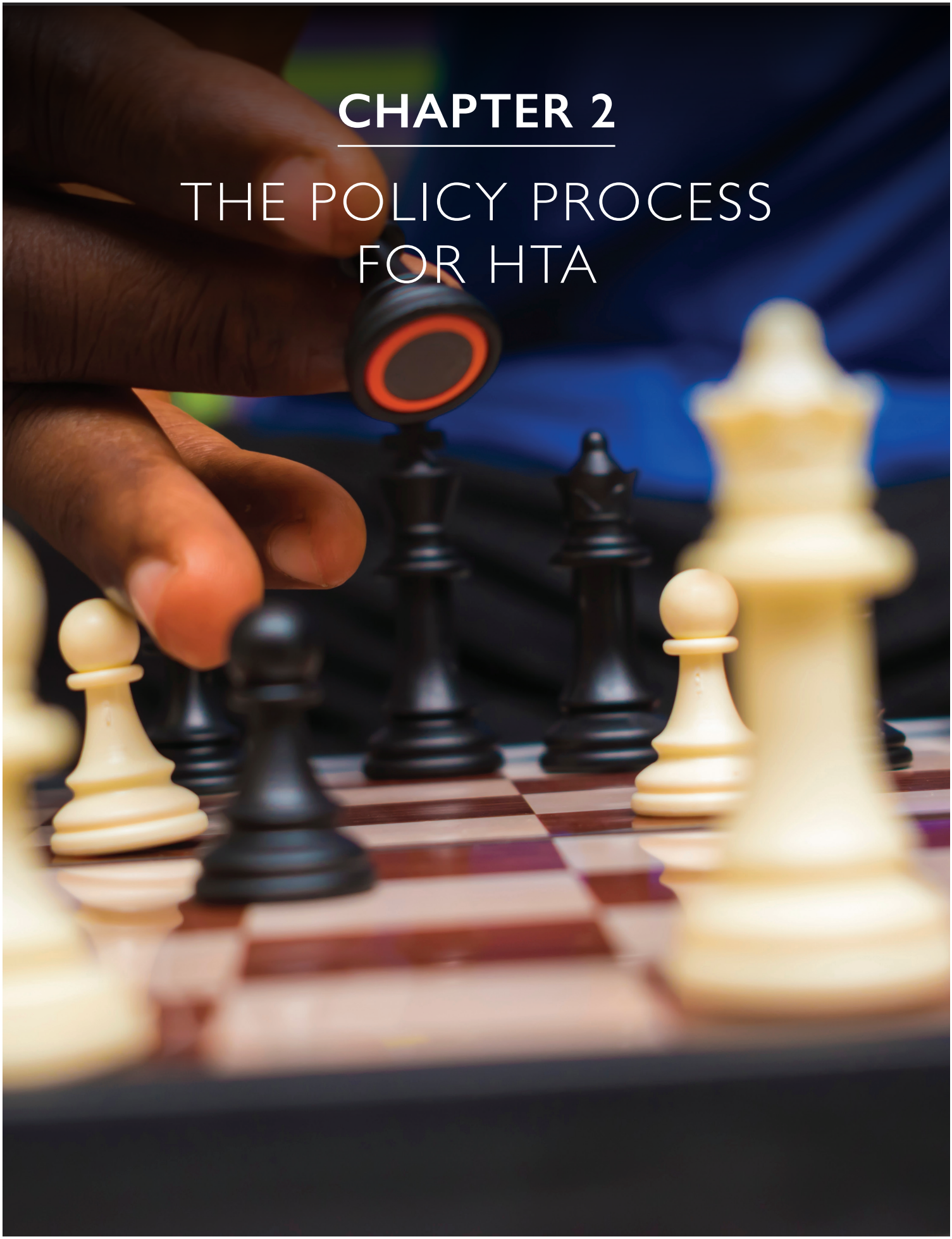


CHAPTER 2

THE POLICY PROCESS FOR HTA

This chapter aims to help readers become familiar with and able to implement policy strategies to introduce systematic and transparent priority-setting processes and HTA in LMICs. We present frameworks and tools for increasing the chances of success.

We have leveraged the stages (heuristic) model, which has been widely used for policy analysis [1–4]. Building on Howlett and Ramesh's adaptation of this model [5], we cover four main stages to implement HTA: agenda setting, policy formulation, adoption/implementation, and impact evaluation. As mentioned before, the stages model provides a useful framework for simplifying policy analysis, but it has some limitations. While there might be some linearity along the process, the interplay among these different stages would also be evident [6, 4]. Limitations aside, this model provides the basis for setting the scene and analyzing the context of interest regarding HTA.

The above mentioned limitations require implementing partners to take a broader approach to help HTA policy development in LMICs [4] by incorporating context, process, and actors' analyses [7]. Instead of just copying and pasting existing models of HTA, considering a country's existing policy dynamics, processes, and institutions and understanding important players' (stakeholders') interests, positions, and power will help test the political waters in deciding how far to pursue HTA as a course of action [8]. To help policy makers, donors, and implementing partners develop a comprehensive stepwise policy approach, this chapter provides insight into:

1. **Getting HTA into the policy agenda:** tools for seizing or creating windows of opportunity for policy action favoring systematic priority setting and HTA. We present examples on how to apply the agenda setting model adapted by John Kingdon [9] to elevate the importance of HTA as a policy solution among others such as price regulation, quality assurance, and resource mobilization.
2. **Considering broader policy analysis approaches helps to understand the context, process, and actors involved in systematic priority setting and HTA.** We build on the 'policy triangle' [7] to analyze content, context, and process to take policy action. Analyzing the context, including existing problems that HTA can address, and existing policies, regulations, and institutions informs the formulation and adoption/implementation stages for HTA introduction.
3. **Integrated frameworks and tools for assessing relevant stakeholders' positions, power, and interest are important for assessing the political feasibility of HTA.** The analysis of the political actors affected by or influencing a given policy has been conducted in different settings, and we provide a list of potential resources and tools that may assist stakeholder analyses.
4. **Additional policy tools that may help implementing partners develop prospective strategies for HTA institutionalization in LMICs are also relevant.** Information retrieved from the local context, existing processes, and stakeholders will help to determine the political feasibility of moving forward. A comprehensive policy analysis should include the plausibility of incorporating principles of good HTA practice (i.e., stakeholder engagement, transparency, communication, and ethical and equity considerations) [10]; the possibility of leveraging existing local capacities and improving coordination; and, since no one single size fits all, the ability to answer questions like: "why?" "when?" and "how to use HTA?" before starting its implementation.

Designing and implementing health policy for HTA will not be simple [8]; nonetheless, if decision makers and implementing partners take incremental steps to introducing HTA rather than disruptive approaches that differ significantly from the status quo, chances of succeeding might be much higher [11].

2.1 SETTING THE AGENDA FOR HTA (SEIZING OR CREATING WINDOWS OF OPPORTUNITY)

As previously mentioned, for HTA to support systematic, evidence-based decisions for health care priority setting, it needs itself to be adopted as a policy. Policy making is a dynamic process because various and changing issues compete to be considered on the political agenda for the attention of policy makers. In this context, agenda setting itself is influenced by the political interests of policy makers and lawmakers. The agenda setting model adapted by John Kingdon [9] could be used to create or seize windows of opportunity to elevate the importance of HTA as a policy solution.

2.1.1 KINGDON'S POLICY STREAMS MODEL

Agenda setting refers to problems that need a public debate or action of public authorities [9]. Different countries and their health systems face a broad array of challenges, including financial strain, limited resources, epidemics, disease burden, and demographic transition. Thus, the process of setting up the political agenda can be competitive among issues to gain the attention of media, professionals, the public, and policy elites (those with decision making authority, power, or connections) [12].

There are different approaches to analyze how policies come to the political agenda for action. We focus on Kingdon's 1984 agenda setting model [9], which has been extensively used in policy analysis. According to the author: "the agenda setting process narrows a set of conceivable subjects to the set that actually becomes the focus of attention" of decision makers. In this model, the dynamics of agenda setting imply the interconnection of three aspects or streams: problems, policies (proposals), and politics.

Kingdon states that the three streams must come together for an issue to be put on policy makers' agenda. As per this model, the three streams may be flowing independent of one another, and it is only on their convergence that a limited window of opportunity is created for policy action [9]. To effect change, the window of opportunity must be seized at that right time [9], because how long it lasts is unpredictable. Windows of opportunity are not created by chance but by policy entrepreneurs or advocates who may exist within the government or among interest groups willing to champion a specific policy intervention. Therefore, to create opportunities, policy advocates must take deliberate and sustained action.

2.1.2 USING THE THREE STREAMS TO SUPPORT HTA INTRODUCTION

Problem: Kingdon defines this stream as where an issue shifts from being an individual problem to a large-scale or public concern that the government recognizes needs to be clearly defined and addressed. In the case of HTA, rising costs for service delivery, new and costly technologies entering the market, issues of quality of health care, or variable access to necessary treatment across the population and accountability are potential motivators for introducing systematic priority-setting processes and HTA as policy solutions [13].

Not all competing problems capture the attention of decision makers, and sometimes dramatic events (focusing events) such as media scandals, disease outbreaks, or political unrest gain their attention. Even a prominent problem can drop off policy makers' agenda if the government feels it has solved it already or if individuals become acclimated to it and turn their attention to the next-in-line subject.

Kingdon further states that policy advocates need to highlight indicators of health system problems to bring them to the government's attention for action. Thus, problems such as increasing costs, high out-of-pocket payments, judicialization of health care, variability of clinical practice, price discrimination, opportunity costs lost due to inefficient allocation of limited resources, or inequity could be triggers that seize the attention of policy makers in favor of HTA implementation.

Policy: The policy stream consists of the ongoing problem analysis and alternative solutions. The implications of different courses of action are relevant but not strong enough to induce policy changes on their own. Many times, policies are developed by experts and stakeholders who are knowledgeable about the problem. Policies often develop when a single institution or academic center has tested the proposed policy/initiative to demonstrate their effectiveness. HTA, for example, has roots in evidence-based medicine practices focused on the individual clinician.

According to some authors [13], HTA institutions could be the result of top-down, bottom-up, or converging problem solutions. Additionally, different settings have adopted different models and contextualized HTA approaches to suit their context; for example, Canada has a decentralized process with provincial HTA processes linked to a national agency, while Spain's process is also decentralized but coordinated within a network that informs the whole Spanish health care system. In England and France, the process is centralized with a national HTA appraisal agency that serves the English National Health Service in the former or the insurance-based care system in the latter [14, 15]. In all cases, analysis of existing problems resulted in HTA as a solution, but on its own it will not be strong enough to induce policy change and will still require political support.

Politics: Operating at a separate level, the politics stream reflects swings of national mood, campaigns, or pressure groups and government changes. The politics stream focuses on the political momentum around an issue leading to the problem being addressed. Kingdon's model refers to perceptions as public concerns that require government intervention. Additionally, public opinion must prioritize the problem for elected lawmakers who need to be responsive to people's requests to maintain electability. Thus, policy advocates need to work with interest groups that support the policy of interest and that have the political power to influence both politicians and the public in favor of a common cause.

In the case of health care, public and political opinion may favor granting access to health services and increasing financial protection for most of the population. However, the benefits of HTA in supporting these goals may be unclear at early stages of the policy process. Therefore, its usefulness needs to be shared and reiterated throughout the stages of adoption and implementation.

Policy advocates need to work with patient groups, clinicians, other health care professionals, and other important players to garner support and build pressure on politicians to support an HTA related policy. The role of both academics and health care professionals may be of paramount importance to shape the mood around systematic and evidence-based priority-setting processes.

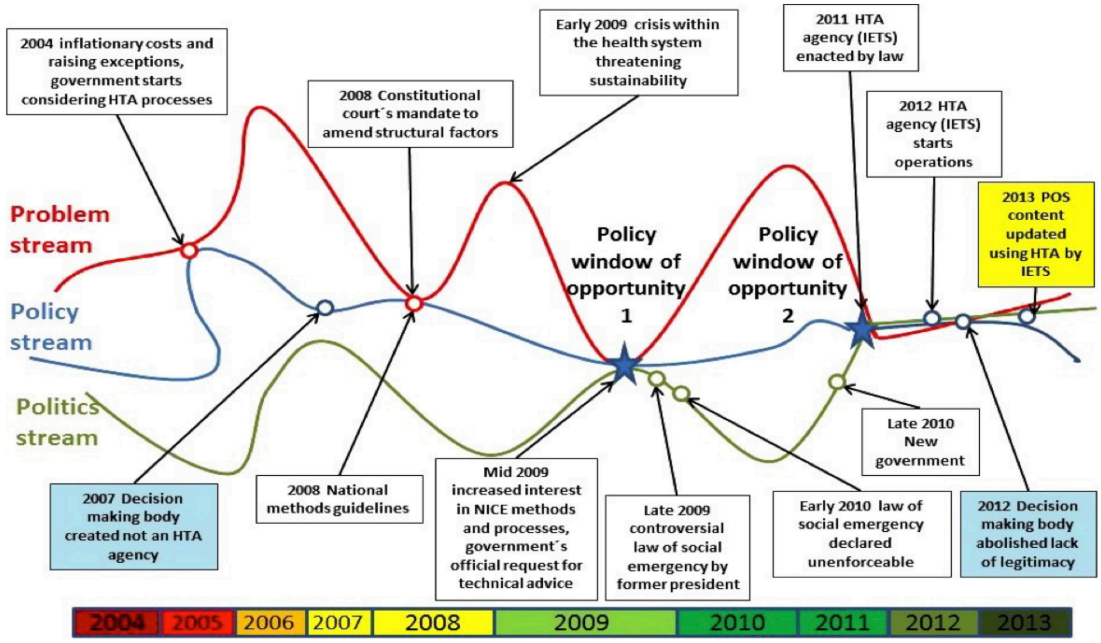
2.1.3 EXAMPLES OF APPLYING THE THREE STREAMS TO HTA IN DIFFERENT SETTINGS

In the three countries below, Kingdon's model was useful to describe the policy process to incrementally introduce more systematic use of evidence to inform decision making and, in some cases, create their own HTA institutions.

- **Indonesia:** In June 2014, the iDSI Steering Group chose Indonesia as iDSI's target country, subject to further detailed in-country scoping. HITAP completed this scoping through a stakeholder workshop in Jakarta in conjunction with PATH. The scoping report confirmed and expanded upon the findings from their initial mapping of Indonesia. In July of same year, the iDSI Steering Group approved the decision to initiate practical support in Indonesia. Since August 2014, iDSI has convened in-country stakeholders and external donors in the HTA policy process and developed technical capacity through different workshops [16].

- **Colombia:** In 2017, Kingdon's model was used retrospectively by a group of researchers to analyze how the local HTA agency (IETS) reached the political agenda and was established in 2012. The study looked at different sources to map out the incremental process from the early 2000s until 2013. In July 2008, a constitutional court statement (T–760) mandated the Executive to correct any structural weaknesses within the system to enhance equity and improve efficiency by equalizing the official benefits package (POS). In 2010, a new president familiar with the UK's NHS and aware of NICE's work catalyzed the HTA policy initiative with IADB support. IETS (the local HTA agency) was finally established in September 2012 and started operations soon after supporting the Ministry of Health and Social Protection (MoHSP) on their interest to periodically update the list of benefits of the POS. "Policy process in this country has been incremental over the use of HTA processes to inform health policies, starting from 'scratch' in the mid-2000s up to the formulation by law 1438 of IETS last January 2011" [12]. Figure 5 presents a pictorial representation of Kingdon's model being used for the analysis of HTA establishment in Colombia in 2012 [12].

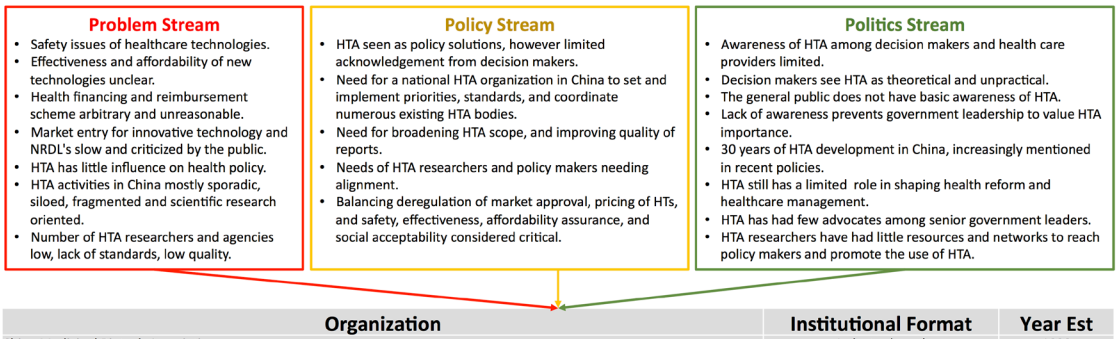
Figure 5. Kingdon's model for agenda setting for HTA institutionalization in Colombia



Source: Castro, 2017 [12]

- **China:** A 2018 article analyzed what factors have influenced the lengthy development of China's HTA initiative and proposed some policy recommendations. It stressed the need for seizing or creating windows of opportunity for HTA using Kingdon's model and taking every opportunity to showcase HTA's value [17] (figure 6). The policy climate for HTA development has been improving in recent years as new health technologies have attempted to enter the Chinese market and population expectations around health care have increased, as has recognition of the value of scientific evidence in general. This created a window of opportunity for policy action that resulted in the establishment of at least four new HTA-specialized institutions in less than a decade. The article emphasized that implementing partners in China should "produce meaningful and influential research with practical implications" to propel the momentum and open (or keep open) the policy window for HTA [17].

Figure 6. Kingdon's model applied to analyze establishing HTA in China



Organization	Institutional Format	Year Est
China Medicinal Biotech Association	Industry-based	1993
Key Lab of Health Technology Assessment (Fudan University), NHFPC	University-based	1994
Division of Evaluation and Translational Research, Development Center for Medical Science and Technology, NHFPC	Governmental institution	1994
Chinese Cochrane Center	University-based	1999
Center for Pharmacoeconomic Evaluation and Research, Fudan University	University-based	2002
Center for Evidence-Based Medicine, Fudan University	University-based	2004
Evidence-based Medicine Center, Lanzhou University	University-based	2005
Division of Health Policy Evaluation and Technology Assessment, China National Health Development Research Center, NHFPC	Governmental institution	2007
Shanghai Health Technology Assessment Research Center Division of Technology Assessment,	Governmental institution	2011
National Center for Medical Service Administration, NHFPC	Governmental institution	2015
Center for Health Policy and Technology Assessment, Peking University	University-based	2017
Research Center for Health Technology Assessment of Hubei Province	University-based	2017

Source: Chen et al., [17], adapted by the authors

These examples indicate that Kingdon's model can be a plausible approach for conducting prospective or retrospective policy analysis focused on agenda setting for HTA. Nonetheless, this model applicability may work differently in settings where the role of pressure groups, civil society organizations, political elites, and the public mood may play vastly different roles.

The HTA process, regardless of the country or health system, seems to have seized the attention of many policy makers [18]. Nonetheless, the emergence of HTA on the policy agenda needs to be considered in the context of other existing policies. Furthermore, HTA establishment is bound to conflict with existing institutions or groups at all policy stages, from agenda setting to implementation and institutionalization [19]. Such conflict can lead to differences in how HTA is institutionalized in different parts of the world, but it may also lead to gaps between the HTA body's mandate and practice [19].

An HTA body may evolve in many ways. Its focus may narrow to specific areas of greatest interest, impact, or value (such as pharmaceuticals) or it may expand if initial experience proves valuable (as in the case of NICE and as is increasingly being documented in in lower-income settings [20]). Global best practices for HTA and priority setting must adapt to the context-specific interplay among ideas, interest, and institutions already in place [19]. Therefore, implementing partners may benefit from using other methods of policy analysis to formulate HTA policies as they are incorporated into existing and operating health systems and as HTA mechanisms evolve over time.

2.2 USING OTHER METHODS OF POLICY ANALYSIS TO FORMULATE HTA POLICIES

In addition to considering health performance indicators, scientific evidence, and cost information, qualitative research may inform HTA policy formulation and support the stages of adoption and implementation. This section presents some policy analysis tools that may assist implementing partners, country policy makers, and local stakeholders to assess specific country context and stakeholders.

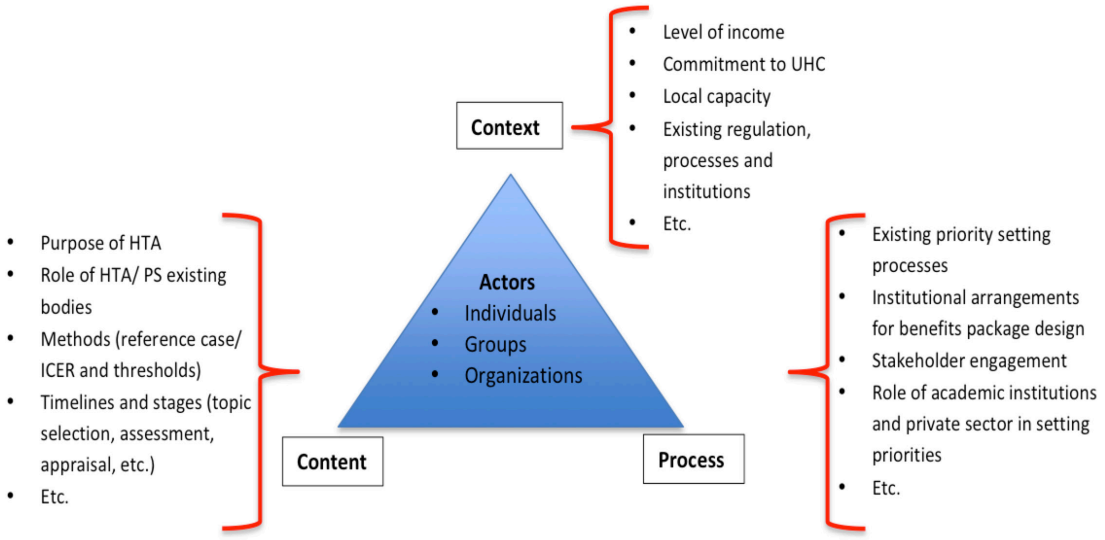
2.2.1 CONTENT, CONTEXT, AND PROCESS ANALYSIS

It is of paramount importance to dynamically analyze content, context, and process throughout the different stages of the HTA institutionalization process. Aimed at informing the HTA policy formulation, adoption, and implementation stages, qualitative research could be used to customize policy content and to identify stakeholders who can hamper or support HTA efforts [21].

Because of potential budget and time constraints to inform pragmatic policy making, we advise thematic content analysis, which allows researchers to look at interview or focus group data to classify, compare, and categorize recurring themes. Interviews or focus groups to depict salient issues from a sample of local (and sometimes international) stakeholders can produce rich data regarding HTA as an intervention [22]. Participant sampling should be purposive and judgmental [23], including individuals representing organizations that can affect the successful implementation of HTA. Semi-structured, short (30–45 minute) open-ended interviews could serve this purpose.

The policy analysis triangle by Walt and Gilson [7], a highly simplified approach, is useful for looking at and summarizing content of existing or non-existing policies for systematic priority setting and HTA, as well as the processes for decision making and how power is used in such health policy. This means exploring the role of the state, civil society groups, and local and international organizations. Figure 7 provides a graphic representation of the policy triangle, applied to HTA.

Figure 7. Policy analysis triangle applied to HTA



Source: Walt and Gilson [7], adapted by the authors

2.2.2 USING STAKEHOLDER ANALYSIS TO ASSESS THE FEASIBILITY OF HTA

Assessing political feasibility requires an analysis of the political actors affected by or influencing a given policy [24]. For HTA, these can include the government (ministries or departments of health and finance); donors; payers (private and public); health care providers; companies; civil society organizations (including patient representatives and general public); health care professionals (doctors and public health specialists); and academics (universities, think tanks, and individuals).

In 2018, Vlad developed a checklist (Mapping Tool) to identify the types of stakeholders who are likely to have a role in priority-setting policy work in LMICs [25]. The checklist was developed to guide iDSI's initial technical support to a new country, but it can be useful for any organization or individual engaging in similar work [25]. This tool includes questions to identify stakeholders and their institutional affiliations.

The checklist will be most useful in settings with limited experience with or resources for stakeholder consultation and participation. Furthermore, once the stakeholders are identified and a specific policy proposal is defined, the checklist can be the first stage in an analysis of potential stakeholder roles [25]. The tool presents three levels for analysis (Nodes (Organizations), Networks, and Environments. Under nodes/organizations, it further categorizes the types of stakeholders into Consumers of Evidence, Producers of Evidence, and Knowledge Brokers. Funders and Development Partners are evaluated under networks. Health System and Research System are explored under environments.

For each stakeholder category, the tool suggests questions that encompass a broad spectrum of types of priority-setting decisions. As each question is addressed, the tool suggests potential functions and roles to consider and specific details to assess stakeholder understanding or positioning on priority setting. Figure 8 presents an adaptation of this tool with some examples developed by the original authors [25] of stakeholder roles in UHC debates in three countries (Philippines, Thailand, and Ghana). This version only extracted information for the first level and category of analysis (Nodes/Organizations and Consumers of Evidence).

The potential list of stakeholders belonging to the category Consumers of Evidence include politicians and politically appointed decision makers, civil servants and non-health professional decision makers, health service managers, health professional groups, the private sector (industry), courts and the judiciary, patients, and the public. Other categories such as Producers of Evidence (academic institutions, independent research institutes, researchers and research managers); Knowledge Brokers (knowledge brokers per se and media organizations and journalists); and Funders and Development Partners (bilateral and multilateral organizations, international foundations) are not included in figure 8 but are also part of the tool.

Figure 8. Stakeholder mapping tool applied to Philippines, Thailand, and Ghana

Level	Category	Type of stakeholder	To be filled				
			Level of governance	Institution Philippines	Institution Thailand	Institution Ghana	Individual actor (if applicable)
NODES (ORGANIZATIONS)	Consumers of evidence	Politicians & politically appointed decision makers	Legislative bodies (e.g., Parliament, Congress and their chambers or committees)	The House of Representatives passed a UHC bill in 2017, whereby "every Filipino is granted the right to health by virtue of citizenship." It also established a Health Technology Assessment (HTA) Council. Three versions of the bill have been approved since then in the Senate. The bill is still under consideration by the Senate, as of May 2018. Each version of the bill had a key proponent in each legislative chamber.			
			Head of government (e.g., Prime Minister, Chief Minister)		The Prime Minister was a key figure for UHC debates in Thailand in the early 2000s, more so than the Health Minister. Other categories of actors are reformist bureaucrats, research institutions, and NGOs.		
			Head of state (e.g., President, Monarch)				
			Federal/Provincial/ state government (e.g., mayors, local government bodies)				
			Ministry of Health			The Health Summit is a national level, joint decision making forum between the Ministry of Health, development partners, and related health actors.	
			Other ministries (e.g., Ministry of Finance)				
			Public organizations (e.g., public health bodies)				
			Government health insurers	In May 2016, the Philhealth Board approved a priority setting process aimed at defining a guaranteed benefit package for the country's National Health Insurance Programme			

Source: Vlad [25], adapted by the authors

There is no single or simple method to assess the characteristics of players involved in policy change [26]. Therefore, we recommend computer-assisted political analysis. *PolicyMaker 4* software [27] is an easy-to-use tool that can help analyze, understand, and create effective strategies to promote a point of view on any policy question or political issue; the tool also provides step-by-step guidance to help conduct the analysis and design

of political strategies to support related policies of interest, in this case for HTA. *PolicyMaker 4* software was used in 2010 and 2011 to inform the nascent stages of the HTA institute of Colombia (IETS) (figure 9) [28].

Figure 9. Stakeholder analysis for introducing HTA in Colombia (2010–2011)

Actor	Interest	Power	Position	Total Score
Health Care Providers: Pharmaceutical companies	Be profitable and well reputed	5	-5	**-25**
Health Care Providers: Clinics & Hospitals	Be sustainable, profitable, well reputed, and invest new technology	5	-3	**-15**
Pressure Groups: Patients association, CSOs	Defend interest of patients with chronic conditions and advocate for access to new health technologies	1	-5	**-5**
Academics: Universities, Think tanks	Produce and disseminate knowledge, support translation into practice, achieve academic reputation	1	5	**5**
Sectional Groups: Medical Associations & Professional Groups	Defend their members' interests, competitive salaries, fair policies, autonomy	3	3	**9**
Health Care Purchasers: Insurers	Be sustainable and well reputed	3	5	**15**
Government: President, MoH, MoF, CRES	Achieve UHC, financial sustainability of an equitable and fair health system, invest in public health/care to increase productivity	5	3	**15**

Source: PolicyMaker [27], adapted by Castro 2010–2011 [28]

Researchers divided actors into different groups: providers (clinics, hospitals, pharmaceutical industry); purchasers (insurers); sectional groups (medical associations and unions); government (Ministry of Health, Ministry of Finance, President, National Commission of Health Regulation-CRES); pressure groups (patients associations, civil society and advocacy groups); and academia (universities, think tanks). Using *PolicyMaker*'s approach and scoring system, researchers assessed each player's position on HTA policy (support, opposition, or non-mobilized), as well as their power (resources available to use in the policy debate) and intensity of position (high, medium, or low) depending on their willingness to use available resources in the policy debate.

After extensive review of documents, public declarations/statements, and interviews available in mass media, researchers scored the power and position of stakeholders in Colombia. Players were ranked on a power scale of 1 to 5 (low to high) and a position scale of -5 to 5 (in which -5 represented high opposition, -3 medium opposition, -1 low opposition, 0 neutral, 1 low support, 3 medium support, and 5 high support. As the analysis confirmed, pharmaceutical companies were expected to be the biggest opponents to the HTA initiative based on their strong financial and lobbying power and the perception of potential risk that a future HTA agency may limit/reduce their profits. This contrasted with insurers and the government, who were expected to be high supporters due to their long-term financial sustainability and universal enrollment interests.

Prospective stakeholder analysis can inform the policy formulation, adoption, and implementation stages, while retrospective analysis serves to monitor and evaluate the progression of different stages. Other sources of information, including stakeholder statements thorough political debate and law enactments as well as public hearings, could help researchers and implementing partners triangulate the findings.

2.3 DEVELOPING POLICY STRATEGIES FOR ADVANCING EXPLICIT PRIORITY SETTING AND HTA

The political feasibility of policy change is determined by the position, power, and perceptions of players [29]. Once these aspects have been assessed, the players' positions might be shifted through bargaining strategies, and their power can be enhanced or reduced by redistribution of assets (e.g., information, financial, interconnections) based on their status (supporters versus contradictors) [29]. The number of players can be modified by reducing their number or mobilizing them according to policy intentions, and their perceptions of problems or solutions can also be shifted through better information, media campaigns, and clarifications to promote or prevent policy change.

Countries' willingness to devote time and resources is related to the joining of the various streams (emergence of windows of opportunity) as in Kingdon's model. When innate interests arise among country players, international partnerships with technical experts in established HTA agencies can allow HTA development and conversations to take place. Such support will increase the likelihood of any policy proposal reaching the implementation stage. In some settings, an international development partner might be needed as the catalyst to sensitize local stakeholders, mainly through high-profile advocacy and broad-based communication to improve awareness. For example, in Thailand, the Wellcome Trust played a major role in sensitizing stakeholders and in the development of the Technology Assessment for Social Security in Thailand, which was an early HTA unit. Other international efforts from partners to sensitize local stakeholders for HTA may include sponsoring field visits and attendance at HTA-related conferences and organizing high-visibility national, regional, or global events. In addition, depending on the target, different techniques are needed to disseminate HTA messages, including research results; mass media can be used carefully if needed during the policy process.

There may be chances not only to seize but also to create windows of opportunity for introducing HTA to the political agenda. As mentioned, urgent problems and crises will rise to the top of priorities. However, for HTA to be implemented as a solution by policy makers, it needs to be technically feasible, aligned with social values, inexpensive, and supported by the public. Finally, the politics stream, bringing together international commitments, national mood, and local policies and aspirations related to UHC in many LMICs, may help create political consensus.

Qualitative policy research may help researchers, donors, and implementing partners introduce or advance priority setting processes using HTA in LMICs. However, the recommendations in this document should not be taken as formulaic steps for policy action as no single size fits all (not even the resources and tools presented in this roadmap).

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CHAPTER 3

FORMULATING POLICIES FOR HTA

Earlier chapters underscore the complexity of the policy making process and the need to understand the context and decisive players for facilitating policy change. Chapter 2 provided proven policy tools to analyze the context; existing processes; and the power, position, and interest of stakeholders to obtain their support for HTA. Once HTA has reached the political agenda and there is willingness to promote policy change (e.g., HTA introduction, promotion, and/or institutionalization), the formal process of policy formulation begins. This chapter has the following objectives aimed to help implementing partners:

- **Break down the HTA process:** We start by identifying the principal objectives of an HTA program and then delineate the differences in the major stages of prioritizing the topics for evaluation, assessment, and appraisal. Finally, we go through the various steps to operationalize an HTA program.
- **Understand the importance of legal frameworks, regulations, and institutional frameworks for HTA:** We discuss these various elements in several countries. Based on the findings, we provide recommendations on potential options for LMICs at different stages of HTA implementation and scale up.
- **Leverage situational and stakeholder analyses for formulating policies for more systematic priority setting:** Each country's health system and policy priorities are unique. Leveraging the findings of the previous chapter, we recommend potential roles of the different stakeholders within the HTA process.
- **Build upon existing capacities:** Even in countries with no or a limited HTA tradition, resource allocation and health coverage decision making processes may already exist, and decision making (albeit with limitations) could already be taking place. HTA processes should be incepted into existing health systems and not the other way around.
- **Identify best practices in the HTA process:** Best practices include stakeholder engagement, communication, and consideration of ethical and equity issues in the HTA process. Our systematic literature review provides several lessons from many countries implementing HTA that would be helpful for LMICs at nascent stages of HTA policy and process formulation.

3.1 HTA AS A POLICY SOLUTION: WHAT FOR? WHEN? HOW?

3.1.1 HTA: A POLICY SOLUTION FOR WHAT?

As mentioned in Chapter 1, the framework from O'Brien and colleagues identifies decisions and policy making that a robust HTA process can inform [1]; nonetheless, the primary focus of this document is to support countries to establish systematic priority setting for resource allocation decisions (across delivery platforms, programs, and technologies). Resource allocation decisions could pertain to identifying best-buy investments for essential medicines lists, designing health benefit packages and identifying the best-buy of public health interventions, and designing investment cases for donors in different disease areas. Therefore, our roadmap provides guidance on the process of HTA in these areas of interest as an approach to create a managed space for stakeholder engagement and fostering legitimacy.

Although different countries in North America, Europe, Latin America, and Asia have been leveraging HTA as a mechanism to engage product developers and guide their research and development priorities based on population needs [2–10], this application of HTA for priority setting is beyond the purview of this document. Nonetheless, this document's scope could also be expanded at a later stage to inform pricing, purchasing, and quality improvement decisions.

Systematic priority setting is one way of promoting more efficient financing for UHC. It entails the explicit consideration of what is relevant given the population, societal values, and ethical considerations [11]. It involves

the assessment of the best evidence on competing health technologies in light of their potential value. HTA fosters the promotion of open discussion, considering the values and preferences of the context in which such decisions will occur. Communication and implementation of decisions are also part of this process.

Health care resource-allocation decisions are complex and involve the assessment and appraisal of available evidence, while bearing in mind societal values and other contextual considerations [11]. Most of the published literature on priority setting and decision making has focused primarily on the technical aspects of quantifying the burden of disease or assessing the cost effectiveness of different interventions. Although these are relevant inputs into the process, priority setting as a whole is a much wider political process because it involves the distribution of benefits and responsibilities throughout society [12].

3.1.2 HTA: WHEN DO WE DO HTA?

Goodman effectively describes the 'moving target problem of health technologies' [13] to reflect their dynamic life cycles. New health technologies are constantly being introduced into the global market, while others are becoming obsolete. Additionally, although new applications of a technology could emerge, pharmacovigilance or technosurveillance could unveil adverse impacts, or price and market competition could shift use recommendations.

In essence, 'when' to conduct HTA is always contextual. It is linked to the objectives of an HTA program. For example, an HTA body may or may not have the responsibility of reassessing a health technology for disinvestment. On the contrary, HTA prioritization of an upcoming breakthrough technology could be reactive or proactive in nature; hence, an HTA body could have a waiting list for future assessments. Thus, the HTA process could create a proactive environment through horizon scanning and early assessment of demand of upcoming technologies.

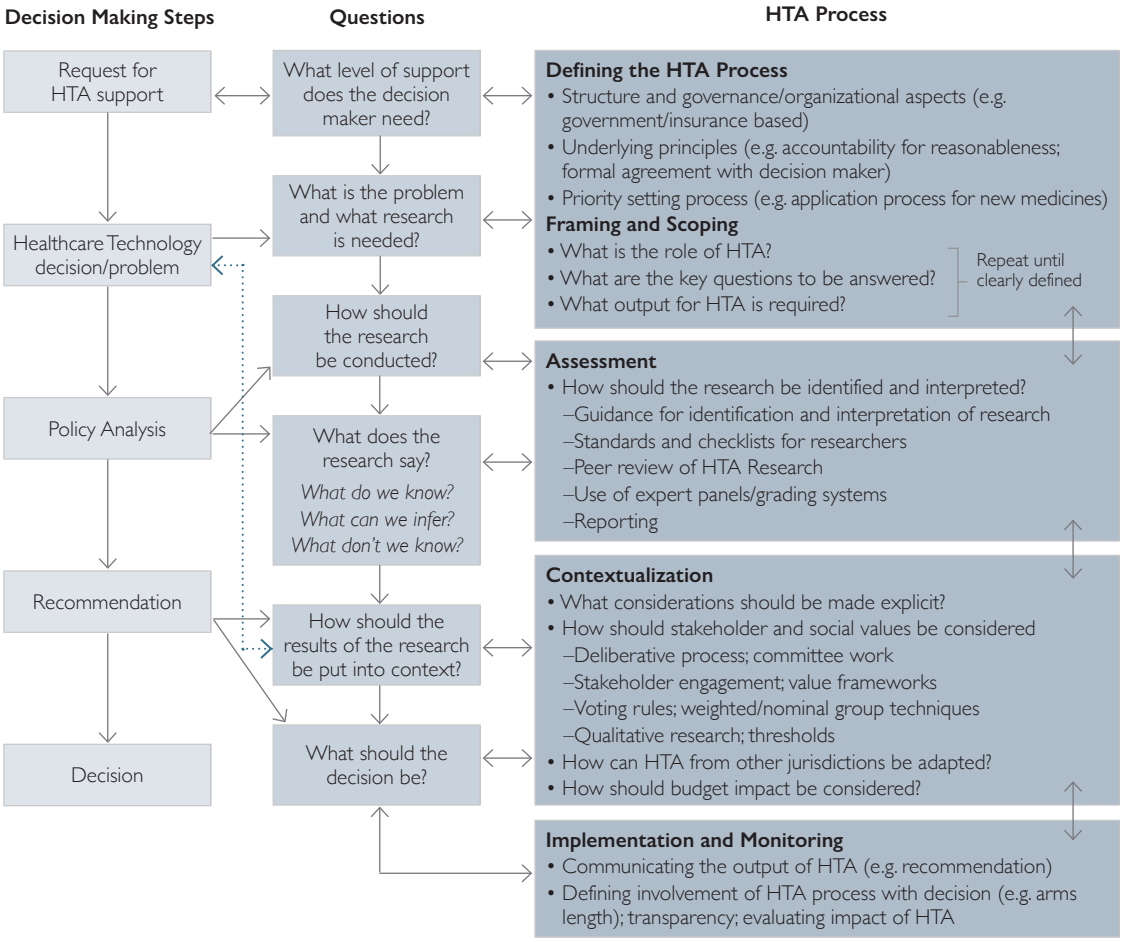
As mentioned, many countries use HTA as a mechanism to engage product developers and guide their research and development priorities based on population needs [2, 3]. This process is referred to as horizon scanning or early stage assessment [13]. In most cases, horizon scanning programs provide rapid assessments of emerging technologies or new applications or future impacts of existing technologies [13]. Organizations and groups with particular interest in horizon scanning (e.g., EuroScan [8]) have developed prioritization criteria for selecting topics. Countries like Canada, Australia, Brazil, South Korea, Spain, and the UK have horizon scanning functions or agencies [8]. The US Centers for Medicare and Medicaid Services and AHRQ also have horizon scanning functions despite the United States' lack of a national HTA agency [8]. In these countries, HTA programs or affiliated agencies or programs have a horizon scanning function that focuses on emerging technologies or new applications or future impacts of existing technologies [13].

Finally, when to conduct HTA is also driven by the stakeholders engaged in the process. Given the multifaceted and political nature of priority setting, patients, clinicians, politicians, donors, or other stakeholders may demand an evaluation or reassessment.

3.1.3 HTA: HOW DO WE CREATE A ROBUST HTA PROCESS?

This section provides a deeper dive into the methods and processes for the assessment component of an HTA program. However, it is important to recognize the various steps involved in creating a robust HTA program. Kristensen and colleagues' work on best practices for HTA implementation for ISPOR provides a framework for understanding the HTA process [14] (figure 10). This framework provides a list of critical questions that need to be answered to operationalize the creation of a robust HTA process.

Figure 10. The HTA process



Source: Kristensen F et al., 2019 [14]

This framework highlights the different components of HTA but adds another crucial aspect for an impactful HTA program—the need to *define the HTA process* itself. This can be characterized through answers to the following questions:

1. Structure and Governance:

a. Legal Framework: Is there a current legal mandate or legislation linked to HTA implementation or establishment of an HTA agency in the country?

b. Institutional Framework and Governance: Will there be an independent agency for HTA or one affiliated with the MoH, or will it be a department within the MOH? Will it be an agency linked to a national health insurance agency or will it be an agency or department within a national research institute? Based on this, what will be the agency's linkage and reporting structure to policy decision making? Which agency, government body, or committee will oversee the HTA agency?

c. Assessment and Appraisal Functions: Which agencies, institutions, or committees will conduct the assessment v. appraisal v. decision making?

d. Binding Power: What will be the binding power of an HTA or HTA institution's recommendation? For example, will outcomes from the HTAs conducted be an essential consideration or an additional point to consider (nonbinding) for decision making?

2. Framing and Scoping:

a. What is the overall objective for HTA (and/or HTA agency) and its role in the health system?

b. What types of questions need to be answered by the HTA and for what products (e.g., medicines, diagnostics, devices, public health interventions)?

c. What is the expected output? A recommendation? A descriptive analysis or reporting of findings?

d. What are the underlying principles with regard to transparency and to ethical, equity, and quality considerations for an HTA process?

e. What is the topic selection process for prioritizing technologies for assessment?

Resource allocation decision making is a complex process that moves from scientific assessment (topic selection, assessment, appraisal) to deliberation to communication of the decisions made [15].

TOPIC SELECTION

It is unlikely that decision makers will be able to assess the value of all health technologies or be fully aware of the costs and benefits of every competing alternative (within and outside the health sector) each time a decision needs to be made. Therefore, it is important to highlight the need for a systematic process for *Topic Selection*. This stage of the process consists of prioritizing those topics (health technologies) that will be evaluated. The number of stakeholders engaged in the topic nomination varies by context [16]. In England for instance, NICE invites submission of potential topics from public health care agencies, health professionals' bodies, industry, academia, and the public [16]. The Swedish SBU invites topics for evaluation from similar entities to NICE, excluding industry [16]. Thailand's HITAP invites public health care agencies and academic/research institutions for topic nomination [16]. In Indonesia, the topic selection process is ad hoc—the national health insurance program has nominated some topics, while HTA team members selected others in the current HTA program [17].

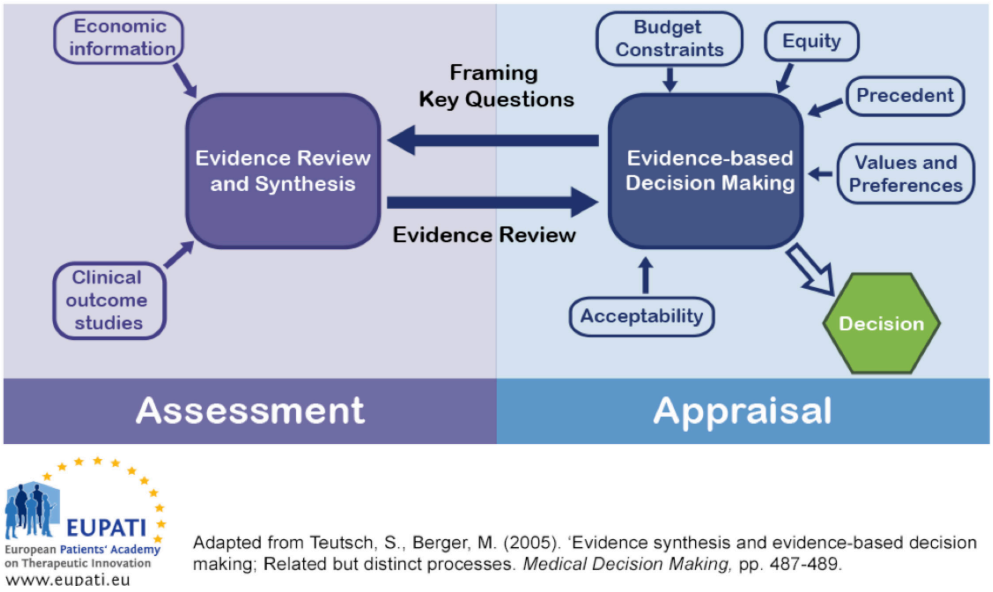
The stage of topic selection could be explicit or implicit, reactive or proactive, dynamic or periodic, and assisted by transparent processes and broad stakeholder engagement or a closed-door exercise. There is no one answer for establishing robust topic selection processes. Being proactive, dynamic, open, and explicit about the selection criteria to assess health technologies seems preferable to ad hoc, reactive, closed-door, and non-transparent approaches to topic selection. Specchia et al. conducted a systematic literature review to identify criteria used for priority setting, including [13]:

- Disease frequency
- Burden of disease
- Patient preferences
- Public interest
- Frequency of use of the technology
- Controversial nature of the technology
- Technical performance
- Efficacy/effectiveness/validity
- Impact on health/quality of life
- Risks/safety
- Economic impact/costs/maintenance cost
- Organizational impact
- Impact on clinical practice
- Risk of inappropriate use of the technology
- Impact on ethical, social, cultural, and/or legal aspects
- Likelihood that HTA results will be implemented
- Impact of HTA results/dissemination of technology
- Availability of scientific evidence

After choosing topics for evaluation, two interconnected components—*assessment* and *appraisal*—may be conducted by separate institutions or the same HTA bodies. While the assessment stage focuses on gathering and synthesizing the best available evidence or critically reviewing and endorsing the evidence submitted from

external reports, the appraisal stage considers assessment results in light of broader factors related to the context of interest, aimed at providing advice or recommendations to decision makers (figure 11). In countries with advanced priority-setting systems, such as England and the Netherlands, there is a clear connection between assessment and appraisal [18]. However, in less developed models for priority setting, the assessment and appraisal components could be disconnected or in some cases nonexistent.

Figure 11. HTA assessment and appraisal



Source: EUPATI, 2015 [19]

ASSESSMENT

An independent group of HTA scholars, the International Working Group for HTA Advancement, has developed a set of principles for the assessment component of HTA [19]. These principles emphasize standards for methods and elements of good practice for HTA bodies to increase their impact on policy decision making and focus on the following four domains [19]:

- Structure of health technology assessment programs
- Methods of health technology assessment
- Processes for conducting health technology assessment
- Use of health technology assessment for decision making

The following chapter goes into detail of these domains for evaluating health technologies. It also provides potential options for structure, methods, and processes for LMICs in different stages of HTA advancement. Here we would like to emphasize that we encourage new HTA bodies to meet the highest level of excellence; however, practical considerations must be explored, particularly at the early stages of implementation.

APPRAISAL

While HTA can form an integral part of a comprehensive continuum for evidence-informed decision making, the process requires transparency and inclusiveness. Recommendations from an appraisal process that

are supported by good evidence and clear reasoning can carry considerable weight. Making HTA results public makes it harder for decision makers not to consider them (*de facto* binding recommendations). If a recommendation departs from available evidence, clear arguments for this deviation must be put forth. We suggest that new HTA institutions explore the working paper from *Ludwig Boltzmann Insitut* that analyzed international appraisal bodies and recommended the following characteristics to be part of the appraisal process [20]:

- The appraisal committee's responsibility should be clearly stated
- The procedural rules governing the appraisal committee's work should be documented and available to the public
- Committee membership should encompass as diverse a set of backgrounds as possible to accurately represent the public in decision making
- Meeting agendas should be publicly advertised well in advance
- Public or stakeholder consultations should be an integral part of the process, preferably both in the prior HTA evidence assessment and in the committee's appraisal
- Earmarked funding should be available for additional evidence collection through pilot testing and trials if needed
- A process to appeal a recommendation should be available

TRANSPARENCY AND LEGITIMACY OF HTA PROCESSES AND RECOMMENDATIONS

It has been said that resource allocation decision making is a complex process that takes place along a continuum that moves from evidence generation to deliberation and communication of the decisions made [15]. Transparency and legitimacy of HTA processes and institutions can affect the impact of recommendations; therefore, implementing partners must bear in mind the principles for good deliberative processes as part of transparent priority-setting policies. Transparency and legitimacy of HTA processes and institutions are important aspects that may increase or reduce the potential impact of recommendations.

Transparent and fair deliberative processes. When new HTA bodies start implementing their deliberative process to inform policy decisions, the Accountability for Reasonableness (A4R) framework developed by Norman Daniels and James E. Sabin [21] shall be considered. A4R argues for four conditions that make deliberative processes behind decision making processes fairer and accountable:

- Publicity condition: Process, factors, and evidence should be publicly available to those affected by the decisions.
- Relevance condition: Problems, data, and solutions should be relevant to those who will be affected by the decisions.
- Revision and appeals condition: All decisions should be revisable in light of the emergence of new evidence or a shift in social values.
- Regulative condition: Institutions in charge of fulfilling the promise of the decision making process should enforce those decisions.

The four conditions compel decision makers to contribute their deliberative capacities to whatever broader public deliberation is conducted through democratic institutions, formally or informally. The arrangements

required by the four conditions are not a replacement for a broader democratic processes. Ultimately, these broader democratic processes have authority and responsibility for guaranteeing the fairness of decisions [21].

Additional resources that can help implementing partners strengthen capacities for more transparent, fair, and participatory deliberative processes for HTA in LMICs include:

- Health technology assessment, deliberative process, and ethically contested issues [22]
- 2020 HTAi Global Policy Forum Meeting, Background Paper: Deliberative Processes in Health Technology Assessment: Prospects, Problems, and Policy Proposals [23]
- The Dynamics of Health Technology Assessment: Is it Just About the Evidence [24]
- Hard Choices in Priority Setting: Reconciling Technical Analysis and Public Participation [25]
- OHE Deliberative Processes in Decisions about Health Care Technologies [26]
- HTA: Algorithm or process? [27]
- Priority setting: towards evidence-informed deliberative processes [28]
- Radboudumc—Evidence-informed deliberative process: A practical guide for HTA agencies [29]

COMMUNICATING HTA RESULTS

All HTA bodies need to continuously use strategic engagement and communication to ensure political and financial support. For example, new HTA bodies should consistently communicate their return on investment for their existence. Some evidence suggests that HTA is a cost-saving endeavor, which means that cutting the HTA budget would be potentially counterproductive to the government's goal [30]. In Ireland, it is expected that HTA saved more than €19 million annually [31]. By effectively communicating the value of HTA activities, institutions may be able to influence three of the main drivers for HTA described in Chapter 1: perception of its potential usefulness, favor stakeholder's position, and securing financial and policy/political support.

HTA results inform decision making at different levels of health systems, so reports must meet the needs of their different audiences. Technical reports should follow best practices (section 3.6) to ensure transparency [32]. Recommendations must be tailored to different audiences using the good principles for knowledge translation and science communications. Reaching and influencing any target audience may require multiple messages and media [33]. At the macro-level, policy makers from departments or ministries of health usually require concrete, timely, and clear information on which to base their discussions; at the meso-level, health care providers and payers require information on the basis of reimbursement, pricing, and coverage recommendations, supplemented with budget estimates and expected targets; at the micro-level, health care professionals, patients, and caregivers also require clear and concrete recommendations, but in plain language. HTA programs should also develop, continue to improve, and adapt their dissemination activities for lay members of the general public. Dissemination planning should start at or before the initiation of each HTA and include costs, time, and other resources allocated and should take into account the culture and existing resources. Reaching and influencing any target audience may require multiple messages and media [33].

Communicating value of HTA activities. In many countries, the main funding source for HTA activities often comes from donors or domestic revenue. Availability of financial resources often rises and falls in the short run due to local and global political, economic, and business cycles. Tightening fiscal space or stagnating international aid requires governments and donors to make difficult decisions to cut costs, and significant justification needs to be put forth from the very beginning to ensure that HTA activities represent good value for money so they can continue in the long term.

3.2 LEGAL FRAMEWORKS AND INSTITUTIONAL STRUCTURE

This roadmap primarily focuses on two common approaches of institutionalizing HTA agencies: top-down or converging modes. Under top-down, governments build on the available legal framework to establish HTA bodies; under converging, they build on existing capacities within academic institutions to advance HTA as a policy intervention. As mentioned in Chapter 1, an HTA agency can also evolve from the bottom up by using resources from academic and research institutions, professional associations, and civil societies using external development and technical support.

3.2.1 INTERNATIONAL AND NATIONAL LEGAL FRAMEWORKS

The WHO constitution declares, "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being." This implies a clear set of legal obligations for countries to ensure access to timely, acceptable, and affordable health care of appropriate quality [34].

Given the resource needs to achieve a high standard of health, WHO noted that the efficient use of resources is a crucial factor in the sustainability of health systems' performance. The World Health Report of 2010 indicated that as much as 40% of spending on health is being wasted [35]. Countries urgently need systematic, effective solutions to reduce such inefficiencies and to enhance the rational use of health technology. Because meeting all health needs with limited resources is impossible, priorities must be set. The national and subnational levels of implementation of the right to health should involve a systematic approach for identifying and implementing cost-effectiveness interventions. This framework of prioritization for resource allocation in achieving the right to health is reflected by the United Nations Committee on Economic, Social, and Cultural Rights.

"The most appropriate feasible measures to implement the right to health will vary significantly from one State to another. Every State has a margin of discretion in assessing which measures are most suitable to meet its specific circumstances. The Covenant, however, clearly imposes a duty on each State to take whatever steps are necessary to ensure that everyone has access to health facilities, goods and services so that they can enjoy, as soon as possible, the highest attainable standard of physical and mental health. This requires the adoption of a national strategy to ensure to all the enjoyment of the right to health, based on human rights principles which define the objectives of that strategy, and the formulation of policies and corresponding right to health indicators and benchmarks. The national health strategy should also identify the resources available to attain defined objectives, as well as the most cost-effective way of using those resources." United Nations CESCR, 2000

In addition to internationally driven pressures, countries also have obligations from their own constitutions, laws, rules, and policies. Constitutional commitments to protecting health differ from setting to setting in both their specificity and focus. By 2011, only a minority of WHO member countries had explicitly enshrined within their constitution's rights to health—public health (14%), medical care (38%), and overall health (36%) [36]. In countries whose constitutions did not expressly provide for the right to health, commitment is inferred from other rights—for example, from the right to a clean and healthy environment in Uganda's constitution and from the right to development in the case of Malawi. In Madagascar, the constitution refers to international human rights instruments, which links to the WHO health as a human right declaration, even if the Madagascar constitution is silent on the right to health itself.

Relevant layers within the legal framework relate to the provision and prioritization of health care. In the case of HTA, governments often explicitly endorse or create agencies or they may pass regulations listing certain evaluation criteria or processes before a new technology is approved.

In the classic example of the 1999 development of NICE in the UK, the HTA agency was deeply integrated into the legal framework guiding the health care system from its inception.

"The Secretary of State for Health, in exercise of powers conferred on him by section 11(1), (2) and (4) of, and paragraph 9(7)(b) of Schedule 5 to, the National Health Service Act 1977 and of all other powers enabling him in that behalf, hereby makes the following Order: (1) This Order may be cited as the National Institute for Clinical Excellence (Establishment and Constitution) Order 1999 and shall come into force on 26th February 1999." "Subject to and in accordance with such directions as the Secretary of State may give, the Institute shall perform such functions in connection with the promotion of clinical excellence in the health service as the Secretary of State may direct." The National Institute for Clinical Excellence (Establishment and Constitution) Order 1999

Similarly, the HITAP in Thailand was developed as a program under the Bureau of Policy and Strategy in the Ministry of Public Health. In addition to the legal framework that allowed for its creation, HITAP also benefits from the legal framework that requires its services. In particular, the revised Medical Device Act B.E.2551 (2008) requires that devices costing upward of 100 million Baht (USD 3.3 million) be assessed on their social, economic, and ethical value prior to achieving market authorization.

"Registrant who wishes to produce or import medical device…shall submit an application to the licensor for the assessment that such medical device has efficiency, quality, standard and safety for use including assessment of its effect and feasibility in economic and social aspects to implement the use of the medical device in appropriateness widely and fairly and after the licensor has issues the assessment certificate it may produce or import." Medical Device Act B.E.2551 (2008), Section 22

Similarly, new agencies in Latin America, North Africa, and Eastern Europe have been implemented by law and with the specific mandate to support resource allocation decisions.

In addition to the legal and policy frameworks that enable the use of HTA for prioritization, some explicitly limit the extent to which a specific assessment methodology can be implemented and the results used. Examples from the United States and Germany explicitly limit the use of value-of-life variables such as quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs) to assess tradeoffs between choices when prioritizing health interventions.

"The Patient-Centered Outcomes Research Institute... shall not develop or employ a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability) as a threshold to establish what type of health care is cost effective or recommended." Compilation of Patient Protection and Affordable Care Act: Subtitle D of Title VI - Sec. 6301

"[a decision based on a threshold per quality-adjusted life year (QALY) gained] should be seen critically. On the one hand, the vast majority of countries in which HEEs contribute to decision-making do not have a (fixed) threshold. On the other, this would be a value judgement, and would thus not fall under the international methodological standards following §139a (4) Sentence 1 according to which only methodological standards apply in the assessments of the Institute." Institute for Quality and Efficiency in Health Card (IQWiG) General Methods, v.5.0. July 2017

Leveraging existing legal frameworks will give implementing partners the foundation to institutionalize HTA bodies and their mandates, while certain policies, existing institutional arrangements, and value judgments will determine the role, character, and tasks that each HTA institution will undertake.

3.2.2 HTA INSTITUTIONAL STRUCTURES

The institutions engaged in the HTA process vary by country and are usually determined by the country context and legal frameworks governing HTA. These subsequently affect the legitimacy and binding power of HTA results. Figure 12 provides examples of institutional structures across countries and the binding power of their recommendations.

Figure 12. Comparative features of institutional HTA structures in selected countries

Country	Legislation	Institutions: Assessment	Institutions: Appraisal	Binding Power
United Kingdom	Legislation in 1999 to make NICE a Non-Departmental Public Body	NICE outsources assessment to a network of academic institutions and the National Institute of Health Research	NICE Technology Appraisal Committee consisting of NHS, patient representatives, care givers, academia, manufacturers	The UK National Health Service (NHS) is mandated to implement the recommendations provided by the technical appraisals (HTAs) conducted by NICE, though it doesn't delve into budget impact of the recommendations. NICE has several other functions (e.g., clinical guidelines, quality standards and performance metrics, sharing of evidence) that are not legally binding but are considered valuable guidelines
Germany	The Federal Joint Committee (G-BA) has the legal mandate to define coverage benefits, including new technologies. G-BA was established by law in 2004	G-BA conducts its own HTAs or commissions the Institute for Quality and Efficiency in Health Care (IQWiG). These reports focus on health policy rather than technologies. Additionally, DAHTA@ DIMDI maintains a national database of HTA research and design information systems to support the research.	G-BA consisting of representatives from physicians, hospitals, sickness funds, and other stakeholders and is the supreme decision making body.	Decisions are binding for SHI
Colombia	IETS established as an independent agency by law 1138 of 2011	IETS outsources to a network of academic institutions and also conducts in-house assessment.	The MoH is in charge of appraising the evidence and promoting broader stakeholder engagement. Appraisal shifted from inclusions to exclusions in 2015.	IETS positive assessment not required for inclusion in national program. Aimed at de-facto binding.
Indonesia	Presidential order mandating use of HTA for determining benefits package	HTA committee staff work with academics in universities to conduct the assessment.	Recommendations of the HTA committee shared with stakeholders and President. President makes final decision on accepting or rejecting HTA committee's recommendation.	HTAC assessment recommendations are not binding. In some cases, even if the President has accepted the committee's recommendations, they are hard to enforce.

Source: Analysis by authors

HTA programs and agencies across the world can have centralized or decentralized structures. In HICs, for example, Spain had different regional agencies in the 1990s that have evolved and grown, including Osteba, AETS, and AETSA. Spain now has eight regional agencies and the Spanish HTA Network (http://www.redets.msssi.gob.es), which acts as the regional coordinating network. The Spanish collaborative approach is based on the strengths of each agency, and health technologies are prioritized for assessment by the MoH's Inter-territorial Health Council [37]. In the United Kingdom, Scotland and Wales have separate HTA agencies that conduct independent HTAs. The Scottish Medicines Consortium (SMC), Scotland's HTA agency, does not

conduct de-novo research but bases its decision on the dossier submitted by the manufacturer [38]. In Canada, Alberta and Quebec provinces have their own HTA agencies separate from the national agency, CADTH.

For LMICs in the early stages of HTA, defining the institutional arrangements for conducting HTA is a good starting point. Resources should be committed to raising awareness among decision makers about what HTA is and its usefulness, limitations, and impact. As awareness levels increase, the uptake and enforcement of the HTA process will also increase. The lesson for LMICs is that HTA institutional structures will develop and evolve based on local contexts and political and economic dynamics.

3.3 SITUATIONAL ANALYSIS TO DEVELOP AN HTA IMPLEMENTATION PLAN

In the previous sections, we discussed the when and how of implementing an HTA process. However, when to initiate policies to advance HTA is also critical. The cultural aspects, local capacity, financial support, policy/political support, globalization, stakeholder pressure, health system context, and usefulness perception are important drivers for successful HTA implementation and should all be considered during the policy formulation stage [39].

Conducting a situational analysis [40] to understand the country context and current environment is an important first step to develop a strategic plan for HTA implementation. HITAP and NICE have developed a conceptual framework for creating a situational analysis [41]. This situational analysis framework focuses on identifying the need, demand, and supply for HTA within a country; a structured questionnaire guides information gathering once stakeholders have been identified [41]. Countries like Cyprus, Estonia, and Turkey have used the Strengths, Weaknesses, Opportunities, and Threats (SWOT) analysis framework for this purpose [42–44]. A desk review of literature, including research papers, policy documents, guidelines, and regulations, may be required to provide further context. Figure 13 provides an example of a SWOT analysis applied to HTA in Cyprus, and figure 14 provides a similar one conducted in India [44, 45].

Figure 13. SWOT analysis applied to HTA in Cyprus

Strengths	Weaknesses
• Cumulated experience • Culture of evidence-based medicine • Centralized decision-making process • Existence of inter-disciplinary teams (Cyprus League Against Rheumatism, Oncology department; Institute of Genetics and Neurology)	• Applied only in public sector • Economics of scale regarding dedicated teams and running costs • Low dissemination amongst practitioners (apart from prescribers) • Willingness to pay not set and arbitrary measure utilized • Ministry of Health's conflicting roles may compromise holistic approach; no diversity during assessment and absence of social stakeholders • Lack of autonomy context • Fragmentation of health services • Applied mainly for medicines
Opportunities	**Threats**
• Introduction of national system will unify market and leverage change • Strong international scientific background of HTA and availability of best practices • Industry supports HTA • Financial crisis requires rationality in decision making and maximization of value for money • Interface management will enable monitoring and performance indicator setting	• Financial recession may compromise decision-making process and shift focus to cost minimization • Small market size may not deter companies from abandoning market in case of negative appraisals

Source: Panagiotis and Talias M, 2013 [44]

Figure 14. SWOT analysis applied to HTA in India

Strengths	Weaknesses
• Declare political will in national health plan 2015 • Commitment by government by establishment of Medical Technology Assessment Board • WHO collaborating center for health research in country • Prior exposure to HTA of staff at various institutions including Indian Council of Medical Research (ICMR)	• No legal provision • No institutional arrangement for HTA agency • Existing capacity needs scale up • Multi-location HTA activity needs synergy
Opportunities	**Threats**
• Indian HTA establishment being monitored at higher levels of government • WHA resolution and inclusion in National Health Plan provide opportunity for global and national partnerships • UHC goals of the National Health Mission are creating need	• Diverse interest of stakeholders a threat for smooth operation of agency • Industry (pharma, medical device, and private hospitals) may oppose • Multi-location HTA poses threat due to ownership • Lack of trained human resources • Long duration of establishment of Indian HTA system

Source: Prince Mahidol Conference 2016 Parallel Session 2.5: Enabling better decisions for Better Health. Embedding Fair and Systematic Processes for Priority Setting for UHC. Presentation by Dr. R Srivastava Indian Council of Medical Research [45]

As highlighted elsewhere [39], cultural and global contexts are important drivers for successful HTA implementation and need to be considered in any situational analysis. The context of early-adopter countries such as Sweden, Canada, Spain, France, and the United Kingdom played a big part in determining the breadth of decision making supported by HTA in these settings [46]. These countries have long-standing traditions of relying on evidence-based information, focusing on quality of care, and promoting the principles of equitable and efficient use of resources [46]. Therefore, their HTA organizations' mandates go beyond informing resource allocation and reimbursement decisions to include improvement in quality of health care, development of quality standards, development of clinical guidelines, and keeping the general public informed throughout the process [46]. The mandates of HTA later-adopters (e.g., Poland, Hungary, Romania, Bulgaria) seem mostly limited to informing reimbursement decisions [46]. As mentioned in Chapter 2, less-affluent countries face challenges such as limited financial resources and research capacity and unavailable or limited local data that may affect the final scope of HTA activities [47]. Additionally, interest in joining the EU may have been an incentive in driving the institutionalization of HTA in some countries [46].

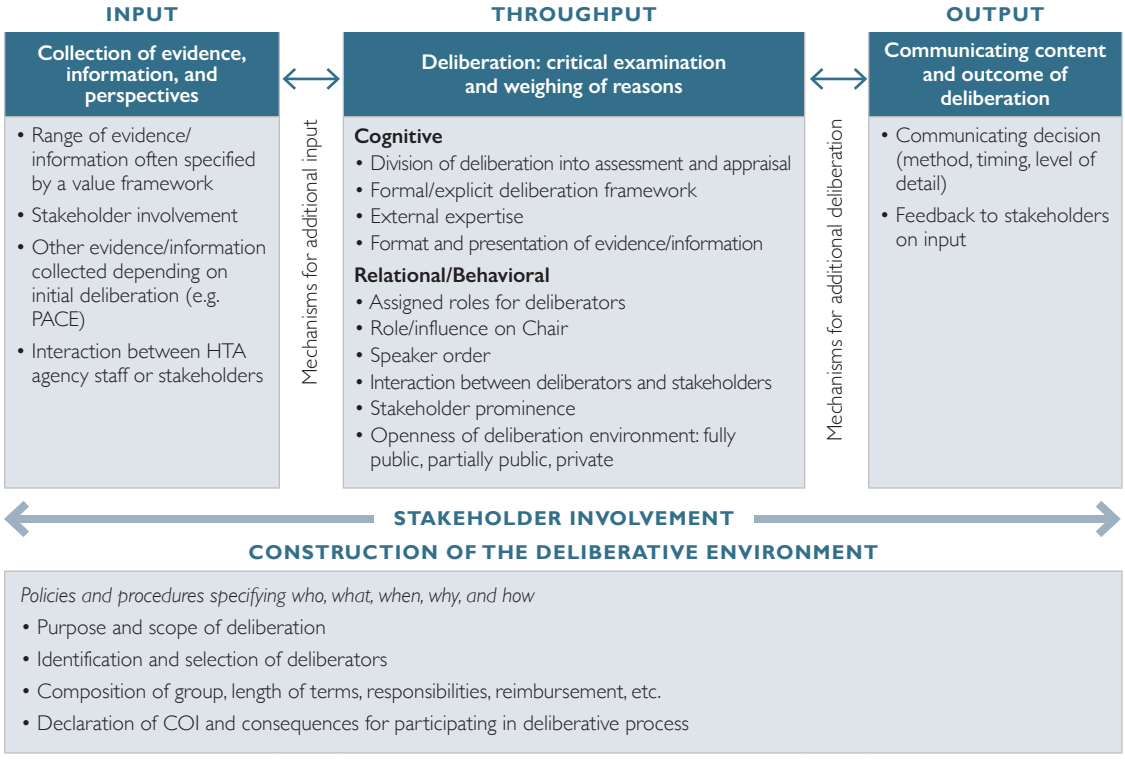
Health system context also plays a major role in policy formulation, and HTA needs to be anchored in the current priorities of the national health programs. In Brazil, for example, HTA was driven by not only the need to increase efficiency in resource allocation but also the increasing judicial intervention regarding coverage decisions and reimbursement mandated by courts [48]. Thus, incorporating a more transparent HTA process to engage and keep stakeholders informed was an important objective for HTA introduction in this country [48]. More recently, in 2014 Indonesia formally established an HTA committee (InaHTAC) in the context of a health sector reform to achieve UHC and resource optimization [17].

Although country-specific HTA health organizations and processes vary according to setting, some procedural principles have been associated with the robust operation of HTA programs and institutions [49, 50]. These include transparency, robust and appropriate methods for combining costs and benefits, explicit characterization of uncertainty, and active engagement with stakeholders [49, 50]. Nevertheless, the current level of application of these principles is considered uniformly poor in many LMICs implementing

HTA practices [51]. Therefore, principles of good practice should be kept in mind during the stages of policy formulation and implementation.

Of paramount importance is the need to highlight active stakeholder engagement to guarantee buy-in and legitimacy of priority setting and HTA processes [52, 53]. Given the divergence in value frameworks of various individuals and institutions, consensus on setting priorities can only be determined through a fair process as highlighted in the A4R framework [52]. HTAi's recent background paper on deliberative processes articulates central principles and provides an operational framework for establishing a fair deliberative process for appraisal of reimbursement decisions [23] (figure 15). Stakeholder involvement is a cross-cutting activity for every component of the process.

Figure 15. Conceptual framework for a deliberative process



Source: HTAi Global Policy Forum, 2020 [23]

3.4 THE POTENTIAL ROLES OF THE DIFFERENT STAKEHOLDERS WITHIN THE HTA PROCESS

HTA is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle [54]. Therefore, the development of HTA (methods and reports) usually requires the combination of a broad mix of skills and profiles that include epidemiologists, health economists, statisticians, health care professionals, and public health specialists. However, the role of other disciplines, such as (bio)ethicists, and other stakeholders, such as academic centers, patient representatives, and companies, varies widely according to setting.

Chapter 2 provides tools for conducting a stakeholder analysis to identify their position, power, and perception with regard to HTA. This contributes to stakeholder management and engagement strategies. Pichon-Riviere and colleagues reviewed the roles and responsibilities of patients and industry stakeholders across countries;

they found that these vary among the different stages of the process for each country [53]. Of importance in the era of advanced globalization is also the role of international organizations and development partners.

3.4.1 ENGAGEMENT OF ACADEMIA

Involving academia is crucial at every stage of the HTA process, from methods development to the assessment and appraisal stages. The concept of HTA itself has roots in academia, and academic research led to what is now broadly considered HTA [55]. A multidisciplinary set of experts (e.g., clinicians, social and political scientists, health economists) contributes to the assessment phase of HTA, and they are often drawn from the network of academic institutions in country. For example, the MoH of Indonesia has identified two additional universities for its network of academic partners from its initial partnership with the University of Indonesia.

Therefore, identifying the academic institutions with capacities related to HTA is an essential part of any situational analysis for LMICs. Examples of potential institutions or institutional arrangements for engagement of academia include:

- **Technical Working Groups:** Sweden, the first country to set up a national HTA agency, had the National Board of Health and Welfare (NBHW), which started assessing new health technologies in the 1960s. NBHW worked with technical working groups from academia and utilized data from clinical trials and disease epidemiology to assess the appropriateness of the technology for the country [56].
- **HTA Organizations Centered in Academic Settings:** Canada has several HTA organizations at the province and national levels, many of which emerged from government funding, while others are based in academic settings [57].
- **Network of Affiliate/Contracted Academic Institutions:** A network of academic or research organizations often conduct the assessment part of HTA [14], as is the case of NICE in the United Kingdome [58], HITAP in Thailand [59], IETS in Colombia [60], and MSAC and PBAC in Australia [61], among others.
- **National Research Agency Linkage to HTA:** The Finnish HTA agency (FinoHTA) has its roots within the Medical Research Council and was housed within Stakes, the National Research and Development Center for Welfare and Health [62]. Stakes was already involved in conducting HTA and building capacity for HTA through international training before FinoHTA was formally created [62]. Prior to the 1997 establishment of the Danish HTA agency (DACEHTA), the Danish Institute of Health Research Services was conducting HTAs in the 1980s [63]. Similarly, NICE in the UK has built upon the foundational work by Cochrane, the emergence of health economics as an academic subject, and prior NHS assessments since the 1980s [64].

In the case of some LMICs with limited capacities, identifying academic institutions that are familiar with HTA concepts or components of the HTA process, such as economic evaluation, may be more feasible. Tanzania provides a great example wherein the policy makers exploring the introduction of HTA identified clinical experts within the system. While Tanzania does not have a specific academic program on economic evaluation, it identified academic institutions that can produce HTA [65]. A similar approach has been followed for capacity building in Ghana [66].

3.4.2 ENGAGEMENT OF HEALTH PROFESSIONALS IN HTA

Health professionals such as doctors, nurses, pharmacists, and laboratory technicians may participate in HTA topic selection discussions, whether it be as individual experts or through their professional associations. They may also be members of multidisciplinary appraisal and recommendation committees at a later stage. Here,

we discuss the role of clinical and other health professionals in adapting HTA recommendations within their practices. HTA conducted at the health care facility level has emerged in the last two decades [67].

In 2006, HTAi initiated an interest group specifically focusing on hospital-based HTA, including its processes, impact, and stakeholder engagement [67]. Models of HTA at the hospital level range from an independent HTA unit or committee to a team doing mini-HTA and a clinical ambassador who shares HTA findings to improve adoption of decisions [67]. The HTA unit model is analogous to a national HTA program with a multidisciplinary team [67]. As per Gagnon et al.'s systematic review of HICs, if the hospital HTA unit has significant engagement with clinical staff, the success of adopting recommendations is higher [67].

Health professional staff must provide local-level data for more context-specific decisions related to changes in guidelines or diffusion of technology within the relevant institution. This includes buy-in for managerial and administrative decisions. The ambassador model has a clinical leader at its core whose leadership and influence highly affects the adoption of HTA recommendations. A review of literature on hospital-based HTA in LMICs revealed that countries such as China, Indonesia, Philippines, Malaysia, Thailand, Argentina, and others in Latin America have introduced hospital-based HTA activities since the early 2000s [68]. Hospital Garrahan's HTA program in Argentina has been active since 2001 [69], while Brazil started a strategic program to foster hospital-based HTA in 2009 [70]. These programs encourage hospital administrators and clinical practitioners to collaborate on the organizational impact of health technologies [70]. Additionally, HTA-related activities promote staff capacity building and mentoring for research projects—further strengthening clinical capacities [70].

3.4.3 PATIENT ENGAGEMENT IN HTA

Patients and other citizens are the end users and beneficiaries of health technologies being considered for inclusion in national programs, so their perspective is critical. The level of patient engagement in a country will depend on the context, cultural norms, institutional and legal frameworks, and available capacities within its HTA system [53]. Different countries engage with patients to varying degrees across the HTA process.

In defining the HTA process and setting priorities, mature HTA systems from European countries such as the United Kingdom, Germany, Netherlands, and Sweden have continuous engagement with patients either through patient councils or by allowing citizens to submit proposals on health technologies for evaluation, such as in the United Kingdom and Spain [53, 71]. Levels and modes of engagement differ based on the purpose.

- **Topic Selection Panels:** In the UK, a patient council is a 30-member panel formally engaged in the HTA process, while any citizen can respond to call for HTA topic selection [53].
- **Patient Associations:** Other countries, such as Thailand, Germany, Spain (regional HTA agencies), the Netherlands, and France, have a consultative process with patient groups or certain patient networks ahead of the priority-setting process but no direct proposal submissions for topics [53, 71]. In Thailand, the UK France, Canada, and Australia, patient representatives comment on HTA scope and protocol [53, 72].
- **Broader-Based Engagement:** In Germany, the scope of the assessment for a specific technology can be commented upon by anyone in the general public. The assessment protocol is provided to the public via the internet and available for comment [53].

Level of patient engagement is also linked to the current country capacity for HTA and the goals identified for its implementation. Countries just starting out, such as Indonesia, do not currently have an explicit patient engagement strategy [17]. This is due to the limited resources (financial and human) dedicated to the HTA process, in addition to a limited tradition of broader stakeholder engagement for decision making. Countries such as Colombia and Mexico that have moved beyond the initial stages of HTA have incrementally engaged with patient groups when designing and running their HTA process [53].

Similarly, patient engagement at later stages of assessment and contextualization (or appraisal) can be targeted or broad based. In most countries, patient groups or individual patients affected by the health technology are engaged in the appraisal process [53, 71]. For example, in Scotland, the SMC has developed a Patient and Clinician Engagement Meeting structure for end-of-life medicines that allows both clinicians and patients to have a greater role in appraising the medicine [73]. France and the United Kingdom disseminate recommendations from the appraisal process and the HTA report to targeted patient representatives or groups [53]. In Brazil, Germany, and Thailand, patient representatives are members of appraisal committees [53, 71].

International networks have dedicated groups devoted to patient engagement process and best practices that are available for reference. HTAi has a patient and citizen involvement interest group devoted to sharing information about processes of patient engagement/involvement and on developing engagement tools for industry, patient groups, and HTA organizations. INAHTA has a newly formed patient engagement learning group for members to share best practices. LMICs' HTA programs or agencies should actively participate in these groups to leverage the resources and best practices.

3.4.4 INDUSTRY ENGAGEMENT

The role of the health technology industry across the HTA process varies across countries depending on their institutional structures. In Latin America, FIFARMA, a pharmaceutical manufacturers association, published a policy paper on the role of industry in the HTA process [53], showing this sector's interest in having a voice in the process. In Switzerland, the industry and insurers participated in the design and use of the HTA process [53]. Similarly, NICE in the United Kingdom included industry representation on the committee working on developing the medical device and diagnostics HTA process. In Australia, New Zealand, Poland, and Hungary, manufacturers are required to submit dossiers on the technology's assessment based on the national guidelines and reference case for economic evaluations [53, 72]. This arrangement may be a starting point for LMICs with limited capacity to develop de-novo in-house evaluations.

Industry engagement can help reduce the asymmetry of information related to the incorporation of new products in competitive markets. Additionally, incorporating their perspectives on HTA while designing the national process, reference case, and guidelines can be benefit consensus building. However, potential conflicts of interest and industry bias need to be accounted for in the consultative process. For this reason, the role of the industry is still highly limited in most countries during the appraisal process to avoid perceived conflicts of interest [14]. Countries such as the UK, Australia, Colombia, and Brazil allow for manufacturers to provide additional information, usually by request [53]. Appealability of a decision based on manufacturer's evaluation of the HTA report and/or process is important for accountable priority setting and HTA [52]. Therefore, countries should allow for manufacturers and other stakeholders to appeal the decision under these circumstances. It is important to note that appealability of a decision differs from revisability of a decision—that is, to reverse or change in a decision based on additional evidence with regard to the technology.

3.4.5 THE ROLE OF INTERNATIONAL PARTNERS, NETWORKS, AGENCIES, AND DONORS

International stakeholders include networks related to HTA such as INAHTA, RedETSA, HTAi, HTAsiaLink, EuroScan, and EUnetHTA. In addition, international donors such as the Bill & Melinda Gates Foundation, Wellcome Trust, World Bank, and Inter-American Development Bank have been involved in global HTA activities. International agencies such as WHO and its regional counterparts such has PAHO have been instrumental in the development of HTA worldwide. International organizations with HTA expertise, including ISPOR, INAHTA, HTAi, HTAsiaLink, HITAP, and iDSI, often sensitize and build capacity building in stakeholders. Financial support from technical and developmental partners is critical to build momentum and strengthen capacities of local stakeholder advocates [74].

"An important initial activity is the sensitisation of key stakeholders, the clarification and discussion of the HTA concept (HTA, EBM, guidelines, cost benefit of medical procedures, etc.). International HTA experts should be contracted to train selected actors from relevant national institutions on up-to-date HTA methodologies and key concepts. On-site visits to other countries where HTA programmes have successfully been established are recommended and are instrumental in building professional networks and in shaping the national HTA concept" [75]

3.5 PRODUCTION COST OF HTA AND SOURCES OF FUNDING

As countries embark on institutionalizing HTA, they are constrained by limited resources, particularly skilled professionals and funding. While there are many competing health technologies awaiting assessment for potential incorporation or reimbursement from public sources, assessing them all is not possible. In practice, HTA institutions (even in affluent settings) must prioritize internal capacity and resources to meet the growing demand for evaluation.

When considering HTA production costs, newly established agencies need to prioritize the allocation of their internal resources during the formulation stage by starting with a narrow scope of activities and growing incrementally. Production costs for HTA vary by the type and complexity of analysis and by the domestic labor costs for conducting such analysis. Complicated and time-consuming analyses have a higher opportunity cost than rapid reviews, which LMICs should consider when budgeting for HTA activities. An EU evaluation for HTA estimated that a rapid HTA assessment, taking as little as one month to prepare, costs around €30,000, while a full HTA report taking up to a year costs €100,000 [76]. The Canadian drug review was priced at CAD 72,000 per evaluation [77], and the Australian Pharmaceutical Benefits Advisory Committee implemented a cost recovery fee of up to 179,000 AUD per evaluation [78, 79].

As mentioned, when building an HTA organization, no one size fits all regarding potential funding sources; however, funding is obviously a requirement for sustainability of these institutions. Globally, most government-led, arm's-length HTA agencies are funded from public sources (e.g., annual budgets, earmarked taxes, levies imposed on insurers); in other cases, private funding (project based or through cost recovery fees) may supplement core public funding. Although it varies, most HTA units affiliated to academic institutions are project or grant based or the result of targeted funding of central institutions that commission collaboration centers or networks of cooperation to conduct HTA.

A significant outcome of the global advancement of HTA is increased collaboration across the world. As noted, global networks such as INAHTA, RedETSA, HTAi, HTAsiaLink, and EUnetHTA have fostered collaboration across regions and countries, resulting in a large knowledge base available to help countries avoid re-inventing the wheel and reduce production costs for HTA. For example, the WHO-hosted Decide Health Decision Hub is a virtual platform that supports knowledge sharing and the INAHTA's database contains over 15,000 reports [80, 81]. Further, the EUnetHTA collaborative network has developed a toolkit that helps HTA agencies adapt HTA reports across regions [82]. The toolkit has checklists and resources that help countries assess the relevance of reports to their context, the reliability of their findings, and the potential transferability of the reports to other countries [82]. Members such as Poland leverage these for their pragmatic HTA models. EUnetHTA also has searchable databases of HTA reports and systematic reviews for country members to leverage. Similarly, the Latin American network of agencies, RedETSA, has a database of HTA reports for countries to potentially adapt to their contexts [83]. This is an important in the context of production cost in that LMICs have resources to leverage and reduce their production costs for HTA.

3.6 CONSIDERING THE PRINCIPLES OF GOOD PRACTICE OF HTA DURING THE FORMULATION STAGE

HTA introduction and institutionalization began in the 1970s, and many high- and middle-income countries have gathered several decades of experience in implementing HTA [55, 57, 62–64, 84]. Given the increase in the adoption of HTA as a standard tool for informing various health system decisions, LMICs can learn from the experiences of these countries.

ISPOR created its HTA Council Working Group to "provide an up-to-date review of current literature that includes guidance on good practices in the use of evidence to inform population-based healthcare decision-making for pharmaceuticals (drugs and vaccines), medical devices, and other health technologies, that is, HTA." [14, 49]. The working group identified the following good practices within the various components of the HTA process:

Define the HTA Process: This includes defining of the broader governance and institutional structures, and the underlying principles governing the HTA process. In the earlier work of the ISPOR working group [14], the best practices with regards to HTA include:

1. Goals of the HTA process should be transparent and explicit
2. HTA should be an unbiased and transparent exercise
3. HTA should include relevant technologies
4. Clear system for setting priorities should exist
5. HTA should involve appropriate methods for assessing costs and benefits
6. HTA should consider a wide range of evidence and outcomes
7. Full societal perspective should be considered in HTA
8. HTA should characterize uncertainty in estimates from HTA
9. HTA should consider issues of generalizability and transferability
10. HTA should involve all relevant stakeholders
11. HTA doers should seek all available data
12. Implementation of HTA should be monitored
13. HTA should be timely
14. Findings need to be communicated appropriately to different decision makers
15. The link between HTA processes and decision making needs to be transparent

All these could be considered part of a checklist to guide the HTA formulation stage described in this chapter. Principles 1 to 4 and 15 are linked to the legitimacy and binding power of the process. NICE in the UK and Germany's IQWIG have explicit guidelines on the HTA process and include a scoping process involving multidisciplinary stakeholders [49], compared to Indonesia's guidelines for HTA in which the recommendations related to the objectives and structure of the process are generalized and the scoping and stakeholder engagement process is not defined. This weakens the adoption of decisions made through the HTA process [17].

As countries move toward more comprehensive HTA programs or agencies, the principles need to be further expanded. Based on the INTEGRATE-HTA framework and the principles of accountability of reasonableness, Oortwijn and colleagues provide an integrated list of best practices for HTA agencies that are aimed increasing their comprehensiveness in addition to the legitimacy of their decisions. Figure 16 [85] presents the judgment criteria to assess the level of comprehensiveness of an HTA process in a specific context.

Figure 16. Judgment criteria to assess the level of comprehensiveness of the HTA process

PHASE	DEFINITION USED
ASSESSMENT PHASE	
Multiple stakeholders are involved in scoping an HTA	Defining the objective and research questions of the HTA by a systematic exploration of relevant aspects from multiple perspectives (e.g., patients, informal caregivers, health professionals, decision makers).
Context is taken into account	Context is defined as the conditions and circumstances that are relevant to the application of an intervention, for example, setting (e.g., hospital) and sociocultural aspects (knowledge, beliefs, conceptions, customs, institutions, and any other capabilities and habits acquired by a group that may influence uptake).
Implementation issues are taken into account	Implementation issues refer to the actual delivery of a health technology and to policy measures and processes or to funding mechanisms (e.g., tax incentives, reimbursement schemes) that directly concern or indirectly influence the implementation of the health technology.
Patient-related factors that influence treatment effects are taken into account	Patients may respond differently to treatments in terms of nature and magnitude of a beneficial effect, the time of onset, and adverse outcomes. It is therefore important to identify factors that influence treatment effects to determine which treatments work best for whom; make medicine more personalized; and improve the valuation of research outcomes.
Patient preferences with regard to treatment outcomes are taken into account	Patients often have different views on the relative importance of certain treatment outcomes. It is widely acknowledged that understanding patients' preferences is important for an accurate assessment and appraisal of the impact of a disease on the patient's quality of life.
Evidence reports and standardized evidence summaries for each assessment aspect are produced	Provide evidence reports and standardized evidence summaries for each assessment aspect (e.g., reports on economics and ethical aspects).
Stakeholder consultation is performed to review the evidence reports	Stakeholders are asked to review the assessment results (i.e., evidence reports/ summaries) with regard to plausibility. The result is an assessment report that includes a critical evaluation of the available evidence and uncertainty and an overview of where evidence is missing.
APPRAISAL/DECISION MAKING PHASE	
The appraisal/decision making process is explicit	The criteria and methods used in the process are well described in a publicly available document.
The appraisal/decision making process is transparent	The procedures used are well described in a publicly available document; the process is open to the public (e.g., public hearings); and the agenda and notes on the meeting are provided in the public domain.
The decisions and the underlying reasons are made public	The final decisions and the underlying reasons are publicly available (e.g., via the Ministry of Health's website and announcement in the official journal).
Stakeholder involvement is clearly specified and open to the public	The names of the stakeholders involved (including those on a specific committee for appraisal/HTA decision making) are publicly available (e.g., via the HTA agency website and notes on the meetings that are provided in the public domain), and the ways in which the views of the stakeholders are taken into account are well described in a publicly available document.
Mechanism(s) to appeal, propose revisions, and receive a reasoned response are in place	Mechanism(s) to appeal, propose revisions, and receive a reasoned response are operational and described in a publicly available document.
Systems are in place to monitor and evaluate the process	Systems to monitor and evaluate the process are operational and described in a publicly available document.

Source: Oortwijn et al., 2017 [85], adapted by the authors

HTA is inherently a systematic process for supporting decisions related to rationing of resources. Therefore, resulting decisions can cause controversy among the various actors with a stake in the process. Based on the principles of accountability for reasonableness, the acceptability of decisions increases if the process is transparent and perceived to be without bias from various interest groups [14, 49]. With agencies that are government funded or within a government institutional structure (e.g., NICE, IQWIG), there is a risk of being perceived as pushing the rationing agenda of local government [49]. NICE, Canada's CADTH, and Sweden's SBU all have institutionalized oversight structures in the form of an independent board consisting of various types of stakeholders to minimize the risk of political capture and promote independence [49]. This alleviates the public's perception of bias, as they act as 'arm's length' institutions, making resource allocation decisions on behalf of the governments but not being part of the government structure themselves. As mentioned earlier, the extent to which various stakeholders are involved in the various stages of the HTA also increases transparency and limits bias.

Finally, most HTA processes focus on evaluating only pharmaceutical products [49]. The complexity of evaluating medical devices, diagnostics, and health interventions limits the scope of HTA in countries with limited capacities and resources. NICE in the UK, IQWIQ in Germany, MSAC in Australia, and HITAP in Thailand are some of the agencies that conduct evaluations for all types of technologies and interventions. Almost all members of the 31 countries involved in EUnetHTA (94%) have processes in place that are related to the assessment of drugs, compared to 68% that assess non-drug health technologies and around 60% that assess both types of health technologies [86]. That said, drug related HTAs still dominate in most of these countries. For LMICs, given the availability of literature and best practices, initiating HTAs for medicines would form a robust base for HTA introduction and future expansion.

As gleaned from the stakeholder analysis and engagement sections, there are multiple audiences for utilizing the findings from the HTA process. Principles 13 and 14 of the above-mentioned list are critical for further increasing the legitimacy and adoption of HTA processes, and in all cases HTA results should be timely and communicated appropriately to decision makers.

Various users of HTA recommendations exist within the country [49]. At a macro level, these could be national policy makers within the ministries of health and finance, purchasers, or insurance organizations, but also political leaders who may deliberate on the recommendations. Other users would be the end users at the micro level, such as clinicians prescribing the health technologies or patients benefiting from them.

As highlighted in Chapter 2, different stakeholders have their own priorities and motivations with regard to HTA and the information disseminated needs to cater to them. On the one hand, policy makers and patients may not be familiar with health economic analyses, so the added value of a recommended technology needs to be articulated in a customized manner to be digestible by that specific audience; on the other, the academic community would expect robust methods and transparency when dealing with uncertainty of estimations. Drummond et al. [49] also underscore that stakeholder engagement at various stages of the HTA process is an effective means of improving communication of HTA findings. Chapters 4 and 5 will delve further into the practices associated with principles 5–12 from the ISPOR Working Group list.

Ethical and Equity Considerations: Saarni and colleagues' [87] critical insight is that HTA is inherently a value-laden construct. HTA value judgements include the appropriateness of a technology with regard to its target population or where the associated condition fits the priorities of the population. Therefore, we would like to emphasize the need for an explicit ethical framework to support such value judgements and to meet the goals of a transparent and unbiased process [88]. There are several guidelines that could be a useful benchmarking tool for LMICs embarking on advancing patient-centered HTA, including:

- **Country Guidelines:** Several countries and networks have guidance documents that provide value frameworks [88] that LMICs can leverage to develop their HTA guidelines. For example, the Austrian, Danish, French, German, Norwegian, Spanish, and Swedish agencies have their own country-specific guidelines, including how to address ethical and equity considerations for HTA.
- **EU Guidelines:** EUnetHTA's core model has a checklist of questions covering ethical issues related to the technology and the HTA process [88]. The methods to address these questions include a guidelines on identifying congruency in stakeholders' value systems. The INTEGRATE-HTA project, funded by the European Commission, provides another framework for developing a comprehensive, patient-centered HTA process for complex technologies, including assessing ethical and other considerations [89].

Another approach already mentioned is the participatory model of engaging stakeholders throughout the HTA process to deliberate or create consensus around ethical considerations within the process. Assasi and colleagues [88] provide an operational framework for including ethical considerations in each step of the HTA process. The framework provides a process and a list of questions to be addressed by the stakeholders involved in each stage.

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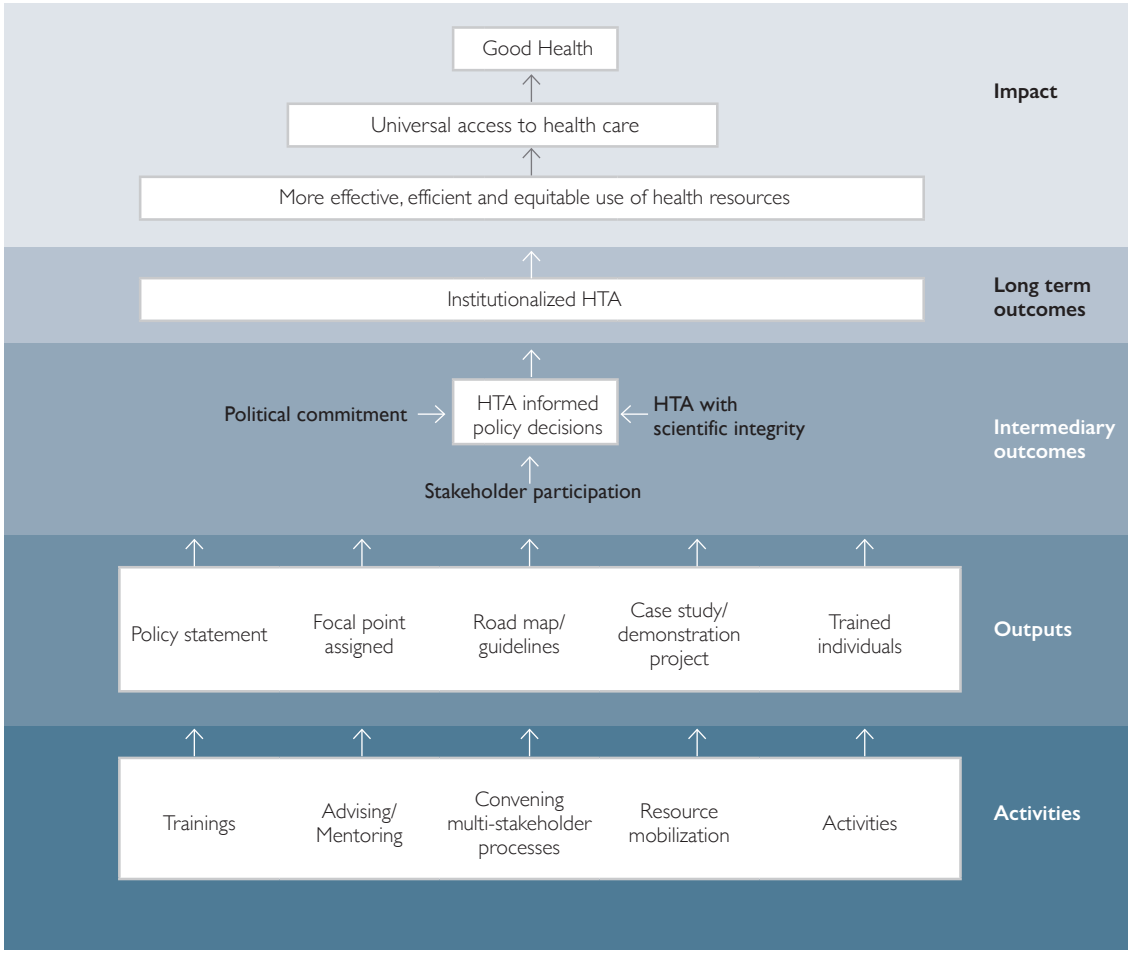
CHAPTER 4

IMPLEMENTING POLICIES FOR HTA

Implementing partners—from policy formulation to implementation—need to understand the elements for HTA institutionalization. Partners may aim to advance an already existing HTA system or start developing a new HTA system of doers and users. In any case, political commitment, stakeholder participation, and scientific robustness are vital. The theory of change developed by Tantivess, et al. [1] outlined activities that lead to HTA institutionalization, including training, advising/mentoring, convening multistakeholder processes, and mobilizing resources (figure 17).

In previous chapters, we discussed political commitments and ways to create and leverage windows of opportunity for policy action. We also discussed the various steps of priority setting, such as identification, topic selection, assessment, appraisal, deliberation, and decision making. In this chapter, we will focus on two critical aspects—methodologies, particularly economic analysis methods, that ensure scientific rigor, and the capacity-building elements needed to ensure meaningful stakeholder participation.

Figure 17. Theory of change applied to HTA



Source: Tantivess et al., 2017 [1]

4.1 METHODOLOGICAL CONSIDERATIONS FOR HTA

Milton Weinstein, one of the founders of medical decision making, once said, "Decisions *will* be made, if not actively then by default [2]." Unfortunately, the default is often arbitrary and can lead to inefficiencies and failure to meet a population's needs [3, 4].

A variety of methodologies can be used to assess resource allocations, which means that results can be hard to compare [5]. This variability can arise from the structure of the analysis (structural uncertainty) or from inputs used to inform the analysis (parameter uncertainty) [6, 7]. The assumptions of analysts will inevitably affect the final estimates. Analyses should therefore be standardized as far as possible so as to minimize variability in methods and assumptions and should explicitly address issues like missing or incomplete data and nonrandomization, which can cause bias [8].

An example of the importance of methods harmonization for HTA is illustrated by studies comparing the potential cost effectiveness of primary prophylaxis versus on-demand treatment for severe hemophilia Results ranged from prophylaxis being "dominant" to being not cost effective (i.e., costing more than €1 million per QALY gained) [9]. The various studies adopted different perspectives; made different structural assumptions; used different time horizons, discount rates, and sources of data; and contained methodological weaknesses [9]. Figure 18 shows the incremental cost-effectiveness ratios (ICERs) and main features of some of these studies [9, 10].

Figure 18. Impact on ICERs of assumptions and parameters

Author	Year	Type of study	Perspective	ICER Result	ICER Interpretation
Miners	2002	Cost-Utility Analysis	Health system	£46,500	Prophylaxis not cost-effective
Risebrough	2008	Cost-Utility Analysis	Societal	CAN$542,938	Prophylaxis not cost-effective
Miners	2009	Cost-Utility Analysis	Health system	£38,000	Prophylaxis not cost-effective
Colombo	2011	Cost-Utility Analysis	Health system	£40,236	Prophylaxis cost-effective
Farrugia	2013	Cost-Utility Analysis	Health system	USD$68,000	Prophylaxis dominant
Castro	2016	Cost-Utility Analysis	Health system	USD$91,494	Prophylaxis not cost-effective

Source: Miners, 2013 [9] and Castro, 2014 [10], adapted by the authors

4.1.1 METHODOLOGICAL GUIDELINES AND REFERENCE CASES

Reference cases are standard sets of analytic practices to improve comparability and quality of HTA reports [11]. In creating country standards, we advise LMICs to leverage existing global resources as a starting point. Policy makers or implementing partners can curate and contextualize the following resources when institutionalizing HTA in their settings of interest, all of which are considered to incorporate best practices for HTA development:

- National Institute for Health and Care Excellence [12]
- The Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG [13]

- Disease Control Priorities [14]
- International Decision Support Initiative (iDSI) reference case [15]
- iDSI HTA toolkit [16]
- ISPOR Good Practices for Outcomes Research [17]
- Global Health Cost Consortium [18]
- European Network for Health Technology Assessment [19]
- Health Information and Quality Authority – Ireland [20]
- Health Technology Assessment Handbook – Danish Centre for HTA (dacehta) [21]
- Benefit-cost analysis reference case [11]
- Methods for Economic Evaluations for Healthcare Programs (Drummond) [20]
- Decision Making in Health and Medicine [22]
- Health Technology Assessment Toolbox for Emerging Settings [23]
- EUnetHTA Core Model [24]
- INTEGRATE-HTA for complex health technologies [25]
- HTA reporting checklist [26]
- Guidelines for the Economic Evaluation of Health Technologies - CADTH Canada [27]

The stepwise approach documented by the NICE reference case in the UK [12] presents a list of components to consider when developing a robust reference case and that could serve as the basis for outlining methodological guidelines in LMICs:

- Defining the decision problem
- Choosing a perspective for costs and outcomes
- Deciding among different types of economic evaluations
- Time horizon
- Synthesis and use of evidence
- Measuring and valuing health effects
- Broad considerations for technology adoption (e.g., equity and evidence on resource use and costs)
- Discounting
- Modelling methods
- Dealing with uncertainty (e.g., companion diagnostics, subgroup analyses)
- Data presentation
- Impact to the health system

Our roadmap is not intended to repeat the contents of existing reference cases. We advise implementing partners to explore guidance from similar settings on specific components of HTA to inform their own needs. For example, countries should adapt the best practices on framing a decision problem, time horizon, or selecting and using or extrapolating best available evidence. The following list highlights some lessons learned from LMICs that have customized reference cases from HICs to create their own country-specific guidelines:

- Health Intervention and Technology Assessment Program - HITAP [28]
- Guide to Economic Analysis and Research - GEAR [29]
- Brazilian Network for HTA (REBRATS) - Methodological Guidance [30]
- Methodological Guidance for Economic Evaluation IETS - Colombia [31]
- Guides Méthodologiques pour les études pharmaco-économiques (Efficience) et les analyses d'impact budgétaire - INEAS Tunisia [32]

4.1.2 METHODOLOGICAL CHALLENGES IN LMICS

While there are some aspects that are worth considering for developing a robust reference case, countries' approaches and preferences may vary in order to accommodate local needs, capacities, and norms [33]. The following section provides an overview on aspects for implementing partners to consider when developing or updating methodological guidelines for HTA in LMICs.

4.1.2.1 CHOOSING THE RIGHT PERSPECTIVE

Should economic analyses reflect all the costs and health-related benefits incurred by all actors due to the adoption of a health care technology? For example, a new drug for diabetes might improve health for a given cost; reduce the need for additional health visits; improve school attendances by children; and free up resources within the health sector or elsewhere (i.e., transportation, caregiver time, productivity loss) that would otherwise be spent for health visits. If the decision maker wishes to take all such consequences into account, researchers would adopt a "societal perspective" to fully capture costs and savings derived from a new drug [34, 35]. However, particularly in LMICs, capturing all costs and benefits may be limited by political values, infrastructural constraints, and data quality and availability [36]. Therefore, in many cases, evaluations to inform resource allocation decisions within the public health system would have a narrower perspective (e.g., that of the payer/health system), as this will fulfill the pragmatic goal to get the direct impact of the technology of interest for a payer's budget [37]. In addition, there are also pragmatic limitations to a societal perspective, especially in multipayer systems where individual budgets address only particular types of cost or benefit or for particular population groups.

4.1.2.2 MEASURING HEALTH BENEFIT

Is the treatment of interest safe? Effective? Answering these questions will require HTA doers to either conduct their own *de-novo* evidence-based evaluation or extrapolate results from elsewhere (whenever possible) to explore health benefits. Elements from the PICO(TS) framework, including Problem/Patient/Population; Intervention; Comparator; Outcome; and (optional) Time or Type of Study and Settings (i.e., inpatient, outpatient) could be used to address these types of questions [38, 39].

HTA doers should consider the use of systematic or rapid literature reviews—the latter gained popularity for their low time and resource use [40]. They should review comparative safety and efficacy studies for both the new intervention and its comparator(s). It is also important to explore issues surrounding publication bias and to understand different innovative approaches to improve reporting, including the use of clinical trial registries

and publication bias detection methods [41, 42]. The comparator(s) should reflect common clinical practice in the jurisdiction in question.

Evaluating health benefits requires measurement, and the unit of choice to measure a health technology's performance is critical. This document discusses three measurement methods: natural units, DALYs, and QALYs.

In evaluating a new immunization outreach campaign, one might consider measuring the number of additional doses delivered, the proportion of children receiving a timely dose, or the proportion of children receiving a complete immunization schedule. These natural units typically look at program outputs and are easily measured. Natural units may also include cases averted or cured, lives saved, and survival times, among others.

QALYs and DALYs act as common metrics to combine quality and quantity of life gained or lost. A QALY represents a full healthy year of life lived, and a DALY represents a year of life lost (due to early death or living in disability or morbidity). For example, assume we are comparing two health technologies using QALYs. The commonly used technology will slightly improve general wellbeing (i.e., from 0.6 to 0.7 or a total difference of 0.1 on a scale from 0 to 1—0 being dead and 1 representing full health) and increase life expectancy by five years, meaning 0.5 QALYs gained (0.1 × 5). The alternative technology would greatly improve wellbeing (i.e., from 0.6 to 0.9, meaning a 0.3 improvement) but minimally increase life expectancy by one year, meaning 0.3 QALYs gained (0.3 × 1).

By evaluating technologies in DALY or QALY terms, researchers can capture the benefits for that specific technology in a single unit to represent value. This allows a comparison between interventions across different health domains. Although QALYs and DALYs stem from the same broad conceptual framework, they are not interchangeable because they are partly based on different assumptions and calculation methodologies (e.g., methods for eliciting quality of life, age-weighting, and disability scores) [43].

There are different population-based survey approaches to estimate utility values (i.e., SF-36 or EQ-5D) as well as methods to elicit values of different health states (i.e., visual analogue scale, time trade-off, standard gamble). This exercise can be labor intensive and challenging for many LMICs. While it is tempting to conduct all evaluations in DALY and QALY terms, they require significant technical expertise and resources that may be prohibitive for new agencies in these settings. An alternative approach, although with caveats, is to extrapolate utility values from other countries with similar political and economic situations. This method is imperfect and should be performed with caution and be fully reflected as part of the limitations in the sensitivity analyses [44].

4.1.2.3 ESTIMATING COST AND USE OF RESOURCES

A question such as *Is an alternative technology (with identical outcome to its comparator(s) less costly*? will only require the assessment of cost. A simple example is two orally administered hypertension drugs considered to be clinical substitutes used daily and with identical schemes—in such a case, it would be enough to prepare a cost minimization analysis considering an annual time horizon [45].

However, other analyses are more complex, such as comparing drugs with different outcomes and profiles (e.g., different cancer chemotherapeutic drugs); a drug versus a medical procedure to gain similar health benefit; supply chain strengthening using drones versus traditional supply chain approaches; or replacing sterilizable syringes with single-use syringes [46]. For these examples, an activity-based costing would estimate volumes, tariffs/fees, and units of consumption associated not only with technology provision and use but also of potential savings or extra financial burden due to complications associated with its use.

4.1.2.4 DETERMINING VALUE FOR MONEY

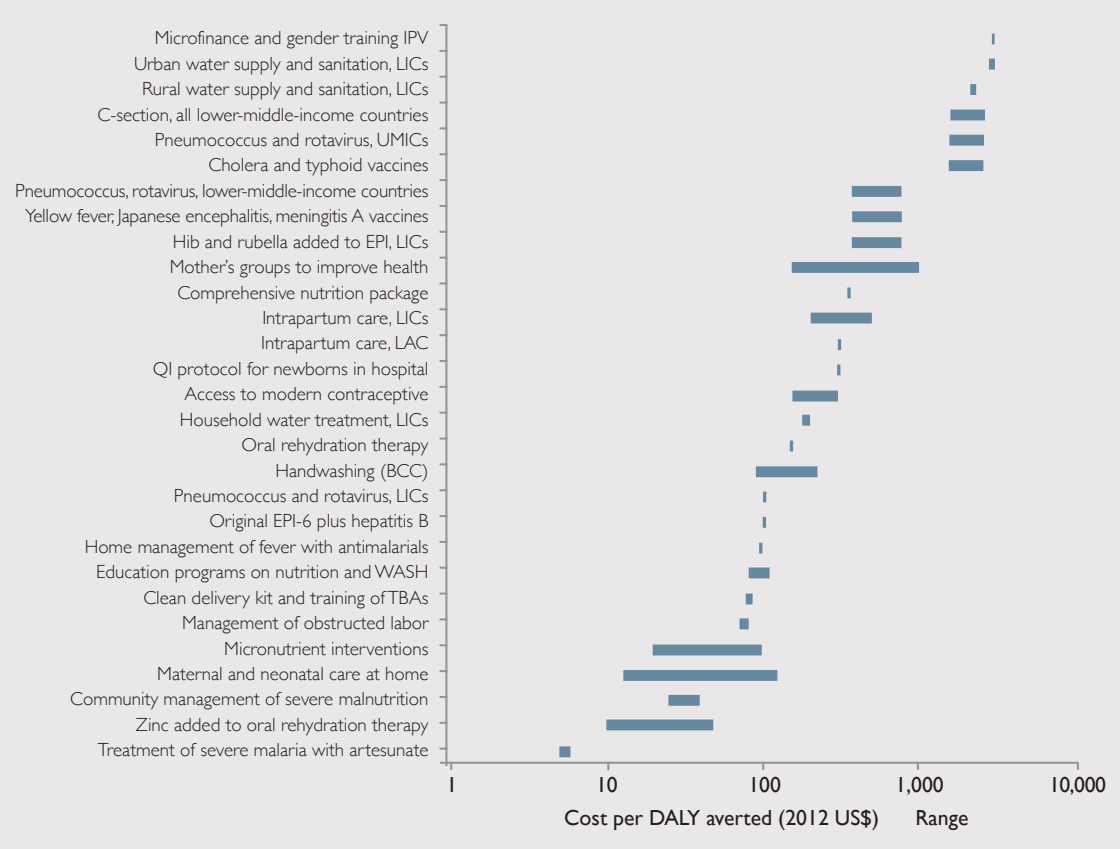
When comparing two dimensions (health benefit and economic impact) to answer the question *Is a new technology a good value for money?* or *Does the technology give more value for money that its comparator(s)*?, the analyst will need to aggregate results to compare both domains—costs and benefits— simultaneously and use a predetermined decision rule to evaluate which treatment provides best value. Three main approaches are used to aggregate both domains and measure health benefit/impact: cost-benefit analyses, cost-effectiveness analyses, and cost-utility analyses.

Cost-benefit analysis (CBA). Expressing both health benefit and costs in monetary terms, CBA aims to assess the effects of policies on overall welfare rather than solely on health. It uses monetary values to measure the extent to which individuals are willing to exchange their income, which can be spent on other things, for the health and non-health outcomes they will likely experience if a policy is implemented. CBA assumes that the preferred policy is that which maximizes social welfare, measured by summing the cost and effects of a policy across individuals and subtracting cost and effects of its counterfactual. With CBA, who receives the benefits and who bears the costs should be addressed separately through policies that directly affect distribution, such as the tax and income-support system [11].

Cost-effectiveness analysis (CEA). Evaluations using natural units to estimate health benefits are relatively easier to produce. They require fewer resources because the health outcomes are typically already being measured and reported in primary studies. CEA also tends to be easier for clinicians to interpret because they use familiar clinical endpoints [47]. However, CEA allows limited comparison between technologies with different outcomes or across disease health areas. If LMICs opt to use natural units to assess value, HTA reports should also consider other dimensions of analysis and their relative weights to allow cross-comparison. Implementing partners should become familiar with CEA's ability to inform decision making; for example, a country may want to identify the best ways to increase vaccine coverage to meet political commitments. CEA may suffice for this. Countries can compare the relative effectiveness (cost per doses delivered) of different interventions such as SMS (short message service) reminders, additional campaign efforts, or conditional cash transfers to strategically inform their decision making [48].

Cost-utility analysis (CUA). Allowing comparison between disease categories, CUA uses cost per QALYs gained or cost of DALYs averted as common metrics to produce an incremental cost-effectiveness ratio for each intervention. For example, to evaluate whether colorectal cancer treatment is cost effective, the exercise would compare the cost-per-QALY (or DALY) of different interventions to a ceiling (threshold) to determine its cost effectiveness. As shown in figure 19, CUA allows decision makers to compare the relative value for money of different interventions across various health domains to develop 'league tables' that list competing interventions and inform their decision making [49]. Some economists dislike the term "cost-utility" analysis on the grounds that neither QALYs nor DALYs are designed to be measures of utility. Analysts will frequently encounter what we here call CUA merely as a form of CEA, and it is worth noting that CUA and CEA might be used interchangeably by different authors. However, they use different units to assess health benefit, as has been described before.

Figure 19. Interventions for children: CEA in disease control priorities



Note: BCC = behavior change communication; EPI = expanded program of immunization; Hib = *Haemophilus influenza* type b; IPV = intimate partner violence; LAC = Latin America and the Caribbean; LICs = low-income countries; QI = quality improvement; TBAs = traditional birth attendants; UMICs = upper-middle income countries; WASH = water, sanitation, and hygiene.

a. Denotes outcome in QALYs (quality-adjusted life years)

Source: Horton et al., 2017 [49]

4.1.2.5 CHOOSING DISCOUNT RATES

Different input parameters, including discount rates, strongly affect the estimations of future costs and benefits. Discounting allows analysts to reflect on the time preference of decision makers and opportunity costs associated with present versus future value of interventions.

Although some of the published reference cases generally apply discount rates for both future costs and health gains, discount rates vary across countries and time periods. For example, the UK uses a 3.5% discount rate, while Colombia uses 5% [31]. Some reference case decisions will be informed by local context characteristics, historic data, or even preferences, and therefore, there is no consensus on what the "correct" discount rate is in all cases.

Discount rates should be part of the sensitivity analyses to consider questions such as what if the intervention's benefit fades in time or the opportunity cost of investing in the technology of interest now versus in the future. Additional developments are ongoing for issuing a recommendation for varying discount rates between health and economic impacts over time [50].

4.1.2.6 USING COST-EFFECTIVENESS THRESHOLDS IN LMICS

Decision makers increasingly seek evidence on costs and outcomes on which to base their conclusions [51]. In the case of CEA or CUA, costs are measured and expressed in monetary terms, but outcomes are stated in either natural or combined units capable of capturing morbidity and mortality to allow cross comparison (e.g., QALY or DALY). However, as said before, a decision rule is not straightforward, and a threshold or ceiling ratio helps decision making. Ideally, such thresholds represent opportunity costs of forgone alternative programs.

Thresholds are useful to start the discussion about the value of a health technology. Many HICs have historically set their own thresholds, such as the rule of thumb of USD 50,000, CAD 50,000, and £30,000 per QALY gained in the United States, Canada, and the United Kingdom, respectively [27, 52–58]. However, the broad nuance in setting up a cost-effectiveness threshold includes refinement using empirical data or considerations related to highly specialized technologies [59–63]. In the context of LMICs, Thailand uses a threshold of 100,000 Baht/QALY gained.

One of the most commonly cited thresholds comes from WHO's Choosing Interventions that are Cost–Effective project (WHO-CHOICE) [64, 65]. It suggests that interventions that avert one DALY for less than a country or region's average per capita gross domestic product (GDP) are *very cost effective*. However, this and other international benchmarks to inform resource allocation decisions have been criticized due to their primary focus on using DALYs (mainly aimed at estimating global burden of disease) and its potential methodological limitation [66].

Some researchers have argued that actual thresholds should be context specific rather than global, and new analyses have incorporated income level and income elasticity to thresholds [67, 68]. A different approach looked at opportunity cost estimates and suggested lower cost-effectiveness thresholds ranging from 1% to 51% GDP/capita for Malawi, 4% to 51% for Cambodia, 11% to 51% for El Salvador, and 32% to 59% for Kazakhstan [69]. Similarly, in HICs, suggested thresholds tend to be lower than those in use (e.g., 0.4–2.2 times GDP for Canada, the Netherlands, the US, or the UK). This evidence suggests that much lower thresholds than one time GDP per capita in LMICs should be considered [31, 70].

Cost-effectiveness ratios have been criticized for their inability to capture the benefits of health care programs, the poor transferability of data that may not reflect the real willingness-to-pay threshold, and the fact that often decision makers are unaware of the costs and benefits of every competing alternative (within and outside the health care sector) for each decision [71–75]. Further, when there are no data, estimations of opportunity costs, including benchmarking to the historic cost, are unreliable [76]. All of these issues are part of the ongoing debate on the use of thresholds, including the value of a life and the value of a life-year [60]. In any case, thresholds should never be used as a stand-alone criterion for decision making [66], but as a starting point for discussions.

4.1.2.7 AFFORDABILITY CONSIDERATIONS

HTA agencies should also look into affordability by asking *Can we afford this technology given our budget constraints*? Health technologies can be assessed as cost effective, but that does not necessarily mean that they will be affordable. Affordability and sustainability of health services depend on the availability of funds [77]. Typically, when conducting a budget impact analysis, HTA doers will focus on the accounting/financial costs or the transaction price, such as pay for nurses and doctors or the cost of medicines or equipment with a specific perspective for the budget holder [78].

An example from Newall et al. looked at HPV vaccinations in 26 LMICs and rotavirus vaccinations in another 15. While less cost-effective programs were less likely to be implemented, very cost-effective programs were not all funded either. CEAs alone were insufficient—affordability needed to be considered as well. These considerations can be conducted together (integrated) or separately [77, 79–82].

There are different approaches for conducting budget impact analyses, usually by forecasting different adoption scenarios by estimating unit costs and volume for the upcoming fiscal year. Beyond the actual cost of technologies and supplies, affordability evaluation should include labor, capital, and cost offsets.

A list of the principal resources available for estimating the budget impact of HTA in LMICs follows:

- Health Technology Assessment Toolbox for Emerging Settings- Best Practices and Recommendations [23]
- Budget Impact Analysis—Principles of Good Practice: Report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force [78]
- Localized country-specific economic analyses, budget impact analysis guidelines in Brazil [83], Colombia [31], Iran [84], and Chile [85]
- Costing and budget impact tools for community health worker, primary health care, specific public health programs [86]
- Modified Budget Impact Analysis checklist for Cost Effectiveness Analysis – example for LMIC budget impact analysis for rotavirus vaccine [87]

4.1.2.8 TRANSFERABILITY OF RESULTS

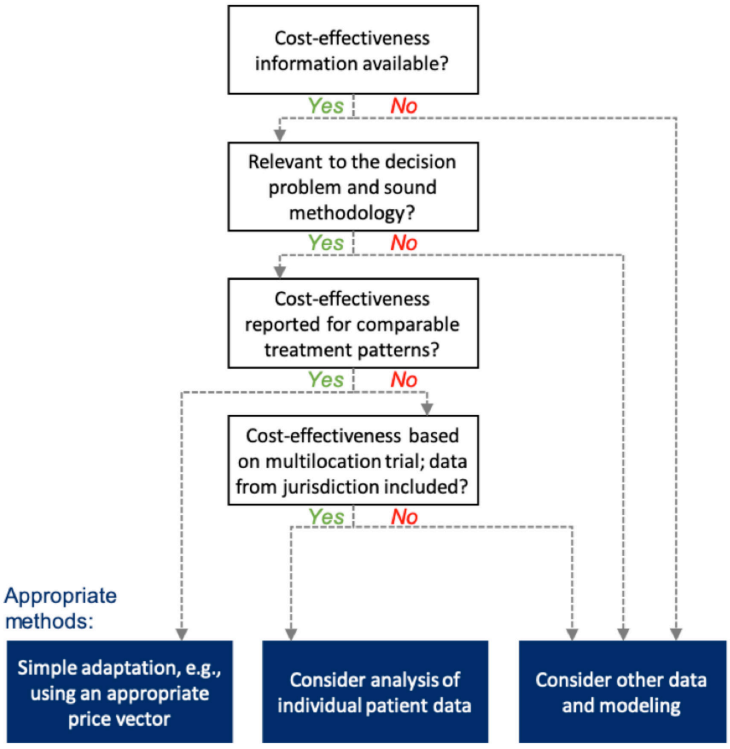
As a new HTA unit identifies a priority decision problem to answer as part of the Topic Selection step, it then must decide how to conduct the technical evaluation and produce robust recommendations. Not all health/health care technology evaluations have to start from scratch (*de-novo*). Generally, clinical analyses have a certain degree of transferability across jurisdictions, while costs and economic estimations are more local in nature [88]. Transferring results of foreign studies (used in the previously mentioned pragmatic HTA approach) may seem helpful in the early stages of HTA adoption. However, this approach is not exempt from criticism and should be done to limit risks of bias (e.g., varying practice patterns, different cost tradeoffs, relevance) [89].

A framework for transferring economic evaluations across jurisdictions helps determine the need to conduct *de-novo* modeling or to adjust previous cost-effectiveness information (figure 20) [90]. This framework explores:

- Availability of published CEAs
- Relevance and quality of study
- Comparability of clinical treatment patterns
- Existence of relevant local data

This framework looks at both the *general knock-out criteria* (decision problems, structural assumptions, treatment patterns, methodological robustness) and *specific knock-out criteria* (contextual issues: local rules for conducting HTA, ability to extrapolate results to population of interest).

Figure 20. Steps for determining appropriate methods for adjusting cost-effectiveness information



Source: Drummond et al., 2009 [90]

An alternative frameworks is a decision chart with a t wo-step process of initial assessment and data transferability assessment [91]. EUnetHTA's HTA adaptation toolkit also provides helpful screening tools to quickly assess the relevance, reliability, and transferability of existing HTA reports (*speedy sifting*) [92]; reports that pass screening will be subject to further evaluation on five domains: technology use, safety, effectiveness, economic evaluation, and organizational elements.

4.1.2.9 TIMELINESS OF ASSESSMENTS

The timeliness of HTA recommendations is of paramount importance for HTA buy-in, and countries often use HTA decisions from other settings to expedite the process despite the methodological limitations. An alternative is a rapid review. WHO and Health Action International (HAI) suggested only one-way adoption of HTA results, in which LMICs with limited HTA capacity can prioritize assessments based on HIC practices where HTA is well established. For example, if an HIC finds that a health technology is not cost effective, it is unlikely to be cost effective in LMICs [93, 94].

Countries such as Ukraine that in recent years have institutionalized HTA use have greatly benefited from the use of rapid reviews. The HTA department has conducted nearly 60 rapid assessment reviews to prepare the list of drugs for central procurement. It used a template covering comparative effectiveness and safety, international guideline recommendations, and HTA recommendations from selected agencies in addition to analyzing budget impact. Local policy makers were satisfied with the process and consequently decided to invest more in the HTA department. In Indonesia, a rapid review of the use of sildenafil to treat pulmonary

arterial hypertension (PAH) found that Thailand's recent CUA had recommended sildenafil to treat PAH patients [95–97], which helped Indonesian policy makers expedite their process.

4.1.2.10 BALANCING HTA DEMAND AND EXISTING CAPACITIES

Although the various types of HTA evaluations require different levels of effort, little information is available on the relative resource requirements to conduct HTA exercises. Figure 21 is adapted from the Duke Global Health Institute and scores the level of effort of peer referencing to other forms of economic analyses [98].

Figure 21. Relative level of effort of peer referencing versus conducting other forms of economic analyses

	A Peer referencing	B Cost analysis Cost minimization Budget impact	C Cost consequences Cost effectiveness	D Cost utility
Information requirements	*	*	**	***
Level of effort	**	**	***	***
Note	Author assumption	"fairly straightforward" "generally, not an expensive endeavor."	"significant time commitment" "need to compile costs, outcomes" for your intervention and alternatives "A CEA is an investment. The costs are high in terms of personnel and study activities and management." "A CBA requires more staff time than a CA or CMA, but likely less staff time than a CEA or CUA."	"Regardless of how a CUA is conducted, it is a complicated analysis." "Contracting someone with economic expertise and a thorough understanding of QALYs or partnering with another experienced organization is recommended."

Source: Developed by the authors, as adapted from Duke Global Health Institute [98]

4.1.2.11 OPPORTUNITIES FOR INTERNATIONAL COLLABORATION ON METHODS AND PROCESSES

In Europe, the EUnetHTA project's strategic objectives were to reduce overlap and duplication of efforts and promote more effective resource use [99]. HTA bodies within the EU can now rely on EUnetHTA guidance and focus mainly on specialized national tasks to improve the evidence base for their decision making [100] while understanding that some HTA components, including costs and practice pattern, may vary [88, 101]. Similar collaboration among global, regional, and subregional networks in LMICs (i.e., RedETSA, HTAsiaLink) is expected to promote greater access to quality, safe, efficacious, and affordable medical products and to address limited capacity and transferability in LMICs [102].

4.1.3 CUSTOMIZING METHODS AND PROCESSES

There is no one right answer regarding HTA methodological approaches, and local stakeholders must balance relevant values, assumptions, and considerations. Methods and processes generally fall under the following two broad categories:

- In countries such as the UK, Canada, and Australia, the focus is on combining cost and benefit in one measure using QALYs, aggregating results through the use of ICERs, and considering thresholds to inform their decisions.
- In contrast, countries such as Germany, France, Italy, Spain, and Japan use a two-step approach, where the first is a clinical-scientific assessment of the benefits, resulting in an "added patient benefit rating." In the second step, this rating will form the basis of a stakeholder deliberation of the cost implications or prices of technologies.

While the first approach centers on standardizing criteria across different disease areas and aspects of health care, the second recognizes that decision making criteria may be difficult in areas of high disease severity and unmet health care needs.

In Chapter 3 we discussed in detail the steps for systematic and transparent priority setting for health/health care, from identification to topic selection, assessment, and appraisal—including incorporating value judgement. In this chapter, we have focused on the methodological considerations and contextual challenges for HTA in LMICs. Methodological considerations aside, results of economic models or cost-effectiveness thresholds should not be blindly used in decision making.

Standard HTA practices may not fully capture relevant societal issues, such as equity and distributional justice; values of health and health states; societal preferences to prioritize key populations; and political decisions on national security, self-reliance, and self-sustenance. Decision making also requires value judgement, which is missing in many of these analyses [103–105]. In fact, in many LMICs, priority-setting and resource-allocation decisions are often inconsistent and unstructured. Important criteria (e.g., budget impact, equity, disease severity) may be missing or have unclear influence on a final decision [106]. The result may be implicit and covert rationing, such as waiting lines, low-quality services, or health care inequities [107]. Therefore, in this section, we also discuss opportunities to expand classic HTA methods to improve its impact on recommendations while still achieving fair and robust deliberative processes.

4.1.3.1 EXTENDED COST-EFFECTIVENESS ANALYSIS

Extended cost-effectiveness analysis (ECEA) quantitatively characterizes equity and financial risk protection policies and non-health outcomes in HTA. ECEA presents health policy assessment in three domains: health gains, private expenditures averted, and financial risk protection (FRP), all per population subgroup (e.g., income quintile, geographical setting). Additionally, by assessing the total costs of the policy, ECEA can calculate the outcomes of health gains and financial protection per dollar (or local currency) expenditure. Therefore, ECEA can assess every policy or intervention by health benefits per monetary expenditure and FRP per monetary expenditure. Policy makers can then visually compare different policies and interventions, taking into account multiple criteria in the decision making process [108, 109].

4.1.3.2 MULTICRITERIA DECISION ANALYSIS

Decision making can be divided into scientific and value judgments [110]. Scientific judgment relies on globally accepted standards defining the quality of evidence. With standardization, scientific judgment is relatively robust regardless of evaluators' positions. Conversely, value judgments are sensitive to evaluator preferences and difficult to standardize, which calls for well-organized, explicit and transparent decision making processes. NICE advisory teams have to make judgments based on both the available science (scientific value judgments) and about what is good for society (social value judgments) [111].

Multicriteria decision analysis (MCDA), with roots outside of the health sector, focuses on finding a compromise between conflicting interests in complex decision making [112]. MCDA methods help people make better choices when facing complex decisions involving several dimensions. "It is especially helpful when there is a need to combine *hard data* with subjective preferences—or consider trade-offs involving multiple decision-makers" [113]. While MCDA has remaining methodological issues (e.g., weighting, double counting) [114], it allows for structured and objective consideration of measurable and value-based factors in an open and transparent way [104]. MCDA can support HTA agencies in LMICs to formulate high-quality, consistent, and transparent recommendations [114].

In a qualitative MCDA, the HTA committee makes a judgment on the overall value of a technology by deliberating on its performance regarding explicitly defined criteria. The distinctive feature of qualitative MCDA that makes it different from intuitive prioritization (without any specific method) is that it uses explicit criteria, including the technologies' performance on these criteria. The use of explicit criteria improves the quality of recommendations as it fosters in-depth consideration of the criteria, including the available evidence, and provides structure to deliberative discussions of the committee. Figure 22 presents a qualitative MCDA of four competing technologies with severity of disease shown as a 4-dot scale, with more dots indicating a more severe disease.

Figure 22. Interpretation of performance matrix in qualitative multicriteria decision analysis

Technologies	Criteria			
	Effectiveness (quality adjusted life years)	Severity of disease	Disease of the poor	Age
Antiretroviral treatment in HIV/AIDS	100	• • • •	✔	15 years and older
Treatment of childhood pneumonia	200	• • • •	✔	0-14 years
Inpatient care for acute schizophrenia	10	• •		15 years and older
Plastering for simple fractures	200	•		all

Source: Baltussen et al., 2009 [114]

Alternatively, quantitative MCDA uses a value measurement model to interpret the performance matrix, followed by deliberation. Figure 23 presents the same four competing interventions with preference scores for effectiveness related to its values following a linear scale. For diseases of the poor, if the technology targets a disease of the poor, it scores 100, otherwise 0. Preference scores for disease severity are scaled between 0 and 100 in proportion to their bullets in the table. Assuming that decision makers have a preference to treat young people over old, 0 to 14 years receives a score of 100, 15 years and older a score of 0, and all ages score 50. Preference scores and relative weight of each aspects are presented here for illustrative purposes only and are arbitrary.

Figure 23. Interpretation of performance matrix in quantitative multicriteria decision analysis

Technologies	Effectiveness	Severity of disease	Disease of the poor	Age	Overall value
Antiretroviral treatment in HIV/AIDS	50	100	100	0	70
Treatment of childhood pneumonia	100	100	100	100	100
Inpatient care for acute schizophrenia	5	50	0	0	7
Plastering for simple fractures	100	25	0	50	48
Weights	40	10	40	10	–

Source: Baltussen et al., [114]

We have argued throughout this roadmap that countries should not reinvent the wheel. Exploring existing approaches, reference cases, and case studies from other LMICs will help them reflect on their current existing capacity to adopt and adapt these approaches to HTA. Figure 24 depicts features of different approaches that LMICs can use to select one methodological approach versus the other [115].

Figure 24. Salient features of different approaches for informing priority setting

	Cost-effectiveness analysis (CEA)	Multicriteria decision analysis (MCDA)	Extended cost-effectiveness analysis (ECEA)	Cost-benefit analysis (CBA)
Reflective of social values	Methods assume that population health gain is the overriding objective.	In principle, method can take into account any possible social values, but care should be taken in structuring the criteria.	Method reflects a key concern in LMICs where avoidance of catastrophic financial payments is important alongside population health gain.	Methods involve modelling all-welfare relevant consequences. Opponents argue that CBA embeds unacceptable value tradeoffs.
Technically robust and justifiable	Method is very well established within the healthcare sector. Guidelines for good practice exist although methodological controversies remain.	Method is well established outside the healthcare sector and popular within the healthcare sector. Several general (i.e., nonhealthcare specific) good practice guidelines exist, but there is not yet a strong body of healthcare-specific guidelines.	Method is a new and established guidelines on good practice do not yet exist.	Method is well-established outside the healthcare sector and popular within the healthcare sector. Several general (i.e., non-healthcare specific) good practice guidelines exist, but there is not yet a strong body of healthcare-specific guidelines.
Easy to understand	Methods can be implemented at various levels of sophistication: more complicated models will be harder for lay people to engage with.	Ease of understanding is one of the principle selling points for these methods. However, appropriately structuring criteria and choosing aggregation rules is subtler than is often appreciated.	Same comments apply as in the case of CEA but with the proviso that some of the additional financial modelling (in particular the concept of insurance value) adds an additional layer of complexity.	Models can be very technical and expression of cost and benefits in monetary terms is often a stumbling block for lay engagement.
Have low cost of implementation	Can be done at varying levels of intensity, from "quick and dirty" to more expensive and robust analyses. Expansion path analysis at the population level involves bringing together clinical and epidemiological data which can be time consuming.	Does not require specialized modelling resources, but requires relatively intensive engagement from stakeholders to supply scores and weights.	Same comments apply as in the case of CEA but with the additional proviso that modelling of financial and payment aspects is required.	Same comments apply as in the case of CEA and ECEA but requires a more extensive modelling of welfare consequences.

Source: Glassman et al., 2017 [115]

4.2 A JOURNEY TO SELF-RELIANCE FOR HTA: INCREMENTAL ADOPTION OF HTA IN LMICS

Self-reliance entails the capacity to domestically plan, mobilize resources, and implement solutions to local development challenges. Development partners such as USAID are reorienting their strategies, partnership models, and program practices to achieve greater development outcomes and work toward a time when foreign assistance is no longer necessary [116]. This journey to self-reliance aims at empowering host country governments and other partners to achieve locally sustained results. Because HTA contributes to sustainable UHC and more efficient resource allocation through systematic priority setting, it could be as means for LMICs to achieve self-reliance.

HTA bodies in LMICs should start small and grow by leveraging in-country existing capacities: "building ship as we sail it"—HITAP's co-founder, Dr. Sripen Tantivess

Evidence shows that national-level HTA capacity and commitment emerge as local systems, institutions, and communities evolve [117]. HTA bodies in LMICs should start small and grow by leveraging in-country existing capacities, as HITAP's co-founder, Dr. Sripen Tantivess said, "building ship as we sail it." An initial ambition of ticking all the boxes of best practices prescribed by decades of development from HICs will not be realistic, particularly at early stages of HTA development.

Established HTA agencies have varying level of adherence with HTA key principles of good practice [118, 119]. More advanced HTA organizations have considerably more resources. There is no single way to conduct HTA that will meet the full spectrum of needs of all decision makers, stakeholders, and societies. HTA organizations will conduct different assessments given their context, including health systems characteristics; institutional structures and governance; statutory authority and mandate; data availability and resources; cultures; traditions; incomes; and local practice patterns, prices, and preferences.

HTA development is context specific and time evolved. NICE in the UK started operation with 30 staff in 1999. IQWiG in Germany started with 17 key personnel in 2004. In China, between 1993 to 2000, only four papers on average were published per year regarding pilot testing HTA [120]. In all cases, capacity and sophistication of methods tend to grow incrementally.

Throughout this document, we have considered variability across settings including different needs, motivations, political momentum, and financial and technical resources available for HTA. As such, we envision a pragmatic and incremental pathway in LMICs in which HTA units start small and with basic methods for assessing and appraising the existing evidence while strengthening their future capacities and competences.

COUNTRIES WITH NON-EXISTING HTA CAPACITY

Conduct peer referencing and rapid reviews, assess comparative safety and efficacy, and conduct cost minimization and budget impact analyses.

This approach optimizes timeliness of HTA evaluations to produce an early positive impact on decision making. Rapid reviews and peer referencing, especially of 'no' decisions conducted in more affluent settings, will help deliver speedy results. Notably, at this nascent phase of HTA development, there would be plenty of caveats around evaluation robustness and contextual applicability; however, this initial model could help the newly

established HTA body become part of the policy process (*insider* status) and help produce stakeholder buy-in. When HTA provides a timely solution to an existing resource allocation problem, it increases the likelihood for further investments. This will allow for more sophisticated, stylized, and context-specific evaluations to grow, contingent on available capacities. This approach is best applied in countries with minimal existing capacities for HTA, including fragile and conflict-affected settings.

COUNTRIES WITH EMERGING AND GROWING HTA CAPACITY

Conduct peer referencing and rapid reviews, assess comparative safety and efficacy, and conduct cost minimization and budget impact analyses, and add more sophisticated economic analyses (cost-consequence or cost-effectiveness), keeping in mind the uncertainty of estimations (sensitivity analyses and develop a reference case).

Many LMICs have some existing HTA capacity and/or have started using HTA reports in some fashion to inform their decision making. These countries should develop country-level methodological standards (reference case) to improve comparability, quality (including sensitivity analysis), and validity. In this phase, countries should aim to reduce fragmentation of HTA capacities (health economists, analysts, research groups) with special emphasis on building capacity to conduct practical CEAs that estimate opportunity costs. Because of the potential technical limitations of using natural units in CEA, countries should feel empowered to explore CUA, which allow for cross-disease comparison (by using QALYs or DALYs). Combining CEA with MCDA is possible if such technical capacities exist. This approach is best suited for countries with some HTA capacity to conduct evaluations with different levels of coordination and binding power or recommendations at a broader policy level.

COUNTRIES WITH FULLY DEVELOPED HTA CAPACITY

Conduct peer referencing and rapid or full reviews; assess comparative safety, efficacy, and effectiveness; assess value of the intervention (CUA or MCDA); and forecast economic impact of implementation, keeping in mind the uncertainty of estimations (sensitivity analyses and more sophisticated statistical methods for HTA. Update reference case in light of new evidence and values). Aim to improve open and transparent deliberative processes.

This level of countries implements HTA evaluations with all main features as described in the reference cases, including:

- Comparative safety, efficacy, and effectiveness assessment
- Value assessment of the intervention(s) of interest (value for money and also considering criteria beyond incremental cost and effectiveness)
- Forecast of implementations' economic impact and broader impact
- Uncertainty analysis (deterministic and probabilistic sensitivity analyses and more sophisticated statistical methods for HTA)
- Updated reference cases reflecting new evidence and values that may include the use of implicit or explicit thresholds

Typically, these countries may have already established HTA organizations and incrementally developed more sophisticated methods, networks of collaboration, stable funding, capacity, and (local) data. HTA institutional

strengthening will revolve around harmonization, coordination, cooperation, and encouragement to take on larger, more ambitious goals for the domestic health system and to contribute to the growing international database of scientific findings. Constant improvement and sustained engagement with stakeholders will improve the transparency, legitimacy, and accountability of decision making.

In summary, the journey to self-reliance for HTA starts with leveraging existing local capacities, starting with small operations, and growing incrementally. Countries may want to seek the highest benchmarks for HTA from the beginning. However, we suggest that a pragmatic incremental approach may be more plausible by considering contextual limitations and drivers for successful and sustainable institutionalization. At the core, HTA aims to better inform complex and dynamic decision making within existing health systems. In their journey to self-reliance, countries should feel empowered to make customized decisions (simplification or sophistication) based on their capacity and needs.

4.3 CAPACITY BUILDING FOR HTA

In the previous chapters, we discussed the global trend of HTA institutionalization and noticed that in some LMICs there is already an existing level of HTA capacity—albeit unstructured and uncoordinated in many of them. Capacity building in HTA is the process by which individuals and organizations develop or strengthen abilities related to understanding, providing input to, conducting, or utilizing HTA for health policy and decision making, as well as developing awareness and support in the environment within which HTA is being used [121]. Beyond developing an inventory of institutional and individual capacities for developing an HTA capacity building plan, countries should examine the full gamut of stakeholders to determine their role as potential doers or users of HTA, including policy makers, funders, health professionals, health economists, epidemiologists, statisticians, civil society, industry representatives, and even mass media.

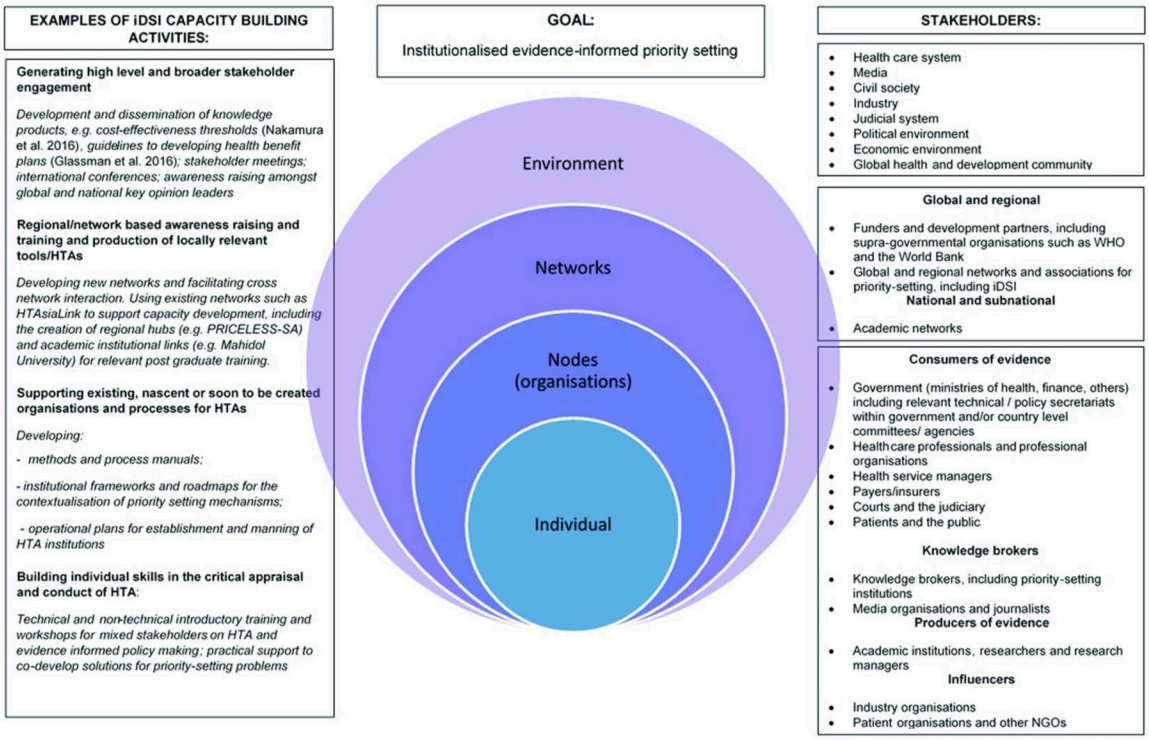
Capacity building should be incremental and tailored to existing needs and envisioned methods. Some empirical evidence shows that it takes a few years for newly established HTA bodies to publish or review their existing reference cases, as they should be tweaked to fit the local context.

By starting early, new institutions will develop expertise as they immerse themselves in the HTA community. This learning by doing approach has been used in many settings. In Australia, draft HTA guidelines were first issued in 1992, and official updates were made in 1995, 2000, and 2006 with continuous input and cooperation from all stakeholders [70]. There is plenty of room for growth for all HTA doers, and the HTA community has increasingly embraced best practices and guidelines that countries can use to build individual or organizational capacities for HTA [122].

4.3.1 ASSESSING CURRENT IMPLEMENTATION CAPACITY

Following the sensitization of key stakeholders and securing initial buy-in, countries need to explore capacity analysis and capacity development. A narrow view of capacity typically involves human resources with experience in conducting HTA. However, the function of individuals and organizations is interlinked with their network and environment as depicted in the Individual, Nodes, Network, and Environment (INNE) framework presented in figure 25.

Figure 25. INNE framework applied to iDSI stakeholders and activities



Source: Li et al., 2017 [123]

The first two steps (individual and nodes/organizations) are typically the primary focus for a new HTA institution. Getting a clear understanding of the current level of capacity allows identification of growth potential. Some areas for growth are low-hanging fruit that require a small amount of time and resources to establish; for example, local researchers can be sensitized through a series of workshops, training, or networking (e.g., participation in international conferences and networks). This activity will allow the country to identify actors to develop an HTA task force.

Developing and acquiring expertise, on the other hand, might require longer-term planning. Training HTA analysts might take years, as would the development of country-specific decision instruments. Countries need to start by leveraging their existing resources. The INAHTA report suggested that internationally trained human resources experts may contribute more meaningfully to an HTA task force. Alternatively, institutions may *leapfrog* the development stage by partnering with a technical organization that will kick-start the process of learning by doing.

While the identification of actors is critical for capacity building, it also helps ensure multisectoral involvement. For example, manufacturers often want to align their expectations—a certain level of revenue and market penetration—with those of the HTA organization [124]. On the other hand, payers expect HTA processes to reduce prices and increase efficiency.

The next two layers (networks and environment) often apply to countries with more developed HTA capacity, although more LMICs have been collaborating, such as through HTAsiaLink. Members of European HTA agencies and programs are partnering to improve HTA coordination. Members of these networks emphasized that collaboration would help avoid duplication and achieve synergy [125].

Understanding the current country capacity landscape in HTA is critically important to meet rising demands given a limited supply of skilled professionals. Countries will need to set a timeline to acquire the skill level to produce rapid and large returns of investment. The resource and skill needs of different HTA methods may help prioritize early investments in capacity building.

4.3.2 CAPACITY-BUILDING REQUIREMENTS FOR TECHNICAL STAFF CONDUCTING ASSESSMENTS (DOERS)

All new HTA institutions need a multidisciplinary team with specific skills. At a minimum, team members need to understand the principles of scientific evaluation and inference and the practical skills to review information to start conducting systematic and rapid reviews. Being able to retrieve published evidence making use of PICO(TS) questions and to report the results of reviews and meta-analyses are important when assessing the best available evidence. Being familiar with approaches to assess the quality of peer-reviewed publications and being able to run costing evaluations are often the first skill sets HTA doers need to develop to run basic comparative (safety, efficacy/effectiveness and cost) analyses.

Countries with a more developed capacity should already have HTA team members with these skill sets. For these settings, capacity building will focus on exploring economic evaluations in terms of both costs and benefits. Simple modeling skills, including the development of decision trees or Markov models, may be introduced to integrate model results with cost effectiveness and utility analyses. Other capacity needs include an understanding of health-related quality of life measures, opportunity costs, incremental cost-effectiveness ratios, DALYs and QALYs (if cost-utility studies are preferred), and sensitivity analyses. In addition, competences are needed to assess ethical, social, cultural, and legal issues; organizational and environmental aspects; and wider implications for the patient, relatives, caregivers, and the population. The EUnetHTA handbook on HTA capacity building includes additional resources for capacity building for implementers [126].

4.3.3 CAPACITY-BUILDING REQUIREMENTS FOR POLICY MAKERS AND USERS OF ASSESSMENTS

HTA users such as government officials, members of appraisal or decision making committees, health care professionals, and patient representatives are often a neglected capacity-building target. HTA users should be able to understand the need to prioritize finite resources for health, the importance of evidence-informed policy and practice, and the need to be transparent and broadly engage stakeholders.

Once users have these basic competencies through training, sensitization, and discussions, they will need to be able to critically read and discuss HTA reports to pick out potential biases, confounding, and forces that may affect the findings such as conflicts of interest among doers and transferability of findings. Users will also need to recognize good practices in HTA processes such as those listed in the *Accountability for Reasonableness* framework (Chapter 3).

In conclusion, HTA uses include benefits package design, reimbursement decision, supply-side drug pricing, price negotiation, and exploring early investment on health technologies research and development [127, 128]. Different methods to conduct HTA have their pros and cons, but what LMICs want to accomplish through HTA will guide their investments. LMICs should start by assessing their existing capacities and take incremental steps into their journey to self-reliance and institutionalize HTA process.

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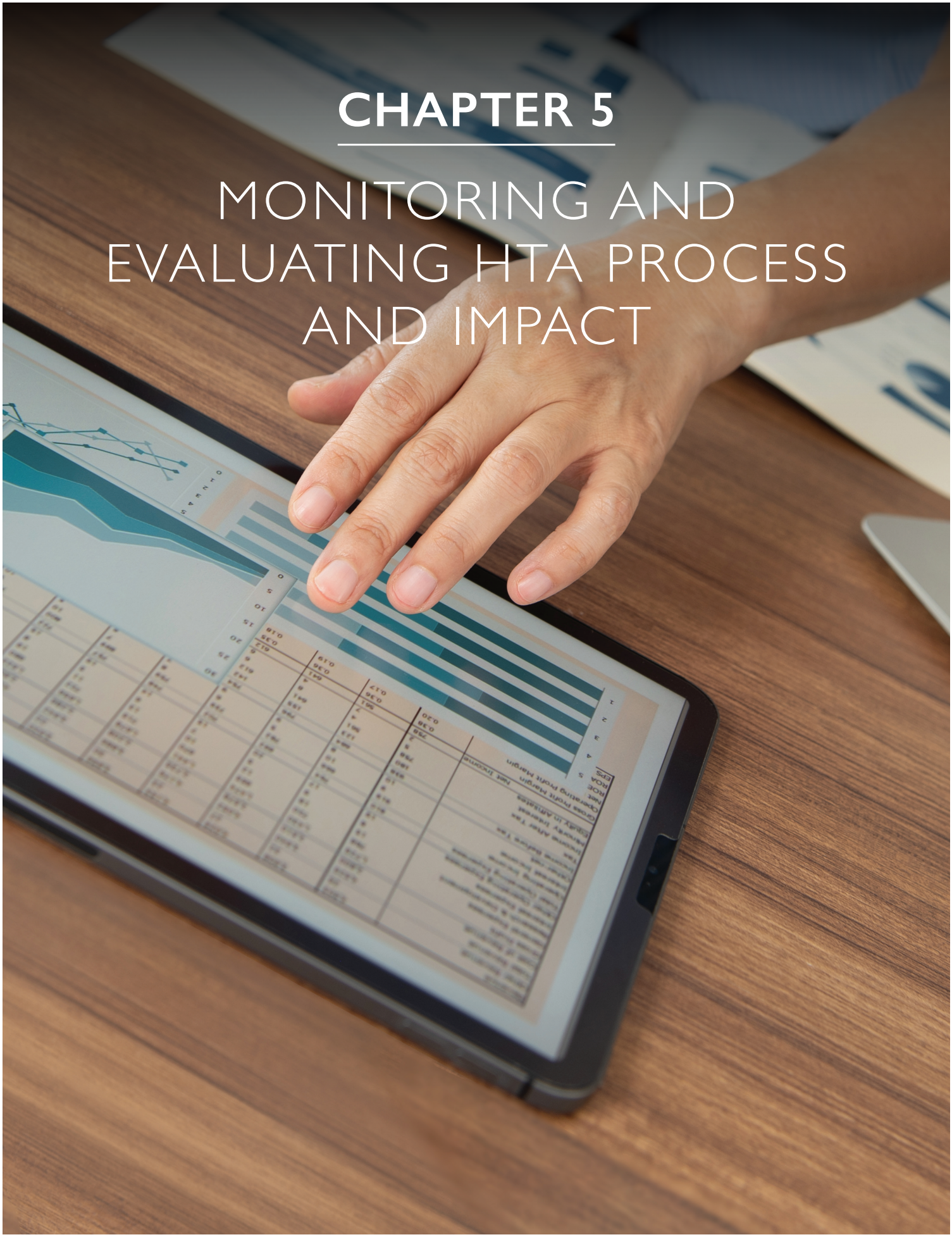


CHAPTER 5

MONITORING AND EVALUATING HTA PROCESS AND IMPACT

HTA is rapidly gaining ground as a strategic policy tool that can support multiple objectives, including informing the value of a technology, guiding reimbursement decisions, setting prices for health technologies, and guiding strategic procurement. HTA can also improve allocation efficiency, reduce the population's financial risk, enhance service quality, drive accountability and buy-in of decision making, and boost constituency satisfaction.

Regardless of the objectives for HTA, performance indicators are needed to monitor and evaluate its impact. Among competing programs, priorities, and funding, HTA evaluation can demonstrate its value as an effective investment to improve health system performance.

In this chapter, we will provide insight into the following monitoring and evaluation components:

- **Identifying approaches, milestones, and performance indicators to assess progress in advancing HTA as a policy solution**
- **Frameworks for evaluating the overall impact of HTA**
- **Baseline and ongoing data collection processes and empirical findings of HTA impact**

The HTA process consists of several stages—identification, topic selection, assessment, appraisal, deliberation, and decision making—that will be the areas for monitoring and evaluation. HTA also requires an institutional structure to support it, which should be evaluated for technical efficiency. Consequently, defining the main milestones and performance indicators to evaluate HTA and monitor its impact involves multiple dimensions, both general and context specific. A major distinction lies between ***assessing the progress of implementing HTA*** as a policy solution versus assessment of the ***overall impact of HTA***. While this chapter examines indicators for these categories as two discrete sets, the progress made in advancing the HTA process, policy, and institutional structures will contribute to the quality of HTA reports and recommendations.

5.1 ASSESSING THE PROGRESS IN ADVANCING HTA AS A POLICY SOLUTION

Although countries may prioritize HTA as a significant goal, countries and implementing partners need to assess progress in advancing HTA as a policy solution. The main principles of good practice for HTA described in previous chapters can serve as the basis for an audit tool to assess HTA agencies' progression to institutionalization [1]. Figure 26 is an example of how the principles can be adapted as a checklist of indicators.

Figure 26. Using the principles of good practice for HTA as a checklist to assess macro performance

	Major principles – macro level	Examples of dimensions to consider in developing subindicators
1	The goal of HTA should be explicit and relevant to its use	HTA Program: Is the goal of the HTA program explicitly stated in its constitution or guidelines? Is it meeting the goals of the types of decisions it is supporting? HTA Report: Is the research question clearly defined (e.g., outcomes, comparators, population)?
2	HTA should be an unbiased and transparent exercise	HTA Program and HTA Report: Are multiple stakeholders involved in the process? Is it open to public? Are findings shared with the public?
3	HTA should include all relevant technologies	HTA Program: Does it assess all types of technologies and interventions (e.g., devices, diagnostics, medicines, vaccines, programs, procedures)? HTA Report: Does the report provide a systematic methodology and evidence for selecting comparators?
4	HTA should consider a full societal perspective	HTA Program: Do the guidelines contain social-, ethical-, and equity-related assessment criteria? HTA Report: Are the relevant stakeholders involved to provide the full societal perspective?
5	Link between HTA findings and decision making processes needs to be clearly defined	HTA Program and Report: Are there explicit criteria for accepting or rejecting the recommendations from HTA (e.g. thresholds)? Is the deliberation rationale shared with the public?

Source: Adapted by the authors from Drummond et al., 2012 and Oortwijn et al., 2013 [1, 2]

WHO's Asia Pacific Observatory on Health Systems and Policies' policy brief on the factors conducive for HTA institutionalization in this region also provides a checklist from the experiences and models in China, Indonesia, Malaysia, South Korea, Thailand, and Vietnam [3]. This checklist is a useful starting point for LMICs thinking about advancing HTA (figure 27).

Figure 27. Checklist of achievement indicators to monitor progress of HTA institutionalization

- ✔ Formal mechanism to link HTA unit and policy makers
- ✔ Full-time group of HTA researchers
- ✔ Use of HTA results in policy implementation
- ✔ HTA process guidelines
- ✔ HTA method guidelines
- ✔ Appointment of HTA focal point agency (*or unit or committee*)

- ✔ Collaboration of domestic stakeholders in carrying out HTA research (e.g., academia, clinical professionals, hospitals/health facilities, patient or representatives, health economists, social science researchers)
- ✔ Domestic HTA training (e.g., educational degrees, certifications, undergraduate or graduate-level courses)
- ✔ Allocation of annual budget to HTA activities by government
- ✔ Policy statement on the willingness to use HTA in policy decision making

Source: WHO policy brief, 2015 [3]

The policy brief also provides significant milestones (features) that indicate when an HTA agency could be viewed as a successful model after moving through the steps outlined in the checklist above (figure 28).

Figure 28. Seven features of a successful HTA agency

1. Independence
2. Financial sustainability
3. Management of conflicts of interest
4. Full-time multidisciplinary staff
5. Extensive networks
6. Good systematic process
7. High-quality research and a quality assurance system

Source: WHO policy brief, 2015 [3]

In 2016, the researchers expanded the initial checklist with further analysis from participating countries [4] (figure 29). The country experts rated achievement of milestones according to their level of importance on a scale of 1 to 4, where 1 was least important and 4 was most important. The researchers then identified the top milestones based on the average score of each indicator.

Figure 29. Milestones for HTA institutionalization in selected Asian countries and regions

Indicator	Country/Region							
	China	Taiwan*	Indonesia	South Korea	Malaysia	Vietnam	Thailand	Average Score
Formal mechanism to link HTA unit and policy makers	4	4	4	4	4	4	4	4
Full time group of researchers	4	4	4	4	2.7	4	4	3.8
Use of HTA in policy	4	4	4	3	3.3	4	4	3.8
HTA process guidelines	4	4	4	3	4	3	4	3.7
HTA method guidelines	4	2	4	3	4	4	4	3.6
Appointment of focal point agency for HTA	4	3	4	2	4	4	4	3.6
Collaboration of domestic experts in HTA research	4	2	4	3	4	4	4	3.6
Domestic HTA training	3	4	4	1	3.3	4	4	3.3
Allocation of annual budget for HTA by government	4	4	4	2	3	3	3	3.3
Policy statement on willingness to use HTA in decision making	4	3	4	2	3.3	4	2	3.2
National HTA database of reports	4	2	3	2	3.7	4	2	3.0
HTA legislation	4	3	2	4	2.3	4	1	2.9
Membership in international networks	4	3	2	3	2.3	3	3	2.9
Post graduate training on HTA subjects	3	4	2	2	3	2	3.5	2.8
Data registry for clinical and economics data for use in HTA	3	2	3	2	3.3	3	2	2.6
International journal publications by researchers	2	2	3	2	2	3	3.5	2.5
National HTA conference	2	3	2	1	3	3	2.5	2.4
HTA as part of undergraduate curricula for health fields	2	3	1	2	2.7	2	3	2.2

*Taiwan is referred to as Chinese Taipei in the original document

Source: WHO policy brief, 2015 [3]

LMICs can customize this checklist based on their own values and priorities regarding milestones or indicators. Additionally, countries can use this as a scorecard to assess progress in HTA institutionalization using a numerical scale; each milestone could be scored to assess levels of progression until full completion. However, each country needs to develop clear operational definitions of milestones and determine if each milestone has the same weight on the impact on health/health care decision making.

5.2. ASSESSING THE IMPACT OF HTA

Once HTA had been institutionalized, it is also valuable to assess overall HTA impact as a demonstration of return on investment in HTA. As noted, it is important to distinguish between evaluating the overall impact of an HTA program as opposed to evaluating the impact of an HTA report. An HTA report is one program output whose impact should be monitored in more detail, keeping in mind principles for best HTA practices, methodological guidelines, quality of reporting, and others.

5.2.1 ASSESSING HTA'S IMPACT ON POLICIES

As stated by Goodman [5], "the impact of HTA is variable and inconsistently understood. Among the most important factors influencing the impact of HTA reports is the directness of the relationship between an HTA program and policymaking bodies and health care decisions". Some HTA reports may directly affect health policies (with varying feasibility of quantifying their impact on the health system and population); nonetheless, even after rigorous analyses, many report recommendations are not adopted into general practice [5]. HTA reports can make an impact by changing one or more of the following policies, which can serve as categories to monitor HTA impact [5]:

- Regulatory policy (e.g., market access of a technology, indication of use)
- Third-party payment policy (e.g., coverage, pricing, reimbursement of a technology)
- Rate of use of a technology
- Clinical practice guidelines
- Clinician awareness and behavior
- Patient awareness and behavior
- Acquisition, adoption, or diffusion of a technology
- Organization or delivery of care
- Research and development priorities and associated spending levels
- Data collection (e.g., to fill evidence gaps identified by HTA reports)
- Marketing of a technology
- Allocation of local, regional, national, or global health care resources
- Investment decisions (e.g., by industry, investors)
- Incentives to innovate

HTA overall can potentially shape broader policies worth measuring, such as training needs, influence on social discourse, and collaboration with other agencies [4].

5.2.2 HTA PERFORMANCE INDICATORS

Performance indicators should be used to map the most important aspects of performance of the different stages of priority setting for health/health care at the country level by focusing on the overall HTA process (identification, topic selection, assessment, appraisal, reporting, dissemination, and implementation in policy and practice). These indicators serve as a baseline for ongoing monitoring and evaluating and quality improvement of HTA and should be collected regularly to help inform strategies and justify HTA expenditures [2].

In 2003, Hailey examined the various determinants of HTA program effectiveness [6]. Starting with the tangible products of HTA (i.e., HTA reports and dissemination of decisions), Hailey provides detailed indicators on the effectiveness of governance, staff and structure, resources, and collaborative and contractual relationships; the process of formulating questions; HTA outputs and outcomes; and the impact of HTA on target audiences [6]. This includes indicators regarding the productivity level of HTA reports, including number and quality of HTA products delivered, accessibility, and timelines. It also includes indicators of impact on different audiences, including whether reports are considered as an important input by policy makers and the binding power of recommendations on policy. The framework provides more than 50 categories of measures and potential modes of assessment, a sample of which are in figure 30. This is an option for countries looking for a more detailed framework to assess the advancement of HTA.

A review conducted for DIMDI in 2005 reported the lack of studies that provide a comprehensive and causal assessment of HTA reports on decision making [7]. However, validated indicators such as those listed by Drummond, Hailey, and Goodman could be used to assess surrogate performance and impact of HTA, although further research is needed to clearly define them. The review also highlighted that most evaluations of HTA reports focus on the assessment methods, but demonstrating a broader causal relationship is difficult because the final impact on health or health systems outcomes is usually multifactorial.

Figure 30. A framework for assessing HTA program effectiveness

Formulation of HTA questions

Issue	Possible Measure	Other Program Areas	Qualifications
Number of assessments requested	Number received/year		A crude measure of input
Requests declined	Number/year	Governance (appropriateness) Resources (feasibility)	Basic measure would need to be supplemented with reasons why
Source of questions	List sources, number per source	Governance (appropriateness)	Some HTA questions may be generated in HTA program with particular targets in mind
Scope of questions—technology, area of healthcare, type of analysis needed	List numbers, areas as indication of activity	Governance	May need to account separately for information/educational initiatives undertaken by program
Policy or administrative questions to be informed by HTA	List type of issuee (e.g. reimbursement decision)	Governance	Questions should be compatible with the program;s mandate
Extent to which the topic has been considered by other HTA programs	Make appropriate reference in individual reports Possibly list other reports considered		Could only be assessed in qualitative terms Note that there will often be a need to consider local issues even if an HTA has been completed elsewhere

HTA products

Issue	Possible Measure	Other Program Areas	Qualifications
Level of Activity	Number of HTA products/year	Formulation of questions Resources	No indication of type or complexity
	By topic, report, or other product		Basic categorization
Quality	Whether externally reviewed		Only one indicator. Some good quality products may not be reviewed
	Whether consistent with recognized guidelines		E.g. INAHTA checklist. Full assessment of this quality would have to be qualitative. Note individual assessments need not consider all attributes of a technology
	Whether transparent as to methods, data, analysis	Governance	Qualitative appraisal needed of a key element
Accessibility	Responses to surveys of targets of whether the products were intelligible and useful	Dissemination Governance	Qualitative appraisal
Time Taken	Record time taken from receipt of request/start of project to completion of HTA product	Formulation of HTA questions Resources Governance	Time may vary considerably. Some elements are outside of control of HTA staff An area where tradeoffs are made to accommodate work programs

Impact of HTA

Issue	Possible Measure	Other Program Areas	Qualifications
Whether report considered	Responses to questionnaire Correspondence received	Dissemination	Likely variable response. Extent of consideration not easy to establish
Recommendation made in HTA products are accepted	References in media releases dealing with policy, program changes Questionnaires, interviews	Formulation of HTA questions	Not all HTAs will include recommendations. Not necessarily a casual link between recommendations and related actions
The HTA demonstrates that a technology meets specific requirements for a program	Comparison of analysis and conclusions of the HTA with published criteria	Formulation of HTA questions	For example, in a situation where minimum standards must be met before some type of approval is given
Material from an HTA product is incorporated into policy or administrative documents	Cite as appropriate		
Information in HTA is used as reference material for future activities	Cite as appropriate		For example, in subsequent developments or refinement of guidelines
Number of HTA products having some impact	Judgments based on input from areas listed above		General guidance on the HTA program but information is likely to be limited

Dissemination

Issue	Possible Measure	Other Program Areas	Qualifications
Vehicles/methods used	Record of mail outs Record of website items Record of media releases, presentations, etc.	Resources Formulation of HTA question	A crude measure of input
Reaction to disseminated material	Responses to surveys of targets		These establish contact with HTA product but not necessarily comprehension
	Hits on websites	Governance (appropriateness)	
	Citations in literature, databases, etc.	Governance	
Related publications in journals, etc.	Citations in literature, databases, responses received	Resources	May give a message to a wider audience; may give additional information to that in HTA

Governance

Issue	Possible Measure	Other Program Areas	Qualifications
Legislative or administrative basis	Statutory or administrative documents	All	
Mandate or specification of program	High level documentation, general availability Operations strategies for local manager	Formulation Targets	
Values	Consistency with basis and mandate		
Interaction with political, other processes external to the program	Possibly a negative—absence of intrusion		
Interaction with HTA program management and staff	Formal meetings—frequency Documented decisions on program	All	Difficult to quantify
Support for generating program resources	Continuity of program budget Availability of resources for new initiatives	Resources	
	Endorsement and approval of external funding	Resources	

Source: Hailey 2003 [6]

5.2.3 USING EVIDENCE-INFORMED DELIBERATIVE PROCESSES TO DEFINE VALUE INDICATORS

Evidence-informed deliberative processes (EDPs) use a systematic approach to identify important values for stakeholders in the HTA process. An example is to identify stakeholder priorities and the values they attribute to those priorities through an explicit and transparent process such as MCDA. Therefore, the impact of HTA and the process is determined from that baseline set of indicators derived through an evidence-based process. If HTA stakeholders deem affordability, cost effectiveness, and equity to be major indicators of priority setting, then the evaluation framework needs to incorporate them [8].

It is also important to have a clear consensus on the definitions of these values—what do patients or clinicians mean by affordability or equitable access? Therefore, involving and meaningfully engaging stakeholders (policy makers, users of guidance such as clinicians, users of the technology such as patients) using deliberation is a critical basis for any EDP [8]. To assess the impact of the deliberative dimensions of priority setting like transparency, buy-in, and trust of recommendations, monitoring and evaluation framework performance indicators should also consider these deliberative processes as a fundamental component for increasing the impact of HTA on decision making. This is in line with productive interactions—the concept of research creating impact.

In 2020, INAHTA concluded important research on the impact and influence of HTA [9]. In line with an EDP approach, INAHTA sought to understand the impact of assessment practices of its member agencies and the influence of their HTA processes [9]. The resulting assessment framework begins with the agency or program's mandate, the stakeholders demanding HTAs, and the type of decisions that the HTA informs. The next part asked participating agencies to list key impact indicators for the HTA reports, the agency, policy, health system, and finally, broader impact. LMICs can use this approach to lay a strong foundation for showing the relevance and legitimacy of their HTA processes. Linking the assessment practices and influence provides a robust approach to understanding whether the outcomes expected from HTA are aligned with the agency's scope of work. See figure 31 for a set of indicators identified by the participants of the survey.

Figure 31: Indicators of impact identified by INAHTA members

Impacts related to the reports (n=10)
- Appropriate format for the HTA to meet requestor's needs
- Quality of the report contents
- Requestor/client satisfaction with the report
- Website or social media indicators (# of website visitors, download rates, app statistic, social media use: retweets, likes, etc.

Impacts related to the agency (n=2)
- Change in awareness about the agency
- Value for money of the HTA report (return on investment to the agency for cost of production of HTA)

Impacts related to the decision/policy makers (n=15)
- Use of report in decision making: decision maker use/consideration of HTA in deliberations
- Influence on decision making: acceptance of recommendations; incorporation of HTA information in decision making
- Change in awareness/ knowledge about the HTA topic
- Change in policy, organizational recommendations, or policy agenda

Impacts related to different levels within the health system (n=21)
- Changes in coverage/reimbursement (addition/removal of technology from benefits catalogue/schedule, formulary listing
- Change in clinical practice, prescribing patterns, technology consumption/use, adoption of technology in hospitals, changes in program development or delivery
- Update of clinical practice guideline or development of new guideline
- Changes in procurement, i.e. (dis)investment in technologies or equipment
- Change in patient health outcomes
- Budget impact and cost savings
- Changes in health system research focus or priorities
- Change in knowledge/awareness about the HTA topic among different stakeholders in the health system

Impacts outside of the health system (n=5)
- Changes to legislation or regulations
- Media coverage (newspaper, radio, television, magazines, social media etc., discussion of or reference to HTA products)
- Parliamentary debates
- Change in knowledge/awareness about the HTA topic outside of the health system

Source: INAHTA, 2020, adapted by the authors [9]

5.2.4 OTHER TOOLS FOR MEASURING HTA IMPACT

Stakeholder-Based Analysis: A 2011 analysis funded by the pharmaceutical industry (European Federation of Pharmaceutical Industries, Pharmaceutical Research and Manufacturers of America, Medicines Australia, and EuropaBio) also provides a useful perspective on measuring HTA impact based on stakeholders' priorities (figure 32). Evidence linking HTA impact to stakeholders has evolved since this study was published.

Figure 32. Potential impact of HTA among stakeholders [10]

Stakeholder	Impact	Potential Measure	Existing Evidence
Patients	Allocate resources on health services that offer greatest benefits	Distribution of expenditure	No analysis that directly relates HTA to impact on allocation of resources
	Speed of access to good value medicines	Impact of HTA review on time to market	HTA clearly increases time to markets relative to markets where manufacturers are free to launch. However, no evidence that HTA increases time relative to markets without HTA. Results in greater restrictions being imposed on reimbursement of medicines but little assessment of the detriment imposed.
	Availability of good value medicines	Diffusion of medicines to patient populations	Mixed evidence. HTA appears to slow diffusion but a positive assessment appears to increase diffusion.
Physicians	Provide information regarding best technical practice	Awareness of changes to clinical practice	Physicians appear to value information but awareness varies considerably.
	Affect clinical standards	Adoption of changes to best clinical practice, reduce variation in patterns of treatment	Mixed evidence but overall HTA is seen to have an impact on clinical standards if funding is available.
Payers	Efficiency of the health system	Cost savings achieved from assessing redundant or inferior technologies	No analysis that directly relates HTA to impact on allocation of resources
	Imposes a direct cost	Cost of the HTA	Broad estimates but no attempt to determine how cost vary by type of HTA
Pharmaceutical Industry	Affect return to innovative medicines	Allocation of resources to products and speed of assessments	Very limited information on the relationship between HTA and price. Analysis of French system shows HTA can associate price to value and even incorporate information over time. Theoretical argument that HTA favor static efficiency over dynamic efficiency and hence lower returns on innovation.
	Predictability of rewards for the future	Consistency between HTA and procurement and	Regional systems show markedly less relationship between the HTA and the ultimate procurement and reimbursement decision.

Source: Wilsdon and Serota, 2011 [10]

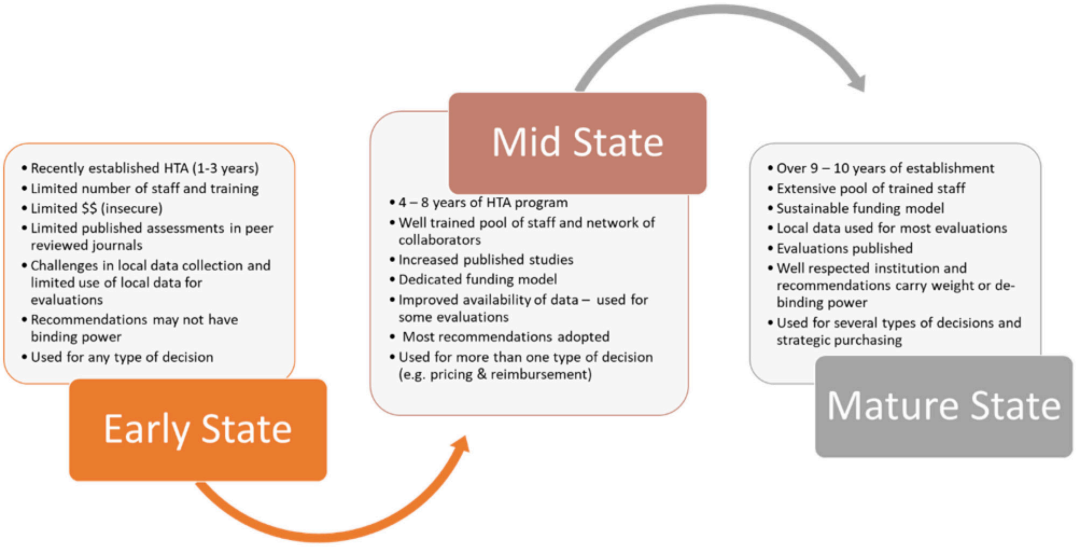
Health Technology Balanced Assessment: Another tool is the Health Technology Balanced Assessment (HTBA) [11]. This has been used to strengthen hospital-based health technology management by aligning strategic planning and actions [11]. The HTBA engages clinicians, hospital managers, and patients in discussions about the impacts of new technologies on the health system and patients [11]. The HTBA guides the decision

making process on use of health technologies, provides a system of checks and balances on internal decision making related to health technology use, and increases transparency and accountability at the organizational level [11]. Although a resourceful option, HTBA seems to have a narrower potential of application to monitor and evaluate HTA impact over overall health systems performance.

Multicriteria Decision Analysis: As discussed in Chapter 4, economic evaluation of new health technologies assessing costs and effectiveness may have limitations in assessing value. MCDA examines a range of effects against a set of criteria, which are scored and aggregated by quantitatively weighting their importance [12, 13]. The principles of MCDA could also be applied when monitoring and evaluating the HTA process. This would entail developing relevant criteria with respect to the goals for an HTA process and their relative weights. For example, criteria could include the expected outcomes from the HTA such as increased transparency in design of benefits package, evidence-based evaluation of health technologies/programs, and cost containment. The effect of the HTA process on the expected outcomes would determine the effectiveness of the HTA program.

HTA programs can be evaluated by "maturity" based on characteristics such as funding availability, staff capacity, local data availability, binding power of recommendations, and the number and type of decisions the program supports (figure 33). Indicators for each state of maturity could be added based on interviews with national and international experts covering areas such as governance, transparency, types of technologies covered, international collaborations, methodological rigor, and number and types of analyses provided by HTA. As mentioned, these will depend on a country's priorities and data availability but could serve as a starting point.

Figure 33. Potential classification of HTA programs' maturity states

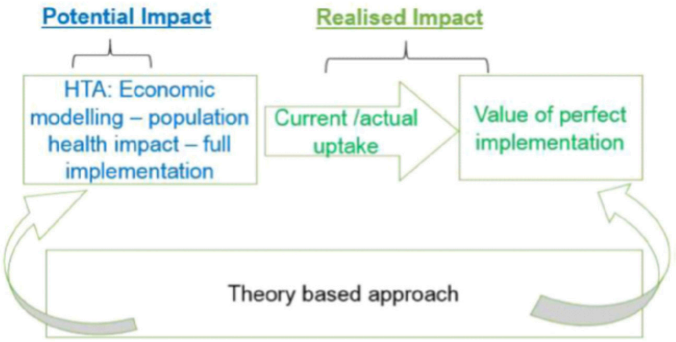


Source: Developed by the authors

In 2015, the iDSI network developed a realistic model for evaluating the impact of an HTA report. The model is used to "predict the expected gain in population health from a policy change given best evidence. This would allow the uncertainty and priorities for research to also be considered. We would then want to understand if HTA has changed policy through direct observation of policy and make a best assessment of the counterfactual. How has that decision been realized? What changes in practice? Is there a decision to recommend or fund or reimburse the intervention? Have clinicians and/or patients changed their practice? Are there additional costs incurred to change practice? Taking observed uptake and implementation, we would calculate the realized expected gain in population health given best evidence" [14].

This model combines economic analyses to calculate the potential impact of an HTA recommendation in economic terms with a qualitative assessment to demonstrate causality [8]. The model's approach compares the actual impact of the intervention to the model results and includes qualitative research to determine the reasons why predicted health benefits were not achieved [14]. Figure 34 provides illustrates this approach and figure 35 provides a summary of the rationale behind such a framework.

Figure 34. Pictorial representation of this approach for measuring the impact of HTA



Source: Grieve and Briggs, 2015 [14]

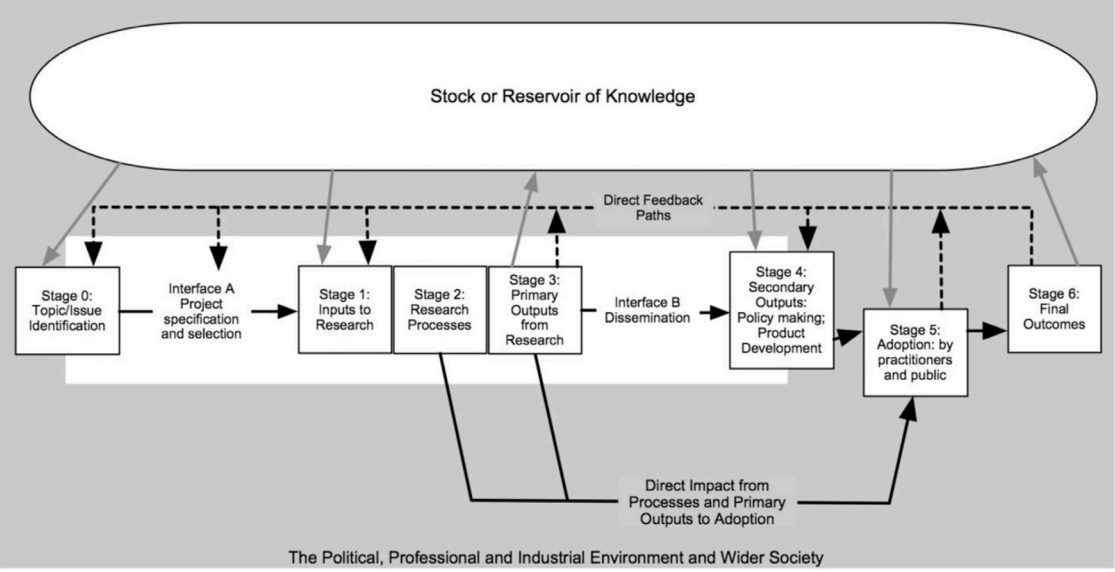
Figure 35. Summary of the rationale behind the approach for measuring the impact of HTA

Summary of conceptual framework	
What is the predicted expected gain in population health from a policy change given best evidence? What is the uncertainty and priorities for research?	Initial HTA model based on available evidence
Has the HTA changed policy?	Observation of policy, best assessment of counter-factual
What is the realised expected gain in population health given best evidence?	Observation of uptake and implementation
How do we explain the difference between expected and actual gain in population health? What is the maximum we can pay to increase uptake?	Qualitative work with relevant stakeholders; quantitative analysis
What implementation activities and policy changes can help address the gap between predicted and realised?	Evidence on cost-effectiveness of implementation activities
What does additional evidence suggest about expected and actual gains in population health?	Update of initial HTA with further evidence from appropriately designed research

Source: Grieve and Briggs, 2015 [14]

HICs such as the Netherlands and the United Kingdom have used the payback model [7, 15], which looks at HTA process components from an input and output perspective and is one of the most commonly referred concept in the context of impact evaluation. Five categories of indicators for outputs and outcomes cover the multidimensional nature of HTA: knowledge creation, research benefits, informing policies, changing health practices, and impact on the broader health care system [15] (figure 36). The Netherlands invited experts to score the indicators in each category and validate the information through group discussion [15]. Primary outputs include publications emerging from the research and secondary outputs include types and numbers of decisions being informed by HTA [15]. The UK's NIIHR commissioned an assessment of the HTA program's impact after its first 10 years using the payback model; the assessment was qualitative and did not include economic evaluations or value assessments [16].

Figure 36. Pictographic description of the payback model

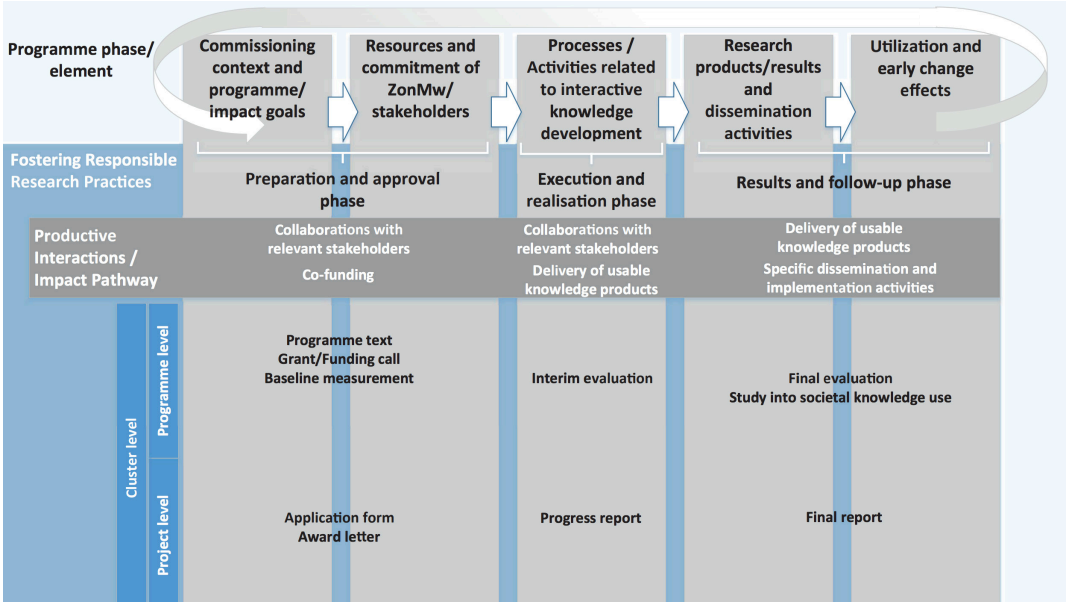


Source: Oortwijn et al., 2008 [15]

More recently, Guthrie et al. concluded an economic assessment on the NIHR HTA program accompanied by case studies for qualitative context-specific findings [7]. In this framework, the health benefits from the technology were given a dollar value and compared to the overall cost of the HTA program [7].

The Netherland's HTA agency ZonMw recently updated its impact assessment framework [17]. Its framework's theory of change is that a collaborative process of knowledge creation via productive interactions (such as collaboration/co-financing/knowledge creation and sharing and implementation activities) will foster knowledge use and responsible research practices. Establishing an HTA program based on these principles leads to greater commitment from stakeholders to shared goals for the program, leading to increased impact and continuous improvement of HTA. These concepts are included as part of the performance indicators and layer the impact assessment framework (figure 37).

Figure 37. ZonMw impact assessment framework



Source: Reijmerink, 2018 [17]

5.3 DATA COLLECTION AND EMPIRICAL FINDINGS OF HTA IMPACT

As noted in the previous sections, there are a vast number of potential models and indicators for assessing HTA. These models assess the HTA process, effectiveness of HTA-related institutional arrangements, and various kinds of impact of HTA (process and report). The type of models and indicators adopted by countries is highly dependent on their local context. The monitoring and evaluation framework will be affected by the country's capacity for monitoring and evaluation (financial and human resources).

Ideally, data on all aspects of HTA performance and impact that are deemed relevant should be collected and assessed. However, collecting locally relevant data for HTA is often a critical challenge in LMICs. For example, many LMICs do not have robust electronic health management records systems or still use paper-based systems. Thus, collecting data related to health outcomes requires substantial resources to conduct surveys or aggregate data. Loss of paper records is also a higher risk in these settings, further affecting the quality monitoring of HTA. However, some data may be easier to collect; for example, in Hailey's monitoring and evaluation framework, indicators such as number of requests, number of requests accepted, number of HTA reports completed per year, and HTA reports completed by specified deadline are straightforward to collect and help determine how productive the newly established HTA body has been [6]. However, indicators related to an HTA report's impact on clinical behavior change, health indicators, or acceptability of HTA may not be as easy to collect or assess because of confounding variables. Assessing the acceptability of HTA would potentially require additional study and investment [6].

Data collection is not a static or one-time activity. Therefore, any of the indicators, frameworks, and/or scorecards used from those listed above or others have to be used on an ongoing basis to assess process implementation or to determine if achievement of HTA program or report goals has been sustained based on measuring indicators. Measuring the effect of HTA on health outcome indicators is difficult because changes are influenced by many factors unrelated to the HTA report or program [1, 5, 6] in addition to needing research and a significant investment of resources [6]. However, as with our advice to advance an HTA program, it is better to start small and incrementally grow. Sufficient information needs to be collected to make the case that HTA represents good value for money and that it serves the needs of those with decision making power. However, investments in data collection could limit resources allocated to the HTA process; therefore, important trade-offs are needed to reach balance.

Most of the empirical findings on the impact of HTA come from HICs, although LMICs are increasingly publishing assessments of HTA program performance and impact. The following section presents a summary of findings from HICs and LMICs that support the cost effectiveness of HTA.

5.3.1 HTA IMPACT FINDINGS FROM HIGH-INCOME COUNTRIES

Sweden. A mixed-methods study showed that HTA reports generated by the Swedish HTA agency SBU [18] had significant impact on policies, clinical guidelines, clinical practice, and clinical research. The review of guideline documents, patient registries, health facility data, and interviews established a strong link between the SBU guidance of the "Yellow" reports and subsequent changes [18]. Yellow reports focus on disease areas and established practices. The authors provided a subjective estimate of the impact of 26 HTA reports generated by SBU between 2006 and 2010 (figure 38) [18].

Establishing a direct causal relationship between HTA recommendations or guidance and changes to policies, guidelines, and practice is not easy to demonstrate, although it was the goal of this study [18]. Additional factors may also influence the decisions and actions to initiate and diffuse policy changes.

Figure 38. SBU "Yellow" reports published between 2006 and 2010: Type of influence, estimated impact, and results

No	Topic	Type of Influence/ Estimated Impact	Results
1	Dementia (2008)	Decision/Moderate	Use of the report for training of municipal caregivers
2	Fortifying flour with folic acid (2007)	Decisions/High	The National Board of Health and Welfare (NBHW) and the National Food Agency did not implement fortification of flour with folic acid
3	Vaccines to children (2009)	Decisions/Low	The report was used by the NBHW and served as a basis for WHO policy
4	Rehabilitation of patients with chronic pain (2010)	Decisions/Moderate	Governmental rehabilitation guarantee and several local care programs
5	Peripheral arterial disease (2007)	Guidelines/High	Implemented by the Swedish Society for Vascular Surgery
6	Patient education in managing diabetes (2009)	Guidelines/High	Implemented in national guidelines (NBHW)
7	Open angle glaucoma (2009)	Guidelines/High	Implemented by the Swedish Ophthalmological Society and Swedish Glaucoma Society
8	Caries (2008)	Guidelines/High	Implemented in national guidelines (NBHW)
9	Endodontics (2010)	Guidelines/High	Implemented in national guidelines (NBHW)
10	Partially dentate or edentulous patients (2010)	Guidelines/High	Implemented in national guidelines (NBHW)
11	Dietary treatment of diabetes	Guidelines/High	Implemented in national guidelines (NBHW)
13	Self-monitoring of blood glucose in noninsulin-treated diabetes (2009)	Guidelines/High	Implemented in national guidelines (NBHW)
14	Intensive glucose-lowering therapy in diabetes (2009)	Guidelines/High	Implemented in national guidelines (NBHW)
15	Tympanostomy tube insertion for otitis media in children (2008)	Guidelines/High	Implemented in guidelines by professional associations
16	Dyspepsia and gastro-esophageal reflux (2007)	Change in practice/High	Trend reversal and decrease in surgical procedures in Sweden after publication
17	Triage methods at emergency departments (2010)	Change in practice/Moderate	An additional 18 emergency departments introduced triage after publication
18	Obstructive sleep apnea syndrome (2007)	Change in practice/Moderate	Decrease in surgical procedures in Sweden and Norway after publication
19	Methods of early prenatal diagnosis (2006)	Change in practice/Moderate	15 of 21 county councils offered the combined test to one extent or another
20	Methods for promoting physical activity (2010)	Change in practice/Moderate	Increase in prescription of physical activity
21	Mild head injury (2006)	Change in practice/High	Number of admissions and bed-days decreased the year after publication with more than 4,000 bed-days.
22	Treatment of insomnia (2010)	Change in practice/Moderate	Changes in pharmaceutical prescriptions in line with evidence-based conclusions in the SBU-report
23	Methods to prevent mental ill-health in children (2010)	Research/High	Led to an invitation by research councils for grants of 30 million euros.
24	Light therapy for depression (2007)	No adequate documentation/ Low	-
25	Drug consumption among the elderly (2009)	No adequate documentation/ Low	-
26	Antibiotic prophylaxis for surgical procedures (2010)	No adequate documentation/ Low	-

Source: Rosen et al., 2014 [18]

Austria. A similar mixed-methods study [19] showed that HTA affected decisions such as reimbursement and disinvestment of technologies. Reports from the 1990s to 2010 were reviewed to assess whether facilities made decisions consistent with the reports (figure 39). The study also included a quantitative analysis on the estimated economic impact of the decisions (figure 40).

Figure 39. Recommendations and decisions for inclusion of new hospital procedures in hospital benefits catalogue

Recommendations by LBI-HTA	No. (n = 42)	%	Decision by hospital financing board	No. (n = 42)	%	Consistency recommendation and decision
Not recommended for inclusion in benefit catalog because limited evidence concerning efficacy and safety available or a lack of net benefit comparison to alternatives	30	72	Not included in benefit catalog	13	31	43%
			Included with restrictions*	17	41	
Recommended for inclusion in benefit catalog with restrictions (and re-evaluation at later stage)	12	28	Included with restrictions*	6	14	50%
			Not included in benefit catalog	5	12	
			Included without restrictions	1	2	
Recommended for inclusion in benefit catalog without restrictions	0	0	n.a.	n.a.	n.a.	n.a.
Total	**42**	**100**		**42**	**100**	

*For example, limited to institutions with specific infrastructure or qualification of personnel, to university hospitals or to specialized hospitals, reimbursement may be subject to interdisciplinary discussion on correct indication, treatment and post-treatment care.

n.a., not applicable

Source: Zechmeister, 2012 [19]

As with the Swedish study, establishing a direct causal impact was not feasible, and other factors influenced decisions. For example, in the case of rationalizing the use of Lucentis for macular degeneration, the much lower cost of the competing therapeutic alternative, Avastin, also helped reduce the consumption of Lucentis. Based on interviews, the researchers estimated the influence of the HTA report (figure 40).

Figure 40. Examples of economic impacts due to rationalization decisions/recommendations

		Size of Impact		
Technology	**Type of impact identified**	**Time period analyzed**	**Unit of analysis**	**Results**
Technologies where over-supply was diagnosed				
EPO in tumor anemia	Reduction in volumes and expenditures	2001–2009	Public hospital association Syria (20 hospitals)	Volumes: –17,437 units Expenditure: –8.2 million €
Immunoglobulins	Reduction in volumes and expenditures	2002–2009	Single university hospital	Volumes: –20,058 units Expenditure: –12 million €
Drug Eluting Stents (DES) vs. Bare Metal Stents (BMS)	Reduction in volumes of DES, slight increase in volumes of BMS, yet big regional variations	2006–2008	All publicly financed hospitals in Austria	Volumes DES: –1,892 units Volumes Bare metal stents: +285
Lucentis® vs. Avastin ® in AMD	Slower increase of Lucentis volumes; Slower increase of expenditure; More patients could be treated	2006–2009	Single opthalmology unit	Avoided extra costs 723,000 € + 1,800 injections possible
Hoemocomplettan ® P	Reduction in volumes and expenditures	2009–2010	Single university hospital	Volumes: –10% to –25% Expenditure: –112,000 to –160,000 €
Tocolysis	No impact identified	–	Austrian province of Styria	–
Technologies where excess prices were diagnosed				
Contrast Media	Reduction in price and expenditures	2008	Viennese public hospital association	Expenditure due to price reductions: –1.1 million €

AMD, age-related macular degeneration; EPO, Erythropoietin

Source: Zechmeister, 2012 [19]

Germany. A study conducted in Germany in 2016 [20] assessed the impact of the HTA additional data requirements and evaluation methods on outcomes related to recommendation of conditionally approved medicines. The authors depicted a list of other potential factors that may reduce HTA impact by comparing the Post Authorization Measures methods and type of data requirements used by European Medicines Agency to those made by the Federal Joint Committee (G-BA) for their appraisals of the medicines (conducted by IQWiG). The study highlighted a certain degree of lack of transparency for reasons for specific data requests, lack of guidelines for submitting data, and limited flexibility in utilization of expert advice or non-clinical study data in the absence of RCTs. In an example of the conditionally approved drug vemurafenib, the removal of conditions was hampered by the issues highlighted earlier, therefore slowing diffusion of a potentially beneficial technology [20].

France. Hospital-based HTA has been implemented for more than three decades in some jurisdictions and might be a proxy for assessing the impact of HTA in clinical practice, but little is known about its effects and impact on hospital budget, clinical practices, and patient outcomes [20]. A pioneering hospital-based HTA agency, the Committee for the Assessment and Dissemination of Technological Innovations (CEDIT), has operated in France since 1982 [21].

A study to assess the impact of CEDIT HTA recommendations gathered data from stakeholder interviews to learn how decisions were made, how knowledge was transferred across recommendations, the impact of recommendations, and specific questions related to the technologies [22]. The study indicated that while CEDIT has considerable impact on technology diffusion in the hospital network, stakeholders used the recommendations differently based on their roles. Technology users used the findings as a potential tool for negotiating for technologies of interest, while administrators used them to make decisions regarding technology use. The study also highlighted the challenges faced in the uptake of recommendations, including a lag between issue and application. This finding help CEDIT improve its dissemination practices.

Ireland. HTA has also become a basis for pricing and reimbursement decision making worldwide. In Ireland, marketing authorization holders submit an HTA dossier to the National Centre for Pharmacoeconomics, which evaluates it and submits a reimbursement recommendation to the Health Service Executive. Technologies that are not deemed cost effective at a threshold of €45,000/QALY gained proceed to HTA-informed price negotiations. Total annual cost savings to the public sector as a result of HTA-informed price negotiations was estimated at more than €19 million [23].

5.3.2 HTA IMPACT FINDINGS FROM LOW-AND MIDDLE-INCOME COUNTRIES

Thailand. HITAP published 162 studies through 2016, 70% of which generated public discussion and at least one-third that translated into policy action [24]. In 2009, HITAP published a very influential report showing that at the price of USD 450 per course (three doses), human papilloma virus vaccine was not a valuable public investment—the vaccine price needed to be reduced by approximately 60% to become cost effective. Three months after the report's publication, manufacturers reduced the price of the vaccine in line with recommendations.

The implementation of HTA guidelines in particular may have an impact on robustness of methods and on the quality of reporting. For example, compliance with best HTA reporting practices in Thailand substantially improved after the publication of the first Thai HTA Guidelines by HITAP in 2008 (figure 41) [24].

Figure 41. Compliance improvement of HTA reporting practices in Thailand

Good Practice	Before (%)	After (%)
Perspective specified	59	88
Comparators described	90	100
Discounting used	50	88
ICER reported	52	97
Uncertainty analysis performed	47	79
Of which, probabilistic sensitivity	43	70
Funding source disclosed	69	75

Source: Culyer et al., 2017 [24], Kittrongsiri and ChalkledKaew (2015) [25]

Colombia. The Colombian HTA agency (IETS) issued recommendations precluding the use of applied behavioral analysis and animal stimulation therapies in patients with non-autism spectrum syndromes due to lack of evidence [26]. Applied behavioral therapies at the time were frequently challenged in courts by patients and care givers. Based on the IETS report, the Constitutional Court of Colombia revised and reversed at least a dozen mandates for coverage (acciones de tutela) costing the system thousands of millions of Colombian pesos [27].

5.3.3 HTA IMPACT FINDINGS FROM MULTIPLE COUNTRIES

A mixed-methods systematic review of 18 studies [28] found that HTA could influence several aspects of decision making. However, it is difficult to evaluate the real impacts of local HTA at the different levels of health care given the relatively small number of evaluations with quantitative data and the lack of clear comparators. As per this study's conclusions, further research is necessary to explore the conditions under which local/hospital-based HTA results and recommendations can impact hospital policies, clinical decisions, and quality of care and optimize the use of scarce resources [28].

Although the effect of HTA on spending for prescription medicines is often studied, less attention is given to its effects on decisions about research and development in the biopharmaceutical industries. A report on the results of a survey of 19 pharmaceutical and biotechnology companies [29] showed that the pharmaceutical industry is adjusting to the realities of today's cost-conscious health care systems by incorporating HTA considerations early on in development decisions. Improving communication and creating collaboration among a range of stakeholders may improve interactions to devise and test new and more efficient processes for HTA in the longer term [29].

HTA reports, if broadly disseminated, have an impact on the stock of knowledge and awareness raising of the topic or disease area of interest. Many HICs and those LMICs with well-established HTA practices have extensive repositories of clinical practice guidelines, protocols, HTA reports, appraisal recommendations, and budget impact analyses that vary according to setting but that attest to the productivity of HTA institutions. When using HTA reports from different settings, as recommended earlier in this roadmap, adaptation to the local context needs to be carefully considered.

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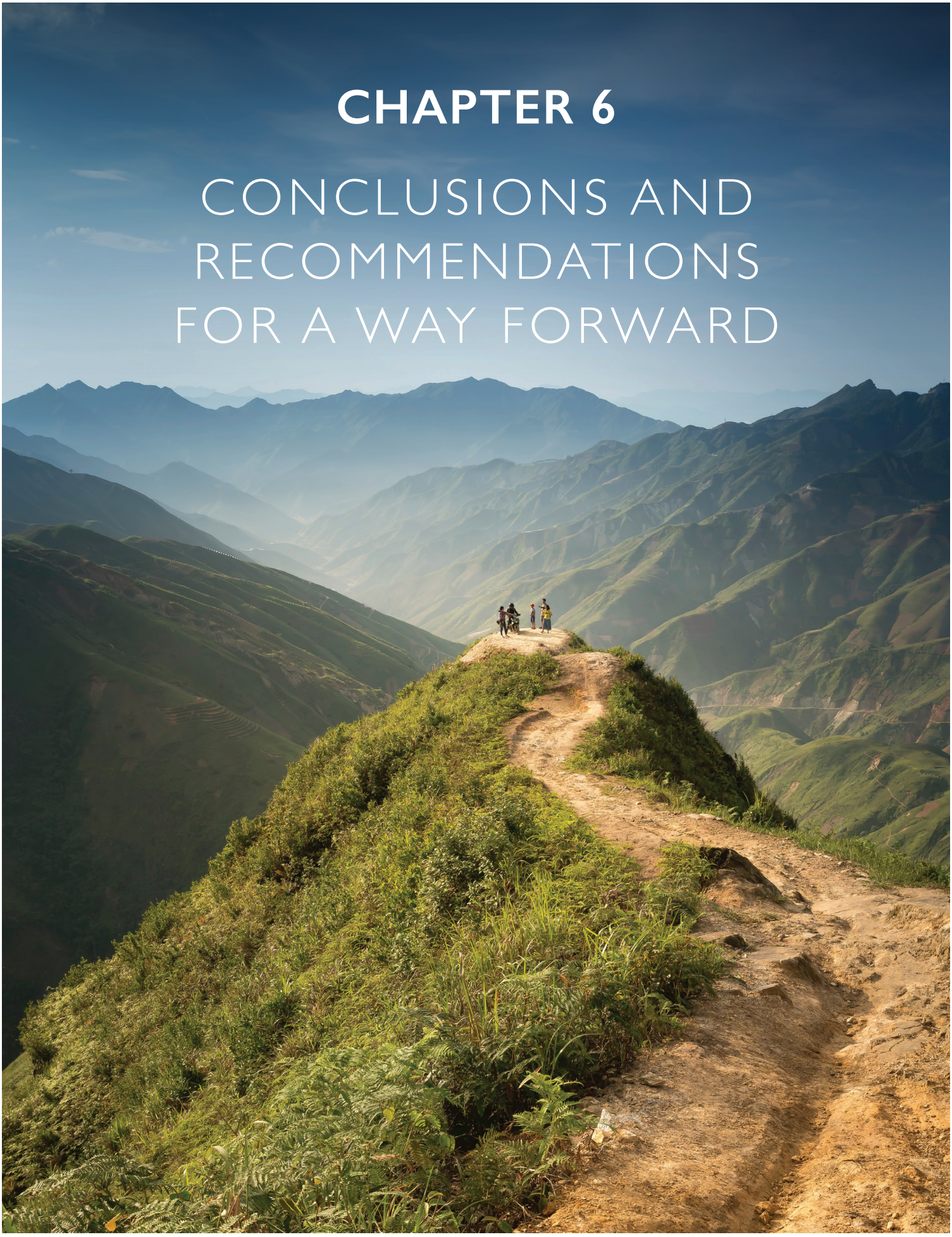
CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS FOR A WAY FORWARD



Quang Nguyen Vinh

HTA has become an important mechanism for supporting priority setting and decision making in many parts of the world, particularly in HICs. While UHC is both a priority and a potential reality for many countries, essential health services still remain unavailable, inaccessible, and unaffordable to many. On the one hand, new health technologies have led to remarkable improvements in health and quality of life but also imposed additional challenges to countries' efforts to achieve UHC. On the other hand, older, highly cost-effective, interventions remain un- or under-provided.

LMICs have limited resources for health and suffer from many risks and uncertainties attached to external funding sources. The widespread waste and inefficiency in the health sector, the intense competition between treatment and prevention of infectious and non-communicable diseases, and the rising health care costs threaten the purchasing power of inherited budgets. Establishing processes that deliver evidence-informed priority-setting decisions and HTA mechanisms and institutions can improve resource allocation decisions in these settings.

This roadmap advocates LMICs to implement HTA using the stages (heuristic) model to simplify the dynamic and contested environment of policy change. We present readers with tools and approaches to help them navigate the process of institutionalizing HTA, from agenda setting through formulation, adoption/implementation to impact evaluation; however, this roadmap's approach and main assumptions will require further testing for their realism and feasibility. In addition to our discussion of the methodology of HTA, the roadmap describes qualitative methods for understanding the local context and the character of its health system, which have a bearing on how HTA might best work and what impediments might need to be removed or at least mitigated. We also stress the importance of using robust HTA methods and evidence-informed deliberative processes to promote legitimacy and buy-in. Transparency of process and involvement of stakeholders are urged as important factors. Finally, monitoring and evaluating HTA progress and overall impact could help guarantee long-term political support and funding for HTA activities.

RAISING AWARENESS OF THE VALUE OF HTA

The lack of common understanding of HTA and how it can support decision making is a major challenge in many LMICs. Awareness of HTA's potential usefulness and limitations as a policy tool to improve systematic priority setting needs to be raised among stakeholders in these settings. To create political will, implementing partners will need to navigate the political landscape of HTA institutionalization.

Recommendations:

- Conducting stakeholder analyses to determine who could be potential champions or strong supporters (within the Ministry of Health or elsewhere) for driving such initiatives is a valuable exercise.
- Implementing partners and policy champions can seize or help create windows of opportunity for HTA policy action by considering the problem, policy, and politics streams in Kingdon's model of agenda setting.
- Identifying HTA players and their interests, positions, and power will help policy makers and champions develop more systematic and better-informed policy strategies for HTA throughout its institutionalization.
- A high turnover of government officials may close windows of opportunity for introducing or advancing HTA. Continuously engaging all stakeholders (existing and new arrivals) will help mitigate that problem.
- Concise and clear messaging strategies help secure political interest of newly appointed decision makers.
- Linking HTA process with UHC and benefits package design can be an important enabler; this could be achieved through legal frameworks such a new national law supporting UHC or through regulation developed by the Ministry of Health.

FORMULATING AN HTA PROGRAM

Although there is no single model for success, it is recommended to strive for an HTA body that is independent and with binding power of recommendations. Nevertheless, a fully independent institutional arrangement would not always be feasible, so a small but technically strong structure protected legally and organizationally from political or external pressure conducting assessments in a transparent manner is acceptable.

Recommendations:

- The formulation and design stages of the HTA body should aim for technical independence but retain an 'insider' status within the policy making process to remain relevant.
- Stakeholders should agree on the reasoning behind implementing an HTA program, as well as the mandate, objectives, and reach of HTA activities.
- There is no one-size-fits-all approach to HTA, and therefore the design should reflect the country context and needs.
- A transparent and well-organized process that uses the best available evidence can be powerful enough to make HTA recommendations *de-facto* binding. This means that decision and policy makers should make explicit the reasoning why they have departed from an evidence-informed recommendation.
- HTA policy formulation should follow the principles of best practice to create buy-in and legitimacy.
- Effective coordination among international organizations, implementing partners, local policy makers, and other stakeholders is critical during policy formulation to avoid duplication and secure local empowerment.
- Taking a leading role from within the local governments at early stages of HTA formulation improves donor and technical assistance coordination as means to serve local needs and expectations.

LEVERAGING HTA EXPERTISE

Globalization provides a great opportunity for LMICs to learn from the available HTA experience from different settings. Some examples come from other LMICs, but most come from HICs with developed HTA organizations, some operating for two decades or more. Implementing partners or policy makers in LMICs may be tempted to copy and paste successful, more advanced models while forgetting the realities in their own settings. Regarding methodological approaches, some countries opt to draw upon principles of comparative safety and efficacy/effectiveness for a narrow set of health technologies, while others would use more sophisticated economic analyses of drugs and medical devices and procedures to inform coverage, reimbursement, procurement, quality, and; more recently, pricing decisions. Although there are different methodological approaches and processes to incorporate HTA results into a deliberative priority-setting process, there are no magic solutions.

Recommendations:

- The major procedural principles should be followed in LMICs while bearing in mind the local context in which they operate.
- HTAs must be timely in relation to the decisions they seek to inform. Simpler studies such as rapid reviews help manage the uncertainty surrounding new technologies while facilitating HTA timeliness and relevancy.
- The pragmatic model of using external HTAs and transferring negative recommendations from other countries may not be an inferior approach. Eastern European countries provide important examples of the potential do's and don'ts of this approach.

- Leveraging existing capacities and structures will always be more efficient than reinventing the wheel.
- Implementing partners should tailor available HTA methods, approaches, tools, and products to their own settings with the short-term goal of fitting it into existing decision making practices and a long-term vision of incremental strengthening, growth, and evolution.
- Local data and studies should be part of a mid- to long-term plan for advancing and building a robust HTA system.
- Many LMICs may not be able to implement CUA, QALYs, or opportunity cost-informed thresholds at the early stages of development. There should be a trade-off between being realistic and ambitious.
- Institutional hubs of national or regional technical expertise can help implementing partners understand the local implications for health technology and transferability assessment.

BUILDING HTA CAPACITY

Capacity refers to the ability of HTA doers to produce robust and fit-for-purpose recommendations, as well as the capacity of HTA users to understand and use HTA outputs to inform their decision making. Capacity is difficult to build but also difficult to keep.

Recommendations:

- Technical, management, and communication capacities in generating and using HTA evidence generally need to be created or strengthened.
- Collaboration with academic institutions (within or outside the country) can expedite further development of HTA experts; nevertheless, retaining skilled staff within HTA units remains a challenge in competitive local and global labor markets.
- Academic institutions can play an important role as HTA doers who are commissioned by HTA bodies to develop reports, once in-house capacity is exhausted.
- National educational programs and degrees in HTA (e.g., health economics) are critical for sustainable institutionalization of HTA. Engagement with the Ministry of Education and the academic community to develop a strategy and operational plan to create HTA degrees or certification programs is important.
- Leveraging e-learning and courses available through international universities, educational programs, or international or regional networks of cooperation could be short-term and less expensive ways to strengthen local capacity.
- International collaboration among HTA bodies, and knowledge sharing at international or regional events can facilitate knowledge transfer and capacity building in less established HTA programs.

IMPLEMENTING HTA

Health care resource-allocation decisions are complex and involve the assessment and appraisal of available evidence while bearing in mind societal values and ethical considerations. HTA is only part of this intricate process.

Recommendations:

- Neither HTA reports nor the results of economic models or CEA should be blindly used in decision making without careful consideration of context and the transferability of results.

- LMICs should aim for the highest attainable standards of their HTA, be transparent about limitations and uncertainty in results, and broadly engage stakeholders.
- Ability to deal with potential conflicts of interest throughout all stages of the process is as relevant as methods themselves for securing legitimacy and buy-in of recommendations.
- LMICs can enhance HTA impact if stakeholders are adequately engaged through a deliberative, transparent, and participatory process. Seeking buy-in from decision makers on using the assessment reports is vital to ensure that the HTA meets their information needs.
- Subnational HTA implementation can be improved through targeted communication strategies, expert opinion leaders or networks, regulatory mandates for implementation, and formal or informal re-evaluation. Promoting a positive environment for collaboration and knowledge and skills transfer across jurisdictions may increase HTA uptake.

ENSURING SUSTAINABILITY AND IMPACT OF HTA

Ensuring HTA establishment and continuity requires both political and financial commitment. Therefore, having a well-planned monitoring and evaluation strategy to justify HTA as a good value-for-money intervention may secure its long-term sustainability and pave the road for countries' journey to self-reliance.

Recommendations:

- Once HTA has been institutionalized, additional international or South-to-South cooperation can sustain operational self-sufficiency.
- Evaluating HTA progress and boosting its impact requires a multisectoral approach comprising an array of decision and policy makers, including the Ministry of Finance, national planning agencies, research and innovation funding bodies, and social protection agencies.
- Research into the successful implementation of HTA remains undeveloped, even in more affluent settings, and further attention shall be paid to HTA implementation research.
- Evidence-informed decisions should be enforceable, meaning the allocation of sufficient resources for implementing decisions emanating from positive recommendations and having the ability to say "no" should evidence results in negative recommendations.
- To facilitate the use and implementation of HTA reports in decision making, incentives within a given health care system must be appropriately aligned with the decisions that are based on/informed by HTA.

The global momentum for HTA, with more than 50 institutions and nearly 40 countries relying on it to inform their resource-allocation decisions, presents an opportunity to further drive the HTA agenda in LMICs. WHO and all major donors, including USAID, DFID, DFAT (Australia), World Bank, Gates Foundation, and the Inter-American Development Bank, support HTA scale up, especially as it links to self-reliance and UHC. In addition, networks such as HTAi, INAHTA, and ISPOR promote cross-country collaborations in different regions to advance a culture of evidence-informed decision making through the use of HTA.

ANNEX 1: SYSTEMATIC LITERATURE REVIEW

A systematic literature review was conducted to gather the evidence base on approaches for implementation and institutionalization of HTA in LMICs. The focus of the literature review was to address the following questions:

1. **What are the barriers to and facilitators of HTA institutionalization?**
2. **What are the motivations for countries to implement HTA?**
3. **What evidence-based guidelines, methods, or institutional frameworks exist for facilitating the adoption and/or institutionalization of HTA?**
4. **Based on country experiences, what are the lessons learned for the adoption and/or institutionalization of HTA?**

The literature review examined HTA programs in any country (i.e., not limited to low-, middle-, or high-income countries). Articles published in peer-reviewed journals as well as gray literature from other relevant organizations were included in the review. The date range of publications was limited to articles published by December 31, 2019. A targeted approach was taken for the gray literature review; articles, guidelines, and other publications were collected from sources such as WHO; Center for Global Development (CGD); International Decision Support Initiative (iDSI); country HTA institutions (e.g., NICE UK, IQWiG Germany, CADTH Canada, HITAP , Indonesia's HTA committee); and international networks for HTA agencies or practitioners (e.g., HTAi, INAHTA, RedETSA, ISPOR). It is recognized that significant literature may be published in a language other than English and therefore this search has been expanded to include articles published in English, French, and Spanish. Other languages have been excluded due to a lack of translation services available. The following databases were searched: Medline, Health Policy reference center, EMBASE, Cochrane, CINAHL, and NHS-EED databases.

Inclusion

- Dates–include articles as late as December 31, 2019
- Geographic–no exclusion
- Languages–articles published in English, French, Spanish

Exclusion

- Hospital-level HTA (focus is on national and/or regional level public sector agencies)
- HTA on specific services/interventions, drugs, technologies (e.g., HTA on oncology drugs)

SEARCH TERMS

Searches included synonyms and subject headings (where available) for the following search concepts: 'health technology assessment', 'barrier', and 'facilitator.'

Health Technology Assessment	Barrier	Facilitator*
Health Technology Assessments	Challenge	Enabl*
HTA	Bottleneck	Promot*
Technology assessment	Impediment	Accelerat*
Resource allocation	Hindrance	Advanc*
Priority setting	Obstruction	
Systematic priority setting	obstacl*	
Multiple Criteria Decision Analysis		
MCDA		
Multi-criteria Decision Making		
MCDM		

#1: ("health technology assessment" OR "technology assessment" OR HTA) AND (challenge OR barrier OR bottleneck OR impediment OR hindrance OR obstruction OR facilitator* OR enabl* OR promot* OR accelerat* OR advanc* OR implement*)

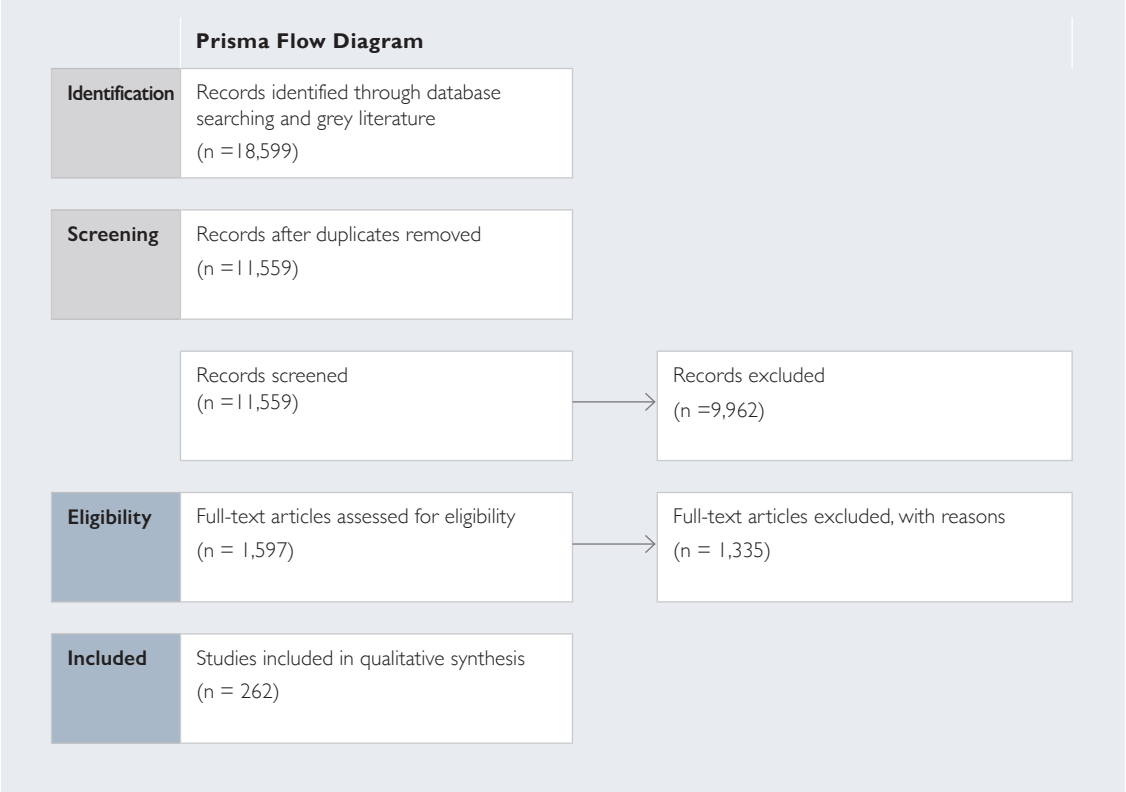
#2: ("resource allocation" OR "priority setting" OR "systematic priority setting" OR health priorit*) AND (challenge OR barrier OR bottleneck OR impediment OR hindrance OR obstruction OR facilitator* OR enabl* OR promot* OR accelerat* OR advanc*)

#3: ("multiple criteria decision analysis" OR MCDA OR "multi criteria decision making" OR MCDM) AND (challenge OR barrier OR bottleneck OR impediment OR hindrance OR obstruction OR facilitator* OR enabl* OR promot* OR accelerat* OR advanc*)

The search was conducted as follows: Each of the three groups will be searched (title or abstract) separately and then combined using "OR"

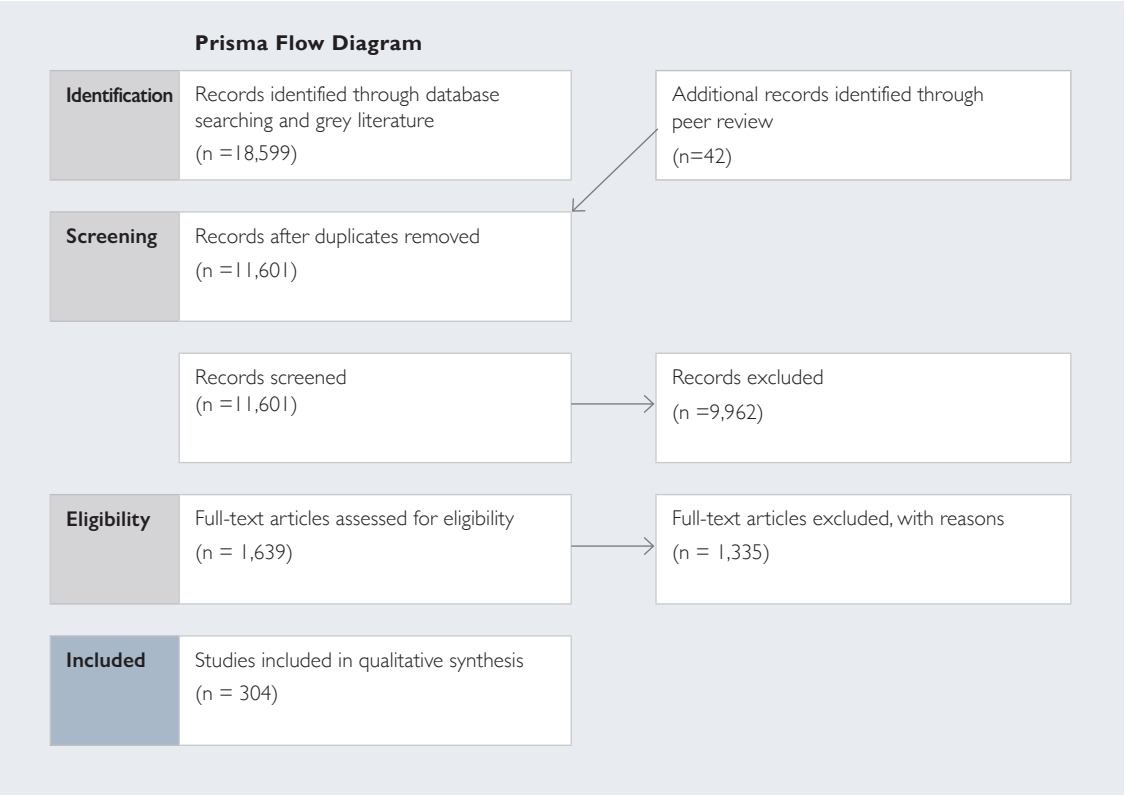
CRITICAL APPRAISAL AND MANAGEMENT OF REFERENCES

The papers were reviewed systematically using PRISMA, which is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. We completed the PRISMA checklist and flow diagram to report and map out the number of records identified, included, and excluded and the reasons for exclusions. A total of 18,599 records were identified through the database searches, targeted literature review, and inputs from global HTA experts. Of the 18,599 records 11,559 were eligible for abstract review and 9,962 records were removed after the abstract review for a full text review of 1,597 articles. Finally, 262 articles were included in the qualitative synthesis of the roadmap.



ANNEX 2: PEER REVIEW PROCESS AND LITERATURE REVIEW UPDATE

A first draft of the Practical Guide for Systematic Priority Setting and HTA Introduction: A Roadmap for Policy Action in Low- and Middle-Income Countries was completed by January 31, 2020. The first draft of the document was shared with global experts on HTA, systematic priority setting, and health financing. A total of 27 global and regional experts, as jointly identified by authors and the USAID Asia Bureau, were contacted to indicate availability and provide feedback to the draft policy document. These experts were representative of the global community of practice, including academia, policy makers from various country governments, leadership and experts from national HTA agencies, leadership and experts from international HTA networks, and intergovernmental and international organizations. Eighteen experts indicated availability for peer review of the document, while some of the seven unavailable experts recommended their colleagues (response rate 92.6%). The authors shared the first draft of the document with available experts on February 7, 2020. Twelve (66.7%) provided feedback, additional references, and comments of varying detail. Experts provided an additional 42 references from both peer reviewed and grey literature. Additional publications included those published and/or accessed by April 15, 2020. The updated PRISMA flow diagram is provided below



GLOSSARY

Canadian Agency for Drugs and Technologies in Health (CADTH): A Canadian national organization that provides research and analysis to health care decision makers.

Cost-Benefit Analysis (CBA): A systematic process to calculate and compare costs and benefits, in dollar value, of a program, decision, or policy.

Cost-Effectiveness Analysis (CEA): A systematic process to calculate and compare costs and benefits, by key outcomes, of a program, decision, or policy.

Cost-Utility Analysis (CUA): A systematic process to calculate and compare between disease categories, CUA uses QALYs gained or DALYs prevented as a common metric to combine quality of life and time of life gained or lost, respectively.

Department for International Development (DFID): A United Kingdom government department responsible for administering overseas aid. According to DFID, the goal of the department is "to promote sustainable development and eliminate world poverty."

Disability-Adjusted Life Year (DALY): A metric used to quantify disease burden. One DALY can be thought of as one year of "healthy" life lost. DALYs combine the years of life lost due to premature mortality in the population and the years lost due to disability for people living with a disease or its consequences.

European Commission (EC): The executive branch of the European Union, responsible for proposing legislation, implementing decisions, upholding the EU treaties, and managing the day-to-day business of the EU.

European Network for Health Technology Assessment (EUnetHTA): A network, established to create an effective and sustainable network for HTA across Europe that could develop and implement practical tools to provide reliable, timely, transparent, and transferable information to contribute to HTA in members states.

Extended Cost-Effectiveness Analysis (ECEA): A cost-effectiveness analysis approach that extends traditional economic evaluation with distributional aspects (such as health and financial one). ECEA thus serves broader objectives than cost-effectiveness analysis in providing guidance in the design of health policies in general and health benefits packages in particular.

Financial Risk Protection (FRP): Safeguards to prevent individuals from suffering financial hardship associated with paying for health care services and a key component of universal health coverage.

Global Alliance for Vaccines and Immunization (GAVI): A public-private global health partnership that was founded in 2000 with the goal of creating equal access to new and underused vaccines for people living in the world's poorest countries.

Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund): An international financing organization founded in 2002 to accelerate the end of AIDS, tuberculosis, and malaria as epidemics.

Gross Domestic Product (GDP): The monetary value of all finished goods and services made within a country during a specific period. GDP provides an economic snapshot of a country and is used to estimate the size of an economy and growth rate.

Health Benefits Package (HBP): The defined list of health care services covered by public monies and the financial terms of such coverage, such as cost-sharing. Some countries use HBPs to meet basic health needs for the entire population; others use HBPs to meet the health needs of specific populations, such as pregnant women, children, the elderly, or the poor.

Health Intervention and Technology Assessment Program (HITAP): A semi-autonomous health technology research unit under Thailand's Ministry of Public Health. HITAP is a core iDSI partner.

Health Technology Assessment (HTA): The systematic evaluation of properties, effects, and impacts of health technologies.

Health Technology Assessment international (HTAi): A global, non-profit, scientific, and professional society for all those who produce, use, or encounter health technology assessment.

Health Technology Balanced Assessment (HTBA): A systematic tool used to strengthen hospital-based health technology management by aligning strategic planning and actions.

High-Income Country (HIC): For the 2020 fiscal year, the World Bank defines a HIC as one that has a gross national income per capita exceeding USD 12,056.

HIV (human immunodeficiency virus): A virus spread through certain bodily fluids that weakens the immune system by destroying T cells or CD4 cells. HIV can progress to acquired immune deficiency syndrome (AIDS), the last stage of HIV infection.

International Decision Support Initiative (iDSI): A multicountry, multidisciplinary partnership of health care practitioners and researchers, launched in 2012 following the publication of a report by the Center for Global Development on priority-setting institutions for better spending on health. Led by the Institute of Global Health Innovation at Imperial College London, iDSI stands for "better decisions for better health."

The International Network of Agencies for Health Technology Assessments (INAHTA): A network that connects HTA agencies to one another to support knowledge sharing and the exchange of information and also to serve as a forum for the identification and promotion of other interests of HTA agencies.

Institute for Quality and Efficiency in Healthcare (IQWIG): A German federal agency responsible for assessing the quality and efficiency of medical treatments, including drugs, non-drug interventions, diagnostic and screening methods, and treatment and disease management.

International Society for Health Economics and Outcomes Research (ISPOR): A global scientific and educational organization for health economics and outcomes research for use in decision making to improve health.

Joint Learning Network for Universal Health Coverage (JLN): A country-driven network of practitioners and policy makers from around the world who co-develop knowledge products to help bridge the gap between theory and practice and extend coverage to people across the globe.

Low- and Middle-Income Countries (LMICs): For the 2020 fiscal year, low-income economies are defined by the World Bank as those with a GNI per capita of $1,025 or less in 2018; lower middle-income economies are those with a GNI per capita between $1,026 and $3,995; and upper middle-income economies are those with a GNI per capita between $3,996 and $12,375.

Management Sciences for Health (MSH): An advisory organization that takes an integrated approach to building high-impact sustainable programs to address critical challenges in leadership, health systems management, human resources, and medicines.

Monitoring and Evaluation (M&E): *Monitoring* refers to a family of methods for data collection and analysis. It is a systematic effort undertaken during the implementation and operation of a project or a policy that is intended to help improve its design and adoption. *Evaluation* is concerned with the outcome of a project or policy and is conducted with the aim of fine-tuning design or informing future projects or policies. It examines longer-term results and identifies how and why activities succeeded or failed. Monitoring is undertaken more frequently than evaluation.

Multicriteria Decision Analysis (MCDA): An alternative to cost-effectiveness analysis that provides a general framework for decision support rather than one specific to the health sector. MCDA is based on the observation that alternative investment opportunities typically have multiple dimensions, and any decision recommendation should be based on the aggregation of the performance of options across these different **dimensions.**

National Health Service (NHS): Publicly funded national health care system for the United Kingdom. It is the largest and oldest single-payer health care system in the world.

National Institute for Health and Care Excellence (NICE): Provides national guidance and advice to the United Kingdom to improve health and social care. Originally created to reduce variation in the avail- ability and quality of NHS treatments and care.

National Institute for Health Research (NIHR): A United Kingdom government agency that funds research into health and care. It is the largest national clinical research funder in Europe

Organization for Economic Cooperation Development (OECD): An intergovernmental economic organization with 37 high-income member countries founded in 1961 to stimulate economic progress and world trade.

Pan American Health Organization (PAHO): The world's oldest international public health agency. Its mission is to lead strategic collaborative efforts among member states and other partners to promote equity in health, combat disease, and improve the quality of life of the peoples of the Americas.

Pulmonary Arterial Hypertension (PAH): A type of high blood pressure that affects arteries in the lungs and in the heart.

Quality-adjusted life year (QALY): A metric used to quantify disease burden. One QALY can be thought of as one year of "perfect health."

Social Health Insurance (SHI): According to WHO, a form of financing and managing health care based on risk pooling. SHI pools the health risks of the people on one hand and the contributions of individuals, households, enterprises, and the government on the other.

Sustainable Development Goals (SDGs): A set of 17 goals that aim to end extreme poverty and hunger, fight inequality and injustice, combat climate change, and more. On September 25, 2015, the leaders of 193 United Nations member states adopted the goals as part of a new global sustainable development agenda. The 17 goals and their targets for 2030 are described at www.un.org/sustainabledevelopment/sustainable-development-goals/.

Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU): An independent Swedish governmental agency tasked with assessing and evaluating methods in use in health care and social services.

United Nations: An international organization established after World War II with the aim to maintain international peace and security and achieve international cooperation. It is the largest, most familiar, most internationally represented, and most powerful intergovernmental organization in the world.

US Agency for International Development (USAID): An independent agency of the United States federal government that is primarily responsible for administering civilian foreign aid and development assistance.

Universal health coverage (UHC): According to WHO, UHC "means that all people and communities can use the promotive, preventive, curative, rehabilitative and palliative health services they need, of sufficient quality to be effective, while also ensuring that the use of these services does not expose the user to financial hardship."

World Health Assembly: A decision making body of WHO that focuses on a specific health agenda. It is attended by delegations from all WHO Member States and determines policies of the organization, appoints the Director-General, supervises financial policies, and approves program budgets.

World Health Organization (WHO): United Nations agency specializing in international public health, founded on April 7, 1948 (now celebrated as World Health Day). Its primary role is to direct and coordinate international health within the United Nations system.

WHO-CHOICE (CHOosing Interventions that are Cost-Effective): An initiative started by the World Health Organization in 1998 to help countries choose their health care priorities. The WHO-CHOICE team works with policy makers at the country level, providing information on cost effectiveness, costs, and strategic planning to help guide decision making.