



MOH/P/PAK/297.15(GU)

**MaHTAS**  
Malaysian Health Technology Assessment Society



# HEALTH TECHNOLOGY ASSESSMENT MANUAL

## FOREWORD

### DIRECTOR GENERAL OF HEALTH MALAYSIA



In all countries, demand for healthcare exceeds the resources available to fund it. Rapid advancement of healthcare technologies such as drugs, biologics, devices, medical / surgical procedures and health programmes, while offering potential improvements in access and outcomes of healthcare services; bring great challenges to the means of priority setting, resource allocation, service delivery and patient care choices. We face with the need to choose between alternative interventions for a given disease, between treating a disease or preventing it in the first place, or between treating one disease as opposed to another. Such decisions require the interpretation of existing,

often incomplete evidence by different types of experts. Hence, the call for Health Technology Assessment (HTA) as a systematic, unbiased, and transparent method of assessing healthcare interventions, bridging the gap between evidence and rational decision making.

Health Technology Assessment is the systematic evaluation of properties, effects or other impacts of healthcare interventions. The main purpose of HTA is to provide input in the decision making about healthcare. In January 2014, the World Health Organisation (WHO) adopted the resolution on health intervention and technology assessment in support of universal health coverage. The Malaysian Health Technology Assessment Section (MaHTAS), Medical Development Division is recognised as the first HTA agency established in Asia in keeping with the Ministry's policy of ensuring that safe, effective and cost-effective health technologies are being used in Ministry of Health (MOH) facilities.

The impact of the assessments carried out by MaHTAS has been in various ways, like formulation of national and MOH policies, providing basis for Clinical Practice Guidelines (CPG) development and decisions for clinical practice, input into purchasing decisions, initiation of programmes and procedures. I am pleased that over the years, MaHTAS has grown and collaborated well with many HTA agencies. MaHTAS has been an active member to the HTAsiaLink, International Network for Agencies of HTA (INAHTA) and to a certain extent the Health Technology Assessment international (HTAi). With such long experience in conducting HTA, the development of this manual is very useful as a guide for healthcare providers in conducting assessment of health technologies.

I would like to congratulate MaHTAS and the Medical Development Division for their commitment in developing this manual. I sincerely hope that this HTA manual will further improve the quality of HTA work in Malaysia.

A handwritten signature in black ink, appearing to read 'Jheh', written in a cursive style.

**DATUK DR. NOOR HISHAM BIN ABDULLAH**  
Director General of Health, Malaysia

## **PREFACE**

This manual is the first manual relating to Health Technology Assessment (HTA) in Malaysia designed as a tool for HTA practitioners and use in teaching. This manual presents updated and new scientific methods and approaches to HTA. It deals with not only the context of HTA namely: safety, efficacy / effectiveness, economic, organizational, ethics, social, and legal aspects but also with the steps in the HTA process. Within the health system, the need for planning and decision-making based on evidence is increasing. For HTA practitioners, this means HTA results could be supplied within a relatively short production time – but without jeopardizing the quality. The formulation of this manual is intended to promote timely production and to further improve the quality of the HTA reports. This manual is aimed at anyone who takes part in planning and production of HTA reports and / or who seeks HTA to be carried out, namely health professionals, political and administrative decision-makers, interest groups, researchers and others who want to adopt an HTA approach.

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Special thanks are extended to the Heads of Units in MaHTAS; Dr Mohd. Aminuddin Mohd. Yusof (Head of CPG unit), Madam Noormah Mohd. Darus (Head of EBM, Research, Training & Economic Evaluation unit), Dr Izzuna Mudla Mohamed Ghazali (Head of Horizon Scanning, Communication & Information Unit) and Dr Roza Sarimin (Head of Monitoring and Implementation of Clinical Practices Guidelines (CPG) & Health Technology Assessment (HTA Unit) for their valuable input in the development of the manual.

We are also immensely grateful to Mr Beh Joo Sin, former research officer at MaHTAS for his contribution with regards to illustrations of the work process included in this manual.

Sincere appreciation is also extended to the members of Technical Advisory Committee for Health Technology Assessment for reviewing and providing constructive comments on the draft manual. Their vast experience and professionalism have facilitated the authors in developing this document.

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# 1. INTRODUCTION

## 1.1. Aim

This manual has been developed to provide guidance for Health Technology Assessment (HTA) practitioners and users on the work process and reporting of HTA.

## 1.2. HTA in general

Health Technology Assessment has been a concept in the field of healthcare since the 1980s, when one witnessed a rapid growth of new medical technologies in relation to limited health budgets.<sup>1</sup> HTA in an original form, was restricted to the assessment of new “technologies”. However, over the years, its focus has expanded to address questions from all levels of decision making in health care. Today, HTA is about assessing interventions on four levels: 1) the technology level (i.e., single drugs, devices, diagnostics etc.), 2) the individual/patient level (i.e., clinical interventions that aim to improve the health of individual patients), 3) the population level (i.e., public health interventions that aim to improve the health of the population, mainly through preventive measures), and 4) to a lesser extent, the policy level (i.e., the ways in which we organize, legislate and finance the health system). As such, it has become an integral part of knowledge chains that exist on each one.<sup>2</sup> In Malaysia, HTA unit was set up in August 1995 and expanded into a section in 2001.

### What is HTA?

Health Technology Assessment is the systematic evaluation of properties, effects or other impacts of health care interventions. The main purpose of HTA is to inform decision making in health care, including decisions made at the individual level, the level of the health care provider or institution, or the regional, national and international levels. HTA may address the direct and intended impacts or consequences of interventions, as well as their indirect and unintended ones. HTA is conducted by interdisciplinary groups using explicit analytical frameworks and drawing from a variety of methods.<sup>2,3</sup>

### Health technology

Health care technology refers to drugs, biologics, devices, equipment, supplies, medical and surgical procedures, programmes, support systems, and organizational and managerial systems.<sup>2</sup>

### What is HTA used for?

The main purpose of HTA is to inform technology-related policy making in health care. HTA contributes to answering questions from decision makers in areas and organizations related to health policy / or practice.<sup>3</sup>

- Primary purpose: to inform decisions relating to national, regional or local



health care systems. Such decisions may relate to the procurement, funding or appropriate use of health technologies

- Secondary purpose: to contribute to global knowledge on assessment of specific technologies – a library function. HTA provides source material for other research, guidelines etc.

### Who and what does HTA inform?<sup>3</sup>

HTA informs the following groups and individuals

**Government agencies, parliaments**

e.g. decisions on regulatory approval, reimbursement, public health programs

**Health care professionals**

e.g. decisions on adoption of technologies, practice guidelines

**Hospital and other health care administrators**

e.g. decisions on equipment procurement, availability of procedures, service delivery

**Private sector insurance**

e.g. decisions on scope and extent of coverage

**Manufacturing industry**

e.g. decisions on product development, marketing

**Patients, carers and their representatives**

e.g. decisions on guidance for treatment and support, access to services; shared decision making with health care professionals

**General public, citizens**

e.g. information for future decisions on health care

Those responsible for or associated with request for assessments are the primary targets and the main focus of HTA. However, the influence of HTA on secondary decision targets through provision of information will often also be important.

### 1.3. HTA and decision makers<sup>3</sup>

Decision makers who use HTA come from a variety of backgrounds.

- HTA will usually be one of several kinds of information used by decision makers.
- Decision makers in many bureaucracies are generalists, without technical expertise.
- There is often volatility in the staffing of policy areas, with short term appointments.
- Clinical groups and other target groups may have gaps in their knowledge of the assessment process and of government requirements.

#### Responsibility

Implicit in the HTA process is the interaction between assessors and decision makers. There are two sides to the contract, and both have responsibilities. Commonly, but not necessarily, the roles and responsibilities of the HTA agency and the decision maker will be separate, though there may be some areas of overlap.

#### HTA agency

An HTA agency should:

- Conduct data collection and analysis competently.
- Present findings clearly and transparently.
- Address the questions that have been asked, and avoid inclusion of non relevant material in its assessments.
- Ensure that assessors without detailed knowledge of clinical practicalities or other areas of expertise seek advice or guidance from appropriate sources.
- Respect the time frame negotiated with the decision makers and inform them of any significant changes and their impact on project implementation.
- Follow-up with decisions makers on the findings and conclusions that were reached in assessments.

#### Decision makers

Decision makers should:

- Make a commitment to the HTA process. They should see that they have an obligation to engage in the process. Requests for HTAs typically require commitment of public funds for the assessments and appropriate allocation of public funding in the areas on which the HTAs provided information.
- Have a clear intention to make use of HTA material when this has been prepared and delivered.
- Ensure that there is continuity of contact with HTA projects within the

decision making structure.

- Inform the HTA agency in a timely manner of any event likely to have an impact on the work in progress, and specifically on any need to adjust the approach or the established time frame.

### **Joint responsibilities**

- Both the HTA agency and the decision maker must be clear on what the question is and how it will be addressed.
- Each party should make efforts to understand the way in which the other works. Decision makers should have some understanding of the methodology and other aspects of the assessment process. HTA agencies should obtain some understanding of the policy making process.
- There should be regular, appropriate contact between the decision maker and assessor.

### **1.4. Types of HTA products**

The increasing demands by decision-makers for shorter production times for HTA reports during recent years have led to the development of different types of health technology assessments. The Quality Assurance Group of International Network of Agencies for Health Technology Assessment (INAHTA) has developed definitions for three types of health technology assessments: 1) HTA report, 2) Mini-HTA, and 3) Rapid Review. These three products types are the commonly produced by INAHTA member agencies.<sup>4</sup>

**Table 1. INAHTA Product Type (IPT) Classification<sup>4</sup>**

Product Type	Description
<b>HTA Report</b>	<ul style="list-style-type: none"> <li>✓ <i>Always:</i> <ul style="list-style-type: none"> <li>• describe the characteristics and current use of the technology</li> <li>• evaluate safety and effectiveness issues</li> <li>• determine the cost-effectiveness of the technology e.g. through economic modelling (when it is appropriate)</li> <li>• provide information on costs / financial impact, and</li> <li>• discuss organizational considerations.</li> </ul> </li> <li>✓ <i>Always</i> conduct a comprehensive systematic review* or a systematic review of high level evidence.</li> <li>✓ <i>Always</i> critically appraise the quality of the evidence base.</li> <li>✓ <i>Optionally</i> address ethical, social and legal considerations.</li> </ul>
<b>Mini-HTA</b>	<ul style="list-style-type: none"> <li>✓ <i>Always:</i> <ul style="list-style-type: none"> <li>• describe the characteristics and current use of the technology</li> <li>• evaluate safety and effectiveness issues, and</li> <li>• provide information on costs / financial impact.</li> </ul> </li> <li>✓ <i>Always</i> conduct a comprehensive systematic review* or a systematic review of high level evidence.</li> <li>✓ <i>Always</i> critically appraise the quality of the evidence base.</li> <li>✓ <i>Optionally</i> address organizational considerations.</li> </ul>
<b>Rapid Review</b>	<ul style="list-style-type: none"> <li>✓ <i>Always:</i> <ul style="list-style-type: none"> <li>• describe the characteristics and current use of the technology, and</li> <li>• evaluate safety and effectiveness issues</li> </ul> </li> <li>✓ <i>Often</i> conduct a review of only high level evidence or of recent evidence and may restrict the literature search to one or two databases.</li> <li>✓ <i>Optionally</i> critically appraise the quality of the evidence base.</li> <li>✓ <i>Optionally</i> provide information on costs/financial impact.</li> </ul>

Note:\* A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusions can be drawn and decisions made (Antman 1992, Oxman 1993)

### 1.5. MaHTAS HTA products

There are three types of reports produced by the Malaysian Health Technology Assessment Section (MaHTAS): 1) HTA report, 2) Technology Review (TR), and 3) Information Brief. Initially, from 1995 to 2000, HTA report was the only type of report produced by the HTA Unit. Increasing demands from the policy / decision

makers for shorter production times for HTA reports locally and internationally has led to the introduction and production of a short form of HTA, called TR (Mini-HTA) since 2001 and Information Brief (Rapid Review) since 2008.

**Issues for assessment are obtained in two ways:**

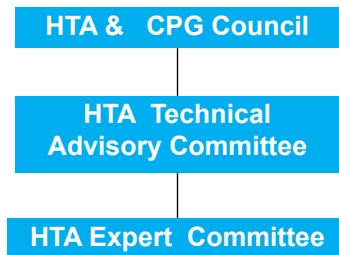
- i) Through letters send by MaHTAS every two years to policy makers and healthcare professionals requesting them to submit issues for assessment (potential HTA issues)
- ii) Received issues for assessment from policy makers or healthcare professionals at anytime throughout the year (ad hoc) via letters or using Request for Health Technology Assessment (HTA) Form which is also available online in the MOH website [potential TR (Mini-HTA) issues]

**Table 2. Short description of MaHTAS HTA products**

Product Type	Description
<b>HTA Report</b>	Characteristics: Based on complex problem or, for instance area of disease. May include alternative technologies. Evaluate safety, effectiveness issues, cost-effectiveness/financial impact, organizational considerations, may also address ethical, social and legal implications. Conduct systematic review.
	Aim: Input for policy / decisions at all levels. Decision can wait (to some extent) based on evidence.
	Time Frame: 8 to 18 months after approval by HTA & Clinical Practice Guidelines (CPG) Council.
	Quality Assurance: Expert committee and externally reviewed.
	Extent of report: Comprehensive report.
<b>TR Report (Mini-HTA)</b>	Characteristics: Based on problem which is of current interest. Reacting to an existing decision problem. Usually focused on one technology. Smaller scope of assessment (evaluate safety, effectiveness issues, cost/financial impact), may also address organizational considerations. Conduct systematic review.
	Aim: Input for policy / decisions at all levels within a short time frame.
	Time Frame: 2 to 4 months after request has been received.
	Quality Assurance: Reviewed by Head of MaHTAS, and may be externally reviewed.
	Extent of report: Less comprehensive report.
<b>Information Brief (Rapid Review)</b>	Characteristics: Based on problem which needs very rapid information response. Usually focused on one technology. Evaluate safety and effectiveness issues. Look for high level evidence or more recent evidence. May restrict the literature search to 1 or 2 databases.
	Aim: Input for decision within very short time frame at certain level (e.g. division / department).
	Time Frame: 2 weeks after request has been received.
	Quality Assurance: Reviewed by head of MaHTAS.
	Extent of report: 2 to 4 pages.

## 2. HTA ORGANIZATIONAL STRUCTURE

The organization structure involved in HTA is represented as follows:



### 2.1. HTA & CPG Council

The HTA & CPG Council chaired by the Director General of Health Malaysia, has representatives from the public, academic and private sectors. The representatives from the public sector include all the Deputy Director General of Health, Directors of Divisions, representative from the State Health Director, and representatives from the Head of Clinical Services in Ministry of Health (MOH). The academic sector has representatives from the Public Medical Faculties, while the private sector representatives include representative from the Association for Private Hospitals Malaysia (APHM), the Academy of Medicine, and the Malaysian Medical Association (MMA). The Council is responsible for approval of issues for the conduct of HTA and the final approval of the HTA report, so as to be adopted as national policy. The HTA & CPG Council is also responsible for the endorsement of the TR (Mini-HTA) report.

The members of the HTA & CPG Council are appointed every two years. The Terms of Reference (TOR) for the HTA & CPG Council is as follows:

- To identify issue and set priorities on technologies for assessment.
- To review and approve HTA reports.
- To review and approved evidence-based CPGs.
- To oversee dissemination and implementation of approved CPGs.
- To set direction on HTA activities.
- To advócate evidence-based health technology related policies.
- To set direction of horizon scanning activity and endore horizon scanning reports.

### 2.2. HTA Technical Advisory Committee

The HTA Technical Advisory Committee (TAC) chaired by the Director of the Medical Development Division, Ministry of Health has representatives from various divisions, research institute, and hospital in the MOH. It has also co-opted Head of Clinical Services in MOH to give technical input on the subject

matter related to the technology assessed. The HTA TAC is responsible for reviewing all HTA and TR (Mini-HTA) reports. If the reports are acceptable to the committee, it will be presented for final approval or endorsement by the Council. In the event that alterations or modifications or changes need to be made to the HTA or TR (Mini-HTA) reports, it would be the responsibility of the author / authors of the report to make the amendments. The HTA TAC is also responsible for prioritisation of HTA issues. The members of the HTA TAC are appointed every two years. The Terms of Reference (TOR) for the HTA TAC is as follows:

- To provide technical input on matters relating to HTA.
- To identify project priorities for the HTA.
- To review activities conducted by HTA Section, Ministry of Health.

### **2.3. HTA Expert Committee**

When a HTA issue has been selected, an expert committee will be set up specifically for the issue. The expert committee would essentially consist of multidisciplinary team involved in the use of the technology. It may also include patient representative. The expert committee is responsible for providing technical input on the subject matter related to the technology assessed. The Terms of Reference (TOR) for the HTA expert committee is as follows:

- To review the draft protocol for the HTA prepared by the authors.
- To provide technical input on the subject matter pertaining to the technology being assessed during the presentation of evidence by the authors.
- To provide input on the recommendation of the HTA report based on the available evidence.
- To review the draft report of the HTA that had been prepared by the authors.

The members of the expert committee will be provided training on the conduct of HTA. All the authors and expert committee of Health Technology Assessment (HTA) and authors of Technology Review (TR) are required to complete a declaration of competing interest detailing the sources of funding, and other possible conflicts of interest (Appendix 1). An explicit statement regarding the above is made in the HTA and TR reports.

### **2.4. Role of HTA Section (MaHTAS)**

The HTA Section (MaHTAS) is involved at all levels – the expert committee, Technical Advisory Committee, and the HTA & CPG Council. The actual assessments for HTA, TR (Mini-HTA) and Information Brief (Rapid Review) are to be carried out by personnel in the HTA Section.<sup>5</sup> The HTA Section (MaHTAS) is the secretariat to the HTA TAC and the HTA & CPG Council.



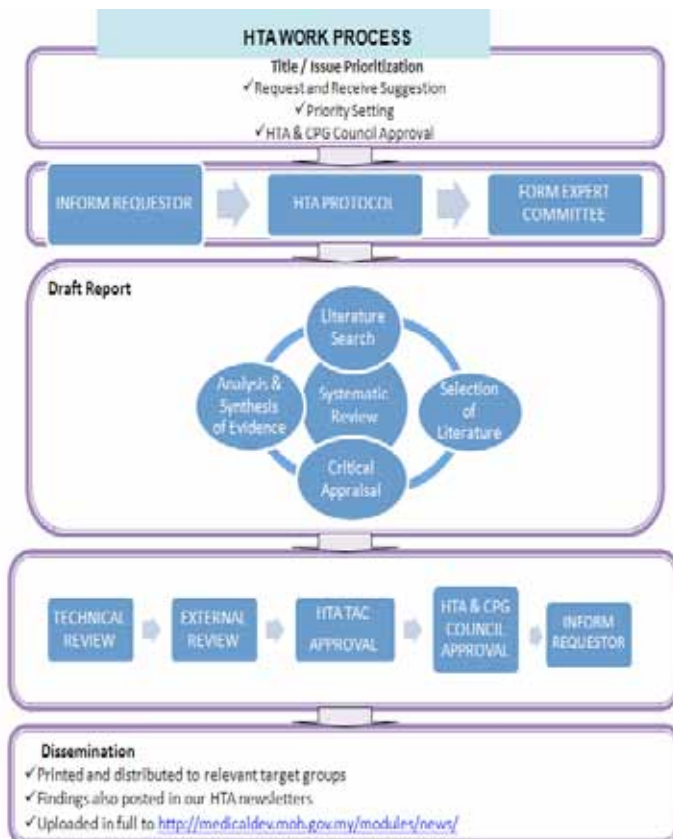
### 3. METHODOLOGIC FRAMEWORK FOR CONDUCTING HTA / TR (MINI-HTA) / INFORMATION BRIEF (RAPID REVIEW)

#### 3.1. Characteristics of HTA

It is now accepted that the characteristic of HTA are: a clear formulation of the problem, an explicit methodology, and a wide scope on the technology, i.e., not only dealing with safety or efficacy / effectiveness. Besides a systematic methodology, the strength of HTA relies on the transparency of the process and in the reporting, which improves the usefulness and generalisability of the findings.<sup>6</sup>

#### 3.2. HTA Work Process

The HTA work process is depicted schematically as shown below:



### 3.2.1. Request of HTA issues

A formal call for HTA issues would be sent out once in every two years to Programme Directors, Division Directors, State & Hospital Directors, Head of Clinical Services, and Head of Allied Health Profession in MOH requesting them and their staffs to submit request / suggestion on health technologies that they would like MaHTAS to conduct an assessment.

**MaHTAS do not accept request for the conduct of HTA from industries because the purpose of the report is for MOH consumption.**

**Request for HTA can be made:**

- i) Manually using **Request for Health Technology Assessment (HTA) Form (Appendix 2)**. This form can be obtained from URL <http://medicaldev.moh.gov/v2/iso/borang.html> or from MaHTAS
- ii) Online at MOH website (*Perhidmatan* Online) or URL [http://eservices.moh.gov.my/ubt/Apl/Permohonan\\_Penilaian.php](http://eservices.moh.gov.my/ubt/Apl/Permohonan_Penilaian.php)

**HTA can be requested for:**

- i) New Health Technologies which is defined as health technologies that have never been introduced in Ministry of Health Facilities and would have implication on national programme and policy
- ii) Existing Health Technologies where there are concerns about safety, efficacy or effectiveness, and economic implications

### 3.2.2. Prioritisation of HTA issues

The number of health technologies needing evaluation far outweighs available resources. Therefore, all HTA agencies must set priorities for their research projects.<sup>7</sup> Given very limited resources for assessment, hence, MaHTAS need to prioritise the issues for HTA. The steps involve in prioritisation of issues is as follows:<sup>8</sup>

- i) **Selection of criteria to be used in priority setting**  
Based on the examples of selection criteria that are used in setting assessment priorities by Goodman CS, the following criteria will be used by MaHTAS in considering issues for HTA:
- Effects on infrastructure and other services (include training, accreditation, education issues, resources, space)
  - Prevalence of disease (include disease burden, number of people affected)
  - Availability of competing technologies (other technologies currently available for the same purpose)
  - Possibility of changing health status (include significance of technology - efficacy / effectiveness, safety, and implication of introduction such as reduction in morbidity, mortality, early detection etc.)
  - Cost (include direct cost or cost-effectiveness, or other cost implication)
- ii) **Assigning relative weights to the criteria**  
Weights would be assigned to the criteria.
- iii) **Preliminary screening of issues**  
Preliminary screening of issues is to be conducted internally to determine its appropriateness for conducting HTA. Issues would be considered inappropriate if it falls into these categories: a) an established technology, b) issue is more appropriate for the conduct of primary research, and c) HTA or TR (Mini-HTA) report is already available.
- iv) **Preliminary search for scientific evidence**  
As soon as the issue is identified as a possible issue for HTA, it should be clarified whether there is sufficient existing knowledge in the area, and whether this knowledge is available. Hence, preliminary search for scientific evidence should be conducted to assist for rating according to the criteria.<sup>1</sup>

**The following information should be retrieved in the initial literature search:** description of the technology, effect of the technology on infrastructure, the number of people whom is applicable, the availability of competing technology, the significance of technology which may include its effectiveness and safety, the economic impact, level of usage and whether there are already HTAs or other types of reports available

nationally or internationally (Appendix 3). The following searches are recommended:

- HTA database
- INAHTA website
- Cochrane Library
- Medline
- EMBASE
- Pubmed

**v) Priority setting exercise**

The priority setting exercise is to be carried out by the HTA TAC committee using the Round Robin Technique. The format used for HTA Priority Setting Exercise is as in Appendix 4. For each issue, each member of the HTA expert committee would assign a score for each of the criteria. The priority score for each issue would then be calculated. The issues would then be rank according to their priority scores. The priority issues would be reviewed to ensure there are sufficient research findings available upon which to base the assessment, and that assessment of these issues would be consistent with the Malaysia Health Plan. Issues which have limited available evidence may be considered for Technology Review (Mini-HTA), instead of HTA.

**vi) Approval of issues for HTA**

Issues that have been prioritised would be presented in the HTA TAC meeting and the HTA & CPG Council for approval. Official feedback would be given to all HTA requestors after the HTA & CPG Council meeting.

**3.2.3. Specification of assessment problem**

One of the most important aspects of an HTA is to specify clearly the problem(s) or question(s) to be addressed; this will affect all subsequent aspects of the assessment. An assessment group should have an explicit understanding of the purpose of the assessment and who the intended users of the assessment are to be. This understanding might not be established at the outset of the assessment; it may take more probing, discussion and clarification with the requestor(s) and the expert committee. The intended users or target groups of an assessment should affect its content, presentation, and dissemination of results. There is no single correct way to state the assessment problem. The elements typically include specifying most or all of the following:<sup>8</sup>

- Health problem of interest
- Patient population (including subgroups as appropriate)
- Technology of interest
- Comparator(s)
- Setting of care
- Provider / clinician delivering the intervention(s)
- Properties, impacts, or outcomes
- Timeframe, duration, or follow-up period
- Study design or type of evidence / data to be included in the HTA
- Target audiences for the HTA findings

One commonly used framework is known as PICOTS (sometimes only PICO or PICOT): **P**opulation, **I**ntervention(s), **C**omparator(s), **O**utcome(s), **T**iming, and **S**tudy design.<sup>8</sup>

#### **i) Policy question<sup>6</sup>**

HTA is policy-driven research, aimed to support decision making. Ideally, the policy question should be worded with close cooperation between the requestor(s) and the assessment group (authors). The policy question reflects the context in which the assessment is carried out. This context is defined by the following aspects (Table 3). The scope of the assessment and its recommendations are determined by the policy question. Thus, the policy question should be clearly stated in the HTA protocol as well as in the technical report (i.e., the detailed document), and the executive summary of the report.<sup>6</sup> The questions listed in Table 3 should be answerable when reading any of these documents.

**Table 3. Aspects Included in the Policy Question<sup>6</sup>**

Question	Examples
Who initiated the report?	Policy makers Healthcare providers Third-party payers Patients' advocate
Who commissioned it?	
Why is an assessment needed right now?	New technology Changes in old technology New indication for old technology New findings Structural / organizational changes Safety concerns Ethical concerns Economic concerns
Which decision is it going to support?	Investment decision Market licensure Inclusion / exclusion from benefits catalogue Planning of capacities Guidance for best practice Investment in further research
Who represents the primary target audience for the report?	Political decision makers Third-party payers Hospital managers / administrators Clinicians Citizens / patients

**ii) Research Question(s)<sup>6</sup>**

Formulating the research question(s) means specifying the policy questions in terms of safety, efficacy, effectiveness, psychological, social, ethical, organizational, professional and economic aspects. The research questions have to specify the target group, the (disease) condition, and the aspects of the technology that are going to be assessed. The formulation of the research questions also implies defining the outcomes of interest for the assessment. Safety, efficacy, and effectiveness of an intervention should be always measured with health-related outcomes: these should be patient-related (e.g., quality of life, mortality, morbidity). Outcomes for assessment of psychological, social, and ethical considerations

are, for example, satisfaction or acceptance. Organizational and professional implications can be addressed with system-related outcomes, such as length of stay or required personnel. Finally, for the economic issues, costs and cost in relation to outcomes (cost-effectiveness, cost-utility, cost-benefit) are the main categories of interest. Table 4 provides examples of outcomes for the different aspects.

**Table 4. Examples of Outcomes for Different Aspects of HTA<sup>6</sup>**

Aspect of assessment	Outcomes
<b>Safety</b>	Mortality directly related to the use of the technology Morbidity/disability directly related to the use of technology
<b>Efficacy/ effectiveness</b>	Change in overall/condition-specific mortality Change in morbidity/disability/disease-free survival Change in quality of life Change in quality-/disability-adjusted life-years (QALYs /DALYs)
<b>Psychological/social/ ethical</b>	Compliance Acceptance Satisfaction Demand Preferences Information/patient advice requirements
<b>Organizational/ professional</b>	Utilization of service Change in treatment location Change in length of stay Change in required personnel, material inputs (e.g., hospital beds) and organizational structure Training requirements
<b>Economic</b>	Cost and changes in cost compared to current practice (if applicable) Cost-effectiveness, cost-utility, cost-benefit

The research questions drives how the rest of the assessment is going to be conducted, the aspects that will be evaluated, and those that will not. The inclusion and exclusion criteria for literature or other sources of data to be reviewed in the assessment also depend on the formulation of the research questions. The research questions need to be formulated in an understandable and answerable way, and should be limited in number.

**Characteristics of research questions include:**

- Clearly worded,
- Answerable,
- Limited in number,
- Address meaningful outcomes, and
- Address other relevant treatment alternatives.

**iii) HTA Protocol**

HTA protocol should be developed to define how the whole assessment is going to be carried out.<sup>6</sup> The HTA protocol will be developed by the reviewers from MaHTAS (authors of the HTA report).

**The content of the HTA protocol includes:** 1) Background information which describe the health problem, current service provision, description of technology under assessment, the requestor(s) and reasons for the request of the HTA, 2) Policy question, 3) Objectives and research question(s), 4) Methods of assessment including search strategy, inclusion and exclusion criteria, critical appraisal of literature, analysis and synthesis of evidence, 5) Report writing (Appendix 5).

Once the HTA protocol has been developed, the HTA protocol would be presented to the HTA expert committee for approval.

**3.2.4. Retrieval of evidence**

One of the great challenges in HTA is to assemble the evidence - the data, literature and other information that is relevant to a particular assessment, and to do so in a timely manner. For a new or emerging topic, this information may be sparse and difficult to find. For many topics, the evidence is readily available, yet profuse and widely varying in quality. Literature searching and related evidence retrieval are integral to successful HTA and the time and resources required for these activities should be carefully considered in planning any HTA.<sup>8</sup>

Searches for HTA and other evidence syntheses aim to be as comprehensive as possible in order to ensure that as many as possible of the relevant studies are identified and included in the synthesis. It is, however, necessary to strike the balance between striving for comprehensiveness and maintaining relevance when developing a search strategy. Increasing the comprehensiveness (or sensitivity) of a search will reduce its precision and will retrieve more non-relevant



articles. Where to search and how extensive the searches should depend on the research question or topic, product type, time frame of the work and resources that is available. Regardless of products, literature searches for evidence synthesis should consist of the following steps:<sup>9</sup>

- i) Structure the research question
- ii) Choose relevant databases / sources for the research question
- iii) Develop individual search strategies for the selected sources
- iv) Review the search results and possibly revise the search strategies
- v) Document and report the search process
- vi) Update the searches (as necessary)

**Two types of studies are used to answer the questions focused upon, namely secondary studies and primary studies:<sup>1</sup>**

- **Secondary studies** are systematic reviews and assessments of published material, e.g. HTA reports, clinical guidelines and systematic reviews.
- **Primary studies** are the individual scientific primary articles in the form of, for example, randomised controlled trials or cohort studies.

The first step in literature search is usually to identify the secondary literature.

### **Initial scoping searches<sup>9</sup>**

It is important to avoid duplication of work, and therefore one should start looking for relevant systematic reviews, HTAs or other evidence syntheses that can answer the specific research question of interest before starting to prepare a new one. Several databases and sources can be used for this purpose. Some examples are:

- Clinical evidence
- Cochrane Database of Systematic Reviews
- Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment Database (HTA)
- Turning Research in Practice (TRIP) database
- McMaster Plus
- NHS Evidence

In addition PROSPERO database can be searched for ongoing systematic reviews.

Reference lists in any relevant but outdated evidence syntheses should be browsed for relevant studies. Reported search strategies should be checked for useful search terms.

Scoping searches will also help to assess the size of the literature and provide advice on approaches, problems and strategies.

### Formulation of search protocol<sup>9</sup>

- **Formulation of a focused question**

A clearly defined and answerable question is the foundation of a good, systematic literature search. Constructing an effective combination of search terms involves breaking down the research questions into 'concepts'

Using the Population, Intervention, Comparator, and Outcome elements from PICO can help to structure the search.

<b>Population Patient problem</b>	<b>Intervention</b>	<b>Comparison</b>	<b>Outcome</b>
<i><b>Describe the group of patients / the problem</b></i>	<i>Which intervention is of interest?</i>	<i>What is the alternative to be compared with the intervention?</i>	<i>Which outcomes are important?</i>

An example: **Does honey help heal wounds?**

<b>Population Patient problem</b>	<b>Intervention</b>	<b>Comparison</b>	<b>Outcome</b>
<i><b>Wounds</b></i>	<i>Honey</i>	<i>No other treatment</i>  <i>Other treatment (for instance antibiotics)</i>	<i>The rate of healing</i> <i>Cicatrizacion</i> <i>Adverse events</i>

PICO is especially suitable for breaking down questions about effects of interventions. Other types of questions might need to be broken down into slightly different concepts. For instance, a diagnostic test accuracy review will typically focus on index test(s) under evaluation and the target condition(s) to be detected.

An example: **What is the diagnostic accuracy of immunochemical faecal occult blood test compared with chemical faecal occult blood test for colorectal cancer screening?**

<b>Target condition</b>	<b>Index test 1</b>	<b>Index test 2</b>	<b>Outcome</b>
<b><i>Colorectal cancer</i></b>	<i>Immunochemical faecal occult blood test</i>	<i>Chemical faecal occult blood test</i>	<i>Diagnostic accuracy</i>

- **Inclusion and exclusion criteria for the search<sup>9</sup>**

It is not always essential to search for every concept of PICO. For example it may be better not to use terms for the outcomes since inclusion might mean that the database being searched fails to show relevant studies simply because the outcome is not mentioned prominently enough in the record, even though the study measured it. It will often be appropriate to search only for the patient / population/problem and intervention.

For each of the elements used, it is important to consider all the possible alternative terms. Decisions about where and how to search could unintentionally introduce bias into the review, so one needs to consider, and try to minimise, the possible impact of search limitations. Searching sources that include grey literature and unpublished studies, such as records of ongoing research, conference, proceedings and theses, can reduce the impact of publication bias. Ideally, no language restrictions should be included in the search strategy. Limiting searches to English language papers can introduce language bias.

Date restrictions should be applied only if it is known that the relevant studies could have been reported during a specific time period, for example if the intervention was only available after a certain date.

- Choice of information sources<sup>9</sup>

What sources to search depends on several factors: type of evidence synthesis, type of question (effect of intervention, diagnostics, etc.), topic of interest and in some cases time limit. Type of question, study design and choice of sources are closely related.

### **Bibliographic databases<sup>9</sup>**

A bibliographic database includes information about journal articles, reports, books, book chapters, etc. Databases differ with respect to journals covered, types of articles included, language, etc. Examples of electronic bibliographic databases:

- ✓ MEDLINE
- ✓ EMBASE
- ✓ PubMed
- ✓ EBM Reviews: Cochrane Central Register of Controlled Trials
- ✓ EBM Reviews: Cochrane Database of Systematic Reviews
- ✓ EBM Reviews: Database of Abstracts of Reviews of Effects (DARE)
- ✓ EBM Reviews: Health Technology Assessment Database (HTA)
- ✓ EBM reviews: NHS Economic Evaluation Database
- ✓ JAMA Network
- ✓ Informa Healthcare
- ✓ Adis International
- ✓ Cumulative Index to Nursing and Allied Health (CINAHL)
- ✓ Alternative and complementary medicine: MANTIS
- ✓ Mental Health: PsycINFO
- ✓ Physiotherapy Evidence Evaluations Database (PEDro)
- ✓ Health Economic Evaluations Database (HEED)

It is often difficult and time consuming to find 'grey literature', but there are databases that record 'grey material', such as OALster and BIOSIS (for conference proceedings).

### **Other Sources**

- ✓ Clinical trials registry
- ✓ Handsearching is an important way of identifying very recent publications that have not yet been included by electronic databases or of including articles from journals that are not indexed by electronic databases

- ✓ Browsing the reference lists of included studies and other key articles should be considered in order to identify further studies of interest

### **Developing search strategies<sup>9</sup>**

- **Search terms**

Try to find synonyms to describe the selected key concepts of the questions. Both text words and subject headings should be used.

- ✓ Text words are words that appear in title and /or abstract of the record. Searching for synonyms (pressure sore; debubitus ulcer), related terms (head; brain), variant spelling (tumor; tumour) and plurals (injury; injuries) will increase the sensitivity of the search.
- ✓ Subject headings in a database are standardized subject terms assigned by indexers that describe the content of the document. Many databases have their own system of subject headings, thesaurus, usually organised in a tree structure from broad terms down to increasingly specific terms. The controlled vocabulary system for PubMed / MEDLINE is called MeSH, which stands for Medical Subject Headings. MeSH is also used in some other databases, like the Cochrane Library and Ovid EBM Reviews. EMBASE uses another system where subject headings system called Thesaurus of Psychological Index terms. Many database interfaces (e.g. Ovid and PubMed) will suggest subject headings that match the search terms. This is also called mapping. Before using the subject heading, it is advisable to take a look at the scope note containing the definition of the subject heading. In the scope note there are many synonyms and related terms that may be used as text words.

Because subject headings differ from database to database, individual search strategies should be developed for selected databases. It is advisable to check all databases for relevant search terms (text words and subject headings) before running any searches. Even though subject headings differ, text word searches in the different databases should be identical.

The following table can be used for the purpose:

	Subject headings in database 1	Subject headings in database 2	Text words	Comments on choices made
P				
I				
C				
O				

- **Search techniques**

- ✓ ***Exploding a subject heading***

A subject heading can consist of several subordinate and more specific terms. If the “explode” function (offered in many interfaces for databases with subjects headings) is chosen, all the subordinate terms are also being search.

- ✓ ***Truncation / wildcards***

Use truncation symbols and wildcards to search for variant forms and words

Truncation: protect\* for protect, protects, protective, protection etc.

Wildcards: wom#n for woman, women

Tumo?r or tumor, tumour

- ✓ ***Proximity operators***

ADJ = Two search terms next to each other, in the given order

ADJ1 = Two search terms next to each other, in any order

ADJ2 = Two search terms within one word from each other, in any order

ADJ3 = Two search terms within two words from each other, in any order etc.

For example:

(hip adj3 replacement\*) for hip replacement(s), hip joint replacement(s), hip and knee replacement(s) etc.

- ✓ ***Phrase searching***

Phrase searching can be done by placing the entire phrase in quotation marks. This technique can be used to search for strings including special characters, numbers, stopwords etc.

✓ **Boolean operators (AND, OR, NOT)**

This is the usual method for combining search terms (both subject headings and text words)

**Search filters<sup>9</sup>**

Search filters are search strategies that are designed to retrieve specific types of records, such as those of particular methodological design. They are composed of a set of search terms based on subject headings, publication types, etc. that describe e.g. a study design. A search filter is combined with the subject search and limits the search to a specific study design.

Search filters focus on:

- ✓ Sensitivity (the proportion of relevant articles that are retrieved)
- ✓ or precision (the proportion of retrieved articles that are relevant)
- ✓ or specificity (the proportion of non-relevant articles that are not retrieved)
- ✓ or a 'best compromise' solution

There is usually a trade-off between sensitivity and specificity. When an attempt is made to maximise one (e.g. sensitivity or specificity) the other operating characteristic suffers.

Search filters should be used with caution. Searching for specific study designs can be problematic due to inconsistencies in reporting by study authors and in the indexing process.

**Evaluation of search strategies<sup>1</sup>**

Once a search has been completed, it is checked whether what one has been looking for has been found. Search strategy may need to be revised.

**Performing and saving searches<sup>9</sup>**

• **Ovid databases**

- ✓ Advanced Search option should be used to search for subject headings and text words, and to combine search lines using Boolean operators (AND, OR).
- ✓ To save search strategy:
  - Select "Save Search History" on the search history page
  - Type a search name in the text box
  - Choose the search type option "Permanent"
  - Click the 'Save' button
- ✓ Create a personnel account to access this feature.

- ✓ By selecting the “View saved” button on the Search History page, a person can:
  - Re-run saved search strategies
  - Edit or delete search lines, and insert new lines within the saved search strategy
  - Edit or delete search lines, and insert new lines within the saved strategy
  - Display the search strategy and copy / paste it to the review (HTA report)
- ✓ Search strategies can be copied from one database to another. This feature can be used to avoid retyping text words in different Ovid databases. Be aware that subject headings must be replaced to match the subject heading system of the selected database.
- **PubMed**
  - ✓ Use MeSH database to search for subject headings and Advanced Search option to search for text words. Advanced search can also be used to combine search lines using Boolean operators (AND, OR).
  - ✓ Create My NCBI account to save changes in PubMed. Saved searches cannot be edited in My NCBI.

## **Management of references<sup>9</sup>**

- **Reference management software**

Searching for documentation for the various products often results in a large amount of references. The best way to handle a large amount of references is to use a reference management programme. Using bibliographic software such as EndNote, Reference Manager or ProCite to record and manage references will help in documenting the process, streamline document management and make the production of reference lists for reports and journal papers easier. In MaHTAS, EndNote is used to manage references.

EndNote is a bibliographic software package which enables a person to create a personal database of references relevant to the person. It enables to:

- ✓ Import references from various databases into EndNote
- ✓ Remove duplicates (references that are found in more than one database, after all references are imported)
- ✓ Insert references from EndNote directly into Microsoft Word



document and automatically generate bibliographies in a variety of styles

- ✓ Categorize, group and annotate references

### **Obtaining full-text articles<sup>9</sup>**

A large proportion of articles are only available through journal subscriptions or direct purchases. However, others can be obtained without charge. Some examples of free-full text journal sources are:

- ✓ BioMed Central
- ✓ PubMed Central
- ✓ Free Medical Journals
- ✓ HighWire Press

Full text of potentially useful article selected from databases, hand searching and reference lists need to be obtained and appraised. This can be done with the help from information specialists or librarians.

### **Documenting and reporting the search process<sup>9</sup>**

The search process should be reported in sufficient detail so as that it could be-run at a later date. It is important to record all searches, including internet searches, handsearching and contacts with experts. Providing the full detail of searches enables readers to evaluate the thoroughness of searching. Each search conducted will have to be listed in a Search Strategy Table as shown in Appendix 6.

The write-up of the searches in the methods section of an HTA report or other evidence synthesis should include information about:

- ✓ PICO concepts that were searched for
- ✓ Databases and other sources searched
- ✓ Date of search
- ✓ Limits applied
- ✓ Cross-reference to the full detailed search strategies

The complete search strategies for each database should be included in an appendix of the report (Appendix 7). The search strategies should be copied and pasted exactly as run, together with the search set numbers. They should not be re-typed as this can introduce errors.

### **Updating searches<sup>9</sup>**

Depending on the scope and timescale of the evidence synthesis, an update of the literature searches towards the end of the project may be required. If the initial searches were carried out some time before

the final analysis is undertaken (e.g. six months) it may be necessary to re-run the searches to ensure that no recent papers are missed.

### 3.2.5. Selection of literature<sup>6</sup>

The selection of the literature that will be definitely included to answer the research questions is a process with consecutive steps to be taken, as summarised in Figure 1. With a systematic literature search, a big number of hits will be obtained. Applying selection criteria (inclusion and exclusion criteria) to the titles and abstracts of articles, these will be separated into relevant and not relevant. The first selection refers to the relevance than to quality of studies. Studies considered to be relevant will be retrieved in full text. Inclusion and exclusion criteria should be defined for all kinds of evidence, rather than only for the literature of efficacy and effectiveness. Selection criteria should be developed in a prospective way to avoid bias when selecting the evidence. Inclusion and exclusion criteria flow from the background information, the research questions, and the availability of evidence. The criteria refer to, for example, patients being treated, outcomes being measured, and aspects of technology being studied. Selection criteria also may refer to study design or other methodology issues. Those criteria may differ for each of the aspects being assessed. The inclusion and exclusion criteria must be documented in the technical report. Every effort should be made to include relevant evidence independent of the language available. This means that language should be used very cautiously as a selection criterion.

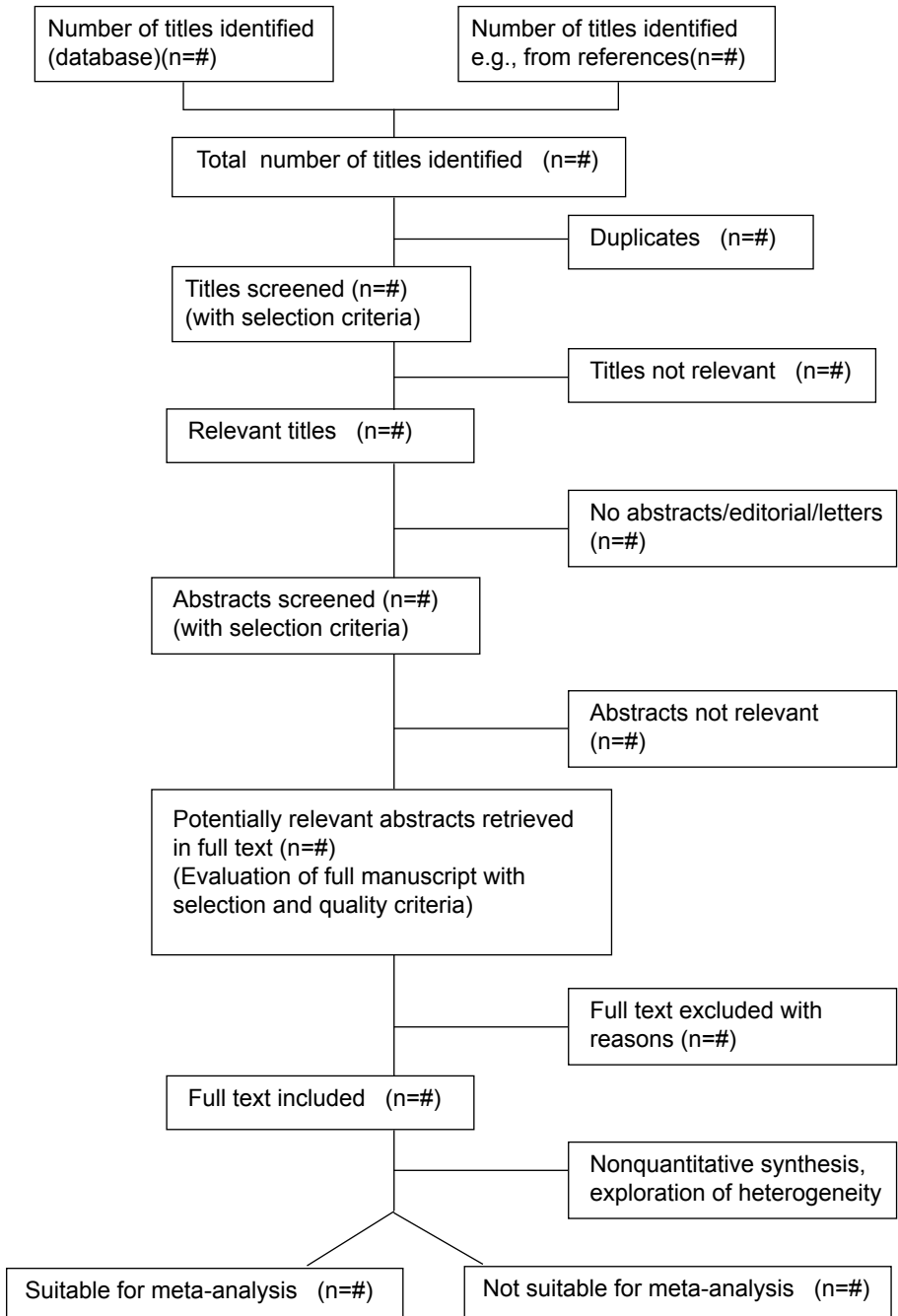
#### **Issues addressed in inclusion and exclusion criteria may include:**

- Population (patient characteristic, condition characteristics),
- Intervention,
- Comparators,
- Outcomes measured,
- Study design, and
- Language

It is recommended that two independent reviewers select the literature to be included; however, this may not always be possible. Based on the inclusion and exclusion criteria, ideally study selection will be carried out independently by two reviewers. The titles and abstracts of all studies will be assessed for the eligibility criteria. If it is absolutely clear from the title and / or abstract that the study is not relevant, it will be excluded. If it is unclear from the title and / or abstract whether the study is relevant or not, full text article will be retrieved together with those having relevant title and abstract.

Ideally, the contents of the full text article will be assessed by two reviewers. Any disagreement should be resolved by discussion. At this point, some studies will be excluded because they are not actually deemed relevant to the research questions, even though they were identified as relevant when the abstract was read. The quality and relevance of all full text articles need to be critically appraised. Studies originally retrieved that do not fulfil the quality criteria will be excluded. Documentation of excluded studies should be provided, along with reasons for exclusions.

**Figure 1. Flow chart of study selection**



### 3.2.6. Critical appraisal of literature

All literature that has been obtained has to be critically appraised. Ideally the critical appraisal should be conducted by two reviewers independently. Appraisal of the validity of the available material is an important component of the HTA.

#### **Assessing the Quality of Primary Data Studies**

Whether the studies are experimental or non-experimental in design, studies varies in their ability to produce valid findings. Validity refers to how well a study or data collection instrument measures what it is intended to measure. **Internal validity** refers to the extent to which the results of a study accurately represent the causal relationship between an intervention and the outcome in the particular circumstances of that study. This includes the extent to which the design and conduct of a study minimise the risk of any systematic (non-random) error (i.e., bias) in the study results. **External validity** refers to the extent to which the results of a study conducted under particular circumstances can be generalised (or are applicable) to other circumstances.<sup>8</sup> Assessments of the internal validity are frequently referred to as ‘assessments of methodological quality’ or ‘quality assessment’. However, the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of studies that evaluates healthcare intervention and Cochrane Collaboration emphasise on the assessment of risk of bias, i.e. the risk that they will overestimate or underestimate the true intervention effect for evaluating each included study in a systematic review.<sup>10,11</sup> According to the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of studies that evaluates healthcare intervention it is important to distinguish between quality and risk of bias and to focus on evaluating and reporting the latter. Quality is often the best the authors have been able to do. For example, authors may report the results of surgical trials in which blinding of the outcome assessors was not part of the trial’s conduct. Even though this may have been the best methodology the researchers were able to do, there are still theoretical grounds for believing that the study was susceptible to (risk of) bias.<sup>10</sup> The risk of bias in the results of each study contributing to an estimate of effect is one of several factors that must be considered when judging the quality of a body of evidence.<sup>11</sup>

#### **Instruments for Assessing Quality of Individual Studies**

A variety of assessment instruments are available to assess the quality of individual studies. Many of these are for assessing internal validity or risk of bias for benefits and harms; others focus on assessing external validity.<sup>8</sup> There are three main ways to assess the risk of bias:

individual components, checklists and scales. There are many scales available, however, the PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of studies that evaluates healthcare intervention caution their used based on theoretical grounds and emerging empirical evidence. Checklists in which specific questions are asked are less commonly used.<sup>10</sup> The Critical Appraisal Skills Programme (CASP) checklist which consists of eight critical appraisal tools designed for Systematic Reviews (SR), Randomised Controlled Trials (RCT), Cohort Studies, Case Control Studies, Economic Evaluations, Diagnostic Studies, Qualitative Studies and Clinical Prediction Rule are one of the tools that are being used by MaHTAS. The checklists are divided into three parts with three broad issues which need to be considered: Section A) Are the results of the review/trial/study valid?, Section B) What are the results?, and Section C) Will the results help locally. The criteria assessed for internal validity in SR include selection of studies, assessment of quality of included studies, heterogeneity of included studies. For RCT, the criteria assess are randomisation, allocation concealment, blinding, explanation on loss to follow-up, and intention to treat analysis. For Cohort study, the criteria assess are selection of the cohort, accurate measurement of exposure and outcome, confounding factors, follow-up adequacy and length. For Case Control study, the criteria assess are selection of the cases and control, accurate measurement of exposure, and confounding factors. For diagnostic study the criteria assess are comparison with appropriate reference standard, all patients get the diagnostic test and reference standard, result of the test influenced by the result of the reference standard, disease status of population clearly described, and methods for performing the test described. For economic evaluation, the criteria assess include comprehensive description of competing alternatives, effectiveness established, effects of intervention identified, measured and valued appropriately, relevant resources and health outcome costs identified, measured in appropriate units and valued credibly, discounting, incremental analysis of the consequences and costs of alternative performed, and sensitivity analysis performed. The example of CASP checklist for RCT is as in Appendix 8.<sup>12</sup>

The Cochrane Collaboration's tool for assessing risk of bias of randomised controlled trial is an example of a component approach which can also be used by MaHTAS. It is a two-part tool, addressing the six specific domains (namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other issues). The tool is summarised in Table 5. Each

domain includes one or more specific entries in a 'Risk of bias' table. Within each entry, the first part of the tool involves describing what was reported to have happened in the study. The second part of the tool involved assigning a judgement relating to the risk of bias for that entry. This is achieved by answering a pre-specified question about the adequacy of the study in relation to the entry, such as judgement of 'Yes' indicates low risk of bias, 'No' indicates high risk of bias, and 'Unclear' indicates unclear or unknown risk of bias.<sup>11</sup>

**Table 5: The Cochrane Collaboration's tool for assessing risk of bias**

Domain	Support for judgement	Review authors' judgement
<b>Selection bias.</b>		
<b>Random sequence generation.</b>	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
<b>Allocation concealment.</b>	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
<b>Performance bias.</b>		
<b>Blinding of participants and personnel Assessments should be made for each main outcome (or class of outcomes).</b>	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
<b>Detection bias.</b>		
<b>Blinding of outcome assessment Assessments should be made for each main outcome (or class of outcomes).</b>	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
<b>Attrition bias.</b>		
<b>Incomplete outcome data Assessments should be made for each main outcome (or class of outcomes).</b>	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
<b>Reporting bias.</b>		
<b>Selective reporting.</b>	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
<b>Other bias.</b>		
<b>Other sources of bias.</b>	State any important concerns about bias not addressed in the other domains in the tool.  If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

QUADAS-2 is another example of a quality assessment tool for diagnostic accuracy studies.



## **Different Study Designs for Different Questions**

RCTs are not the best study design for answering all evidence questions of potential relevance to an HTA. Other study designs may be preferable for different questions. For example, the prognosis for a given disease or condition may be based on a follow-up studies of patient cohorts at uniform points in the clinical course of a disease. Case control studies, which are usually retrospective, are often used to identify factors for diseases, disorders and adverse events. The accuracy of a new diagnostic test (though not its ultimate effect on health outcomes) may be determined by a cross-over study in which patients suspected of having a disease or disorder receive both the new (“index”) test and the “gold standard” test. Non randomised trials or case series may be preferred for determining the effectiveness of interventions for otherwise fatal conditions, i.e., where little or nothing is to be gained by comparison to placebos or known ineffective treatments. Surveillance and registries are used to determine the incidence of rare or delayed adverse events that may be associated with an intervention. For incrementally modified technologies posing no known additional risk, registries may be appropriate for determining safety and effectiveness.<sup>8</sup>

### **3.2.7. Grading of evidence (Evidence hierarchies)**

All full text articles used for the assessment would need to be graded according to standard grading scales e.g. the U.S./Canadian Preventive Services Task Force for efficacy / effectiveness study (Appendix 9) or graded according to NHS Centre for Reviews and Dissemination (CRD) University of York, Report Number 4 (2<sup>nd</sup> Edition) for diagnostic accuracy study (Appendix 10). It is suggested that all reviewers use the same grading system.<sup>13,14</sup>

### **Working with Best Evidence**

In health care as well as other fields, there are tradeoffs between wanting to rely on the highest quality of evidence and the need to derive useful findings when the evidence of the highest quality is limited or unavailable. “Best evidence” is not based on a single evidence hierarchy and is not confined to internal validity. Even where traditional high-quality evidence with internal validity does exist (e.g., based on well-designed and conducted RCTs or meta-analysis of these), complementary evidence from other study designs (e.g., practical clinical trials, observational studies using registry data) may be needed to determine external validity. Where there is little or no high-quality evidence with internal validity, it may be necessary to pursue lower quality evidence for internal validity, such as non-randomised clinical trials, trials using historical controls, case series,

or various types of observational studies, while documenting potential forms of bias that might accompany such evidence.<sup>8</sup>

### **3.2.8. Analysis and synthesis of evidence<sup>6</sup>**

The next step to be taken is the extraction of the relevant data for the assessment from included studies and its synthesis in a way that allows comparison among studies. Data to be extracted are mainly determined by the research questions. It is strongly recommended that customized extraction sheets be used. As with the selection of studies, the process of data extraction should be done by more than one person; however, this is not always possible. The way the data were extracted need to be reported.<sup>6</sup>

#### **Data extraction strategy**

Data will be extracted from the included studies by a reviewer using a pre-designed data extraction form and checked by another reviewer. Disagreements will be resolved by discussion. Summary of the abstracted data is presented in evidence table (Appendix 11). Details on: (1) methods including study design, (2) study population characteristics, (3) type of intervention, (4) comparator(s), (5) outcome measures for safety, efficacy/effectiveness, economic, organizational, social, ethical, and medico-legal implications will be extracted. The extracted data will be presented and discussed with the expert committee. The evidence that has been obtained has to be analysed, addressing various aspects: safety, efficacy/effectiveness, cost implication, and organizational issues. For certain HTA topics, ethical, social, and medico- legal implications may have to be taken into consideration.

#### **Methods of data synthesis<sup>6</sup>**

Once the evidence has been gathered, it has to be synthesised either non-quantitative (qualitative) or quantitatively. The use of evidence tables to summarise study characteristics and study results is the best way to synthesise the evidence in a non-quantitative form (which always precedes a quantitative synthesis). In non-quantitative synthesis, consistency of results throughout studies or heterogeneity among studies (e.g., differences among patients or relevant details of intervention) can be explored. Furthermore, lack of valid or relevant evidence can also be identified. In the non-quantitative synthesis of information, explicit criteria for validity and quality of the studies have to be followed. Thus, the non-quantitative synthesis is closely related to the appraisal process. In non-quantitative synthesis data will be presented in tabulated format with narrative summaries.

The decision as to whether a quantitative synthesis can be performed, and if so, which result can be pooled into what comparisons, will be made from the results of non-quantitative summary of the available evidence. If significant heterogeneity among studies or lack of validity of results identified, a quantitative synthesis may not be indicated. There are different methods for performing a quantitative synthesis for HTA. However, the most extended one is the used of meta-analysis.<sup>6</sup>

Meta-analysis refers to a group of statistical methods for combining (or “pooling”) the data or results of multiple studies to obtain a quantitative estimate of the overall effect of a particular technology (or other variable) on a defined outcome. The combination may produce a stronger conclusion than can be provided by any individual study. Meta-analysis typically is used for topics that have no definitive studies, including topics for which non-definitive studies are in some disagreement. Evidence collected for HTA often includes studies with insufficient statistical power (e.g., because of small sample size) to detect any true treatment effects. By combining the results, a meta-analysis may have sufficient statistical power to detect a true treatment effect if one exists, or at least narrow the confidence interval around the mean treatment effect.<sup>8</sup>

Table 6 gives an overview of the factors that should be taken into consideration when choosing a method of meta-analysis.<sup>6</sup>

**Table 6. Factors to Consider When Using Quantitative Synthesis (Meta-analysis)**

<p>Why does the meta-analysis approach seem possible and appropriate?</p> <p>Which studies are being included in meta-analysis and why?</p> <p>Which comparisons are going to be made and why?</p> <p>Which outcome measures are chosen and why?</p> <p>Which summary statistics (OR, RR, WMD) are chosen and why?</p> <ul style="list-style-type: none"><li>• Type of data (e.g., binary, continuous)</li><li>• Consistency of treatment effects across trials</li><li>• Ease/plausibility of interpretation of summary estimate</li></ul> <p>Which weighting method is used?</p> <ul style="list-style-type: none"><li>• Reliability when sample sizes are small</li><li>• Reliability when events are rare</li><li>• Degree of imbalance in allocation ratios among groups</li></ul> <p>Is heterogeneity explored? Possibilities to consider heterogeneity:</p> <ul style="list-style-type: none"><li>• Meaning of a meta-analysis depending on degree of disagreement between studies</li><li>• Use of random effects model</li><li>• Accounting for variations in treatment effects (e.g., meta-regression, stratified analysis)</li></ul> <p>Is the presence and possible effect of publication bias taken into account?</p> <p>Is a sensitivity analysis carried out?</p>
----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

In addition to assessing the problem of publication bias, robustness of results of a meta-analysis should be tested. This is done through sensitivity analysis, which enables an assessment of how sensitive results are to changes in included studies (e.g., studies of lower quality or studies suspect of double publication) or in statistical methods of synthesis (random effect model, fixed effects model).<sup>6</sup>

### **Assessing the Quality of a Body of Evidence**

There is a need to assess the quality (or strength) of cumulative body of evidence. Systematic reviews assemble bodies of evidence pertaining to particular evidence questions. Although each body of evidence may comprise studies of one type, e.g., RCTs, they may also comprise studies of multiple designs. Many approaches have been used to assess the quality of a body of evidence since the 1970s. In recent years, there has been some convergence in these approaches, including by such organizations as the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group (Balshem 2011), the Cochrane Collaboration (Higgins 2011), the US Agency for Healthcare Research and Quality Evidence-Based Practice Centres (AHRQ EPCs) (Berkman 2014), the Oxford Centre for Evidence-Based Medicine (OCEBM Levels of Evidence Working Group 2011), and the US Preventive Services Task Force (USPSTF) (US Preventive Services Task Force 2008). According to the GRADE Working Group, more than 70 organizations, including international collaborations, HTA agencies, public health agencies, medical professional societies, and others have endorsed GRADE and are using it or modified versions of it (GRADE Working Group 2013).<sup>8</sup>

Increasingly, organizations such as those noted above consider the following types of factors, dimensions, or domains when assessing the quality of a body of evidence:<sup>8</sup>

- Risk of bias
- Precision
- Consistency
- Directness
- Publication (or reporting) bias
- Magnitude of effect size (or treatment effect)
- Presence of confounders that would diminish an observed effect
- Dose-response effect (or gradient)

Each of these dimensions is described briefly, below:<sup>8</sup>

**Risk of bias** refers to internal validity. For a body of evidence, this

refers to bias in the overall or cumulative observed treatment effect of the group of relevant studies, for example, as would be derived in a meta-analysis. The quality of a body of evidence is subject to various types of bias across its individual studies. Among these are selection bias (including lack of allocation concealment), performance bias (including insufficient blinding of patients and investigators), attrition bias, and detection bias.<sup>8</sup>

**Precision** refers to the extent to which a measurement, such as the mean estimate of a treatment effect, is derived from a set of observations having small variation (i.e., are close in magnitude to each other). Precision is inversely related to random error. Small sample sizes and few observations generally widen the confidence interval around an estimate of an effect, decreasing the precision of that estimate and lowering any rating of the quality of evidence.<sup>8</sup>

**Consistency** refers to the extent that the results of studies in a body of evidence are in agreement. Consistency can be assessed based on the direction of an effect, i.e., whether they are on the positive or negative side of no effect or the magnitudes of effect sizes across the studies are similar. One indication of consistency across studies in a body of evidence is overlap of their respective confidence intervals around an effect size. Investigators should seek to explain inconsistency (or heterogeneity) of results. The quality of a body of evidence may be lower when there are no plausible explanations for inconsistent results.<sup>8</sup>

**Directness** has multiple meanings in assessing the quality of evidence. First, directness refers to the proximity of comparison in studies, that is, whether the available evidence is based on a “head-to-head” (i.e., direct) comparison of the intervention and comparator of interest, or whether it must rely on some other basis of comparison (i.e., directness of comparisons). Second, directness refers to how many bodies of evidence are required to link the use of an intervention to the impact on the outcome of interest (i.e., directness of outcomes). Third, directness can refer to the extent to which the focus or content of an individual study or group of studies diverges from an evidence question of interest. Directness, may be characterised as the extent to which the PICOTS of the studies in a body of evidence align with the PICOTS of the evidence of interest. This type of directness reflects the external validity of the body of evidence, i.e., how well the available evidence represents, or can be generalised to, the circumstances of interest.<sup>8</sup>

**Publication bias** refers to unrepresentative publication of research reports that is not due to the quality of the research but to other characteristics. This includes tendencies of investigators and sponsors to submit, and publishers to accept, reports of studies with “positive”

results, such as those that detect beneficial treatment effects of new intervention, as opposed to those with “negative” results (no treatment effect or high adverse events rates). One approach used for detecting possible publication bias in systematic reviews and meta-analysis is to use a funnel plot that graphs the distribution of reported treatment effects from individual studies against the sample sizes of the studies. The use of the terms, publication bias and reporting bias, varies. For example, in the GRADE framework, reporting bias concerns selective, incomplete, or otherwise differential reporting of findings of individual studies.<sup>8</sup>

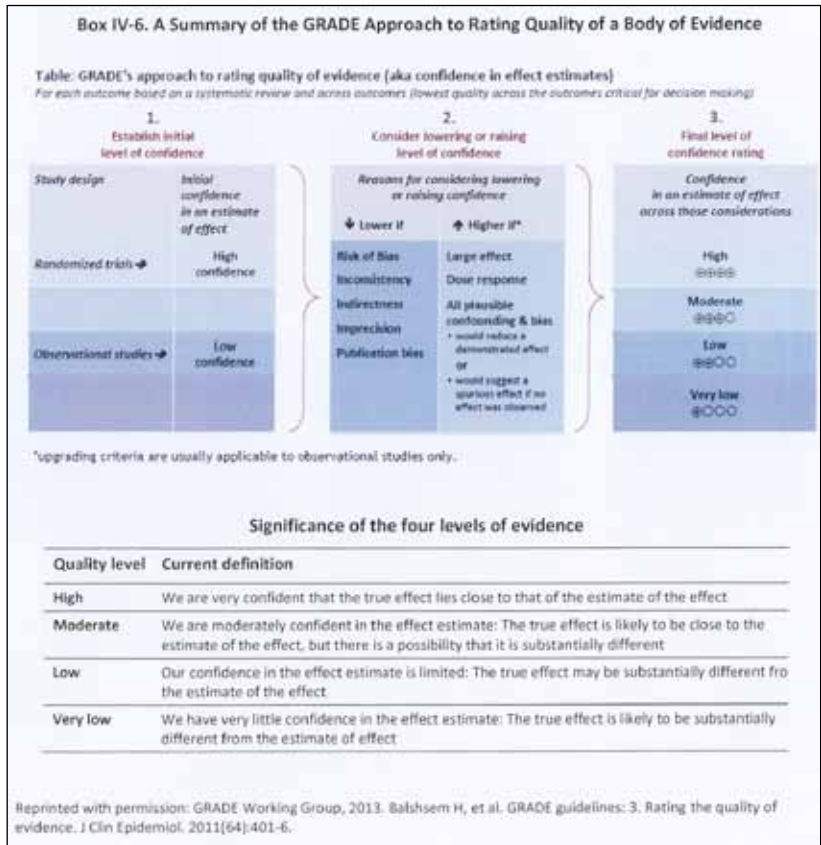
**Magnitude of effect size** can improve confidence in a body of evidence where the relevant studies report treatment effects that are large, consistent, and precise. Overall treatment effects of this type increase confidence that they did not arise from potentially confounding factors only. For example, the GRADE quality rating approach suggests increasing the quality of evidence by one level when methodologically rigorous observational studies show at least a two-fold change in risk ratio and increasing by two levels for at least a five-fold change in relative risk.<sup>8</sup>

**Plausible confounding that would diminish observed effect** refers to instances in which plausible confounding factors for which the study design or analysis have not accounted would likely have diminished the observed effect size. That is, the plausible confounding would have pushed the observed effect in the opposite direction of the true effect. As such, the true effect size is probably even larger than the observed effect size.<sup>8</sup>

**Dose-response effect** (or dose-gradient) refers to an association in an individual study or across a body of evidence, between the dose, adherence, or duration of an intervention and the observed effect size.<sup>8</sup>

Among the important ways in which appraisal of evidence quality has evolved from using traditional evidence hierarchies is the accounting for factors other than study design. For example, as shown in Table 7, the GRADE approach to rating quality of evidence starts with a simplified categorization of study types, i.e., RCTs and observational studies, accompanied by two main levels of confidence (high or low) in the estimate of treatment effect. Then, the rating scheme allows for factors that would raise or lower a level of confidence. Factors that would lower confidence in evidence would include, e.g., risk of bias, inconsistency across the RCTs, indirectness, imprecision and publication bias; factors that would increase confidence include, e.g., large effect size and an observed dose-response effect. The final levels of confidence rating (high, moderate, low, very low) are shown at the right, and defined in the lower portion of that table.<sup>8</sup>

**Table 7. A summary of the GRADE Approach to Rating Quality of a Body of Evidence**



The GRADE approach may be used by MaHTAS when rating the quality of a body of evidence.

### 3.2.9. Economic Analysis Methods

Studies of costs and related economic implications comprise a major group of methods used in HTA. Interest in cost analyses has accompanied concerns about rising health care costs, pressures on healthcare policymakers to allocate resources, and the need for health product makers and other technology advocates to demonstrate the economic benefits of their technologies.<sup>8</sup>

## Main Types of Economic Analysis in HTA

Main types of economic analysis used in HTA include the following:

- *Cost-of-illness analysis*: a determination of the economic impact of an illness or condition (typically on a given population, region, or country) e.g., of smoking, arthritis, or diabetes, including associated treatment cost
- *Cost-minimization analysis*: a determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes
- *Cost-effectiveness analysis (CEA)*: a comparison of costs in monetary units with outcomes in quantitative non-monetary units, e.g., reduced mortality or morbidity
  - *Cost-utility analysis (CUA)*: a form of cost-effectiveness analysis that compares costs in monetary units with outcomes in terms of their utility, usually to the patient, measured, e.g., in QALYs
  - *Cost-consequence analysis*: a form of cost-effectiveness analysis that presents costs and outcomes in discrete categories, without aggregating or weighting them
- *Cost-benefit analysis (CBA)*: compares costs and benefits, both of which are quantified in common monetary units
- *Budget-impact analysis (BIA)*: determines the impact of implementing or adopting a particular technology or technology-related policy on a designated budget, e.g., of a drug formulary or health plan

### The differences in valuation of costs and outcomes among these alternatives.<sup>8</sup>

Analysis Type	Valuation of costs <sup>1</sup>		Valuation of outcomes
Cost of Illness	\$	vs.	None
Cost Minimization	\$	vs.	Assume same
Cost Effectiveness	\$	÷	Natural units
• Cost Consequence	\$	vs.	Natural units
• Cost Utility	\$	÷	Utiles (e.g., QALYs)
Cost Benefit	\$	÷ or <sup>2</sup> -	\$
Budget Impact	\$	vs.	None <sup>3</sup> or maximize various <sup>4</sup>

<sup>1</sup>Any currency  
<sup>2</sup>Cost-benefit ratio (÷) or net of costs and benefits (-)  
<sup>3</sup>That is, determine impact of an intervention/program on a designated non-fixed budget  
<sup>4</sup> That is, maximize some outcome within a designated fixed ("capped") budget



## Basic formulas for determining CEA, CUA, and CBA.<sup>8</sup>

Box V-2. Basic Formulas for CEA, CUA, and CBA

A: Technology A  
C: Technology C (a comparator)

**Cost-Effectiveness Ratio:**

$$CE \text{ Ratio} = \frac{\$Cost_A - \$Cost_C}{Effect_A - Effect_C}$$

For example: "\$45,000 per life-year saved" or "\$10,000 per lung cancer case averted"

**Cost-Utility Ratio:**

$$CU \text{ Ratio} = \frac{\$Cost_A - \$Cost_C}{Utiles_A - Utiles_C}$$

Utiles, units of utility or preference, are often measured in QALYs. So, for example: "\$150,000 per QALY gained" or "\$12,000 per QALY gained"

**Cost-Benefit, Ratio Approach:**

$$CB \text{ Ratio} = \frac{\$Cost_A - \$Cost_C}{\$Benefit_A - \$Benefit_C}$$

For example: "Cost-benefit ratio of 1.2"

**Cost-Benefit, Net Benefit Approach:**

$$CB \text{ Net} = (\$Cost_A - \$Cost_C) - (\$Benefit_A - \$Benefit_C)$$

For example: "Net cost of \$10,000"

## Attributes to consider when designing and reviewing cost analyses:<sup>8</sup>

- Comparator
- Perspective
- Outcomes /endpoints selected
- Efficacy vs. effectiveness
- Data capture methods
- Direct costs (health care and non healthcare)
- Indirect costs (e.g., loss of productivity)
- Actual costs vs. charges/prices
- Marginal costs vs. average costs
- Time horizon analysis
- Discounting
- Correction of inflation
- Modelling use
- Sensitivity analysis
- Reporting results
- Funding source

The Critical Appraisal Skills Programme (CASP) checklist is being used by MaHTAS to appraise economic evaluation studies

### **3.2.10. Reporting of an assessment (Formulate findings, conclusion and recommendation)**

The HTA report can then be drafted based on the evidence that has been obtained. The reporting of HTA should include at least three kinds of documents:<sup>6</sup>

- Technical report (full HTA Report)
- Executive summary report
- Abstract

#### **Technical Report (full HTA Report)**

Although HTA reports are primarily addressed to local agents (decision makers, clinicians, etc.), their findings may also be of interest for the International scientific / HTA community. Those readers need to be able to assess the relevance and quality of previous HTA reports when they are considering previous HTA knowledge in their assessment. The technical report should include comprehensive information on all issues covered in undertaking HTA report. The steps undertaken, tools used (e.g., protocols), and evidence included and excluded should be documented in this comprehensive report. There are different elements that can be included in the technical report to enhance transparency and comprehensiveness in an understandable way (Table 8).<sup>6</sup> A checklist for HTA reports has been prepared by INAHTA as an aid to furthering a consistent and transparent approach to health technology assessment (Appendix 12). A general theme is the clear identification in an HTA report of what has been done in the assessment and of any significant limitations in the analysis.<sup>15</sup>

#### **Discussion of findings should include:**<sup>15</sup>

- The relationship of the results obtained to the question being assessed by the assessment.
- There should be a clear interpretation of the results. It will be helpful to include comment on their likely relevance to clinical practice and to the health care system.
- Comment on missing or uncertain information, and the reliability of the analysis.

#### **Conclusion(s)**<sup>15</sup>

The report should reach clear conclusion(s), which will make reference to the question addressed by the assessment and, where appropriate, its context. The conclusion should flow from the evidence that has been reviewed.

## **Recommendation(s)**

Recommendation(s) will be made based on the evidence retrieved and taking into consideration the followings as in the GRADE approach:

- Quality of evidence
- Balance between the benefits and harms
- Resource implications
- Organization/social/ethical/medico-legal implications
- Values and preferences

It may be helpful for the HTA report to include directions for future research and implications of their findings for policy.<sup>15</sup>

**Table 8. Structure example for an HTA Report**

---

- Title
  - Disclaimer
  - Contact Details
  - Authors and information specialists
  - Expert committee
  - External reviewers
  - Acknowledgement
  - Disclosure (Conflict of interest)
  - Executive summary
    - Background
    - Technical Features
    - Policy question
    - Objectives
    - Methods
    - Results
    - Conclusion
    - Recommendation
  - Abbreviations
  - Background
    - Description of health problem
    - Current service provision
    - Description of technology under assessment
    - Requestor(s) and reasons for request for the assessment
  - Technical features of the assessed technology
  - Policy question
  - Objectives
    - Research questions
  - Methods
    - Literature search strategy
      - ✓ Databases
      - ✓ Year range
      - ✓ Restriction (limits)
      - ✓ Other kind of information resources
    - Study selection
      - ✓ Inclusion criteria
      - ✓ Exclusion criteria
    - Critical Appraisal of literature
      - ✓ Assessing quality of individual studies
    - Grading of evidence
    - Analysis and synthesis of evidence
      - ✓ Data extraction strategy
      - ✓ Methods of data synthesis
      - ✓ Assessing the quality of a body of evidence
  - Results
    - Number of studies identified
    - Number and types of studies included
    - Number and types of studies excluded
    - Flow chart of study selection
    - Description of included studies including risk of bias  
**(context – may or may not apply to each HTA)**
    - Safety
    - Efficacy / Effectiveness
    - Economic analysis
    - Organizational issues
    - Social/ethical/medico-legal implications (optional)
    - Other perspectives (stakeholders, patients, consumers) (optional)
  - Discussion
  - Conclusion(s)
  - Recommendation(s)
  - References
  - Appendices
    - Hierarchy of evidence
    - Health Technology Assessment Protocol
    - Literature Search strategy
    - Critical Appraisal Tools used
    - Evidence table (included studies)
  - List of excluded studies
-

### **Executive summary report**

Executive summary report is (should be) addressed to local decision makers (executives, clinicians), stressing a summary of conclusions and recommendations, because these are the kind of information sought by local decision makers. Methodologic aspects of the assessment are usually underrepresented in the executive summary, since they are not of much interest to the target audience.<sup>6</sup> The structure for writing the executive summary is as shown in Appendix 13. Other type of summary such as consumer summary may also be reported.

### **Abstract**

Recommendations already exist on how to write a structured abstract for the INAHTA Database. The abstract must be written in English. The aspects to be included in the abstract are in Appendix 14.

#### **3.2.11. Technical Review and External Review**

The draft HTA report will be sent for technical review to the head of MaHTAS, the expert committee and to experts in the field, either locally or abroad for comments and feedback. Feedback obtained may be used to modify the draft HTA report before it is being submitted to the HTA TAC for review.

#### **3.2.12. Approval of HTA Report**

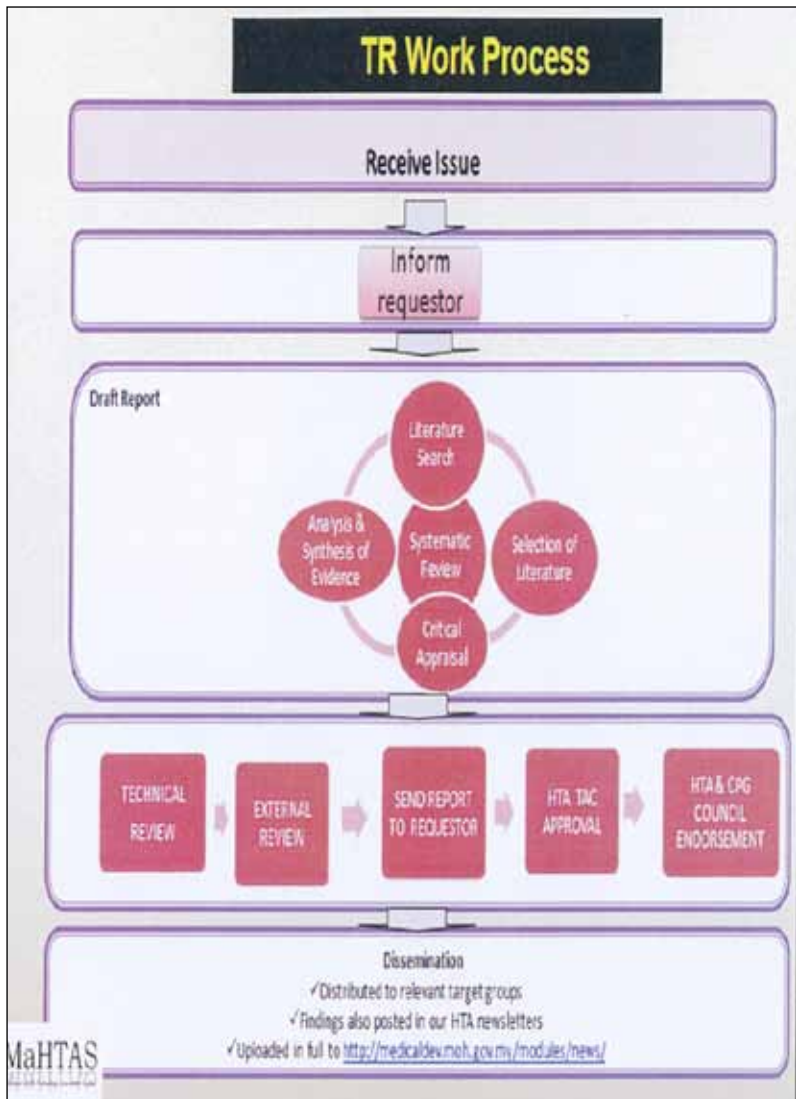
The draft HTA report would be presented by the author(s) to the HTA TAC during the HTA TAC meeting. The report would be reviewed and discussed. In the event that alterations or modifications or changes need to be made, amendments would be made first and then the final draft HTA report would be sent to the HTA & CPG Council members and presented to the HTA & CPG Council for final approval.

#### **3.2.13. Feedback to requestor(s)**

Once approved, official feedback would be given to the requestor(s) to inform them to utilise the HTA report as an input for decision or policy making related to the health technology.

### 3.3. TR (Mini-HTA) Work Process

The TR (Mini-HTA) work process is depicted schematically as shown below:



The process of conducting technology review is less complex compared to the conduct of HTA. Issues received do not undergo prioritisation and do not need approval by the HTA & CPG Council. The assessment is usually conducted by reviewer(s) and does not involve the formation of expert committee.

### **3.3.1. Receive Issues for TR (Mini-HTA)**

Technology Review (Mini-HTA) will be conducted by MaHTAS based on requests received via letters or online using HTA Form. Issues for TR (Mini-HTA) are usually received from health personnel in Ministry of Health (MOH) or other government agencies via letters or HTA Request Form available on-line at MOH website throughout the whole year. Once an issue has been received, the suitability of conducting a TR (Mini-HTA) for the issue would be assessed. The MOH Heads of Clinical Services advice may be sought to determine the suitability of conducting a TR (Mini-HTA) for the requested issue. If the issue is found to be suitable for the conduct of TR (Mini-HTA), head of MaHTAS would assign a reviewer to conduct the assessment on the technology.

### **3.3.2. Inform requestor**

Official feedback would be given to the requestor to inform them on the decision made regarding their request and also the time-line for conducting the assessment which is usually two to four months from the date the request is received by MaHTAS.

### **3.3.3. Conduct systematic review**

The scope of assessment is limited to safety, efficacy / effectiveness, and cost / financial impact. It may also address organizational considerations. However, the steps involved in the assessment are similar to HTA:

- Literature search
- Selection of literature
- Critical appraisal
- Analysis and Synthesis of Evidence

### **3.3.4. Reporting of an assessment**

The TR (Mini-HTA) report will be drafted based on the evidence that has been obtained. The reporting of TR (Mini-HTA) should include at least three kinds of documents:<sup>6</sup>

- Technical report [full TR (Mini-HTA Report)]
- Executive summary report
- Abstract

### **Technical Report [full TR (Mini-HTA Report)]**

The technical report should include comprehensive information on all issues that are covered in undertaking TR (Mini-HTA) report. The steps undertaken, tools used and evidence included and excluded should be documented in this comprehensive report. There are different elements that can be included in the technical report to enhance transparency and comprehensiveness in an understandable way (Table 9).



**Table 9. Structure example for TR (Mini- HTA) Report**

---

- Title
  - Disclaimer
  - Contact Details
  - Authors and information specialists
  - External reviewers
  - Disclosure (Conflict of interest)
  - Executive summary
    - Background
    - Objective/Aim
    - Results and conclusions
    - Recommendation (after HTA TAC meeting)
    - Methods
  - Background
    - Description of health problem
    - Current service provision
    - Description of technology under assessment
    - Requestor(s) and reasons for request for the assessment
  - Objective / Aim
  - Technical features of the assessed technology
  - Methods
    - Searching
      - ✓ Databases
      - ✓ Year range
      - ✓ Restriction (limits)
      - ✓ Other kind of information resources
    - Study selection
      - ✓ Inclusion criteria
      - ✓ Exclusion criteria
    - Critical Appraisal of literature
      - ✓ Assessing quality of individual studies
    - Grading of evidence
    - Analysis and synthesis of evidence
      - ✓ Data extraction strategy
      - ✓ Methods of data synthesis
      - ✓ Assessing the quality of a body of evidence
  - Results and Discussion
    - Number of studies identified
    - Number and types of studies included
    - Description of included studies including risk of bias  
**(context – may or may not apply to each Mini-HTA)**
    - Safety
    - Efficacy / Effectiveness
    - Economic analysis
    - Organizational issues (optional)
    - Social/ethical/medico-legal implications (optional)
    - Limitation
  - Conclusion(s)
  - Recommendation(s) after HTA TAC meeting
  - Appendices
    - Literature Search strategy
    - Hierarchy of evidence
    - Evidence table (included studies)
-

## **Executive summary report**

The structure for writing the executive summary for TR (Mini-HTA) Report is as shown in Appendix 15.

### **Abstract**

Recommendations already exist on how to write a structured abstract for the INAHTA Database. The abstract must be written in English. The aspects to be included in the abstract are in Appendix 14.

#### **3.3.5. Technical Review**

The draft TR (Mini-HTA) report will be sent for technical review to the head of MaHTAS and will be amended by the author (if necessary) before sending it for external review.

#### **3.3.6. External Review**

The draft TR (Mini-HTA) may be sent to experts in the field for comments and feedback. Feedback obtained may be used to modify the draft TR (Mini-HTA report) before it is being submitted to the HTA TAC for review.

#### **3.3.7. Send report to requestor**

The draft TR (Mini-HTA) report would be sent to the requestor and relevant personnel in the MOH informing them on the findings based on the retrievable evidence. This report is usually drafted until the conclusion.

#### **3.3.8. Approval of TR (Mini-HTA) Report**

The draft TR (Mini-HTA) report would be presented by the author to the HTA TAC during the HTA TAC meeting for approval. The report would be reviewed, discussed and recommendation on the technology would be finalised based on the discussion during the meeting. In the event that alterations or modifications or changes need to be made, amendments would be made first and then the final draft TR (Mini-HTA) report will be sent to the HTA CPG Council members. The summary of the findings of the TR (Mini-HTA) report would be presented to the HTA & CPG Council for endorsement. Once the report has been endorsed by the HTA & CPG Council, a letter would be sent to the requestor to inform them of the final recommendation.

#### **3.3.9. Conversion of TR (Mini-HTA) Report to HTA report**

Occasionally, some issue where TR (Mini-HTA) has been conducted would also undergo detailed assessment (HTA) for the following reasons:

- i. Body of evidence has significantly increase, or
- ii. More detailed assessment is required by policy maker or HTA & CPG Council members.

### **3.4. Information Brief (Rapid Review) Work Process**

The Information Brief (Rapid Review) work process is depicted schematically as shown below:



#### **3.4.1. Receive Issues for Information Brief (Rapid Review)**

Information Brief (Rapid Review) will be conducted by MaHTAS for issue which needs very rapid information response. The issue usually focused on single technology and the scope of the assessment is limited to safety and efficacy / effectiveness. The head of MaHTAS would assign a reviewer to conduct the assessment on the technology.

#### **3.4.2. Literature search**

Literature search would be conducted to search for high level evidence or more recent evidence. The search may be restricted to one or two databases. The evidence retrieved would then be selected. The reviewer may critically appraise the quality of the evidence (optional).

#### **3.4.3. Report writing**

Once the evidence has been retrieved and selected, the reviewer would then write the report. The format for the Information Brief (Rapid Review) is as shown in Appendix 16.

#### **3.4.4. Technical review**

The draft Information Brief (Rapid review) will be sent for technical

review to the head of MaHTAS and will be amended by the author (if necessary).

#### **3.4.5. Feedback to requestor**

The Information Brief (Rapid review) would be sent to the requestor as an input for decision / policy making related to the health technology.

## **4. DISSEMINATION OF HTA/TR (MINI-HTA) REPORTS**

Dissemination of HTA findings and recommendations, whether for internal use by the sponsoring organization or into the national or international health information mainstream, must be carefully planned and implemented in order to enable any HTA to achieve its purpose. Dissemination of HTA findings and recommendations must inform decisions and policies for improving population risk factors, patient care, health outcomes, and resource allocation, as appropriate.<sup>8</sup>

Once the HTA and TR (Mini-HTA) reports have been approved or endorsed by the HTA & Council, it would be printed and disseminated to the relevant target groups. Findings of the HTA and TR (Mini-HTA) reports will also be posted in HTA newsletter and facebook. The HTA or TR (Mini-HTA) reports will also be uploaded in MOH website (full report and executive summary). The reports are to be made available via mobile application (myMaHTAS – android and IOS application). The reports are link to the INAHTA database. The findings of the reports will also be published in peer reviewed journals and will also be presented at seminars or conferences.

## **5. MONITORING IMPACT OF HTA/TR (MINI-HTA) REPORTS**

Measuring and demonstrating the impact (or influence) of HTA reports is important in many HTA agencies. In MaHTAS the impact of HTA or TR (Mini-HTA) reports is monitored using the MaHTAS User Feedback Form (Appendix 17). Besides that, INAHTA had developed a framework for reporting on HTA impact (Appendix 18) to be used by members to record, measure and share the impact of HTA reports produced by their member agencies. INAHTA members are requested to provide information on HTA reports that have shown some indication of impact on decision making by government at the regional, national and international level(s). Impact reports are requested no less than six months after the HTA report's publication date.<sup>16</sup>

## **6. UPDATING HTA/TR (MINI-HTA) REPORTS**

Updating of HTA or TR (Mini-HTA) reports will be carried out with the appearance of significant new evidence.

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## Appendix 1

### DECLARATION OF COMPETING INTEREST

HTA is the systematic evaluation of properties, effects or other impacts of health care interventions. The main purpose of HTA is to inform decision making in health care, including decisions made at the individual or patient level, the level of the health care provider or institution, or the regional, national as well as international levels. HTA may address the direct and intended impacts or consequences of interventions as well as their indirect and unintended ones. HTA is conducted by interdisciplinary group using explicit analytical frameworks and drawing from variety of methods.

HTA recommendations are important for decision making process. Thus it is important to ensure that HTA processes are done in a systematic and transparent method. Potential conflict of interest may occur among the health technology assessors including analysts, panel members, or other experts involved in reviewing the evidence and making recommendations. A conflict of interest may be in any form such as financial or other interest that conflict with one's contributions in a assessment group because it could impair that person's objectivity or could create an unfair advantage.

All the authors and expert committee of Health Technology Assessment (HTA) and authors of Technology Review (TR) are required to complete a declaration of competing interest detailing the sources of fundings, and other possible conflicts of interest. An explicit statement regarding the above is made in the HTA and TR reports.

### DECLARATION OF COMPETING INTEREST

1. Have you in the last three years accepted the following from any pharmaceutical and medical device industries that may in any way gain or lose financially from the results of your work (in relation to this health technology):

- A fee for speaking?
- Fund support for research?
- Funding for publication?
- Consultancies?

If so, please declare the occasion or event and the organization that provided you with financial support.

Organization	Event

2. Have you, during last three years, been employed by an organization that may in any way gain or lose financially from the results or conclusion of this assessment or systematic review?

If so, please declare the organization and the nature of your relationship with that organization.

Organization	Event

3. Do you have any competing financial interest such as investments or directorships? If so specify.

Organization	Event

4. Do you belong to a political party, special interest group or hold deep personal or religious convictions that may have affected what you have written/contributed and that reader s should be aware of when reading your paper?

Organisation/personal beliefs that could be perceived as influencing your work.

5. List the source(s) of funding for the development of this HTA/TR

---

---

---

Signature .....

Name .....

Work place .....

Title of HTA/TR  
that you have  
contributed .....

Date .....

*I understand that this declaration will be retained by the HTA Section Administrator and made available on inspection of the HTA Section, Ministry of Health Malaysia.*

*\* The Ministry of Health Malaysia requires all the authors, expert committee and external reviewers to fill in this form.*





**REQUEST FOR HEALTH TECHNOLOGY ASSESSMENT (HTA)  
PERMOHONAN UNTUK PENILAIAN TEKNOLOGI KESIHATAN (PTK)  
APPLICABLE FOR GOVERNMENT AGENCIES ONLY  
UNTUK KEGUNAAN AGENSI KERAJAAN SAHAJA**

1. Name of technology  
(Nama teknologi)

2. Short description of technology  
(Penerangan ringkas teknologi)

3. Reason for requesting Health Technology Assessment (HTA)  
(Sebab-sebab Penilaian Teknologi Kesihatan (PTK) dipohon)

4. Issue/problems related to technology  
(Isu/masalah berkaitan dengan teknologi ini)

5. Size & strength of evidence on this technology (cite key references if available)  
(Saiz dan kekuatan bukti saintifik atas teknologi - sila nyatakan rujukan-rujukan utama jika ada)

6. Name of applicant  
(Nama pegawai yang memohon)

7. Designation  
(Jawatan)

8. Address of work  
(Alamat bertugas)

Telephone (Telefon)

Email

Attachment for additional file :

(Lampiran sekiranya ruangan tidak mencukupi)

Note:<sup>h</sup> Technology refers to drugs, equipment, surgical and medical procedures, health programmes, organizational and support systems for delivery of healthcare

Nota:<sup>h</sup> Teknologi kesihatan merujuk kepada ubat, peralatan perubatan, prosedur klinikal, program, organisasi dan sistem sokongan untuk penyampaian perkhidmatan kesihatan

**For further information please contact :**

Health Technology Assessment Section(MaHTAS)

Medical Development Division

Ministry Of Health Malaysia

Level 4, Block E1, Precint 1

Government Office Complex

62590 Putrajaya, Malaysia

Tel : 0388831229 / 0388831246

Fax : 0388831230

Email : htamalaysia@moh.gov.my

**Sebarang Pertanyaan dan Maklumbalas Sila Hubungi :**

Cawangan Penilaian Teknologi Kesihatan

Bahagian Perkembangan Perubatan

Aris 4, Blok E1, Kompleks E

Pusat Pentadbiran Kerajaan Persekutuan

62590 Putrajaya, Malaysia

## Appendix 3

### FORM A: HEALTH TECHNOLOGY ASSESSMENT ISSUES FOR PRIORITY SETTING EXERCISE

YEAR

<b>Name of technology</b>	
<b>Reasons for request</b>	
<b>Requesting officer</b>	
<b>Technology description</b>	To include picture if available.
<b>Effect on infrastructure</b>	
<b>Number of people whom applicable</b>	To mention the disease burden in the world and in Malaysia.
<b>Availability of competing technology</b>	
<b>Significance of technology</b>	<p>Mention number of hits from the available databases: Via OVID (Medline, HTA database, Systematic Review, DARE, RCT, NHS economic evaluation, EMBASE), PubMed, Horizon scanning.</p> <p><b>Effectiveness: (Summary of evidence)</b> HTA, systematic review, RCT, and other study design. If many choose the highest quality and summaries few studies (less than 5).</p> <p><b>Safety</b> To mention main adverse events. Also to mention USFDA, CE mark if relevant.</p>
<b>Cost / cost-effectiveness</b>	To mention cost if no cost-effectiveness / cost-utility analysis.
<b>Level of usage</b>	
<b>Other related problems / issues</b>	
<b>References</b>	

HTA TAC MEETING NO./YEAR

# Appendix 4

## HTA PRIORITY SETTING EXERCISE FORMAT: YEAR

NO.	CRITERIA & WEIGHTAGE					SCORE
	↑EFFECTS ON INFRASTRUCTURE & OTHER SERVICES (include training, accreditation, education issues)  ↑Weightage	↑PREVALENCE (include disease burden, number of people affected)  ↑Weightage	↓AVAILABILITY OF COMPETING TECHNOLOGIES (other technology currently available for the same purpose)  ↑Weightage	↑POSSIBILITY OF CHANGING HEALTH STATUS (include significance of technology -efficacy/ effectiveness, safety and implication of introduction such as reduction in morbidity, mortality, early detection etc.)  ↑Weightage	↑COST (include direct cost or cost-effectiveness, or other cost implication)  ↑Weightage	
	(20)	(20)	(20)	(20)	(20)	%
1						
2						
3						
4						
5						
6						
7						
8						
9						

I S S U E S

**HEALTH TECHNOLOGY ASSESSMENT (HTA) PROTOCOL  
TITLE:**

- 1. BACKGROUND INFORMATION**  
To include requestor and reasons for request
- 2. POLICY QUESTION**
- 3. OBJECTIVES**  
Research questions
- 4. METHODS**
  - 4.1. Search strategy**
  - 4.2. Inclusion and exclusion criteria**
    - 4.2.1. Inclusion criteria**
      - Population
      - Intervention
      - Comparators
      - Outcome
      - Study design
      - English full text articles
    - 4.2.2. Exclusion criteria**
      - Study design
      - Non English full text article
  - 4.3. Critical Appraisal of literature**
  - 4.4. Analysis and Synthesis of evidence**
    - 4.4.1. Data extraction strategy
    - 4.4.2. Methods of data synthesis
- 5. REPORT WRITING**

## Appendix 6

### SEARCH STRATEGY TABLE

#### SEARCH STRATEGY (HTA TITLE)

Date	Data base	Keywords	Year Publications	Other limit	No. of search	No. of relevant title	No. of relevant abstract	No. of full text article used	Notes

## Appendix 7

### SEARCH STRATEGY (example of a search strategy)

#### MEDLINE® In progress and other Non-Indexed Citations and Ovid Medline® 1946 to present.

- 1 Muscle spasticity/
- 2 (muscle adj1 spastic\*).tw.
- 3 spastic\*.tw.
- 4 Spasm/
- 5 (Spasm\* adj1 (muscular or ciliary body or muscle or generalized)).tw.
- 6 Spasm\*.tw.
- 7 Spinal Cord Injuries/
- 8 (spinal cord adj1 (injur\* or contusion or traum\* or laceration\*)).tw.
- 9 (spinal adj1 (cord traum\* or cord injur\* or cord contusion\*)).tw.
- 10 Cerebral Palsy/
- 11 (spastic\* adj diplegia\*).tw.
- 12 (cerebral pals\* adj1 (hypotonic or monoplegic or athetoid or quadriplegic infantile or monoplegic infantile or atonic or spastic\* or dyskinetic or congenital or mixed or dystonic rigid or dystonic-rigid or diplegic infantile or rolandic type)).tw.
- 13 cp.tw.
- 14 cerebral palsy.tw.
- 15 (Infantile cerebral palsy adj1 (quadriplegic or diplegic or monoplegic)).tw.
- 16 brain injuries/
- 17 (injur\* adj1 (traum\* brain or mild traum\* brain or brain traum\* mild or diffuse brain or focal brain or acute brain or brain)).tw.
- 18 (brain injur\* adj1 (traum\* or acute or focal or diffuse)).tw.
- 19 (encephalopath\* adj1 (post concussive or post-concussive or traum\* or post-traum\* or post traum\*)).tw.
- 20 (brain adj1 (traum\* or laceration\* or contusion\*)).tw.
- 21 (cortical adj1 contusion\*).tw.
- 22 traumatic brain injury.tw.
- 23 tbi\*.tw.
- 24 Diffuse Axonal Injury/
- 25 (injur\* adj1 diffuse axonal).tw.
- 26 dai\*.tw.
- 27 diffuse axonal injury.tw.
- 28 axonal injur\* diffuse.tw.
- 29 BRAIN HEMORRHAGE, TRAUMATIC/
- 30 (h?emorrhage\* adj1 (traumatic cerebellar or traumatic brain)).tw.
- 31 (traum\* adj1 (cerebellar h?emorrhage\* or brain h?emorrhage\*)).tw.
- 32 brain stem hemorrhage, traumatic/
- 33 (traum\* adj1 (brainstem h?em\* or brain stem h?em\* or bulbar h?em\* or medullary h?em\* or pontine h?em\* or midbrain h?em\* or h?em\* brain stem or h?em\* brainstem)).tw.
- 34 (h?em\* adj1 (traumatic medullary or traumatic bulbar or post-traumatic brainstem)).tw.
- 35 cerebral hemorrhage, traumatic/
- 36 (traum\* adj1 (cerebral h?em\* or intracerebral h?em\* or cerebral parenchymal h?em\* or brain h?em\* cerebral or cerebral intraparenchymal h?em\*)).tw.
- 37 (h?em\* traum\* adj1 (intracerebral or cerebral)).tw.
- 38 Multiple Sclerosis/
- 39 (disseminated adj1 sclerosis).tw.
- 40 ms.tw.
- 41 multiple sclerosis.tw.
- 42 Multiple Sclerosis, Chronic Progressive/
- 43 (multiple sclerosis adj1 (secondary progressive or primary progressive or progressive relapsing or chronic progressive or remittent progressive)).tw.
- 44 Stroke/
- 45 (Stroke\* adj1 (cerebr\* or acute)).tw.
- 46 (cerebrovascular adj1 (apoplexy or accident acute or accident\*)).tw.
- 47 (Brain adj1 vascular accident\*).tw.
- 48 cva\*.tw.
- 49 cerebrovascular accident.tw.
- 50 stroke\*.tw.
- 51 acute cerebrovascular accident\*.tw.
- 52 Dystonia/
- 53 (dystonia adj1 (paroxysmal or limb or muscle or diurnal)).tw.
- 54 dystonia.tw.
- 55 Hypoxia, Brain/
- 56 (anoxi\* adj1 (encephalopath\* or brain damage or brain or cerebral)).tw.

57 (Hypoxi\* adj1 (brain or encephalopath\* or cerebral or brain or brain damage)).tw.  
58 Hypoxia-Ischemia, Brain/  
59 ((Brain or cerebral or encephalopath\*) adj1 (isch?emia\*- anoxi\* or isch?emia\* anoxi\* or isch?emia\* hypoxia or isch?emia\*- hypoxi\* or hypoxia\*- isch?emia\*or hypoxi\* isch?emia\*)).tw  
60 acquired brain injury.tw.  
61 or/1-60  
62 Baclofen.tw.  
63 Lioresal.tw  
64 Gablofen.tw.  
65 Baclosan.tw.  
66 (injection\* adj1 (intrathecal or intraspinal or spinal)).tw.  
67 Baclofen/  
68 Injections, Spinal/  
69 Muscle Relaxants, Central/  
70 (muscle relaxant\* adj1 (central or centrally acting)).tw.  
71 Infusion Pumps, Implantable/  
72 drug delivery systems implantable.tw.  
73 ((implantable adj1 (infusion pump\* or peristaltic pump\* or perfusion pump\*)).tw  
74 62 or 63 or 64 or 65 or 67 or 69 or 70  
75 66 or 68 or 71 or 72 or 73  
76 74 AND 75  
77 Baclofen/  
78 Lioresal.tw.  
79 Gablofen.tw.  
80 Baclosan.tw.  
81 Administration, Oral/  
82 (oral adj1 (drug administration\* or administration\*)).tw.  
83 Dantrolene/  
84 (dantrolene adj1 sodium).tw.  
85 dantrolene.tw  
86 dantrium.tw.  
87 Diazepam/  
88 Diazepam.tw.  
89 Valium.tw.  
90 Cannabinoids/  
91 Cannabinoids.tw.  
92 4-Aminopyridine/  
93 4 aminopyridine.tw.  
94 4-aminopyridine.tw.  
95 Pymadine.tw.  
96 Botulinum Toxins/  
97 (botulinum adj1 toxin\*).tw.  
98 botulin.tw.  
99 BTX.tw.  
100 BoNT.tw.  
101 Botox.tw.  
102 Exercise/  
103 (exercise\* adj1 (isometric or aerobic or physical)).tw.  
104 exercise\*.tw.  
105 physical therapy.tw.  
106 muscle stretching exercises/  
107 (stretching adj1 (exercise muscle or static active or static-active or static passive or static-passive or passive or active or static or dynamic or relaxed or isometric)).tw.  
108 Phenols/  
109 Phenol\*.tw.  
110 Injections, Spinal/  
111 (injection\* adj1 (intrathecal or intraspinal or spinal)).tw.  
112 108 or 109  
113 110 or 111  
114 112 and 113  
115 Rhizotomy/  
116 Rhizotom\*.tw.  
117 Dorsal rhizotom\*.tw.  
118 Placebo Effect/  
119 (placebo adj1 effect\*).tw.  
120 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 114 or 115 or 116 or 117 or 118 or 119  
121 61 and 74 and 75 and 120



## Appendix 8

### CASP Checklist for RCT



## 11 questions to help you make sense of a trial

### How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a randomised controlled trial:

- Are the results of the trial valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 11 questions on the following pages are designed to help you think about these issues systematically.

The first two questions are screening questions and can be answered quickly. If the answer to both is **yes**, it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a **yes**, **no** or **can't tell** to most of the questions. A number of prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

There will not be time in the small groups to answer them all in detail!

**These checklists were designed to be used as educational tools as part of a workshop**

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## (A) Are the results of the trial valid?

### Screening Questions

1. Did the trial address a clearly focused issue?

Yes

Can't tell

No

Consider: An issue can be "focused" in terms of

- The population studied
- The intervention given
- The comparator given
- The outcomes considered

2. Was the assignment of patients to treatments randomised?

Yes

Can't tell

No

Consider:

- How was this carried out, some methods may produce broken allocation concealment
- Was the allocation concealed from researchers?

## Is it worth continuing?



### Detailed questions

3. Were patients, health workers and study personnel blinded?

Yes     Can't tell     No

Consider:

- Health workers could be; clinicians, nurses etc
- Study personnel – especially outcome assessors

---

4. Were the groups similar at the start of the trial?

Yes     Can't tell     No

Consider: Look at

- Other factors that might affect the outcome such as age, sex, social class, these may be called baseline characteristics

---

5. Aside from the experimental intervention, were the groups treated equally?

Yes     Can't tell     No

6. Were all of the patients who entered the trial properly accounted for at its conclusion?

Yes  Can't tell  No

Consider:

- Was the trial stopped early?
- Were patients analysed in the groups to which they were randomised?

## (B) What are the results?

7. How large was the treatment effect?

Consider:

- What outcomes were measured?
- Is the primary outcome clearly specified?
- What results were found for each outcome?
- Is there evidence of selective reporting of outcomes?

8. How precise was the estimate of the treatment effect?

Consider:

- What are the confidence limits?
- Were they statistically significant?

## (C) Will the results help locally?

9. Can the results be applied in your context?  
(or to the local population?)

Yes

Can't tell

No

Consider:

- Do you have reason to believe that your population of interest is different to that in the trial?
- If so, in what way?

10. Were all clinically important outcomes considered?

Yes

Can't tell

No

Consider:

- Is there other information you would like to have seen?
- Was the need for this trial clearly described?

11. Are the benefits worth the harms and costs?

Yes

Can't tell

No

Consider:

- Even if this is not addressed by the trial, what do you think?

## Appendix 9

### DESIGNATION OF LEVELS OF EVIDENCE

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
- III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

**SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)**

## Appendix 10

### HIERACHY OF EIDENCE FOR TEST ACCURACY STUDIES

Level	Description
1.	A blind comparison with reference standard among an appropriate sample of consecutive patients
2.	Any one of the following
3.	Any two of the following
4.	Any three or more of the following
5.	Expert opinion with no explicit critical appraisal, based on physiology, bench research or first principles.

Narrow population spectrum

Differential use of reference standard

Reference standard not blind

Case control study

**SOURCE: NHS Centre for Reviews and Dissemination (CRD) University of York, Report Number 4 (2<sup>nd</sup> Edition)**

## Appendix 11

### EVIDENCE TABLE

**Evidence Table : Effectiveness / Safety / Cost-effectiveness  
Question :**

Bibliographic citation	Study Type/Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow-up (if applicable)	Outcome measures/ Effect size	General comments

Note: LE (Level of evidence)



## Appendix 12

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### A checklist for HTA reports

This summary form is intended as an aid for those who wish to make a record of the extent to which a health technology assessment report meets the 14 questions given in the checklist.

It is NOT intended as a scorecard to rate the standard of HTA reports — reports may be valid and useful without meeting all the criteria that have been listed.

Item	Yes	Partly	No			
<b>Preliminary</b>						
1. Appropriate contact details for further information?						
2. Authors identified?						
3. Statement regarding conflict of interest?						
4. Statement on whether report externally reviewed?						
5. Short summary in non-technical language?						
<b>Why?</b>						
6. Reference to the policy question that is addressed?						
7. Reference to the research question(s) that is/are addressed?						
8. Scope of the assessment specified?						
9. Description of the assessed health technology?						
<b>How?</b>						
10. Details on sources of information and literature search strategies provided?						
Search strategy	Databases	Year range	Language restriction	Primary data	Other kind of information resources	
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Complete reference list of included studies	List of excluded studies	Inclusion criteria	Exclusion criteria			
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			
11. Information on basis for the assessment and interpretation of selected data and information?						
Method of data extraction described?	Critical appraisal method (for quality assessment of the literature) described?	Method of data synthesis described?	Results of the assessment clearly presented, e.g. in the form of evidence tables?			
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			
<b>Context?</b> (may or may not apply to each HTA)						
(Medico-) legal implications considered?	Economic analysis provided?	Ethical implications considered?	Social implications considered?	Other perspectives (stakeholders, patients, consumers) considered?		
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>		
<b>What then?</b>				Yes	Partly	No
12. Findings of the assessment discussed?						
13. Conclusions from assessment clearly stated?						
14. Suggestions for further action?						

## Appendix 13

### EXECUTIVE SUMMARY FOR HTA REPORT FORMAT

 <p><b>MaHTAS</b> Malaysian Health Technology Assessment Section</p>	<b>Title</b>
<b>Authors:</b>	<b>Background</b>
<b>Expert Committee:</b>	<b>Technical Features</b>
<b>External Reviewer:</b>	<b>Policy Question</b>
<b>Information Specialist:</b>	<b>Objectives</b>
<b>Disclaimer:</b>	<b>Methods</b>
<p>This Health Technology Assessment has been developed from analysis, interpretation and synthesis of scientific research and/or technology assessment conducted by other organizations. It also incorporates, where available, Malaysian data, and information provided by experts to the Ministry of Health Malaysia. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of the review. For further information please contact:</p>	<b>Results and conclusions</b>
<p>Health Technology Assessment Section (MaHTAS) Medical Development Division Ministry of Health Malaysia Level 4, Block E1, Precinct 1 Government Office Complex 62590 Putrajaya.</p>	<b>Recommendation</b>
<p>Tel: 603 8883 1246</p>	
<p>Fax: 603 8883 1230</p>	
<p>Available at the following website: <a href="http://www.moh.gov.my">http://www.moh.gov.my</a></p>	
<b>Year</b>	
	<i>Executive Summary</i>

## Appendix 14

 <b>INAHTA Brief</b>		<i>Issue 20XX/00X</i>
<b>Title</b>	(Add text)	
<b>Agency</b>	(Add text)	
<b>Reference</b>	(Add text)	
<b>Aim</b>	(Add text)	
<b>Conclusions and results</b>	(Add text)	
<b>Recommendations</b>	(Add text)	
<b>Methods</b>	(Add text)	
<b>Further research/reviews required</b>	(Add text)	
<b>Written by</b>	(Add text)	

## Appendix 15

### EXECUTIVE SUMMARY FOR TR (MINI-HTA) REPORT FORMAT

 <p><b>MaHTAS</b> Malaysian Health Technology Assessment Section</p>	<p style="text-align: right;"><b>Title</b> <b>Executive Summary</b> [Adapted from the report by AUTHOR NAME]</p>
<p>Review Group Membership</p>	<p>Introduction</p>
<p>MaHTAS Reviewer:</p>	<p>Objective/Aim</p>
<p>Information specialist:</p>	<p>Results and Conclusions</p>
<p>External Reviewer:</p>	<p>Methods</p>
<p><b>Disclaimer:</b> Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It is subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.</p>	
<p>For further information please contact:</p>	
<p>Health Technology Assessment Section (MaHTAS) Medical Development Division Ministry of Health Malaysia Level 4, Block E1, Precinct 1 Government Office Complex 62590 Putrajaya.</p>	
<p>Tel: 603 8883 1246</p>	
<p>Fax: 603 8883 1230</p>	
<p>Available at the following website: <a href="http://www.moh.gov.my">http://www.moh.gov.my</a></p>	
<p>Year</p>	
<p>Executive Summary</p>	

## Appendix 16

### INFORMATION BRIEF (RAPID REVIEW) FORMAT

MEDICAL DEVELOPMENT DIVISION  
MINISTRY OF HEALTH MALAYSIA

INFORMATION BRIEF

TITLE:

---

PURPOSE

BACKGROUND

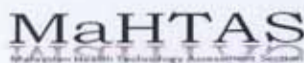
EVIDENCE / INFORMATION SUMMARY

CONCLUSION

REFERENCES

Prepared by:

Date



## MaHTAS USER FEEDBACK

Title of Health Technology Assessment (HTA) / Technology Review (TR) :

.....

1. Your contact information.	
Name : Designation* : Organization* :	Phone : E-mail :  *Compulsory to fill
2. How would you rate the report? (Please tick (✓) one of the following)	
HTA/TR	<input type="checkbox"/> Excellent <input type="checkbox"/> Good <input type="checkbox"/> Fair <input type="checkbox"/> Poor <input type="checkbox"/> Did not read <input type="checkbox"/> Will read later
3. How did you use this report? (Please tick (✓) all that apply.)	
<input type="checkbox"/> Influence or develop policy / decisions <input type="checkbox"/> Influence operational procedures / practices <input type="checkbox"/> Influence guideline formulation <input type="checkbox"/> Change awareness or increase understanding of the issue <input type="checkbox"/> Influence or make operational / capital funding decision <input type="checkbox"/> Others ( please specify ) <input type="checkbox"/> Did not use for the above purpose <i>Comments (please provide specific examples of use where possible. You can use separate paper for your comments )</i>	
4. Regarding the technology, how is it currently being used in your organization or area of jurisdiction?	
<input type="checkbox"/> Not in use and not being considered <input type="checkbox"/> In use – full implementation <input type="checkbox"/> Not in use but under review / considered <input type="checkbox"/> Not applicable <input type="checkbox"/> In use – partial or pilot implementation <input type="checkbox"/> Others ( please specify ) <i>Comments ( You can use separate paper for your comments )</i>	
5. How well did the report meet your needs? (Please tick (✓) one of the following)	
<input type="checkbox"/> Really well <input type="checkbox"/> Well <input type="checkbox"/> Not so well <input type="checkbox"/> Not at all <i>Comments ( You can use separate paper for your comments )</i>	

Please return the completed survey to  
 Health Technology Assessment Section/ MaHTAS, Medical Development Division,  
 Ministry of Health Malaysia,  
 Level 4, Block E1, Parcel E, Presint 1, 62590 Putrajaya.  
 Tel: 603-88831229/1246/1247  
 Fax: (603) 88831230  
 e-mail to [htamalaysia@moh.gov.my](mailto:htamalaysia@moh.gov.my) (Attn. Dr. Jumaiah Sabirin)  
 This form is downloadable from <http://medicaldev.moh.gov.my>

**INAHTA – Framework for reporting on impact of HTA reports**

Before completing the form, you are kindly asked to carefully review the accompanying instructions.

To complete the form, please put the marker on the grey areas to write text and double click on the squares to tick them. The form should be sent to the INAHTA Secretariat via email [secretariat@inahta.org](mailto:secretariat@inahta.org)

<b>A. Agency:</b> [Write here]	<b>B. Name of technology:</b> [Write here]	B.1 [Add any needed qualification – eg particular application]
<b>C. Date of this record:</b> [M/Y]*	<b>D. Date of HTA report:</b> [M/Y]	<i>The date of the record should be <u>not less than 6 months</u> after the publication date of the HTA report</i>
<b>E. Origin of HTA request.</b>	[Give the name or type of organisation that made the request. This might be government – related (eg health ministry) or non – government (eg professional body). If the report was not solicited from outside the agency, please indicate this]	
<b>F. Purpose of HTA</b>	F.1 [Tick] <input type="checkbox"/> 1 Coverage decisions <input type="checkbox"/> 2 Capital funding decisions <input type="checkbox"/> 3 Formulary decisions <input type="checkbox"/> 4 Referral for treatment <input type="checkbox"/> 5 Program operation <input type="checkbox"/> 6 Guideline formulation <input type="checkbox"/> 7 Influence on routine practice <input type="checkbox"/> 8 Indications for further research <input type="checkbox"/> 9 Other [Write here]	F.2 [Single sentence of explanation/qualification, if needed]
<b>G. HTA conclusions</b>	[1 or 2 sentences]	



## The HTA Impact Framework

p. 2/2

<b>II. Indications of impact</b>	<b>H.1. [Tick one or more]</b> <input type="checkbox"/> 1. HTA considered by decision – maker <input type="checkbox"/> 2. HTA recommendations/ conclusions accepted <input type="checkbox"/> 3. HTA demonstrated that technology met specific program requirements <input type="checkbox"/> 4. HTA material incorporated into policy or administrative documents <input type="checkbox"/> 5. HTA information used as reference material <input type="checkbox"/> 6. HTA linked to changes in practice <input type="checkbox"/> 7. HTA linked to changes in health status <input type="checkbox"/> 8. No apparent impact <input type="checkbox"/> 9. Other [Write here]	<b>H.2</b> [1 or 2 sentences to give further information]
<b>I. AGENCY'S opinion on level of impact</b>	<b>I.1. [Tick 1]</b> <input type="checkbox"/> 1. No apparent influence <input type="checkbox"/> 2. Some consideration of HTA by decision maker <input type="checkbox"/> 3. Informed decisions <input type="checkbox"/> 4. Major influence on decisions	<b>I.2</b> [1 or 2 sentences indicating basis reasons for opinion]  [indicate whether unintended influence led to a change in HTA procedure]
	<b>I.3</b> Indicate any unintended influence that the HTA had [Write here]  Did the unintended influence lead to a change in HTA procedure? [Yes/ No]	
<b>J. EXTERNAL opinion on level of impact of the HTA</b>	<b>Source of opinion:</b> [Write here] [Tick 1] <input type="checkbox"/> 1. No apparent influence [Write here] <input type="checkbox"/> 2. Some consideration of HTA by decision maker [Write here] <input type="checkbox"/> 3. Informed decisions [Write here] <input type="checkbox"/> 4. Major influence on decisions [Write here]	



INAHTA – The International Network of Agencies for Health Technology Assessment  
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