NATIONAL CANCER GRID

COLLABORATION FOR CANCER CARE

2026

ADAPTIVE HEALTH TECHNOLOGY ASSESSMENT IN INDIA- METHODS MANUAL

DRAFT

Published by

National Cancer Grid, Mumbai, India

NATIONAL CANCER GRID

COLLABORATION FOR CANCER CARE

Contributors

C S Pramesh
Manju Sengar
Sajith Kumar S
Anuja VR
Akshita Vikani
Ankita Ahire
Adrian Gheorghe
Abha Mehndiratta
Veronica Alfie
Fernando Argento
Andres Pichon Riviere

AHTA in India- Methods Manual

NATIONAL CANCER GRID
COLLABORATION FOR CANCER CARE

National Cancer Grid (NCG)

Published Online: https://www.ncgindia.org/
Release Date – June 2026

Contact:
National Cancer Grid
Tata Memorial Hospital,
Dr. E Borges Road,
Parel, Mumbai 400012
Maharashtra, India
Email - ncg@tmc.gov.in

Acknowledgments

The National Cancer Grid (NCG) gratefully acknowledges the valuable guidance and technical inputs provided by several experts and collaborating institutions during the development and refinement of this Adaptive Health Technology Assessment (aHTA) methods manual.

We sincerely thank Dr. Daniel A. Ollendorf, Non-Resident Fellow, Center for Global Development and Former Director, Center for the Evaluation of Value and Risk in Health, Tufts Medical Center for his methodological insights and continued support in strengthening the conceptual and analytical framework for adaptive HTA. We also acknowledge the contributions of Dr. Shankar Prinja (Post Graduate Institute of Medical Education and Research) for his expertise in health economics and health technology assessment in the Indian context. We also thank colleagues from the Center for Global Development (CGD), including Dr. Javier Guzman, Dr. Peter Baker, Ms. Srobhana Ghosh, and Dr. Tom Drake, for their continued engagement and technical inputs on adaptive HTA methodologies and policy translation.

We are grateful to Professor Andrés Pichon-Riviere (Institute for Clinical Effectiveness and Health Policy – IECS) for sharing international experiences and methodological perspectives that informed the development of this framework.

The development of this manual has benefited from collaborative discussions and exchanges with experts and institutions including the National Health Authority (NHA), the Center for Global Development (CGD) and the Institute for Clinical Effectiveness and Health Policy (IECS). Their insights have helped strengthen the methodological clarity and policy relevance of this document.

Table of Contents

List of Tables

List of Figure

Executive Summary

India continues to make progress toward improving population health and expanding access to healthcare services. Achieving these goals requires systematic approaches to evaluate whether health technologies, medicines, diagnostics, and care pathways deliver meaningful clinical benefits while representing efficient use of limited healthcare resources. Within oncology, this need is particularly pronounced. The number of new cancer medicines, diagnostics, and treatment technologies is rapidly increasing, while treatment costs continue to rise. At the same time, cancer care systems must ensure equitable access, sustainability, and quality across a large and diverse population.

Health Technology Assessment (HTA) has emerged globally as a key tool to support such evidence-informed decision-making. HTA involves the systematic evaluation of the clinical effectiveness, safety, economic impact, and broader implications of health technologies. In India, the Health Technology Assessment in India (HTAIn) programme under the Department of Health Research has been established to support such evaluations at the national level. However, the volume and pace of emerging technologies—particularly in cancer care—can make it difficult to conduct full HTAs for every decision question within the timelines often required by clinicians, programmes, and policymakers.

Adaptive Health Technology Assessment (aHTA) provides a complementary approach that enables rapid synthesis and contextualisation of available international clinical and economic evidence for the Indian setting. By leveraging existing HTA reports and economic evaluations from other jurisdictions, aHTA can generate timely evidence signals on value for money, affordability, and implementation considerations while maintaining transparency about uncertainty and transferability.

The National Cancer Grid (NCG) in collaboration with HTA in India (HTAIn) and Center for Global Development (CGD) has developed this methods manual to provide a structured framework for conducting aHTA in oncology and related decision contexts. The framework aims to support clinicians, policymakers, and programme planners by enabling transparent, standardised, and timely evaluation of cancer technologies and services, while maintaining appropriate safeguards and well-defined pathways to full HTA if the aHTA does not provide evidence for the technology with certainty

This methods manual includes methods, analytical, and process components that together create a systematic approach to aHTA. While the components are discrete, they are interrelated and follow a logical sequence (see process flowchart in Figure ES1). The key components are summarised below:

Topic selection and prioritisation: A structured, criteria-based process to identify candidate topics, prioritise them for assessment, and determine whether aHTA, full HTA, or no HTA is appropriate.

Scoping: Definition of the decision problem, including the target population, intervention, relevant comparators, and outcomes of interest (PICO), along with key contextual boundaries for the assessment.

Acquiring evidence: Identification of relevant clinical and economic evidence from international sources—including HTA reports, systematic reviews, and economic evaluations—and extraction of key data for analysis.

Combined analysis and contextualisation: Synthesis of clinical evidence, assessment of transferability, and adjustment of economic results for the Indian context, with explicit reporting of assumptions and uncertainties.

Evidence summary and recommendation: Preparation of structured evidence tables and interpretation of India-adjusted results to assess likely value for money, potential affordability considerations, and key implementation issues.

Deliberation: Structured discussion of the evidence by relevant experts and stakeholders to interpret findings, consider contextual factors, and arrive at a recommendation with clearly documented rationale.

Overall, the aHTA framework is intended to complement the broader HTA ecosystem in India by providing a systematic and transparent mechanism for rapidly assessing technologies where timely evidence is needed. When applied transparently and in coordination with national HTA processes, this approach can support prioritisation of topics, inform policy discussions, and identify areas where more comprehensive HTA or additional local evidence generation is required.

1. Introduction

1.1 Background

India has made significant economic progress over the past decades, leading to improvements in living standards and expanded access to services. However, substantial disparities in health outcomes and access to healthcare persist across regions and population groups. Public spending on health has historically been limited, and a large share of healthcare costs continues to be borne by households through out-of-pocket expenditure. Such expenditures can be financially catastrophic for vulnerable populations and remain a major challenge for equitable access to healthcare (1). In response, India has undertaken several policy initiatives aimed at strengthening the health systems to move towards Universal Health Coverage (UHC). Achieving these goals requires systematic approaches for evaluating whether health technologies, medicines, diagnostics, and care pathways provide meaningful clinical benefits while representing efficient use of limited health system resources.

Health Technology Assessment (HTA) has emerged as an important tool to support such evidence-informed decision-making. Through structured evaluation of clinical effectiveness, safety, economic impact, and broader system implications, HTA can guide decisions related to benefit packages, clinical guidelines, procurement strategies, and technology adoption within the health system. Within oncology, the need for structured evaluation mechanisms is particularly important. Cancer care is evolving rapidly, with frequent introduction of new medicines, diagnostics, and treatment technologies. At the same time, the scale of the disease burden and the increasing cost of cancer therapies pose challenges for health systems seeking to balance innovation, affordability, and equitable access to care.

The National Cancer Grid (NCG) represents a nationwide network of cancer centres, research organizations, and patient groups which strives towards improving the quality of cancer care across India. As part of its mandate to support evidence-informed cancer care and policy discussions, NCG has initiated efforts to strengthen structured approaches for evaluating clinical and economic evidence relevant to cancer technologies and services. Given the large number of existing and emerging oncology interventions and the practical constraints of conducting full HTAs for every decision question, there is a need for a complementary and pragmatic approach that can rapidly synthesise available international evidence and interpret

it for the Indian context. Adaptive Health Technology Assessment (aHTA) provides such an approach by systematically identifying existing clinical and economic evidence, assessing its transferability to India, and generating contextualised insights to support timely decision-making.

The Health Technology Assessment in India (HTAIn), established under the Department of Health Research, currently serves as the national institutional mechanism for conducting and coordinating HTA studies to support evidence-informed healthcare decision-making in India. HTAIn undertakes systematic evaluations of the clinical effectiveness, safety, cost-effectiveness, and broader health system implications of medicines, devices, diagnostics, procedures, and public health programmes through its network of regional resource hubs and centres. However, the growing volume of technologies requiring assessment, particularly in rapidly evolving fields such as oncology, poses practical challenges for conducting full HTAs within available timelines and resource constraints. In such settings, aHTA can function as a complementary evidence-generation approach within the broader HTAIn ecosystem by rapidly synthesising and contextualising existing international evidence to support preliminary policy discussions, topic prioritisation, price negotiations, procurement decisions, and identification of technologies that require escalation to full HTA. When implemented using transparent methods and clear safeguards, aHTA can help strengthen the efficiency and responsiveness of the existing HTA process while remaining aligned with HTAIn oversight and methodological standards.

This methods manual describes the framework for conducting aHTA in a transparent and structured manner. The approach focuses on rapid evidence synthesis, contextualisation of economic evidence, and clear documentation of assumptions and uncertainties. The objective is to support clinicians, policymakers, and programme planners with timely evidence signals while maintaining clear safeguards and defined pathways for escalation to full HTA when more detailed analysis is required.

1.2 Objective and scope of the manual

Rapid advances in health technologies and expanding policy needs require timely review of both new interventions and potential additions to the Health Benefit Package (HBP), alongside periodic reassessment of existing services as evidence accumulates on clinical and economic impact. Conducting full HTAs for all such topics is often impractical due to time and

resource constraints, highlighting the need for a structured, time-bound adaptive approach to generate decision-relevant evidence efficiently.

This manual provides a standardized, practical methodology for conducting adaptive health technology assessments (aHTA) in India using a time-bound, stepwise process. Its objectives are to: (i) Define a common workflow from topic selection to recommendation, ensuring consistency across assessment teams; (ii) Specify minimum methodological standards for rapid evidence identification, extraction, appraisal, and context interpretation; (iii) Describe transparent approaches for economic evidence to India, including structured Incremental Cost Effectiveness Ratio (ICER) adjustment methods, price-related scenario analysis where available, and clear reporting of assumptions and uncertainty; (iv) Set out governance and quality assurance requirements (roles, review checkpoints, conflict-of-interest management, documentation, and version control); and (v) Provide standard report structures and templates so that the outputs are comparable, decision-ready, and suitable for deliberation, programme use, guideline development, and pricing/procurement discussions.

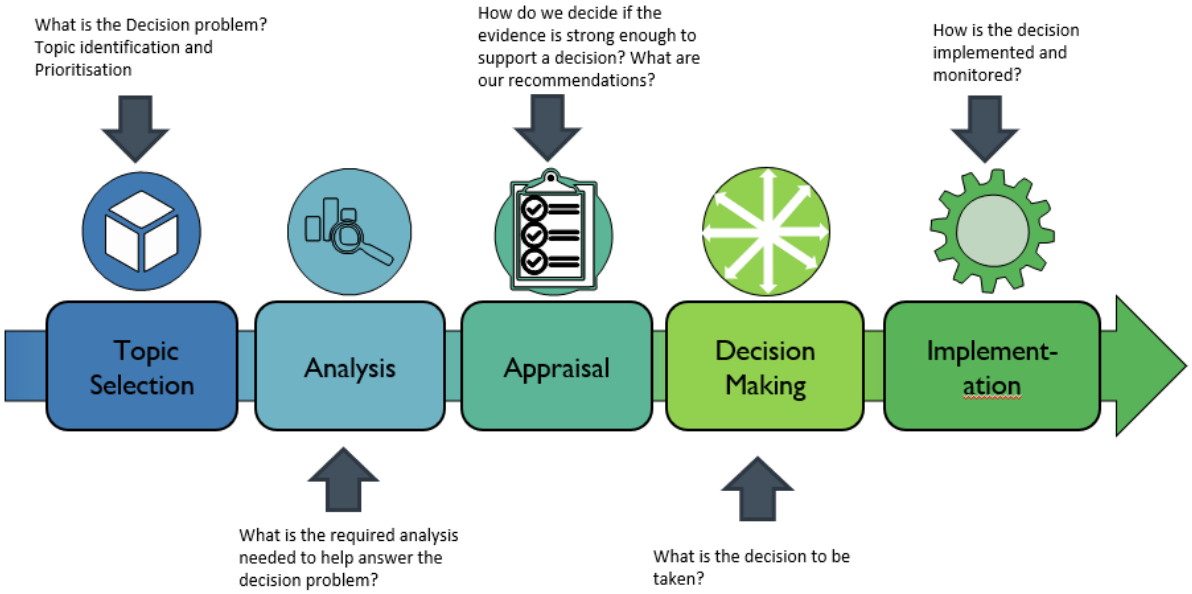
The scope of this manual is limited to aHTA conducted primarily by leveraging existing evidence (HTA reports, systematic reviews, clinical studies, and published economic evaluations) and adapting it to the Indian decision context. It covers: Topic nomination and Prioritisation; Scoping using Population, Intervention, Comparator, Outcome framework (PICO) and Indian care pathways; Rapid evidence acquisition and Data extraction; Combined clinical and economic appraisal; Contextualisation to India (costing inputs, prices, and key contextual differences); Structured handling of transferability and uncertainty, including explicit escalation to full HTA when required; Preparation of an evidence summary and recommendation package; and deliberation, documentation, publication, and update triggers. This manual does not replace full HTA and does not prescribe de novo model development as a default approach; it provides a structured framework for rapidly synthesising and adapting existing international evidence to generate context-relevant, decision-oriented insights, while clearly identifying situations where full HTA or additional evidence generation is required.

1.3 Overview of Full HTA

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 equitable, efficient, and high-quality health system" (2). The multidisciplinary aspects of HTA are on full display during the analysis, appraisal, and decision-making processes (Figure 1.1), since these elements have clinical, economic, actuarial, and ethical components.

Figure 1.2: The Full HTA Process



Source: iDSI

Clinical assessment requires specific training in systematic literature review and clinical epidemiology; analyses are conducted both quantitatively (e.g., meta-analysis or indirect treatment comparison) and qualitatively. Cost-effectiveness and budget impact analyses extrapolate clinical benefits and risks over intermediate- and long-term time horizons and are often the result of complex programming and simulation modeling. The deliberative and decision-making aspects of HTA are purposefully created to embody ethical constructs of stakeholder inclusion, transparency, impartiality, and fairness. Often, independent committees appointed by HTA bodies wrestle with contextual issues that are related to but lie outside of the analytic and quantitative frameworks in arriving at a decision or recommendation.

In some countries, health interventions must go through an HTA process before they are approved for use or funding. Examples include Australia's Pharmaceutical Benefits Advisory Committee (PBAC),(3) Canada's Drug and Health Technology Agency (CADTH)(4), England's National Institute for Health and Care Excellence (NICE), (5) New Zealand's Te Pātaka

Whaioranga – Pharmac, (6) and Thailand's Health Intervention and Technology Assessment Program (HITAP)(7). Many countries explicitly consider the cost-effectiveness of a new technology in relation to an implicit or explicit threshold for what is considered a wise investment in that setting (e.g., £25,000-35,000 per quality-adjusted life year [QALY] gained in United Kingdom). Conversely, treatments that have insufficient benefits and/or those that are deemed too expensive will not be recommended unless there are important considerations outside of cost-effectiveness.

The HTAIn unit, which is situated in the Department of Health Research, to collate and generate HTA evidence related to the clinical effectiveness, cost-effectiveness, and safety of medicines, devices, and health programs. There is also a growing body of economic evaluation work currently being conducted by universities and regional resource centres across the country. While HTAIn's capacity and influence is growing there is a need to conduct reviews on many more services and technologies. In addition, full HTA assessments may take six to nine months on an average to complete, and some decisions need to be taken in a much more abbreviated timeline. Finally, there remain gaps in technical capacity, training, and local data to inform de novo economic and clinical assessments in India, so an alternative approach is required.

1.4 Overview of Adaptive HTA

Given the challenges to conduct a full HTA for all interventions of interest, aHTA may be a possible solution to ensure that available clinical and economic evidence is used to inform decisions on whether to include, modify, or remove certain benefits.

Overall, aHTA is a structured approach to selecting and conducting a pragmatic and context-adapted HTA analysis. It produces efficient HTA results by adjusting for analytical time, data, capacity required, and leverages information from other settings where possible. Hence, aHTA can leverage or adapt available international clinical data, economic evaluations, models and/or decisions from the published literature or established HTA agencies to inform policy decisions, whilst accounting for uncertainty considerations, differences in cost structures and health systems between settings, and contextual and other nonquantifiable factors specific to the local context.

While aHTA is still a growing and evolving discipline, an increasing number of HTA agencies are using adaptive or rapid methods to assess whether a full HTA is needed, thereby shortening the time it takes to gain an insight into the value argument for a given technology. Examples include the efforts of Instance Nationale de l'Évaluation et de l'Accréditation en Santé (INEAS),(8) the HTA authority in Tunisia, which recently evaluated trastuzumab for breast cancer based on previously published systematic reviews and cost-effectiveness studies as well as local data on pricing and clinical practice;(9) and in Romania, where international evidence and adjustments to cost-effectiveness analyses done elsewhere were used to determine the maximum price at which medicines would be cost-effective locally (10).

Apart from these, aHTA is increasingly being explored internationally as a pragmatic complement to full HTA, particularly in settings where rapid decisions are required and sufficient international evidence is already available. A global scoping review identified multiple countries using adaptive or rapid HTA approaches, including Canada, the United Kingdom, Ireland, Scotland, Singapore, Malaysia, South Africa, and the Philippines, mainly for time-sensitive decisions, lower budget-impact technologies, or preliminary evidence generation. In India, aHTA applications are still at an early stage but several important methodological and pilot studies have been published. Ghosh et al. conducted a pilot aHTA study evaluating ten cancer interventions in India through rapid review of international HTA reports and economic evaluations, demonstrating that aHTA can provide feasible, resource-sensitive evidence for oncology decision-making while also identifying topics requiring escalation to full HTA (11). Chauhan et al. assessed the validity of adapting international economic evaluations to the Indian context and showed that although adapted ICER estimates can support rapid topic prioritisation and early policy discussions, results may vary considerably from full Indian economic evaluations and therefore require careful interpretation and explicit uncertainty reporting (12). In addition, Kaur et al. and related Indian methodological initiatives have contributed to developing structured approaches for evidence transferability, rapid contextualisation, and adaptation of international HTA evidence for Indian decision-making (13). Collectively, these studies highlight both the potential and current limitations of aHTA and reinforce the need for transparent methods, standardised reporting, and clear safeguards when applying adapted evidence in the Indian context.

Table 1.1 provides a comparison between full HTA processes and aHTA, along with the trade-offs to consider between the steps taken in each approach. As noted in the detailed sections that follow, an aHTA approach may have several variants depending on specific needs.

Table 1.1: Differences between Steps Taken in Full and Adaptive HTA

	Full HTA	Adaptive HTA	Trade-offs
Timeline	6–9 months	1–3 months	• Level of comprehensiveness • Speed
Topic selection	Detailed topic selection process with established criteria. Developed and institutionalised priority setting mechanisms.	Shortened process might have abbreviated criteria and/or opportunistic process; can be triggered by urgent local or national need	• Identifying low-hanging fruit • Local relevance • Range of topics
Analysis	De novo clinical and economic evaluation (e.g., CUA)	Review of HTAs or other published literature, adaptation of economic evaluation, and other measures	• Accuracy • Quality • (Un)certainty • Building capacity
Data sourcing	Local studies, primary data collection, systematic literature review and/or meta-analyses as needed	Pragmatic and structured search based on targets known to authors	• Level of comprehensiveness
Appraisal	Multistakeholder group guided by agreed principles appraising evidence and making policy recommendations	Might have an abbreviated appraisal process	• Level of HTA system improvement and health system strengthening
Implementation	Wide ranging policy changes could include adjustment to HBPs, essential medicines lists (including appropriate indications), price negotiations, reimbursement decisions, clinical guidelines, care pathways, and quality standards.		• Mobilising HTA institutionalisation

Source: C. Nemzoff, F. Ruiz, K. Chalkidou, A. Mehndiratta, L. Guinness, F. Cluzeau, and H. Shah, "Adaptive Health Technology Assessment to Facilitate Priority Setting in Low- and Middle-Income Countries. BMJ Global Health 6, no. 4 (2021). http://dx.doi.org/10.1136/bmjgh-2020-004549. (14)

1.5 Core principles

This manual is grounded in four core principles that guide the conduct and interpretation of adaptive HTA in India.

Transparency: All key decisions- topic selection rationale, scope, evidence sources, inclusion/exclusion decisions, data extraction, assumptions used for Indian contextualisation, and uncertainty handling, should be explicitly documented so that users can understand how conclusions were reached and what drives them.

Consistency: A common process, minimum evidence standards, and standard reporting templates should be applied across topics and assessment teams. Consistency enables comparability of findings across technologies, supports institutional learning, and improves credibility in deliberation.

Proportionality: The depth of analysis should be matched to the decision need, available evidence, expected budget impact, and urgency. When evidence is strong and results are far from decision boundaries, a streamlined approach may be sufficient; when evidence is limited, transferability is weak, or results are close to the decision threshold, the process should escalate to full HTA, or a conditional recommendation linked to further evidence generation.

Equity and fairness: Assessments should consider distributional impacts alongside average cost-effectiveness- who benefits, who bears costs, implications for financial risk protection, access barriers, and variation across settings and states. Where relevant, the assessment should explicitly highlight equity trade-offs and implementation considerations that may affect real-world benefit.

2. Overview of the Indian aHTA process and institutional set-up

2.1 Where aHTA will be used

HTA is already institutionalised in India through HTAIn, which undertakes evidence generation on topics received from the NHA, state governments, and other stakeholders, including innovators through the web portal. AHTA is currently used in a limited way by a few centres, but there is growing interest in expanding its use as a pragmatic, time bound approach to support evidence needs that cannot be met through full HTA alone. Any such use must align with HTAIn's mandate and processes; aHTA should be viewed as a complementary approach that supports HTAIn's decision-making pipeline rather than a parallel system.

Within this framework, aHTA can be used in three main decision pathways. First, aHTA can support health benefits package revisions and public health programme decisions by rapidly synthesising available clinical and economic evidence to generate directional value-for-money and affordability signals and to identify topics that warrant escalation to full HTA. Second, it can support clinical guideline development and updates, particularly in areas with fast-evolving evidence, by summarising benefits, harms, and economic considerations in a standard format while clearly stating uncertainties and evidence gaps. Third, it can inform pricing, procurement, and negotiation by contextualising published cost-effectiveness findings to India (with explicit assumptions and uncertainty) and presenting price–value scenarios that can guide price discussions, procurement planning, and prioritisation.

AHTA may be especially relevant in high-innovation areas such as oncology, where the number of technologies and indications is large (including frequent entry of generics, biosimilars, and newer diagnostics and devices), making it difficult to undertake full HTAs for every candidate intervention within required timelines. In such situations, aHTA can provide structured, transparent evidence summaries for time sensitive decisions, with clear safeguards, it is not a substitute for full HTA and should trigger full HTA or local evidence generation when transferability is weak, uncertainty is high, or conclusions are highly assumption sensitive.

2.2 Structure, Roles and responsibilities

AHTA requires coordinated inputs from technical, clinical, and policy facing functions, delivered within a short timeline and documented to a common standard. Defining

responsibilities up front ensures that each stage from scoping and evidence synthesis to appraisal and recommendation, has clear ownership, appropriate review, and transparent accountability.

NCG HTA cell: HTA team associated with the NCG receives topics, records them in the tracking system, confirms eligibility for aHTA/HTA, sets timelines, coordinates meetings, manages documentation and version control, and ensures required disclosures and administrative checks are completed. Once the assessment is done, the identified topics will be forwarded to HTAIN. The team will also ensure that reports follow the approved format and are submitted for review and deliberation.

Regional Resource centres (RRCs): The technical team at HTAIn RRCs conducts the aHTA as per the approved protocol. The team conducts the evidence collection, required economic adaptation, analysis, and reporting as per the manual, documents assumptions and uncertainty, and drafts the final aHTA report/policy brief for review. The health economists in the resource centres will lead economic components, interpretation and adaptation of published economic evaluations, selection and implementation of ICER adjustment approaches where applicable, identification of India-relevant cost inputs, and preparation of affordability/budget-impact analysis when required. They will ensure transparent reporting of uncertainty and key value drivers and assist in structuring conclusions aligned to decision needs.

Clinical Advisors/Subject Experts: Provide clinical input to ensure that the decision problem reflects real-world practice, including current care pathways, relevant comparators, subgroup definitions, dosing/usage patterns, and feasibility of implementation. They validate clinical assumptions used in contextualisation, interpret clinical relevance of evidence, and support identification of outcomes that matter for decision-making.

Quality Review: The study team will conduct method and content checks before deliberation, using standard checklists (scope completeness, evidence integrity, transparency of assumptions, consistency of reporting, and appropriateness of conclusions) developed for aHTA.

Technical Appraisal Committee: The HTAIn, TAC will review the final evidence and deliberates on recommendations. The committee will ensure methodological adequacy,

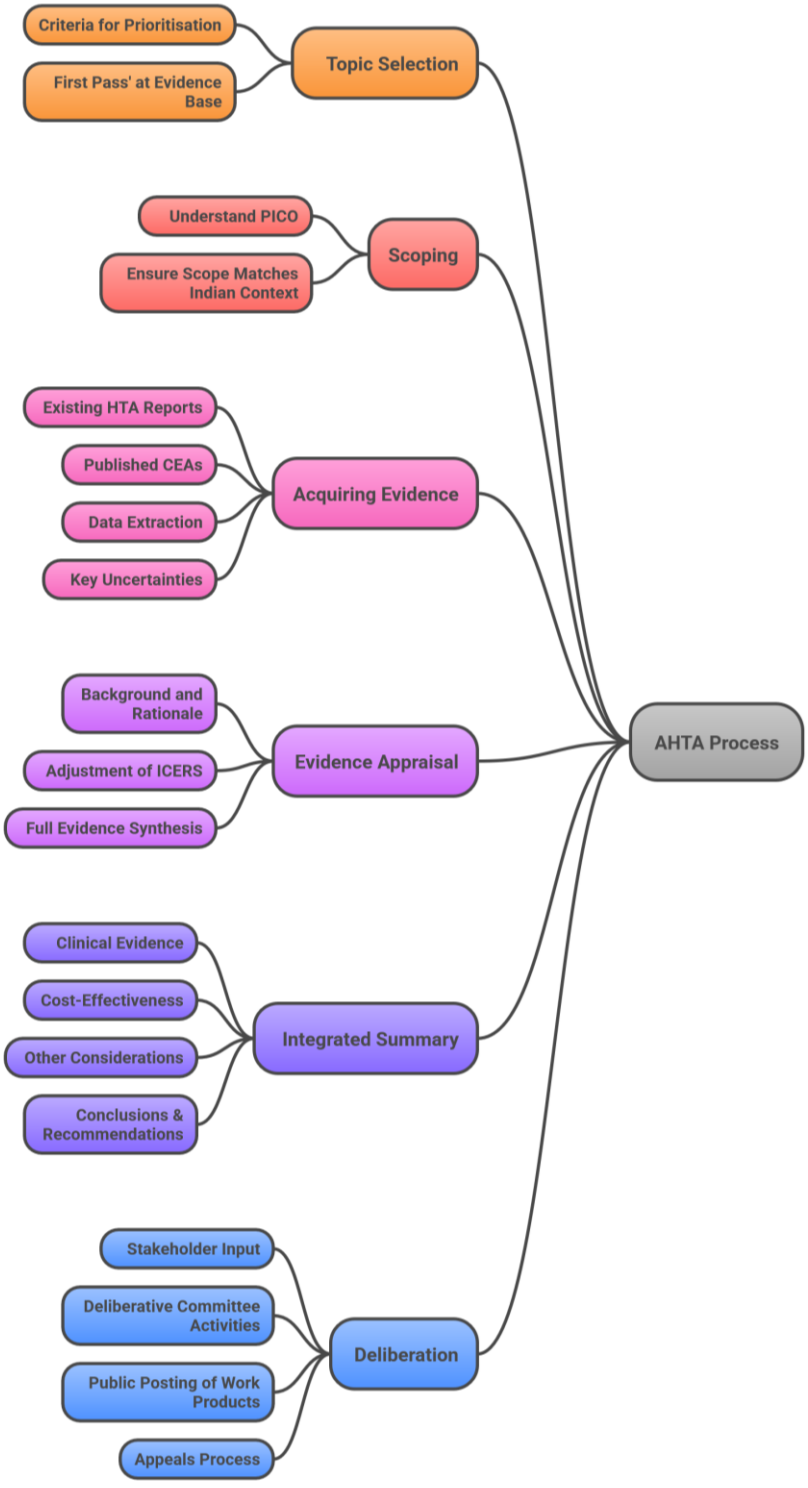
assesses decision-relevance, considers broader system factors, and issues an outcome (e.g., proceed/adopt, do not proceed, conditional/limited use, or refer to full HTA). It also records the rationale and any conditions or evidence-generation requirements.

2.3 Process flow of aHTA

The process described below is developed based on the collaborative efforts of HTAin, NCG, and health services researchers and health economists from the Center for Global Development, Argentina's Instituto de Efectividad Clinica y Sanitaria (IECS). A core working group created an outline for the methodologic and process approach, which was vetted and refined with the larger group.

The key components of the process are presented in Figure 3 and described in further detail in the sections that follow. The efforts associated with each step are intended to draw a balance between integration of critical information, speed, and full appreciation of how the Indian context differs from that of other settings.

Figure 3.1: The Proposed aHTA Process



While the steps in the process are followed in chronological order, however there is no requirement that this be strictly adhered to. For example, stakeholder input may be obtained at multiple points during the process rather than only during the final deliberative stage. The upcoming sections explain each of the steps in detail.

3. Topic Selection and Prioritisation

3.1 Topic nomination sources and intake process

NCG implements a structured, transparent, and documented procedure for receiving, prioritising and shortlisting topics and recommend it to the HTAIn for aHTA/HTA. The procedure is designed to manage the volume of requests, improve the efficiency of early-stage screening, and ensure that nominated topics align with national priorities and the broader HTA ecosystem in India, with appropriate coordination with HTAIn.

3.1.1 Topic nomination sources

Topics are nominated through multiple established channels using a standardised submission system: Nominations from clinicians and academic units within NCG can nominate the topics based on observed technology gaps, uncertainty in care pathways, emerging evidence, expected economic burden, and access or equity implications in cancer care.

Open call nominations: Like HTAIn topic submission system, stakeholders can submit topics to support network-wide identification of priority decision questions.

3.1.2 Standardised topic submission and intake

Topics can be submitted based on observed technology gaps, uncertainty in care pathways, emerging evidence, expected economic burden, and access or equity implications in cancer care through a standardised submission form (available here in the link) aligned to the HTAIn intake format to support network-wide identification of priority decision questions.

The form captures the minimum required information for screening and prioritisation, including decision rationale; PICO elements; current standard practice and proposed comparators; availability of international HTA/economic evidence and key clinical trials; expected implications for access and equity; and relevant contextual references. Such information is expected to come in the PICO format so that the topic scope and its relevance to the Indian context can be considered. Table 3.1 summarises the PICO and provides examples for each element. As part of the nomination, submitters should provide any available evidence of the potential or realised benefits of the technology on health outcomes. The PICO will be revisited after an aHTA process has begun to ensure that international evidence matches the intended scope.

Upon receipt, the NCG HTA team conducts an initial screening for duplication and completeness. Submissions missing essential elements are returned to the contributor with specific requests and are taken forward only after the required information is provided. As part of intake, nominated topics are cross-checked with HTAIn to confirm whether the same topic is already completed or under evaluation within the national pipeline. Topics taken forward for assessment are documented for coordination with HTAIn, consistent with HTAIn's role as the national custodian for HTA decision processes.

3.1.3 Structured clarification and documentation

For complete submissions, the aHTA coordination team conducts a brief structured clarification interaction with the topic submitter to confirm decision intent and refine the scope. This step verifies PICO definitions, comparator relevance to Indian practice, key evidence sources, and the anticipated decision use (e.g., guideline update, procurement, pricing). The discussion outcomes and scope clarifications are documented as part of the topic intake record.

3.2 Prioritisation criteria

Regardless of whether full HTA or aHTA is considered, it is important to have a process by which topics are selected and prioritised based on the level of impact expected; note that potential impact could be positive (e.g., possible health gain), negative (e.g., high cost), or mixed. Topic prioritisation is based on multiple considerations and the trade-offs between them. The topic submitted has to follow a standardised structure, usually in population, intervention, comparator and outcome (PICO) format (Table 3.1). Consideration of each nominated topic is first made by NCG HTA team and then linking in HTAIn to take a final decision on allocation to RRCs.

Table 3.1: PICO Elements for Nominated Topics

Parameter	Definition	Example(s)
Population	The health condition or disease addressed by the technology; the burden of disease; key subgroups or other populations of interest, such as the following: • Age range • Stage or severity of disease • Prior therapies attempted • Types of symptoms • Disease subtypes	• Secondary progressive form of multiple sclerosis • Moderate-to-severe rheumatoid arthritis with prior TNF inhibitor treatment • Adults age ≥ 65 with mild cognitive impairment and imaging evidence of Alzheimer's disease
Intervention	Full description of the intervention of interest as well as the details involved in delivering the treatment Its licensing status in India, including indicated populations(s) and uses	• Robot-assisted laparoscopic prostatectomy • Osimertinib •
Comparator	Current approaches to treating or managing the condition Guideline-listed standard treatments or workflows specific to India	• Open radical retropubic prostatectomy • Erlotinib • Best supportive care
Outcomes	The key outcomes of interest for the technology: patient-centred longer-term outcomes or intermediate measures that have been validated to predict longer-term outcomes ***Nominators should also provide evidence of real or potential beneficial impacts of the technology on these outcomes.***	• Survival/mortality • Progression-free survival • Quality of life • Changes on disability or functional scales • Hospitalisation • Complications/ adverse effects

Submitters are welcome to include additional information supporting the topic nomination, such as the following:

- Price (including potential discounts)
- Available evidence on value proposition (e.g., cost-effectiveness or other benefits)
- Expected uptake and utilisation
- Ethical, patient-level, and social considerations
- Laws, statues, or policies that may impact technology use in India
- Justification for consideration of the topic as high priority
- Feasibility considerations (e.g., training and certification)

Once the topic submission and initial checking is completed, the seven criteria for topic prioritisation (Table 3.2) are individually scored in terms of priority on a 1–5 scale, where 5 indicates highest priority for undertaking an aHTA. Scores should be accompanied by a brief written justification.

Table 3.2: aHTA Topic Prioritisation Criteria

Criterion	Score 1	Score 2	Score 3	Score 4	Score 5	Remarks
Public health importance / disease burden	Very low burden and negligible contribution to overall morbidity/mortality	Low burden with measurable but limited morbidity/mortality impact	Moderate burden or confined to specific subgroups	High burden with substantial morbidity or mortality	Very high burden; major contributor to morbidity/ mortality or priority programme area	
Clinical impact and unmet need	No or negligible additional benefit	Marginal benefit over existing options	Moderate benefit or benefit in limited subgroups	Substantial benefit or addresses clear unmet need	Transformational benefit or first effective option	
Economic impact / budget relevance	Negligible cost or minimal budget impact	Low unit cost or small eligible population	Moderate cost or uncertain budget impact	High unit cost or large eligible population	Very high cost and/or major budgetary implications	
Urgency of decision	No immediate policy decision required	Decision can be safely deferred	Medium-term decision anticipated	Decision required in the near term	Immediate or time critical decision required	
Availability of international evidence	Little or no published evidence	Fragmented or low-quality evidence	Some relevant HTA/ CEA evidence with limitations	Multiple relevant HTAs or CEAs available	Strong, consistent international HTA and economic evidence	
Feasibility and suitability for aHTA	Requires de novo modelling or primary data	Major transferability concerns	Feasible with substantial assumptions	Feasible with manageable uncertainty	Highly suitable for aHTA; minimal adaptation required	
Potential to inform multiple decisions	One-off or highly narrow decision	Limited applicability	Relevant to more than one setting	Applicable across programmes or states	High reuse potential (HBP, guidelines, pricing, procurement)	

Interpretation guidance: Total possible score: 7–35. If score is **≥26:** High priority; **26–18:** Moderate priority (subject to feasibility review); **<18:** Lower priority or consider alternative evidence pathway.

Generally, a criteria score of 26 or higher will be considered as high priority and 26-18 is with moderate priority for consideration by the NCG HTA cell. In addition to the general criteria described above, there are additional considerations that can be used to help determine if aHTA is warranted and feasible for a given topic. These are distinct considerations at play when determining whether a given topic should be assessed via an adaptive or full HTA pathway. These additional criteria are listed in Table 3.3, along with examples of their application.

Table 3.3. Additional Criteria for aHTA Determination

Criteria	Description	Examples of Potential Actions
Nature of the evidence	The types of study designs, outcomes measured, and size of the evidence base	• Large, randomised trials reporting patient-relevant outcomes → aHTA • Small clinical studies reporting intermediate or surrogate outcomes → full HTA
Local data	Differences in health system, population, patient characteristics, or other aspects require local data?	• No → aHTA • Yes → full HTA
Timing of the decision	Whether a decision on a technology is urgent or less pressing	• < three-month time frame → aHTA • ≥ three-month time frame → full HTA

Despite the application of the potential criteria, there may be grey area in determining the best and most expedient path to take, so the additional criteria should be considered suggestions. In addition, while an urgent timeline typically leads to aHTA as the more feasible option, a given topic may be a high enough priority and associated with enough uncertainty that full HTA is warranted regardless.

3.3 Case study

Topic: *Cost effectiveness of Ribociclib as a first-line treatment for confirmed HR-positive, HER2-negative Metastatic Breast Cancer in Postmenopausal women in India: An Adaptive Health Technology Assessment*

Nomination source and why it entered the pipeline: *Nominated by NCG clinicians and prioritized based on high-burden metastatic breast cancer care needs and the emergence of a high-cost targeted therapy (Ribociclib) already approved for use in India, with an immediate requirement to understand value for money for package and access decisions.*

Prioritisation criteria met: *Metastatic breast cancer represents advanced disease with high mortality and sustained treatment needs - International trial evidence (MONALEESA-2) indicates improved outcomes when added to endocrine therapy - High unit price in India with potential for substantial financial impact if scaled - Multiple international sources available (HTA reports and published economic evaluations) enabling rapid evidence synthesis and adaptation - Need for timely decision support for coverage/package consideration and price related discussions.*

Why selected for aHTA vs full HTA: *Selected for aHTA because sufficient international HTA and economic evaluation evidence existed with a matching PICO, allowing ICER adaptation to India within a short timeline. A full HTA was not prioritised at this stage because rapid, decision-oriented evidence was required and the key uncertainty was expected to be price-driven, which can be examined efficiently through adapted ICERs and scenario interpretation.*

Output: *Topic prioritisation done using an excel sheet and the score recorded and an explicit suitability decision documented: Eligible for aHTA.*

4. Scoping

4.1 Defining the decision problem in the Indian context

Defining the decision problem is the foundation of an aHTA and determines the relevance and usefulness of the final recommendation. In the Indian context, this step requires translating a broad clinical or policy question into a clearly specified, decision-focused problem that reflects local disease burden, care pathways, financing arrangements, and policy levers. The decision problem should explicitly state who is making the decision, what decision is being informed, and how the evidence will be used (e.g., coverage consideration, guideline inclusion, price negotiation, or procurement planning). Clarity at this stage avoids scope drift, inappropriate evidence transfers, and misinterpretation of results.

This stage recognises variation in treatment access across public and private sectors, availability of generics or biosimilars, typical sequencing of therapies, and real-world constraints such as affordability and programme budgets. The output of this step is a concise decision problem statement that specifies the intervention(s), relevant population(s), comparator(s) grounded in Indian practice, outcomes of interest, and the intended decision use.

4.2 PICO framework

Once the topic has been appropriately prioritised and triaged to aHTA, the scoping process will begin with a description of the decision problem as it relates to the Indian context and the definitions, comparisons, and outcomes that will define the evidence to be used in the assessment.

The PICO framework, first employed in the topic selection process described in Section 3.2, is revisited and expanded on to determine if the project scope matches the available international evidence (see Table 4.1). Importantly, an aHTA is only feasible if the PICO matches between current or anticipated clinical practice in India and the defined scope for available international evidence. If this is not the case, the aHTA effort should be abandoned and full HTA considered in its place.

Table 4.1: PICO Definition of a Project Scope

Parameter	Definition	Example(s)
Population	The definition of the population and indication should be very specific. While not exhaustive, elements to consider could include: • Age range • Stage or severity of disease • Prior therapies attempted • Disease subtypes	• Colorectal cancer in screening-eligible population (age 50+)
Intervention	This should include a full description of the intervention of interest as well as the details involved in delivering the treatment.	• Annual testing followed by optical colonoscopy as necessary
Comparator	The comparator should be standard of care in clinical practice, or on a menu of alternatives recommended in clinical guidelines. More than one comparator can be included. There should be a CEA, clinical trial data, or robust comparisons available comparing the intervention against the selected comparators for the target population.	• Optical colonoscopy alone every 5 years
Outcomes	The key outcomes of interest for the technology should be listed. They should be patient-centred, longer-term outcomes or intermediate measures that have been validated to predict longer-term outcomes. Evidence of useful surrogate or intermediate outcomes should be available through their use in cost-effectiveness models.	• Survival/mortality • Quality of life • Cases averted
Market Price or cost per unit of drugs in India	Price or cost per unit should be provided for both the intervention and comparators. For chronic therapies an annual price should be estimated based on dosing and administration schedules. If there are additional costs associated with administration and/or monitoring these should be included.	• Test cost + cost of interpretation
Subgroups of interest	Specify if there is an interest for the results of a specific subgroup in addition to the overall population.	• Demographics • Cancer risk strata
Regulatory and safety evidence	The indication as well as conditions of use (e.g., dose, route) should be specified	• Capacity to self-test with FIT

AHTA team should not undertake the scoping exercise in isolation. Rather, this represents a key opportunity to engage patients and caregivers, clinical experts, technology manufacturers, and others to refine the scope for anticipated use in India and provide a basis for comparison to the international evidence.

4.3 Case study

***Final PICO**:*

***Population:** Postmenopausal adult women with confirmed HR-positive, HER2-negative metastatic breast cancer.*

***Intervention:** Ribociclib + endocrine therapy (letrozole); Ribociclib 600 mg orally once daily for 21 days followed by 7 days off (28-day cycle) + letrozole 2.5 mg once daily.*

***Comparator:** Endocrine therapy alone (aromatase inhibitors), including letrozole 2.5 mg once daily and/or anastrozole 1 mg once daily, consistent with available evidence.*

***Outcomes:** Progression-free survival, overall survival, ICER per life-year gained, and ICER per QALY gained.*

***Key scope boundaries:** Studies with postmenopausal population only, aligned with MONALEESA-2 evidence included, while studies focused on pre-/peri-menopausal women or mixed populations without separable postmenopausal results; studies using comparators outside aromatase inhibitor–based endocrine therapy; and decision questions requiring de novo Indian pathway modelling beyond aHTA scope.*

***Output:** A written scoping note (decision question + final PICO + inclusion/exclusion boundaries and drug approval details along with its price in India) was finalised and approved for evidence acquisition and review.*

5. Acquiring Evidence

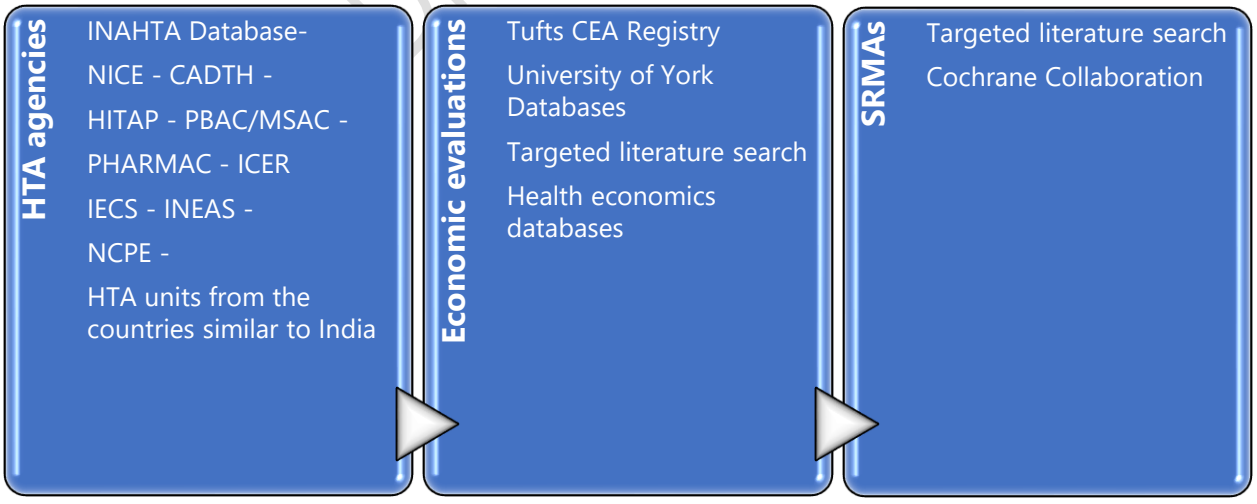
5.1 Evidence sources and search

Once the topic has been selected and the scope written, the next step is to collate the internationally available evidence on the topic. The set of evidence to be accessed is designed to be comprehensive yet pragmatic, and rapidly accessible. There are three possible sources of evidence:

- Reports from HTA agencies
- Published systematic reviews and cost-effectiveness analyses (CEAs)
- Newly published clinical evidence

The aHTA process should be hierarchical in nature. That is, the first review should be of relevant HTA reports. This can be supplemented with published CEAs, ideally conducted in relevant middle-income settings. Finally, only if there is an insufficient amount of HTA/economic evaluation evidence available then other systematic literature reviews and/or more recent clinical studies should be sourced. Further details on the selection process can be found in the sections that follow. Representative sources and approaches for access are presented in Figure 5.1.

Figure 5.1: Hierarchical Selection of Potential Sources of Evidence



MSAC: Medical Services Advisory Committee (Australia); NCPE: National Centre for Pharmacoeconomics (Ireland); PBAC: Pharmaceutical Benefits Advisory Committee (Australia).

HTA Reports

A comprehensive source of HTA reports can be found at a freely available site maintained by the International Network of HTA Agencies (INAHTA). Figure 5.1 lists a selection of the most influential HTA bodies worldwide, but the INAHTA database may be used to search for other reports that may be relevant to aHTA decision-making context. Note that the INAHTA database also integrates information that was previously collated by the University of York's Centre for Reviews and Dissemination (CRD). This database includes records through March 2015, including HTA reports, economic evaluations, and systematic reviews (both published and affiliated with Cochrane).

Published Cost-Effectiveness Analyses

In addition to HTA evidence, there may be published stand-alone CEAs studies. Given the possibility that many such evaluations are available and the potential additions to the workload they may represent, it is recommended that priority be given to those CEAs conducted in middle-income settings that may be relevant to the Indian context (e.g., similarities in health systems or per capita income). CEAs evaluated in high-income settings may also be considered if the scope and perspective are a close match (e.g., a US-based evaluation using a Medicaid perspective, with similar demographics to AB-PMJAY).

Economic evaluations may be identified in one of the databases maintained by the York CRD. In addition, Tufts University maintains a detailed registry of over 12,000 published CEAs that measure health benefits using the quality-adjusted life year (QALY) or disability-adjusted life year (DALY). There are also literature databases that may provide a more direct link to economic evaluation given their focus on the social sciences. The two databases most commonly accessed are PsycINFO and EconLit.

Systematic Reviews

Systematic reviews and meta-analyses should be considered only if relatively few available HTA reports represent a good match to the Indian context. While there is no firm threshold for this, it is suggested that a minimum of three relevant HTA reports be available; if this is not the case, a search can be conducted for additional systematic reviews. These analyses may be identified in specifically curated databases, such as the library of systematic reviews maintained by Cochrane. Studies published in peer-review journals may be accessed through

a targeted search of electronic literature databases. It is recommended that for pragmatic purposes the search be limited to PubMed and EMBASE, the two largest compilations that focus on the English-language literature. Both databases include a search filter for systematic reviews.

5.2 Search strategy

The evidence search for aHTA follows a rapid and targeted strategy designed to identify relevant HTA reports and economic evaluations efficiently while maintaining transparency and reproducibility. The objective is not to conduct a full systematic review but to locate the most relevant existing assessments and studies that can inform adaptation to the Indian context. The search typically follows an HTA-first approach, beginning with targeted searches of HTA agency websites and repositories to identify existing appraisal reports, cost-effectiveness assessments, and technology review documents related to the intervention and population of interest. These sources often contain synthesised clinical and economic evidence that can be directly adapted or used as primary inputs for the aHTA.

In parallel, bibliographic databases are searched to identify published economic evaluations and related evidence. At minimum, the search includes PubMed for peer-reviewed literature and the Tufts Cost-Effectiveness Analysis Registry for structured records of cost-effectiveness studies. Search terms are constructed around the intervention, disease/condition, and economic evaluation terms (e.g., cost-effectiveness, cost-utility, ICER). The search strategy is designed to be focused and time-efficient, typically limited to the most relevant databases and HTA sources rather than an exhaustive multi-database search. Where appropriate, additional targeted searches of key HTA agencies or reference lists may be conducted to ensure that major assessments are not missed. For transparency, the search date, sources searched, and key search terms should be documented in the report as appendix. The results of the search are then screened against the predefined PICO and eligibility criteria, with included studies recorded in the evidence map and extraction tables presented in the report.

5.3 Data Extraction

Once the searches have been conducted and relevant documents have been selected for review, a data extraction template is used to standardise the information aggregated to facilitate comparisons and provide consistency in reporting across selected documents. The

data extraction template consists of background information on the type of evidence as well as information on the key findings relative to intervention effectiveness, safety, cost-effectiveness, and other concerns. All this evidence is extracted using a separate template (see below sections 5.3.1 to 5.3.4).

5.3.1 Background Information

The data extraction sheet begins with a section on background information to identify and contextualise the studies within the hierarchy of evidence and confirm that the information in the document under review matches the decision problem in the scope (Table 5.1).

Table 5.1: Data Extraction Sheet: Background Information

Data point	Description
Country	The primary country of the document or analysis to help understand how generalisable the results are to the Indian context
Analysis/document type	Detail whether the document is an HTA, systematic review, individual study, or other to determine where it lies in the hierarchy of evidence
Link	Web address for the document (and additional citation information if available)
Title	Full title of the document
Author	Names of the authors of the document, if appropriate
Date	Date of the report to contextualise when the recommendations were made
Population	The target population identified in the report
Intervention	The name of the intervention in the report
Comparator(s)	The name of the comparator(s) in the report
Funding source	The type of entity funding the study or report (e.g., government, industry, or foundation)
Quality	Study or review quality rating, as appropriate

It is also important to rate and report the overall quality of the study identified. The updated CHEERS checklist is used for an assessment of economic evaluations, while the AMSTAR 2 tool allows for appraisal of systematic reviews, and the Cochrane Risk of Bias tool focuses on the quality of individual clinical studies.

5.3.2 Clinical Evidence

Clinical evidence is necessary to determine the anticipated benefit and potential harms of the treatment (Table 5.2). The PICO exercise will determine what outcomes are most appropriate for the disease area and treatments under study. Regardless of the area of focus, however, there is consistent guidance regarding the type of information to extract, which includes the following:

- Absolute estimates of treatment effect (e.g., rates, means, or medians)
- Relative estimates of treatment effect (e.g., odds ratios or relative risks)
- Measures of variance, including standard deviation/error, confidence intervals.
- P-values for treatment comparison
- For meta-analysis: number of contributing studies and weighting factors used

It is important that all relevant clinical outcomes are extracted and reported from each document to gain an understanding of all potential benefits that need to be considered. All data extracted should include both the point estimates to define the benefit and measured of variance with associated p-values to understand the uncertainty around the benefit.

The quality rating tools described previously tend to focus on the clarity and detail with which elements of systematic reviews or individual studies are reported. There may be additional nuances in the evidence base that should be described outside of strict quality rating. For example, a placebo-controlled clinical trial conducted in patients who responded to prior therapy may overstate the benefit of a new treatment; this is a structural and design issue rather than a concern of reporting quality. Space should be allocated in data collection to describe these issues in further detail.

Table 5.2: Data Extraction Sheet: Clinical Evidence

Data point	Description
Study name	Title, author, year
Type of study	Study design, geographic settings, number of patients
Comments on clinical benefit	Note anything unusual or noteworthy about the findings
Outcome	Point estimate for outcome of interest (e.g., %, mean), separately for intervention and comparator, or measure of between-group difference
Measure of variance	Standard deviation, standard error, 95% confidence interval, and the like
P-value	Measure of statistical significance of the comparison
Utility weights	Detail the source of the utility weights for all health states included in the model, note if the values were taken from the literature or if local data was applied
Limitations, critiques, and residual uncertainties regarding the clinical evidence	Limitations on generalisability to the Indian context (e.g., differences in disease severity, subpopulation differences, or bias in study design or sampling strategy), uncertainties from limited follow-up, major differences between study protocol and typical clinical practice, and so forth
Safety evidence	Rate of serious adverse events for intervention and comparator; identification of any specific adverse event types that occur with more frequency in the intervention or comparator group; rate of discontinuation due to adverse events
Other considerations	Mention of other contextual issues, such as complex implementation or treatment delivery, specialised training required, and so forth

5.3.3 Cost-Effectiveness Evidence

Cost-effectiveness evidence will primarily be extracted from HTA agency assessment reports or published economic evaluations from international jurisdictions. This evidence is typically based on the outputs of a simulation modeling exercise, although occasionally CEAs are integrated directly into a randomised clinical trial. The key data points that may be considered useful for decision making involve extracting information on costs, health-related quality of life, estimates of cost-effectiveness and budget impact, conclusions or recommendations based on findings, and an assessment of the quality of the evaluation (Table 5.3).

Table 5.3: Data Extraction Sheet Data Points: Cost-Effectiveness Analysis

Data point	Description
Study-level characteristics	Important study descriptors, including (a) perspective (e.g., health system or societal); (b) time horizon; (c) discount rate; (d) unit costs of intervention and comparator; (e) currency used; (f) currency year; (g) exchange rate
Intervention costs	The costs associated with the intervention, disaggregated if available (e.g., treatment costs, resource use costs, adverse events, administration costs, other relevant costs)
Comparator costs	The costs associated with the comparator, disaggregated if available
Incremental costs	The difference in costs between the intervention and comparator
Intervention QALYs	The QALYs associated with the intervention
Comparator QALYs	The QALYs associated with the comparator
Incremental QALYs	The difference in QALYs between interventions
ICER	The incremental cost-effectiveness ratio
Cost-effectiveness threshold	The threshold to which the ICER was compared in the study publication or HTA assessment, noting any adjustments due to special conditions (e.g., rare disease, end of life, paediatric)
Recommendation or conclusion	Whether the intervention was recommended or the study concluded that it was cost-effective. Detail any required price discounts required or additional restrictions on use.
Generalisability concerns or other uncertainties	Key concerns regarding the generalisability of the findings to India, such as implementation, practice or health-system differences, training requirements, and so forth Key uncertainties with study or model findings, including the most sensitive parameters identified
Quality	Quality of the study or model using the CHEERS checklist

5.4 Quality appraisal and weighting of economic evaluations used for ICER adaptation

When multiple economic evaluations are available for a single intervention, their methodological quality and reporting standards often vary substantially. Treating all studies as equally informative can dilute decision relevance and lead to misleading adapted ICERs. aHTA therefore requires a structured approach to screen, rate, and prioritise economic evaluations before they are used for adaptation.

Mandatory quality screening before ICER adaptation: All identified economic evaluations should undergo a minimum quality appraisal prior to inclusion. Studies that fail to meet essential criteria like unclear comparator, absence of incremental results, or non-transparent methods etc. should be excluded from ICER adaptation and referenced only as background information, if at all.

Use of a structured quality and reporting checklists: AHTA should apply a concise, standardised checklist to assess methodological and reporting quality. Existing tools such as the CHEERS reporting standards and key domains from Drummond's checklist provide an appropriate foundation, but should be applied in a simplified, decision-oriented manner suitable for rapid assessment. The focus should be on elements that directly affect ICER credibility rather than exhaustive scoring. Each study should be rated qualitatively (e.g., high, moderate, or low confidence for adaptation), with brief justification.

Prioritisation rather than averaging: Adapted ICERs should be derived preferentially from high or moderate confidence studies. Studies with low confidence should not be used to generate primary adapted ICERs and should not be mixed with higher quality evidence. Where multiple high-quality studies exist, results should be compared for directional consistency.

Handling mixed quality evidence: If only low or moderate quality studies are available, this limitation must be explicitly stated, and conclusions should be framed as highly conditional.

Documentation requirement: The final aHTA report should include a table summarising the quality appraisal of all included economic evaluations and clearly indicate which study or studies informed the adapted ICERs. This ensures transparency and prevents implicit weighting of poor-quality evidence.

5.5 Transferability screening and key Uncertainties

Transferability screening is a structured assessment of whether evidence generated in other settings can meaningfully inform the Indian decision problem, and which elements require cautious interpretation. This step explicitly identifies what can be transferred with reasonable confidence and where uncertainty is introduced through contextual differences, ensuring that conclusions are appropriately qualified and that escalation to full HTA is triggered when required.

Screening should focus on core dimensions that materially affect decision relevance, clinical pathway alignment, resource use and cost structure, population characteristics, and outcome measurement. Relative treatment effects and health outcomes are often more transferable than absolute costs, whereas results driven by local prices, utilisation patterns, or delivery models are more sensitive to context. Key uncertainties arising from these differences must be explicitly documented, including their likely direction and magnitude of impact on conclusions.

The output of this step is a concise transferability and uncertainty summary that identifies dominant drivers of results, flags parameters with high uncertainty, and states whether findings are robust to plausible ranges. This summary should directly inform interpretation of results, recommendation wording, and the decision to proceed, apply conditions, or escalate to full HTA.

5.5.1 Uncertainty in ICER Estimates

As previously described, most CEAs are the result of a simulation modeling effort that in many cases extrapolates short-term clinical data through a treatment pathway that has multiple decision points and is assessed over the very long term. This requires making numerous assumptions, which are associated with multiple uncertainties. It is therefore crucial that the data extraction captures the level of uncertainty in the results.

The base case cost-effectiveness results will typically rely on point estimates. These are often tested in multiple types of sensitivity analyses. It is important to characterise these results in detail to ensure understanding of how consistent the conclusions may be when parameters are varied and whether some parameters affect the results more than others. Understanding the effect of the full range of potential parameters helps determine whether the model

sensitivities would be pronounced when generalised to India.

5.6 Ensuring quality and credibility of adapted ICERs

Adaptation of ICERs from international studies to the Indian context introduces unavoidable uncertainty, particularly when cost structures, prices, and care pathways differ substantially. To strengthen the credibility and appropriate use of adapted ICERs, aHTA must apply explicit quality checks before results are interpreted or used for recommendations. This section outlines minimum safeguards to assess whether an adapted ICER is sufficiently reliable for decision support or whether escalation to full HTA is warranted.

5.6.1 Assessment of ICER drivers in the source study

In addition to documenting uncertainty, it is also important to note whether there are other underlying drivers of the results to make clear how the clinical effects and cost offsets might play out in India. This is particularly important when the issue at hand is understanding how to translate international evidence to India.

As an example, suppose a new treatment might become cost-effective if it would displace significant resource use involved in delivering the current standard of care. To use a UK example, the treatment might cost £10,000 more but because patients are healthier for longer and don't require additional care, it could save the health system £15,000. However, this savings might not be generalizable to India, and then the results would change. Taking the same example, the treatment could cost ₹10,000 more but due to the differences in clinical practice between India and the UK, the difference in resource use and associated costs might mean that it only saves ₹5,000; then, conclusions around cost-effectiveness might change.

Another common driver of cost-effectiveness is the comparability of the clinical benefits. If the clinical benefits are quite similar between a new treatment and the comparator, then even small differences in price can have a great impact on the cost-effectiveness. For example, if the QALY gain with a new treatment is 0.02, a £250 increase in incremental costs from £500 to £750 would increase the ICER from £25,000 per QALY gained to £37,500, potentially changing conclusions about cost-effectiveness. However, if the QALY gain was 0.3, the change in costs would change the ICER very slightly (from £1,667 to £2,500 per QALY gained) and not necessarily change the conclusions.

Another significant driver of cost-effectiveness is the expected duration of treatment. In cancer treatment, for example, many new therapies are prescribed on a treat-to-progression basis, where therapy continues until there is evidence that the disease has returned or progressed to a more severe level. In contrast, many older chemotherapy drugs, and even can greatly affect the incremental costs associated with treatment as patients progress through disease states. While keeping cancer in remission and avoidance of disease progression are desirable health outcomes, the expectations regarding duration of treatment are important to keep in mind when interpreting results and considering costs to the system.

5.6.2 Use of sensitivity analysis outputs to inform adaptation

Where available, one-way sensitivity analysis results (e.g., tornado diagrams) should be examined to understand how changes in individual parameters affect the ICER and probability sensitivity analysis (PSA) results for overall variability in ICER. These results allow the assessment team to judge whether plausible Indian values for key parameters would materially alter conclusions. Quantitative values from tornado diagrams and CE Plane can be extracted using digital graph-reading tools (e.g., WebPlotDigitizer) when numerical results are not tabulated and should be used to inform scenario ranges rather than point estimates.

5.6.3 Consistency checks across multiple evidence sources

When more than one HTA or economic evaluation exists, adapted ICERs should be compared across sources to assess directional consistency rather than numerical convergence. Consistent conclusions across studies strengthen confidence, whereas wide divergence signals structural uncertainty and supports escalation to full HTA.

Price-ICER plausibility assessment

For interventions where price is a key driver, adapted ICERs should be interpreted alongside explicit price- ICER or price value scenarios. If small changes in price lead to large shifts across the decision threshold, results should not be treated as definitive and should instead be used to inform negotiation or conditional recommendations.

Threshold proximity and decision risk

Adapted ICERs that fall close to the decision threshold with high uncertainty require heightened caution. Where results lie within a narrow margin around the threshold, or where relative ranking across interventions is unstable, aHTA findings should not be used to make

exclusionary decisions and should prompt either conditional use or referral for full HTA.

Documentation and transparency requirements

All assumptions used in adaptation, including parameter substitutions, price sources, inflation or PPP adjustments, and proxy measures must be explicitly documented in the report.

5.7 Case study

HTA-first sources searched: *Evidence acquisition followed an HTA-first approach by searching HTA agency repositories/websites (for full HTA reports). A structured search was conducted in PubMed and the Tufts Cost-Effectiveness Analysis Registry, supplemented by targeted search to capture HTA reports/studies relevant to the decision question.*

Study types included: *Full HTA/appraisal reports that reported cost-effectiveness evidence for Ribociclib in the target indication - Published cost-utility/cost-effectiveness studies reporting incremental costs and effects and ICERs for Ribociclib plus endocrine therapy versus endocrine therapy comparators.*

Selection decisions: *Studies were screened against the pre-specified PICO. Included studies matched the postmenopausal HR+/HER2− metastatic breast cancer population and compared Ribociclib plus endocrine therapy to aromatase inhibitor–based therapy. Studies were excluded if they: (i) focused on pre-/peri-menopausal populations or mixed populations without separable postmenopausal estimates, or (ii) used non-AI comparators that did not align with the scoped comparator set. The selection process reported as PRISMA flow chart in the result section (appendix 2 and the search strategy along with number of hits and search date is reported in the appendix of the report.*

Extraction outputs: *A structured extraction sheet capturing study setting, perspective, cost year, intervention/comparator costs and outcomes, incremental values, ICERs, thresholds, and key cost-effectiveness drivers; and summary tables prepared for inclusion in the report.*

Output: *Final evidence base documented as 3 HTA reports (UK, Switzerland, Canada) and 8 economic evaluations identified for aHTA adaptation. The characteristics of the identified studies reported as a table in the final report.*

6. Combined Evidence Analysis and contextualisation

Once collection of data on comparative clinical and cost-effectiveness is finished, the full evidence package can be analysed. The intent is to provide a comprehensive view on the accumulated information on the effectiveness and cost-effectiveness of the intervention under review; its safety; the level of confidence the decision maker should have in the evidence; and any remaining uncertainties that should be considered. The sections that follow provide a step-by-step guide to the key elements of the appraisal.

6.1 Background on Topic and Rationale for aHTA

The appraisal should begin with background information on the disease in question, its epidemiology in India, the current burden of the disease, and ways in which the intervention of focus might address the burden. The rationale for aHTA should then be described in detail, including how the criteria set forth in Section 3 were fulfilled.

6.2 Clinical Evidence Synthesis

Synthesis of the evidence on clinical benefits should include summary tabular presentation of data on the outcomes of interest from available clinical studies, statements about the statistical and clinical significance of the findings, and the results of any other quantitative assessments of the data. An overall summary of the evidence of clinical benefit (e.g., in terms of whether it is consistently positive, mixed, and so forth) should be provided to aid in summarising the overall net health benefit.

As with clinical benefits, harms should be summarised in tabular form. Safety data collected in clinical trials is often not subject to significance testing, as most of these studies are powered to detect differences in efficacy. Nevertheless, important safety signals may be revealed by the data. In addition to the three main types of adverse events captured in clinical trials as highlighted in Section 5, other potential harms may be captured. For example, established therapies may have been subject to long-term observational studies for safety surveillance purposes (e.g., risk of lymphoma among those with autoimmune disease who received TNF inhibitors).

In addition to separate summation of the benefits and risks of a given intervention, the overall quality and strength of the evidence base should be summarised. Overall quality is simply an assessment of the quality of individual studies and reviews that make up the evidence base

(e.g., three of five reviews were of higher quality, two of four individual studies, and so forth). The strength of evidence is more complex and multifactorial, and typically involves assessment of multiple domains, as shown in Table 6.1.

Table 6.1: Domains Considered When Assessing Strength of Evidence

Domain	Description
Directness	Whether (a) the evidence links directly to an outcome of interest or is based on a surrogate; and/or (b) whether comparisons are head-to-head or indirect
Consistency	Whether available studies produce findings in the same direction or with a comparable magnitude of effect
Precision	The degree of certainty surrounding effect estimates
Reporting or publication bias	Selectively reporting on only certain outcomes or only studies with positive findings
Other possible domains	
Dose–response	Effect size grows proportionally to level of exposure to the intervention
Plausible confounding	Artificial reduction in observed effect size due to confounding factors
Strength of association	A large enough magnitude of effect that it is not likely to be a result of confounding

Source: N.D. Berkman, K.N. Lohr, M. Ansari, M. McDonagh, E. Balk, E. Whitlock, J. Reston, et al. Methods Guide for Comparative Effectiveness Reviews (Rockville, MD: US Agency for Healthcare Research and Quality, 2013).

Many organisations score these domains individually and then provide an overall grade for the evidence based on the level of confidence that the estimate of benefit lie close to the true observed effect. In other words, if the evidence scores well on all domains, the confidence might be *high*. If the evidence rates well for the key domains but is mixed on others, confidence might be rated *medium*. And if there are serious questions about precision, consistency, and the like, confidence might be *low*. Finally, data might be considered *insufficient* to make a determination about strength of evidence, but it is likely that the topic would have been diverted from the aHTA pathway before engaging in a review in such a case. Some organisations have conveyed this through a stoplight graphic: green for high confidence, yellow or orange for medium, red for low, and no color or a strikethrough symbol

for insufficient.

An assessment of the generalisability of the findings to the Indian context should also be made. Attention should be paid to differences in the population studied relative to candidate patients likely to receive the treatment in actual practice, differences in disease severity and underlying risk between the study populations and the target population in India, considerations regarding treatment implementation and access, and other issues. Along with strength of evidence, a generalisability assessment speaks to the likelihood that the observed treatment effect will be realised in the Indian context. Key generalisability considerations are described further in Table 6.2.

Table 6.2: Key Generalisability Considerations

Domain	Description
Feasibility	Delivery of the intervention as reported in clinical studies should be possible in the local context, or variation by setting should be measurable (e.g., facilities with versus without specialised training).
Coverage	Adequate coverage of the intervention is available or gaps in coverage are identifiable (e.g., urban versus rural).
Acceptability	The intervention should be acceptable to patients, caregivers, and clinicians, and challenges to acceptability are identified (e.g., social norms for STD prevention).
Representativeness	Populations in clinical studies should be generally reflective of the target population for the intervention, or gaps in representation should be identified (e.g., underrepresentation of minority racial or ethnic groups).
Needs of future recipients	Support services necessary to ensure adherence to treatment in typical practice should be identified (e.g., educational materials or case management).
Impact on care pathway	The extent to which benefit extends beyond disease in trial versus target population should be noted (e.g., spillover effects of treatment in high-risk individuals versus a more general population)

Source: C. Bonell, A. Oakley, J. Hargreaves, V. Strange, and R. Rees. "Assessment of Generalisability in Trials of Health Interventions: Suggested Framework and Systematic Review," BMJ 333, no. 7563 (2006): 346–49.

6.3 Cost-Effectiveness Synthesis

6.3.1 Adjustment of ICERs to Indian Context

Data extraction in Section 5 focused on collection of information on costs, health benefits, and ICERs as reported in the original HTA appraisals or published studies. Because these estimates come from a variety of settings, the ICERs should be adjusted to reflect their likely translation to India. There are several options available to make this calculation. It is recommended that, data and circumstances permitting, all three adjustments be made for the purposes of evaluating the consistency of findings across them.

Simple Adjustment

In many circumstances, particularly in the case of high-priced drugs, the cost of the intervention itself is the main driver of the cost-effectiveness results. In such cases, a straightforward adjustment may be informative, and can be made by multiplying the study-reported ICER by the ratio of the price in India to the price in the study country, as follows:

$ICER_A = ICER_O * (P_A / P_O)$

Where $ICER_O$ is the reported ICER in the study country; P_A and P_O are the drug (or other intervention) prices in India and the study country, respectively; and $ICER_A$ is the ICER adjusted for India.

Moderate Adjustment

When the price or cost of the intervention in India is known, it may be possible to generate an extrapolation of cost-effectiveness if enough detail is reported in the relevant economic evaluations or through derivation of clinical study findings. Specifically, a monthly cost of treatment is estimated, along with a mean or median duration of treatment (in months) from the clinical study or a CEA for both the intervention and its comparator. An incremental cost is generated based on the price and duration of treatment, and this is divided by the ratio of the number of additional months of treatment with the intervention to 12, the number of months in a full year of life. This of course requires the availability of data on treatment duration and is useful for chronic therapies only. The formula is as follows:

$ICER_I = (C_I * M_I) – (C_C * M_C) / ((M_I – M_C) / 12)$

Where C is the monthly cost and M is the number of months of treatment; and lower case I

and lowercase C are the intervention and comparator, respectively. The result considers the costs added by the intervention as well as the benefit of longer treatment, expressed as a proportion of an additional year of life. Note that "valuation" of health is approximated here by duration of treatment, based on the assumption that longer treatment duration for chronic therapy is associated with better outcomes. While this is a relatively crude assumption, it may nevertheless be informative for considering the benefits of treatment when therapy is anticipated to be ongoing for the longer term.

Complex Adjustment Cost and Outcome–Adjusted ICER

A more complex formula may be used if it is expected that there are multiple types of costs that might affect an ICER adjustment, not merely the cost of the intervention, and/or differences in the underlying epidemiology of disease and its trajectory between countries. This will involve separate adjustment of costs and QALYs.

Costs should be recorded in both the currency and year in which they are reported or publication year and converted to INR and inflated to the most recent year to allow for comparisons across studies. Currency conversion can be accomplished using exchange rate and GDP-based purchasing power parity (PPP) data tables from the World Bank, and inflation adjustment should be based on the India Consumer Price Index (CPI) for Health, maintained by the Ministry of Statistics and Programme Implementation or World Economic Outlook Database maintained by International Monetary Fund (IMF). If costs are reported separately for the intervention and its comparator, they should be adjusted separately and then the incremental costs recalculated. If only incremental costs are available, these should be adjusted. The basic formula for these calculations is as follows:

a. Converted cost = PPP GDP per capita, India / PPP GDP per capita, study country
b. Inflation factor = CPI for health, India, current year / CPI for health, India, year of reporting or publication
c. Adjusted cost = (Study reported cost * converted cost) * inflation factor

Data points for health-related quality of life capture the health benefits gained. This might be an increase in overall survival, a reduction in disability, and/or other more nuanced improvements in patient quality of life. This will be calculated for each intervention and comparator, then presented in terms of QALYs gained. As with costs, QALYs should be

presented as reported and adjusted for the Indian context. In this case, data will be required either on life expectancy from the diagnosis or onset of the disease in question, or if not available, the overall life expectancy, in both India and the study country, which is also available from the World Bank. Alternatively, it may be more appropriate to adjust for the differences in quality of life if such data is available. QALY adjustment should be done separately for the intervention and comparator, if feasible; if not, incremental QALYs should be adjusted. The straightforward calculation for this formula is presented below.

d. Conversion factor = Life expectancy from diagnosis or birth, India (recent year) / Life expectancy from diagnosis or birth, study country (recent year)
e. Adjusted QALYs = Study reported QALYs * conversion factor

Once both costs and QALYs have been adjusted in this manner, the adjusted ICER for India is simply calculated as:

$ICER_A = \Delta Cost_A / \Delta QALY_A$

Where $ICER_A$ is the adjusted ICER for India, $\Delta Cost_A$ are the incremental adjusted costs (i.e., intervention–comparator), and $\Delta QALY_A$ are the incremental adjusted QALYs. Note that this calculation does not take into account the possibility that utility values (i.e., the level of value individuals attach to a given state of health) may also differ between India and the original settings; in many cases, however, these models employ a complex framework that includes multiple health states, and it may not be possible to disentangle the values attached to each state for such an adjustment.

IECS extended Adjustment

Modified formula by the Institute for Clinical Effectiveness and Health Policy (IECS) for estimating the ICER adjusted to the local currency unit

$$a\_ICER(in\ LCU) = \frac{(O\_original\_\Delta\text{Costs} * \text{Cross country and temporal adjustments}) + \text{a\_Int\_Int\_cost} - \text{a\_Comp\_Int\_cost}}{O_{\Delta\text{QALY}} * \text{QALYCorrector}}$$

Where, $ICER_a$ (in aLCU): Adjusted incremental cost-effectiveness ratio, expressed in the local currency of the analysis country (aLCU).

O_Original_Δcosts is the incremental cost, not directly associated with intervention or comparator (represents the difference in costs, which is not directly associated with the

treatment or comparator). These may include costs related to hospitalizations, follow-up care, management of complications, or other non-pharmacological interventions.

It is calculated as: "o_Other_ΔCost"="Tot_ΔCost"-("Int_Int_Cost"-"Comp_Int_Cost")

Where:

Tot_ΔCost: The total cost difference between the scenario with the intervention of interest and the scenario with the comparator.

Int_Int_Cost: The total cost of the intervention in the scenario with the intervention of interest.

Comp_Int_Cost: The total cost of the intervention in the scenario with the comparator.

All costs in this term are expressed in the original study's local currency (oLCU).

Cross-country and temporal adjustment: This adjustment factor accounts for differences between the country and year in which the original study was conducted and the target context of analysis by the product of factors that have to be multiplied.

Exch_rate: Exchange rate between oLCU and aLCU (1 × Exch_rate = 1 oLCU in aLCU).

a_Int_Int_Cost: Cost of the intervention in the intervention arm, in the analysis country's currency (aLCU).

a_Comp_Int_Cost: Cost of the comparator in the comparator arm, in aLCU.

o_QALY_Diff: Incremental QALYs (intervention arm – comparator arm) from the original study.

QALY_corrector: Adjustment for baseline health expectations between countries, calculated as aHALE / oHALE.

aHALE: Healthy life expectancy in the analysis country.

oHALE: Healthy life expectancy in the original study country.

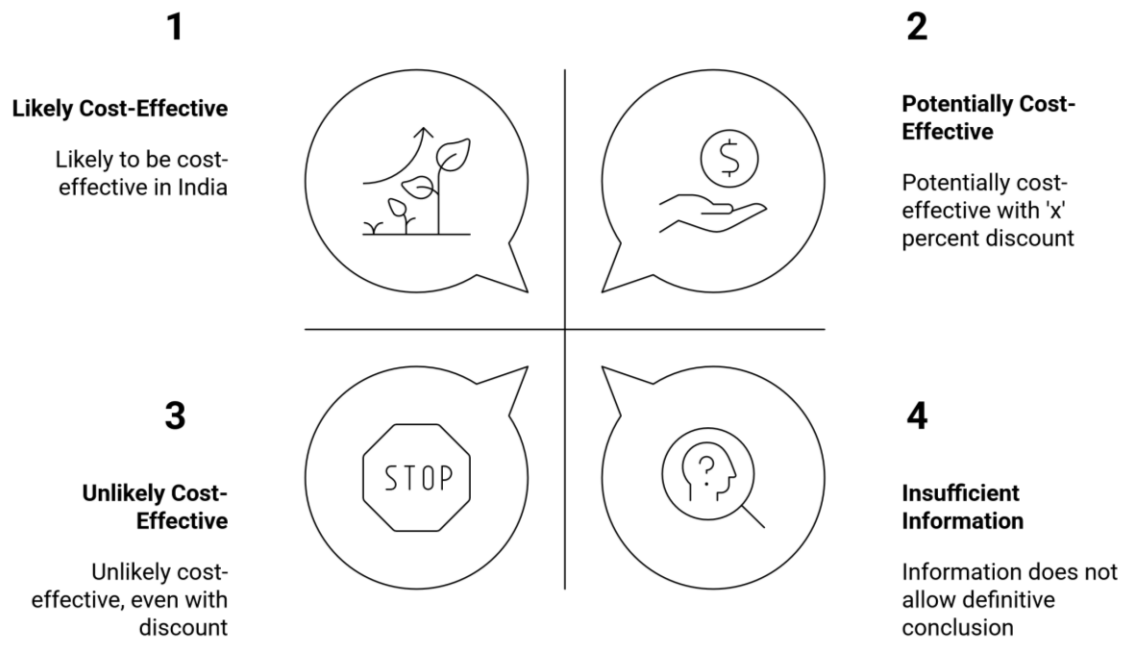
6.3.2 Comparison to Indian Thresholds

After an adjusted ICER is calculated, it should then be compared to available cost-effectiveness thresholds or benchmarks for India. ICERs close to or below the threshold can be considered to represent potentially cost-effective uses of Indian budget and resources,

while those above the threshold would likely not be. It should be noted, however, that the adjusted ICERs are all the result of some extrapolation, and therefore likely not accurate as findings from a de novo model constructed for the Indian context might be.

6.3.3 Cost-Effectiveness Summary

Available cost-effectiveness data should be summarised in detail. This should include the number and quality of external economic evaluations considered. All adjustments made to the cost-effectiveness estimates for India should also be described in detail. A summary judgment should be made on whether the technology is likely to be cost-effective in India, based on both the results of original CEA studies as well as the adjusted estimates made. A possible list of categorical assignments could include the following:



The purpose of these categories is to provide a summation of the evidence and the potential policy directions to take regarding cost-effectiveness. It is intended to be distinct from the evaluation of clinical evidence so that policy priorities might be put in place (e.g., to highlight a technology with major clinical potential that nevertheless requires substantial negotiation to become cost-effective, or a technology of marginal value that may not benefit from further negotiation). An assignment of category 4 might necessitate collection of further evidence or commissioning of a full HTA.

6.4 Estimated Budget Impact

In addition to cost-effectiveness, an estimate of the budget impact should be made to assess affordability. This involves estimating the current spending on the standard of care and calculating how much spending would change by introducing the new technology.

Estimating current spending is relatively simple- the size of the population that is currently receiving care is multiplied by the cost of standard treatment. This is compared against the costs of care following the introduction of the new technology. Given that the new technology may not replace the existing technology completely, the new cost of care has two components- the costs related to the proportion who still receive standard treatment and the costs related to those who shift to the new technology. In addition, the new technology may increase access, and so an adjustment must be made to include such patients.

This is a relatively simple approach and does not account for potential cost offsets because this data is usually not easily available. Cost offsets are costs avoided because of improvements in efficacy and/or safety, which offset a proportion of the additional cost of a new healthcare intervention.

There are several components necessary to estimate a simple analysis of the budget impact of adopting a new technology:

A. Number of eligible patients

B. Cost of standard treatment

C. Proportion of the population that will receive the new technology will be estimated using the HTAIn budget impact guideline.

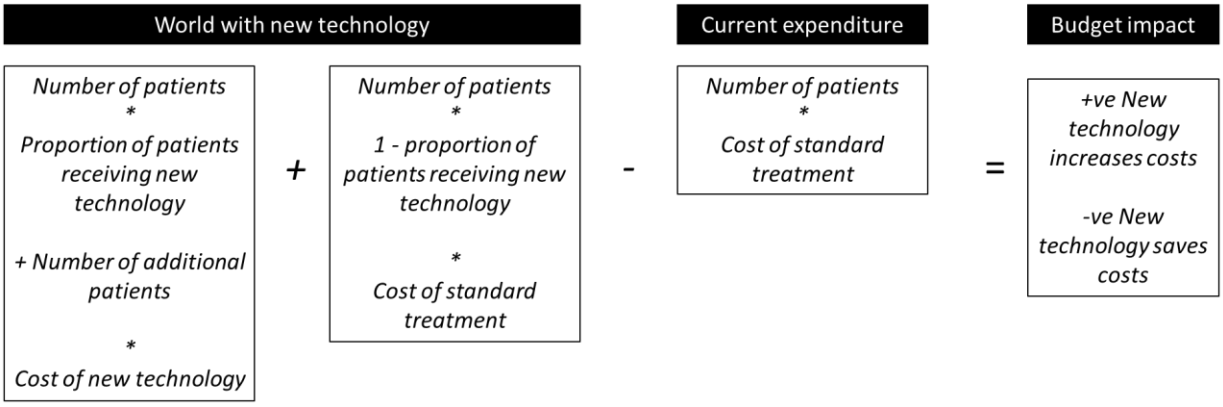
D. Number of additional patients that will receive the new technology (e.g., subgroup that could not access standard care but can receive the new treatment)

E. Cost of the new technology

The budget impact is then assessed using the formula, which is explained in Figure 6.1.

Budget impact = ((((A * C) + D) * E) + ((A * (1–C)) * B)) – (A*B)

Figure 6.1. Explanation of Budget Impact Formula



For example, suppose standard treatment is currently provided to 50,000 individuals and costs $1,000 per year. That would entail that current expenditure is $50 million.

Supposing the new treatment is expected to take 65 percent of the current market, be available to an additional 5,000 patients, and will cost $5,000 per year. Multiplying the size of the current population by 65 percent yields a total of 32,500 individuals. Adding 5,000 new patients raises this figure to 37,500 and multiplying the resulting number by $5,000 yields a total cost of $187.5 million introduced by the new treatment.

The size of the population that will continue to receive standard treatment is (50,000 x 0.35), or 17,500 individuals. Multiplying this figure by the annual cost of $1,000 yields total costs of $17.5 million. Together the total cost in a world with the new technology is $205 million. Subtracting the current expenditure of $50 million entails that there is a budget impact of $155 million for introducing the new technology in one year.

6.4.1 Budget Impact Summary

Budget impact is an important consideration that is related but distinct from cost-effectiveness. A valuable therapy on an individual basis may be nevertheless unaffordable when made available to a large population. The threshold of acceptance is dependent on what any given payer or health system feels that it can absorb. It is recommended that the following categorical conclusions be considered:

A. Absorbable budget impact given current estimates

B. Prioritisation of treatment or other managed access recommended

C. Significant budget impact challenge

As with cost-effectiveness, the purpose of this categorisation is to provide a summary judgment and indicate when policy actions may be necessary. Interventions rated as category "B" will require some sort of process to prioritise treatment for the sickest patients or those in most need. For category "C", it is likely that policy activity will have to involve entities outside the NHA (e.g., supplemental public health or other governmental funding).

6.5 Price Benchmarking

Price benchmarking uses a formula to convert the drug prices paid for the intervention from India and a benchmark country to determine how much more or less India is paying for the same drug relative to its GDP. Prices are adjusted for GDP per capita (GDPpc) to address different levels of affordability. The price in the HTA reference country, as a proportion of its GDPpc, is compared to the price in India, as a proportion of India's GDPpc. (The method for price benchmarking is taken from Ruth Lopert and colleagues' work.)

$$\frac{\text{Drug price in country}}{\dfrac{\text{Country GDP PC}}{\text{Benchmark country GDP PC}} \Big/ \text{Drug price in benchmark country Adjusted for currency}}$$

6.6 Interpreting uncertainty

Finally, a separate evaluation should be made of the key uncertainties presented by the available data. From a clinical perspective, challenges in study design and conduct, such as small sample size, use of surrogate endpoints with an uncertain relationship to key outcomes, short-term follow-up, and crossover trial design, may all contribute to uncertainty in assessment of the results and conclusions. Other concerns such as strong treatment effect observed in a placebo or standard care control group may limit understanding of the magnitude of benefit. From a cost-effectiveness standpoint, uncertainties may arise around the impact of drug prices, treatment effects, and other objectively defined parameters, and may also be manifested in assumptions required, such as the wraparound services required for a technology, subsequent treatment in the case of lack of efficacy or adverse events, extrapolation of clinical trial endpoints to longer-term outcomes, and the like.

Uncertainties may also arise from ICER adjustment. Cost offsets realised in the country of

origin may not be feasible in India due to differences in clinical practice, for example. An oncology product may be followed in sequence by another agent that is not available in India. Or the comparator's pricing may be different than expected. Such uncertainties should be noted in both general terms as well as in consideration of the adjusted ICERs.

Documentation should include a complete description of the uncertainties observed and their relation to the level of confidence in the conclusions, the need to monitor for new evidence and/or update the review in the short term, or other concerns.

6.7 Case study

Clinical synthesis: *Clinical effectiveness was anchored to the MONALEESA-2 trial evidence for the scoped population (postmenopausal HR+/HER2− metastatic breast cancer). The trial evidence showed improved clinical outcomes with ribociclib plus letrozole compared with endocrine therapy alone, and this was summarised in the report as the key clinical benefit signal. Safety/harms were noted based on the trial and HTA summaries, with an explicit statement that conclusions on value for money depend mainly on costs and prices rather than uncertainty about clinical benefit.*

Economic adaptation: *The complex adjustment method was applied. Costs from each included economic evaluation were converted using PPP and inflated using India's health CPI to a common reference year (2023), then used to compute India-adjusted incremental cost, incremental QALY, and ICER.*

Benchmark/threshold: *India's 2023 one GDP per capita benchmark of ₹205,249 per QALY was used for interpretation.*

Key assumptions: *Transferability of relative clinical benefits from international evidence; adjustment of costs across settings and years through PPP and inflation; effectiveness alignment through life-expectancy adjustment where required; interpretation focused on threshold-relative conclusions.*

Uncertainty approach: *Uncertainty was handled through explicit documentation of transferability limits and identification of key cost-effectiveness drivers; results were interpreted as ranges across studies rather than a single pooled estimate.*

Output: *India-context results: Adjusted ICERs consistently exceeded the benchmark, with values spanning multiple-fold above one GDP per capita. One HTA report and one economic evaluation reported insufficient evidence to draw definitive conclusions, and these were flagged accordingly. A summary table in the report presented both reported and India-adjusted ICERs.*

Key uncertainty drivers: Drug price in India and cost assumptions were identified as the dominant drivers of the adapted ICERs; evidence limitations in some sources contributed additional uncertainty.

Escalation check: Studies with insufficient evidence were marked as "not decision-conclusive" within aHTA; escalation to full HTA was considered appropriate if decision-making required higher certainty or if conclusions fell near the benchmark threshold.

7. Evidence summary and reporting

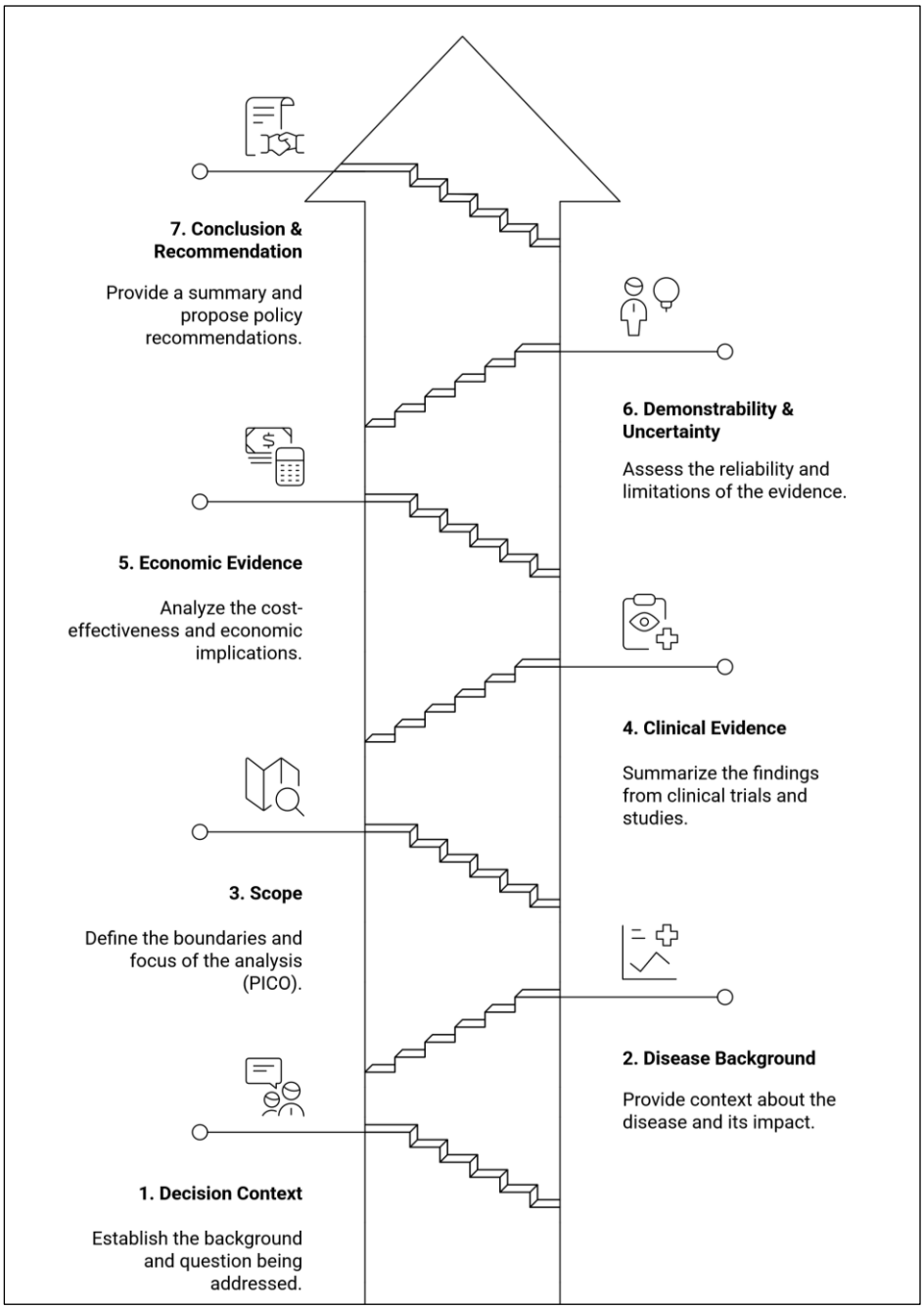
Following synthesis and adjustment of clinical and cost-effectiveness evidence, an integrated summary should be prepared that describes the major conclusions of the analyses, the recommendation to the independent committee that will deliberate on the topic, and a detailed description of the rationale for the recommendation.

7.1 Standard policy brief/report structure

AHTA outputs should be presented in as a report and a standardised policy brief that is concise, decision-oriented, and aligned with HTAIn reporting practices. The purpose of standardisation is to ensure that decisions are made consistently in the similar way across all decision problems and decision makers can quickly identify the decision question, understand the evidence base, interpret value and uncertainty, and see the recommended next steps without navigating extensive technical detail.

To balance speed with transparency, detailed methods, search strategies, data extraction tables, and calculations should be placed in appendices, while the main document focuses on synthesis, results, uncertainty analysis and interpretation.

Each aHTA policy brief/report should follow a fixed structure and include the following core sections:



7.2 Evidence summary tables

Evidence summary tables are used to present the key findings of the aHTA in a clear and structured format that supports rapid interpretation by decision-makers. These tables synthesise the main clinical and economic results from the identified studies while highlighting the relevance of the evidence to the Indian context and the main sources of uncertainty.

Clinical evidence summary table: This table summarises the main characteristics and outcomes of the clinical evidence informing the intervention. Key elements include the study or trial name, population characteristics, intervention and comparator, primary clinical outcomes (e.g., survival or disease progression), and a brief note on the certainty or strength of the evidence. The aim is to provide a concise overview of the clinical benefit and potential harms associated with the technology.

Economic evidence summary table: This table presents the main features and results of the economic evaluations identified during the search. It generally includes the country or setting, analytical perspective, model type, time horizon, reported incremental costs and outcomes, the original ICER, and the cost-effectiveness threshold used in the source study. This allows comparison of economic findings across different settings.

Adjusted ICER results table: This table presents the India-adjusted results derived from the economic evidence. It typically includes the study source, reported incremental costs and QALYs (or life-years), adjusted incremental costs and QALYs for India, the resulting adjusted ICER, and the benchmark used for interpretation (e.g., one GDP per capita). This table provides the final set of results used to assess whether the intervention represents value for money in the Indian context. Together, these tables provide a concise and transparent summary of the evidence base and form the primary inputs for the interpretation of results and the final recommendation in the aHTA report.

7.3 Summary Recommendation

The summary assessment of clinical benefit, cost-effectiveness, budget impact, and other considerations should take the form of a recommendation to the independent appraisal committee. Based on the ratings and categorisations described in the previous sections, the following four possible recommendations can be made:

- *Adopt:* The treatment should be adopted without limitation.
- *Adopt with limitations:* The treatment should be adopted, conditional on limiting activities such as price negotiation, prioritisation for a subset of candidate patients, or other limitation.
- *Do not adopt:* The treatment should not be adopted.
- *Further research required:* There are too many uncertainties regarding

implementation at this point, so the decision should be tabled until additional information is obtained or full HTA is commissioned.

7.4 Case study

Standard tables/figures used: The report used a fixed set of decision-oriented tables and summary elements to make findings easy to interpret:

Key study characteristics table summarising included sources by type (HTA reports vs economic evaluations), setting, perspective, cost year, comparator, outcomes reported, key drivers, data gaps, and confidence notes for each included source.

Main results table presenting reported ICERs and India-adjusted ICERs along with final conclusions.

The conclusion was written in a directional, conditional style rather than as an absolute statement, explicitly linking the recommendation to the evidence strength and key uncertainty drivers. The phrasing followed the pattern, "not cost-effective at current drug prices"

Condition/uncertainty note: *"Based on adapted ICERs from available international evidence; results are primarily price-driven; the probability of being cost effective at the current drug price and cost effectiveness threshold is very low/low/moderate/high"*

Output: *A complete policy brief/report package was finalised with version control, consisting of: (i) the decision question and scope, (ii) methods summary and evidence sources, (iii) evidence tables and adjusted ICER results, (iv) uncertainty and transferability statement, (v) recommendation category and conditions, and (vi) appendices (search strategy, extraction sheet, and calculation notes).*

8. Deliberation and recommendations

An important component of both full and adaptive HTA is deliberation by a technical appraisal committee independent of the HTA assessment team. Ideally, the makeup of this committee should represent the broader stakeholder community and include patients or patient advocates, clinicians, health-system representatives, technology manufacturers, and state and national health agency representation. Procedures should be in place to recuse individuals from discussing a topic in which they have a conflict of interest.

Independent deliberation ensures an impartial approach to decision making whilst basing the decisions on the best and most complete evidence available. While the deliberative process varies by setting, guidance has recently been developed around the structure and the conduct of HTA deliberation. This includes a checklist for the major considerations to keep in mind while developing a deliberative process. The details of deliberation are outside the scope of this manual, but the checklist has been included in an appendix as a resource.

8.1 Stakeholder Input

A key component of any HTA deliberation is a formal process by which stakeholders can provide input into the conduct of an appraisal, the discussion of the results, and the decisions made. These processes should be well-documented and clear so that any stakeholder knows of the opportunities to participate and how to participate in them. Stakeholders for aHTA reviews may include individual patients and patient advocacy groups, individual clinicians and clinical societies, and industry and health-system representatives.

Regardless of the opportunities considered for stakeholder process, it will be important to document the approach to be taken, provide links to submission forms and other resources, and make contacts available to stakeholders for assistance in navigating the process.

8.2 Public Posting

It is recommended that the aHTA process be as transparent at possible. All work products as well as transcripts of discussions and the recommendations made should be posted publicly and be freely accessible. This should include, but should not necessarily be limited to the following:

- Project scope
- Draft and final report
- Any technical appendices, including all calculations made to adjust for Indian context
- Report recommendations
- Written comments and transcripts of oral comments from stakeholders
- Committee decision and rationale

8.3 Case study

Main decision considerations-

Value for money: India-adjusted ICERs from multiple sources were well above the India benchmark, indicating poor value at current prices.

Feasibility: The intervention is clinically implementable, but financial feasibility under existing packages was the limiting factor.

Equity/access signals: Potential risk that adoption could widen access gaps if only patients able to pay out-of-pocket could benefit, while public coverage remains constrained.

Uncertainty: Some sources had insufficient evidence; overall conclusions were primarily price-driven rather than driven by uncertainty in clinical benefit.

Final recommendation category and conditions: *Do not adopt under existing health benefit packages at current Indian prices. Reassessment is recommended if lower-priced alternatives become available (e.g., biosimilars/generics) or if material price reductions occur; if such changes arise, a rapid reassessment should be undertaken before reconsideration for inclusion.*

9. Implementation, monitoring, and updating

The value of an aHTA lies in its ability to translate evidence into clear, actionable inputs for decision-making. AHTA outputs should therefore be explicitly mapped to the decision pathway they are intended to inform, with clear statements on how the findings are to be used, by whom, and within what timeframe. This linkage ensures that rapid assessments do not remain standalone technical documents but are integrated into existing policy, guideline, and procurement processes.

For HBP updates and programme decisions, aHTA outputs should inform whether an intervention warrants consideration for inclusion, exclusion, or conditional inclusion, and whether escalation to full HTA is required. For clinical guideline updates, aHTA reports should provide structured summaries of benefits, harms, economic signals, and uncertainty to support recommendation, subgroup restrictions, or deferral decisions. For pricing and procurement, aHTA outputs should present negotiation-relevant information such as price value or price budget impact scenarios, while clearly stating assumptions and limits of transferability. In all cases, recommendations should specify next actions and any conditions attached to use.

9.1 Key performance indicators (KPIs)

KPIs are required to monitor whether the aHTA process is delivering timely, consistent, and decision-relevant outputs, and to support continuous improvement. KPIs should be defined at programme level and reviewed periodically by the Secretariat and the Core Committee.

Timelines: Standard turnaround times should be specified for each stage (topic acceptance to final recommendation). Delays and their causes should be documented to inform process refinements.

Completion and escalation rates: Programmes should track the proportion of topics completed within timelines, the share concluded through aHTA, and the proportion escalated to full HTA or issued as conditional recommendations. These indicators help assess whether topic selection and feasibility screening are functioning as intended.

Update triggers: Pre-defined triggers should be recorded at the time of recommendation, such as significant price changes, entry of generics or biosimilars, publication of new pivotal evidence, changes in standard of care, or substantial deviations in utilisation or budget

impact. Triggers should specify the type of update required.

Post-decision review plan: Where feasible, aHTA outputs should be linked to a light post-decision review plan, outlining what indicators will be monitored and when reassessment is expected. This will ensure that rapid decisions remain responsive to new evidence and system changes.

9.2 Post-implementation review and evidence update cycle

Post-implementation review ensures that aHTA-informed decisions remain appropriate as evidence, prices, and practice evolve. Given the rapid and adaptive nature of aHTA, reassessment should be trigger-based rather than periodically by default, with clearly defined criteria recorded at the time of recommendation.

Rapid reassessment triggers should include price changes (including negotiated reductions or generics/biosimilars), publication of new pivotal clinical evidence or updated HTA conclusions, changes in standard of care or treatment sequencing that affect comparator relevance, and observed deviations in utilization or budget impact that materially differ from assumptions. When triggered, reassessment should follow a shortened pathway focused on the changed parameter(s) rather than repeating the full aHTA.

Reassessment outcomes should be limited to confirming the existing recommendation, revising conditions, or escalating to full HTA if uncertainty increases or conclusions approach the decision threshold. All updates should be documented with version control, and superseded recommendations should be clearly archived.

9.3 Annual methods update process

The aHTA methods manual should be treated as a living document that is periodically refined based on implementation experience, methodological advances, and stakeholder feedback. An annual update cycle provides a structured mechanism to incorporate learning while maintaining stability and consistency in ongoing assessments.

The update process will be coordinated by the HTAIn secretariat, with inputs from technical teams, clinical networks, health economists, and the other stakeholders. Proposed revisions may arise from recurring implementation challenges identified through KPIs and post-decision reviews, new methodological evidence on rapid reviews, economic adaptation, transferability, or uncertainty handling, feedback from users and decision-makers on clarity

and usability, and alignment needs with evolving national HTA practices or international standards. Revisions should focus on clarifying guidance, correcting identified weaknesses, strengthening safeguards, and standardising approaches that have proven feasible in practice.

All updates should follow a documented process, proposed changes are collated, reviewed for methodological validity and consistency with HTAIn processes, and approved through the designated governance mechanism. Each revised version should be clearly dated and versioned, with a shortchange log summarising what has been modified and why. This approach ensures transparency, supports institutional learning, and avoids ad hoc or inconsistent methodological changes.

10. Limitations and appropriate use of aHTA

10.1 Common pitfalls

Experience with aHTA highlights several recurring pitfalls that can undermine decision relevance if not explicitly identified and managed. Recognizing these risks early is essential to avoid over-interpretation of results and inappropriate recommendations.

Transferability failures occur when key elements of international evidence do not align with Indian context, such as differences in treatment pathways, baseline risk, access patterns, or cost structures. In particular, the absolute cost estimates and incremental costs are highly sensitive to local prices, utilization, and delivery models. Failure to clearly flag these differences can give a false sense of precision. AHTA outputs should therefore remain directional when transferability is limited and should trigger escalation to full HTA where results hinge on non-transferable assumptions.

Inappropriate comparator selection is a frequent source of bias. International studies may use comparators that are not relevant or widely used in India or may reflect outdated standards of care. AHTA should focus on studies with comparators that reflect current Indian practice and explicitly document the mismatch if there is anything and restrict conclusions accordingly or recommend full HTA.

Unstable or uncertain prices including ongoing negotiations, confidential discounts, anticipated generic or biosimilar entry, or state level price variation can substantially alter value-for-money conclusions. Recommendations should clearly state price conditions under which conclusions hold and define triggers for reassessment when prices change.

10.2 Good practice safeguards

To ensure that aHTA supports sound decision-making despite compressed timelines and reliance on transferred evidence, specific safeguards must be applied systematically throughout the assessment process. These safeguards are embedded at defined stages of the workflow and documented through standard forms and outputs within the aHTA report. Their purpose is to prevent over-interpretation, maintain methodological transparency, and ensure timely escalation to full HTA when required.

First, explicit escalation rules must be applied at predefined checkpoints, particularly during the pause point following evidence acquisition and preliminary appraisal. Escalation to full

HTA should occur when international evidence cannot be reliably transferred to the Indian context, when key parameters cannot be localised using credible data sources, or when adapted ICER estimates fall close to the decision threshold and conclusions are highly sensitive to reasonable changes in assumptions. The escalation decision, along with its rationale, must be formally documented as part of the study record.

Second, transparent documentation of assumptions and methodological choices must be maintained across all stages of the assessment. This includes recording the search strategy and evidence sources, justification for study inclusion or exclusion, ICER adjustment methods applied, and any limitations related to data availability. These elements are captured in the evidence extraction sheets, evidence summary tables, and methodological notes included in the final report.

Third, explicit reporting of uncertainty must accompany all adapted results. aHTA outputs should avoid presenting single point estimates as definitive conclusions when the evidence base contains important uncertainties. Key uncertainty drivers—such as intervention price, treatment duration, utilisation assumptions, or generalisability of outcomes—should be identified and reported in the evidence summary and deliberation sections. Where quantitative sensitivity analysis is not feasible, qualitative scenario descriptions or ranges should be provided to inform interpretation.

To operationalise these safeguards, Table 10.1 summarises where each safeguard is applied within the aHTA process and how it is documented.

Table 10.1 Operational safeguards in the aHTA process

Safeguard	Stage of aHTA process	How it is applied	Documentation/output
Transferability screening	Evidence acquisition and appraisal	Assess whether clinical pathways, comparators, and cost drivers are sufficiently similar to the Indian context	Transferability notes in evidence extraction sheet
Escalation to full HTA	Pause point after evidence appraisal	Triggered when transferability is weak, evidence is insufficient, or results are highly uncertain	Pause point decision record
Transparent documentation	Evidence searches and appraisal	Record search sources, study selection decisions, and adjustment methods used	Search log, extraction sheets, methodological notes
Uncertainty identification	Evidence synthesis and interpretation	Identify major drivers affecting ICER estimates and document variations across studies	Evidence summary tables
Conditional interpretation	Deliberation and recommendation	Frame conclusions as directional where uncertainty remains significant	Recommendation notes in final report
Reassessment triggers	Recommendation and reporting	Specify conditions under which the assessment should be revisited (e.g., price change, new evidence)	Final report and policy brief

11. Conclusion

The aHTA framework is intended to provide a structured, transparent, and pragmatic approach for generating timely evidence to support health policy and programme decisions. By systematically identifying and synthesizing available international clinical and economic evidence, the framework enables rapid assessment of the potential value, affordability, and policy relevance of new or existing health technologies. The results are presented in a clear and standardized format that facilitates informed deliberation by clinicians, policymakers, and programme managers, while maintaining transparency for broader stakeholders.

At the same time, the framework emphasizes careful consideration of transferability, as differences in interventions, prices, population characteristics, clinical pathways, healthcare delivery systems, and local standards of care can substantially influence the applicability of international evidence to the Indian context. Adapted estimates should therefore be interpreted with appropriate caution, particularly for technologies associated with high uncertainty, significant budget impact, or major contextual differences. In general, adaptive approaches may be most appropriate when existing international evidence is relatively consistent, when technologies are clearly cost-effective or cost-ineffective in relation to decision thresholds, and when the financial risks of incorrect decisions are modest. Conversely, technologies with high budgetary implications, substantial uncertainty, or strong dependence on local healthcare delivery contexts may require comprehensive HTA and additional local evidence generation.

Overall, the aHTA framework is designed to complement the existing HTA ecosystem in India by providing a practical method to rapidly screen and assess technologies where timely decisions are needed. When applied transparently and in coordination with HTAIn processes, it can help prioritize topics, support evidence-informed policy discussions, guide the selection of technologies requiring full HTA, and identify areas where further local data collection or comprehensive assessment is necessary.

Further Readings

General:

- "Adaptive Health Technology Assessment." Video. National Health Authority posted October 18, 2021. https://www.youtube.com/watch?v=oegIn_cWdmI.
- Alcaraz, A., V. Alfie, L. Gonzalez, S. Virgilio, S. Garcia-Marti, F. Augustovski, and A. Pichon-Riviere. "Evidence-Informed Update of Argentina's Health Benefit Package: Application of a Rapid Review Methodology." *International Journal of Technology Assessment in Health Care* 38, no 1 (2022): e24. https://doi.org/10.1017/S0266462322000034.
- Heupink, L.F., E.F. Peacocke, I. Saeterdal, L. Chola, and K. Frønsdal. "Considerations for Transferability of Health Technology Assessments: A Scoping Review of Tools, Methods, and Practices." *International Journal of Technology Assessment in Health Care* 38, no 1 (2022): E78. https://doi.org/10.1017/S026646232200321X.
- Nemzoff, C., A. Mehndiratta, P. Baker, and H.A. Shah. "Rapid Priority Setting in Low- and Middle-Income Countries." Blog post. Center for Global Development, April 26, 2021. https://www.cgdev.org/blog/rapid-priority-setting-low-and-middle-income-countries-potential-adaptive-health-technology.
- Teerawattananon, Y., C. Painter, S. Dabak, T. Ottersen, U. Gopinathan, L. Chola, K. Chalkidou, et al. "Avoiding Health Technology Assessment: A Global Survey of Reasons For Not Using Health Technology Assessment in Decision Making." *Cost Effectiveness and Resource Allocation* 19 (2021): 62. https://doi.org/10.1186/s12962-021-00308-1.
- WHO DECIDE Network Cost-Effectiveness Data Across Settings (CEDAS) Working Group. "Technical Document on Transferability of Cost-Effectiveness Methods and Evidence." Working draft. Accessed July 30, 2023. https://drive.google.com/file/d/1UWHHc_Ug8J3PJryEncp2CdcsijktoJa5/view.
- WHO, "HTA and Benefit Package Survey Summary 2020/2021." https://app.powerbi.com/view?r=eyJrIjoiYzMyZDY4NDEtY2VmOC00YjNhLTgzZWUtMDU0MTlhODNlZmMyIiwidCI6ImY2MTBjMGI3LWJkMjQtNGIzOS04MTBiLTNkYzI4MGFmYjU5MCIsImMiOjh9&pageName=ReportSection6010075c0d83085bc926

Country Specific:

- Canada: https://www.cadth.ca/about-cadth/what-we-do/products-services/rapid-response-service
- England/Wales: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation
- EUNetHTA adaptation toolkit- https://www.eunethta.eu/wp-content/uploads/2011/01/EUnetHTA_adptation_toolkit_2011_version_5.pdf
- Ireland: https://www.ncpe.ie/submission-process/process-flochart/

- Netherlands: https://www.zorginstituutnederland.nl/over-ons/werkwijzen-en-procedures/evaluatie-effecten-producten-zorginstituut
- Philippines: https://hta.doh.gov.ph/philippine-hta-methods-guide/
- Romania: https://media.hotnews.ro/media_server1/document-2012-03-15-11748944-0-raportul-institutului-nice-engleza.pdf
- South Africa: https://www.knowledgehub.org.za/system/files/elibdownloads/2021-07/3.%20HTA%20Methods%20Guide_draft_v1.2_14Jun21.pdf
- Thailand: https://www.hitap.net/en/documents/165667
- Tunisia: https://www.ineas.tn/sites/default/files//ineas.hta_.guide_etudes_pharmacoeconomiques.pdf
- United States: https://icer.org/our-approach/methods-process/

References

1. Ambade M, Sarwal R, Mor N, Kim R, Subramanian SV. Components of Out-of-Pocket Expenditure and Their Relative Contribution to Economic Burden of Diseases in India. JAMA Netw Open. 2022;5(5).
2. O'Rourke B, Oortwijn W, Schuller T. The New Definition of Health Technology Assessment: A Milestone in International Collaboration. Int J Technol Assess Health Care. 2020;36(3):188.
3. PBAC Outcomes [Internet]. Pharmaceutical Benefits Scheme, Australian Department of Health and Aged Care; 2023. Available from: https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes
4. CADTH [Internet]. Available from: https://www.cadth.ca
5. NICE [Internet]. Available from: https://www.nice.org.uk
6. Te Pātaka Whaioranga – Pharmac [Internet]. Available from: https://pharmac.govt.nz
7. HITAP [Internet]. Available from: https://www.hitap.net/en
8. INEAS [Internet]. Available from: https://www.ineas.tn
9. Jameleddine M, Grati H, Jebali MC, Kouki M, Gutierrez-Ibarluzea I, Toumi M, et al. Trastuzumab in the Treatment Of HER2-Positive Early And Locally Advanced Breast Cancer: The First HTA Report Of INEAS-Tunisia. Value Health. 2019;22(S3):S511.
10. Lopert R, Ruiz F, Chalkidou K. Applying Rapid 'De-facto' HTA in Resource-Limited Settings: Experience from Romania. Health Policy. 2013;112(3):202–8.
11. Ghosh S, Pramesh CS, Sengar M, Ranganathan P, Ruiz F, Wadasadawala T, et al. Exploring adaptive health technology assessment for evaluating 10 cancer interventions: insights and lessons from a pilot study in India. BMJ Evid-Based Med [Internet]. 2025 Jan 2 [cited 2025 Sept 14];bmjebm-2023-112490. Available from: https://ebm.bmj.com/lookup/doi/10.1136/bmjebm-2023-112490
12. Chauhan AS, Sharma D, Mehndiratta A, Gupta N, Garg B, Kumar AP, et al. Validating the rigour of adaptive methods of economic evaluation. BMJ Glob Health [Internet]. 2023 Sept [cited 2025 Sept 12];8(9):e012277. Available from: https://gh.bmj.com/lookup/doi/10.1136/bmjgh-2023-012277
13. Kar SS, Sivanantham P, Ravel V, Mehndiratta A, Tyagi K, Ollendorf DA. Cost-effectiveness of emicizumab prophylaxis for haemophilia A with inhibitors: an adaptive health technology assessment for the Indian setting. BMJ Evid-Based Med [Internet]. 2024 May 6 [cited 2025 Sept 14];bmjebm-2023-112492. Available from: https://ebm.bmj.com/lookup/doi/10.1136/bmjebm-2023-112492
14. Nemzoff C, Ruiz F, Chalkidou K, Mehndiratta A, Guinness L, Cluzeau F, et al. Adaptive Health Technology Assessment to Facilitate Priority Setting in Low- and Middle-Income Countries. BMJ Glob Health [Internet]. 2021;6(4):e004549. Available from: http://dx.doi.org/10.1136/bmjgh-2020-004549

Appendices

Appendix 1. Quality assessment check list

A quality assessment check list is used to assess the credibility and suitability of published economic evaluations considered for the ICER adaptation to the Indian context. This checklist is mandatory for all aHTAs that adapt or transfer ICERs from other settings. Each domain is rated as **Adequate, partially adequate** or **Inadequate** with brief justification. Overall confidence is derived qualitatively (High / Moderate / Low) and used to guide inclusion, weighting, or escalation.

No.	Criterion	Adequate	Partially adequate	Inadequate	Comments
	Section A. Decision problem and relevance				
A1	Decision problem clearly stated (population, intervention, comparator, outcome)				
A2	Comparator(s) clinically relevant and clearly justified				
A3	Intervention and comparator reflect current clinical practice in source setting				
A4	Study objective aligned with decision-making (not exploratory only)				
Section B. Clinical effectiveness and outcomes					
B1	Clinical effectiveness based on systematic evidence (RCTs/meta-analysis)				
B2	Relative treatment effects transparently reported				
B3	Outcomes relevant for HTA decision-making (e.g., survival, QALYs)				
B4	Quality-of-life measurement clearly described				
B5	Clinical uncertainty explored in sensitivity analysis				
Section C. Model structure and assumptions					
C1	Model type and structure clearly described and justified				
C2	Time horizon appropriate to disease and intervention				
C3	Health states and transitions clinically plausible				
C4	Key assumptions clearly stated and justified				
C5	Structural uncertainty discussed or tested				

Section D. Costing methods and resource use					
D1	Perspective clearly stated and appropriate				
D2	Cost components comprehensively identified				
D3	Unit costs and resource use separately reported				
D4	Price year and currency clearly specified				
D5	Cost drivers clearly identified				
Section E. Analysis and reporting of results					
E1	Incremental costs and effects reported				
E2	ICER clearly calculated and interpretable				
E3	Results consistent with methods described				
E4	Conclusions supported by results				
E1	Incremental costs and effects reported				
Section F. Uncertainty and sensitivity analysis					
F1	One-way sensitivity analysis conducted				
F2	Key drivers identifiable (e.g., tornado diagram or table)				
F3	PSA conducted				
F4	Parameter uncertainty clearly interpreted				
F5	Decision uncertainty acknowledged				
Section G. Transferability and adaptation relevance (aHTA-specific)					
G1	Clinical pathway broadly comparable to India				
G2	Cost drivers identifiable and adjustable				
G3	Results not dominated by non-transferable parameters				
G4	ICER not extremely sensitive to single unobservable parameter				
G5	Suitable for scenario-based adaptation				
Section H. Transparency, funding, and conflicts					
H1	Funding source disclosed				
H2	Conflicts of interest reported				
H3	Methods and data sources reproducible				
Overall confidence judgement					
	Overall confidence for ICER adaptation				**Tick one**
	High confidence	suitable as primary source for adapted ICER			☐
	Moderate confidence	suitable with caution and scenarios			☐
	Low confidence	not suitable for ICER adaptation			☐

Appendix II: PRISMA Flow chart