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HTA Core Model for Medical and Surgical Interventions
v 1.0r

was developed by

Work Package 4

The HTA Core Model

Work Package 4 Lead Partner: FinOHTA, Finnish Office for HTA, Finland

December 2008
General information on the European network for Health Technology Assessment, EUnetHTA

Background
Health Technology Assessment (HTA) is increasingly used in European countries to inform decision- and policy-making in the health care sector. Several countries have integrated HTA into policy, governance, reimbursement or regulatory processes. Therefore, the EU and Member States in 2004 expressed the need for a sustainable European network for HTA.

EUnetHTA was established to respond to this need. The European Commission and Member States co-funded the three year project (2006–2008) with the aim to develop a sustainable network and information resources to inform health policy making (1, 2, 3). The project, which was based on three prior projects, connected national HTA agencies, research institutions and health ministries and enabled an effective exchange of information and support to policy decisions (4).

What is health technology assessment?
EUnetHTA used the definition of health technology offered by the International Network of Agencies for Health Technology Assessment (INAHTA): “Any intervention that may be used to promote health, prevent, diagnose or treat disease, or for rehabilitation or long-term care. This includes pharmaceuticals, devices, procedures and organisational systems used in health care” (5).

EUnetHTA defined health technology assessment (HTA) as “a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe effective, health policies that are patient focused and seek to achieve best value”.

EUnetHTA aims and strategic objectives
The EUnetHTA project was established to create an effective and sustainable network for HTA across Europe that could develop and implement practical tools to provide reliable, timely, transparent and transferable information to contribute to HTAs in Members States.

The strategic objectives of the EUnetHTA project were to:
- reduce duplication of effort in order to promote more effective use of resources
- increase HTA input to decision making in Member States and the EU in order to increase the impact of HTA
- strengthen the link between HTA and health care policy making in the EU and its member states
- support countries with limited experience of HTA.

Structure of EUnetHTA
The EUnetHTA Partnership involved 64 organisations: 1 Main Partner, 33 Associated Partners, and 30 Collaborating Partners. In total, 33 countries (Europe: 25 EU and 2 EEA countries (Norway, Iceland), Switzerland and Serbia; outside Europe: Australia, Canada, Israel, USA) participated in the project. The list of partners is accessible at: www.eunethta.net
Management and leadership
EUnetHTA governance structure consisted of
- the Steering Committee which comprised the heads of each of the Associated Partners or representatives appointed by the head. The head of the Main Partner chaired the Steering Committee. The Steering committee mandated the the management of the network to:
- the Executive Committee representing the Main Partner and Work Package Lead Partners,
- the Secretariat under the leadership of the Main Partner which provided managerial support to the overall project and ensured ongoing contact to the DG SANCO.

Collaborating Partners participated in the work packages and received internal communication on a regular basis.

The modes of operation of the network were described in a standard operating procedures (SOP) manual, a communication strategy, and supported by virtual and face-to-face meetings, website (with the Members Only work area), regular e-newsletter and other types of communication tools. The Associated Partners agreed on 3-year work plan during the first Steering Committee meeting and project results were presented at the EUnetHTA Conference “HTA’s Future in Europe”, in journal articles and conference presentations.

Work Packages and major results
The scientific work in the EUnetHTA project took place in separately managed Work Packages (WPs), each led by a Lead Partner. The following major results were achieved:
- A well functioning network of partners and colleagues from HTA agencies, research institutions and health ministries (WP1 - DACEHTA/National Board of Health, Denmark)
- A well functioning Information platform and website (www.eunethta.net) (WP2 - SBU, Sweden and Co-Lead Partner – DIMDI, Germany)
- Internal evaluations that helped to adjust work plans (WP3 – NOKC, Norway)
- A comprehensive, evidence-based and validated common framework for HTA information (HTA Core Model) applied to two types of technology to produce generic Core HTAs a) on medical and surgical interventions (Drug Eluting Stents) and b) on diagnostic technology (Multislice CT coronary angiography) (WP4 - FinOHTA, Finland)
- A handbook instructing in the use of the Core HTA Model (WP4 - FinOHTA, Finland)
- An Adaptation Toolkit (and a guidance document) composed of a series of checklists and resources which address the relevance, reliability and transferability of data and information from existing reports (WP5 - NCCHTA, UK)
- A book "Health technology assessment and health policy-making in Europe” (WP6 - DACEHTA/National Board of Health, Denmark)
- A web-based Stakeholder Open Forum, a Draft Stakeholder Policy and Discussion Topic Catalogue; (WP6 - DACEHTA/National Board of Health, Denmark)
• Web-based tools for information sharing on the monitoring of new promising technologies and information service on emerging technologies (WP7 – HAS, France, and Co-Lead Partner- LBI/HTA, Austria)
• A handbook on HTA capacity building (WP8 - CAHTA, Spain)
• A proposal for a permanent EUnetHTA Collaboration after two rounds of public consultation (WP1 - DACEHTA/National Board of Health, Denmark)

Based on best practice each Work Package developed the methods suitable for their purpose, which is described in WP-specific products. The Lead Partners were responsible for coordination within the WP, for bringing work forward, producing and reporting results, for sending management information reports to the Main Partner and for responding to internal evaluation questionnaires.

The next phase
Through a series of internal and public consultation rounds, the network developed a Proposal for the EUnetHTA Collaboration (published June 16, 2008) detailing the approaches for the future development of the network. A group of founding partners was established after this to implement the proposal for EUnetHTA Collaboration.

References
5. INAHTA: http://www.inahta.org/GO-DIRECT-TO/Members/ (downloaded 20 October 2008)
HTA Core Model for Medical and Surgical Interventions

This document is a revised version of the final project deliverable on the 31st of December 2008.

The HTA Core Model will be developed further within the EUnetHTA Collaboration. The most recent version of the Model should be used when conducting assessments.

The HTA Core Model is subject to Terms of Use.

For the most recent version of the Model and the Terms of Use, please visit http://www.eunethta.net.
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Editors' Notes

This is the final version of this document. It represents a considerable amount of work by many people across Europe. The document is divided into chapters, most of which present one domain of work within HTA. In the beginning of each chapter the main authors have been listed. Several others, however, have contributed to the work. Their names can be found in the chapter "Teams” of this report.

Each chapter describing domains of the HTA Core Model contains the following sections:

- Domain description: what this domain is about?
- Methodology: what kind of research methodology is typically used (or should be used) within this domain?
- Assessment elements: what is being studied within this domain (in more detail), what are the topics and issues within this domain?
- References

A validation of the draft version of this document, published in July 2007, has been performed. Results of the validation as well as feedback acquired through a public consultation have been considered when finalizing this document.

The HTA Core Model represents a novel method of performing and reporting HTA and hence the current version requires further testing and refinement. Future development will take place within the EUnetHTA Collaboration. Users of the HTA Core Model should always utilize the most recent version, available through www.eunethta.net.

An online tool to support easier utilization of the Model is under construction. It will be available in 2009.

The HTA Core Model is subject to Terms of Use, available through www.eunethta.net.
WP4 Teams

The work on different domains has been done as a collaborative effort of WP4 teams. Each team consists of investigators that are responsible for writing the sections of the report and reviewers whose task is to provide support and feedback to investigators in their team. Each team has also a coordinator on behalf of FinOHTA.

Notice that not all persons indicated as authors of this documents are listed below as team members. This is due to the fact that the persons within WP4 teams changed at least partially between the two models that were designed during the project. In the context of some domains, the same (or almost the same) text was finally used in both model documents. The authorship of such texts is acknowledged in both model documents.

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Introduction

Kristian Lampe, Finn Børn Christensen, Marjukka Mäkelä, Inger Norderhaug, Alberto Ruano Ravina, Marcial Velasco Garrido, Ilona Autti-Rämö

The organization of health technology assessment (HTA) and the settings in which HTA agencies operate vary considerably across countries. According to a recent study there are also significant differences in the practical application of HTA. HTA is usually defined as a multidisciplinary field of research, but the extent of analysis varies. Whereas in some countries HTA merely studies the clinical effectiveness and perhaps safety and cost-effectiveness of technologies, agencies in other countries apply a broader perspective and consider also other issues, such as ethics, or organisational, social or legal aspects of technology.

Differences in health care systems and in the organization of HTA probably explain a large part of the variance in international HTA. On the other hand, differences in how HTA is perceived, understood or used in various parts of the world may have an important impact on the way it is performed and used. Hence different applications of HTA may exist even in settings where there are no substantial differences in the health care system or in the organization of HTA.

The varying implementation of HTA internationally and even within Europe makes sharing of information difficult and reduces the applicability of foreign HTA results for one’s own purposes. This applies even in cases where use of assessment produced elsewhere would be feasible because of low context-dependency of their results.

Another problem in importing assessment results of HTAs is the non-standardized information structure of reports. An HTA report can be seen as a collection of information which represents the result of an assessment process. Information in the reports is typically organized in a specific – though very rough – structure that follows the traditional headings of a scientific publication (abstract, background, methods, results, conclusions and references). This structure varies somewhat depending on the local characteristics of HTA (i.e. inclusion

Definitions of HTA

Technology assessment in health care is a multidisciplinary field of policy analysis. It studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology.

INAHTA 2007

Health technology assessment (HTA) is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value. Despite its policy goals, HTA must always be firmly rooted in research and the scientific method.

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of recommendations section or appendices which document stakeholders' positions, etc.). Besides variation in the number of sections, the internal structure of chapters also varies. Currently, most - if not all - reports represent a mixture of plain text and evidence tables, lacking an in-depth structure that would enable easy access to various pieces of information - either by humans or computers. Different sections contain pieces of information that are quite difficult to extract or analyze without reading the whole report and using substantial human effort in merely identifying those parts of the data that are of greater interest for one’s own purpose.

The need for clear structure, transparency, and rigorous handling of information in any HTA leads to a need for standardisation. Steps towards definition of some standards at the international level have been done by INAHHTA (checklist) and the previous European Projects (EUR-ASSESS, ECHTA/ECAHI).

The exchange of HTA reports across borders is an important means to enable each national HTA agency to work more efficiently. There are examples of HTA reports being successfully adopted across agencies, but also of duplication. Developing a core model for HTA will aim to increase the use of HTA-reports across agencies.

Practical advice on how to conduct HTA is available in earlier European projects and relevant national guidelines. In the European context we refer particularly to the Working Group 4 - "Best practice in undertaking and reporting HTA" - of the ECHTA/ECAHI project. The core model developed within the EUUnetHTA project builds on earlier work and aims at being more specific when a) operationalising the questions that should be asked and answered within an HTA and b) defining and standardising the fine structure of the final product - the HTA report. This is explained in more detail in the next chapter "General design".

### Research methods in HTA

HTA applies a number of research methods, many of which draw from the general development in evidence-base healthcare. Often information is collected through production of a systematic literature review that brings together and summarises the available evidence in the scientific literature. Further joint estimates of the effects of technology can be produced through meta-analyses of available studies. Whenever adequate information is not available, primary research may be warranted. Currently randomised controlled trials represent the state-of-the-art method in providing reliable data particularly on questions regarding effectiveness. Also many other research methods can be and are used in HTA, e.g. register studies, surveys and focus group interviews. Preferred or most suitable methodology varies between HTA agencies and the aspects and contexts of assessment.

Various research methods have been well documented in scientific literature. The core model for HTA does not redefine these basic scientific methods, but it employs all available research methods whenever feasible. Detailed descriptions of the methods can be found in relevant literature and standards.

Sometimes the scientific paradigm that the researchers base their work on may strongly affect the design and results of HTA. An important example can be seen in innovation research, where two models have different starting points. The (linear) diffusion model perceives new technology as an external stable entity that is brought to a (health care) system and induces changes. A competing paradigm, the translation model, presumes that technology undergoes
changes in the environment it is brought into (such as a health care setting). Hence the final impact will not depend on the original technology only. Application of these two paradigms is discussed further in the chapters on social and organisational aspects of HTA.

**Ethics of HTA**

The HTA Core Model assumes that ethical aspects of health technologies should be considered in HTAs. Ethics, however, has also a broader application within HTA. The assessments themselves should be designed in such a way that key ethical principles are considered and respected.

In order to safeguard against unethical use of technologies and to emphasise beneficial uses of technologies, every HTA process should be performed considering the following ethical issues:

- The driving forces (and valued interests) to perform the assessment at this stage should be identified, including the stakeholders and the whole HTA organisation.
- The morally relevant reasons for performing / not performing a HTA on this topic should be identified.
- The interests of the producers of the technology should be identified.
- It should be identified whether there are related technologies that are morally contentious.
- The interests of the content expert group should be discussed openly so that the work can be conducted in an objective and independent way.
- The choice of end points in the assessment has to be carefully considered.
- The morally relevant issues related to the selection of meta-analysis and studies to be included in the HTA have to be identified.
- The scope of the HTA and choice of research methods (e.g. inclusion of other aspects of assessment than effectiveness in the literature searches).

These issues are discussed in further detail in the appendix below.

**References**

2. European Network for Health Technology Assessment. Definition of HTA. http://www.eunethta.net/HTA/
Appendix: Ethical considerations within HTA process

Every HTA process should be performed considering the following ethical issues:

- The driving forces (and valued interests) to perform the assessment at this stage should be identified, including the stakeholders and the whole HTA organisation. Are there particular interests that make this technology subject to assessment (pressure from producers, patient groups or professionals, costs)?
- The morally relevant reasons for performing / not performing a HTA on this topic should be identified. Is the topic a significant public health issue? Is the technology likely to benefit public health? Are HTA resources wisely spent on this topic? Is the topic a priori morally contentious? Is there fear of presenting unpopular results? Has the technology already been implemented without proper, objective evaluation? Is the technology being used beyond its actual target group? Have the costs exceeded the resources?
- The interests of the producers of the technology should be identified. Developers and producers are interested in promoting their technology which influences the distribution and use of technologies. What are the financial interest in respect to "well doing"?
- It should be identified whether there are related technologies that are morally contentious, or if the technology is a novel, innovative mode of care. It is important to identify, from the beginning, whether there are ethically relevantly similar technologies in use. They may provide useful casuistic background for the ethical analysis. On the other hand, novel, innovative technologies may pose unexpected ethical problems and value conflicts, which may justify extra emphasis placed on ethical analysis.
- The interests of the content expert group should be discussed openly so that the work can be conducted in an objective and independent way. It is morally important to evaluate the relationship between professionals and the industry with respect to the development and use of the technology in question. What are their final interests? Is the technology of relevance for the professional identity and development?
- The choice of end points in the assessment has to be carefully considered. The choice of end points lead to questions that of moral relevance. What is the aim of technology - to reduce mortality, increase functional status, improve quality of life, lengthen disease-free time, save money? Are there other stakeholders with possible gains or loses that should be evaluated? The decision on endpoints has also an impact on the inclusion criteria of original studies and thus may not reflect the entire existing literature on the technology in question.
- The morally relevant issues related to the selection of meta-analysis and studies to be included in the HTA have to be identified. The choice of endpoint affects the inclusion criteria for original studies to be accepted. What to do when the quality criteria are not filled by any existing studies or when no RCT studies exist - especially when the technologies are
already being used? When is it necessary to continue with the HTA even if no RCTs are available?

- The scope of the HTA and choice of research methods (e.g. inclusion of other aspects of assessment than effectiveness in the literature searches).
  
  The literature searches focused only on the effectiveness of the technology in question seldom give access to articles relevant to other domains of assessment (e.g. the ethical, social or organizational analysis). Ethically relevant issues may be identified during the entire HTA process and the literature searches are thus possible first after their identification. The literature search should cover other related technologies with similar ethical challenges. The detailed presentation of questions and experiences related to a (ethically relevantly) similar technology are important, as they may help decision makers identify relevant issues and adopt coherent policies.
General design

Kristian Lampe, Finn Børørum Kristensen, Marjukka Mäkelä, Inger Norderhaug, Alberto Ruano Ravina, Marcial Velasco Garrido

The HTA Core Model

The HTA Core Model is an attempt to define and standardise elements of an HTA. The model tackles particularly the two problems of HTA reports presented in the introduction: variation in the contents and lack of a refined (detailed and standardised) structure.

First the HTA Core Model facilitates a shared understanding of what belongs to HTA. In other words, it suggests what kinds of information one could find in an HTA report - and perhaps should find in an ideal comprehensive assessment. As a consequence, it can contribute to reducing the differences in content across local (national, regional, etc.) reports. This process, however, should not be understood as an attempt to completely standardise HTAs. There may be valid reasons for differences in the contents of local assessments. The aim of EUnetHTA is to provide the HTA community with a Model that makes it easier for researchers to take into account important aspects of assessment and address them in a cohesive manner.

Secondly, the Model enables future international, systematic and even automated use of HTAs through a shared and more detailed structure. The Model can also be used for educational purposes within HTA.

Different types of technology - such as drugs, devices or interventions - may require different kinds of assessment. The current model is an application or a "subset" of the HTA Core Model and limited to medical and surgical interventions. Another model for diagnostic technologies has been produced within the project as well.

The HTA Core Model builds on earlier work of projects EUR-ASSESS\textsuperscript{1}, HTA Europe\textsuperscript{2} and ECHTA/ECAHI\textsuperscript{3} as well as on other theoretical guidance\textsuperscript{4-6}. It is loyal to the definitions of HTA that emphasize the multidisciplinary nature of assessments. The current first version employs the following nine domains that were originally identified in the EUR-ASSESS project:

1. Current use of the technology (implementation level)
2. Description and technical characteristics of technology
3. Safety
4. Effectiveness
5. Costs, economic evaluation
6. Ethical aspects
7. Organisational aspects
8. Social aspects
9. Legal aspects
The current approach draws also from recent developments in information science. It goes a step beyond earlier methodological guidance that has strongly relied on the classical structure of a scientific paper and constructs an **ontology** for HTA. The aim is to facilitate extraction and usability of information.

**Ontology of HTA**

In philosophy, an ontology has traditionally been a theory of *being* or *existence*, i.e. a description of what types of things exist. In recent times, the term has been increasingly used slightly differently in the context of information management - the semantic web in particular. In such contexts, one of the key aims has been to assign meanings to pieces of information and to describe the relations between concepts. Hence an ontology of postal addresses may define that "zip code" and "postal code" essentially describe the same data, although the heading is different. A range of postal codes may in turn describe a range of codes within one city.

Ontologies typically make it easier for both humans and computers to understand information and its context. They also promote the usefulness of information beyond the system or setting in which they were produced or originally used. Such application is particularly relevant for European HTA, since the use of foreign HTAs essentially requires extraction of data from foreign reports and appraisal of its usability in local settings. When data extraction is made easier through well-defined structure and when meanings of each piece of information are clear, the application of foreign data is likely to be less complicated than before.

Increased standardisation of the way of searching, handling, and presenting of information may lead to better use of informatics within HTA in the future and promote a clearer systematic approach that is more easily reproducible. Similar problems related to presentation and use of information have been well noted within many other medical settings, e.g. in the development of electronic patient records. Structuring information is a key field of research and development in knowledge representation and artificial intelligence. Due to the difficulties in utilizing non-structured data, modern information applications tend to go towards well-defined information structures that enable transparent, verifiable and standardized extraction, analysis and other use of data - with or without the help of computers.

**Assessment elements**

The basic unit of the model is an **element**. It defines a piece of information that describes the technology or the consequences or implications of its use. In the context of clinical research, an element may describe a clinical outcome (e.g. reduction of symptoms), whereas in social science an element may describe the impact of technology on patient's life (e.g. ability to work). The nature of elements may vary across domains, since the consequences and implications are understood and studied differently in each domain. The common denominator for all elements is that they **provide information** that may be useful when deciding on the use or non-use of any given technology.
As the number of possible elements of HTA is very large, perhaps infinite, the model is limited to

a) elements that deal with context-independent information and  
b) elements that are particularly significant from the viewpoint of HTA (even if these would not be easily transferable).

These two features of elements are not mutually exclusive. An element may be both context-independent and very important. In this model context independent information is such information on any given technology that is transferable to another context (e.g. another geographical area, health care system or policy setting). Transferability and importance are discussed further below (see "Element cards" and "Inclusion in the core").

It would also be possible - and perhaps useful - to perceive any piece of information contained in an HTA report as an assessment element (such as details on original policy question, literature search, or conclusions). At this phase, however, the ontology excludes such elements.

The globalisation of health care interventions challenges HTA institutions to develop methods to share the assessment work and results. It is expected that future HTAs which are conducted using the core model can be more easily utilized in another region or country. This assertion builds on a key hypothesis of the EUnetHTA project, which is that by reaching clarity on and describing what the core of HTA consists of, this will lead to much better opportunities to share what can be shared in the production of HTA – be it a completely new HTA with a prospectively produced core or sharing of existing HTA from other settings.
Basic concepts

The ontology of HTA is structured according to the following basic concepts:

Domain
A wide framework within which the technology is considered. An angle of viewing the use, consequences and implications of any technology. A standard set of domains is agreed on within the project.
Currently the following domains (headings slightly modified from EUR-ASSESS) are considered:
1) Health problem and current use of technology,
2) Description and technical characteristic of technology,
3) Safety,
4) Clinical effectiveness,
5) Costs and economic evaluation,
6) Ethical analysis,
7) Organisational aspects,
8) Social aspects,
9) Legal aspects.

Topic
A more specific area of consideration within any of the domains. One domain is divided into several topics. Similar topics may be addressed within more than one domain.
Examples:
Clinical effectiveness / Life expectancy;
Current use of technology / Regulatory status;
Societal aspects / Ability to work;
Societal aspects / Economic self-sufficiency

Issue
An even more specific area of consideration within any of the topics. One topic typically consists of several issues, but it may also contain only one issue. An issue is expressed as a question. Such questions may be similar to research questions within scientific studies.
Examples:
Clinical effectiveness / Mortality / What is the effect of the intervention on the mortality caused by the target disease?;
Clinical effectiveness / Mortality / What is the effect of the intervention on the mortality due to other causes than the target disease?;
Current use of technology / Regulatory status / Has the technology been approved by relevant authorities in the EU?

The combination of a domain, a topic and an issue defines a single assessment element. The model structure is based on such domain-topic-issue combinations. Each element is described in more detail in an element card (see below).
Similar issues may exist within different domains, perhaps even within different topics of one domain. Such overlaps do not constitute a problem in this model, since the combination of domain-topic-issue reveals the context of an issue.

If two issues that look similar at the first glance are genuinely different, i.e. they would be analyzed differently from the viewpoint of two different domains (or topics), they constitute two separate elements. If on the other hand the issue is largely perceived and analyzed similarly within both domains (or topics), it constitutes only one assessment element that is common to both domains.

The current version of the model contains a total of 133 assessment elements. The number of topics within each domain ranges from 3 to 8 and the number of issues from 6 to 25. On average each topic is divided into 3 issues. Details are available in the following table.

Table 1. Number of topics and issues in the domains.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Topics</th>
<th>Issues</th>
<th>Issues per Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health problem and current use</td>
<td>6</td>
<td>19</td>
<td>3.2</td>
</tr>
<tr>
<td>Description and technical characteristics</td>
<td>3</td>
<td>15</td>
<td>5.0</td>
</tr>
<tr>
<td>Safety</td>
<td>5</td>
<td>15</td>
<td>3.0</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>4</td>
<td>18</td>
<td>4.5</td>
</tr>
<tr>
<td>Costs, economic evaluation</td>
<td>5</td>
<td>6</td>
<td>1.2</td>
</tr>
<tr>
<td>Ethical analysis</td>
<td>8</td>
<td>15</td>
<td>1.9</td>
</tr>
<tr>
<td>Organisational aspects</td>
<td>4</td>
<td>11</td>
<td>2.8</td>
</tr>
<tr>
<td>Social aspects</td>
<td>3</td>
<td>9</td>
<td>3.0</td>
</tr>
<tr>
<td>Legal aspects</td>
<td>7</td>
<td>25</td>
<td>3.6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>45</td>
<td>133</td>
<td>3.0</td>
</tr>
</tbody>
</table>
**Element cards**

Each assessment element is described in further detail in *element cards*. These descriptions are generic in nature, i.e. they are not specific to any technology. The basic set of cards and their content in the model is constant. Hence the cards do not change depending on technology. Any changes to the cards alter the whole model. It should be emphasised, however, that the model at hand applies only to medical and surgical interventions - not to any type of health technologies.

The practical application of the cards, i.e. how to use the model, is explained in detail below.

Examples of element cards are included at the end of the general design section. The following information is available in each card:

<table>
<thead>
<tr>
<th>Information</th>
<th>Explanation</th>
<th>Format</th>
<th>Defined by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Element ID:</td>
<td>An individual code for each element.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domain:</td>
<td>The domain within which the element belongs to.</td>
<td>Standard list</td>
<td>General design team</td>
</tr>
<tr>
<td>Topic:</td>
<td>The topic within which the element belongs to.</td>
<td>Standard list</td>
<td>Each team within their domain. In collaboration with the general design team.</td>
</tr>
<tr>
<td>Issue:</td>
<td>The specific question within the aspect and topic. Should be in the form of a question.</td>
<td>Standard list</td>
<td>Each team within their domain.</td>
</tr>
<tr>
<td>Clarification:</td>
<td>A brief clarification that explains what the issue is about. Clarification is not necessarily needed if the issue is self-explanatory.</td>
<td>Free text.</td>
<td>Each team within their domain.</td>
</tr>
<tr>
<td>Importance:</td>
<td>Defines how important it is to consider the particular issue when conducting HTA. This importance has to do with significance from the viewpoint of HTA. This is not always the same as &quot;relevance&quot; in a particular policy context.</td>
<td>3 categories: Critical Important Optional</td>
<td>Initially within each team. Wider consensus sought from all project participants.</td>
</tr>
<tr>
<td>Information sources(s):</td>
<td>An explanation of how to find answers to this particular issue. What methodology to use? If there are several possible methodologies, which are preferred? Where to find relevant information?</td>
<td>Free text</td>
<td>Each team within their domain.</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Transferability:</td>
<td>An estimate about the transferability of data or other findings from one context to another.</td>
<td>3 Categories: Complete Partially Not</td>
<td>Initially within each team in collaboration with WP5. Wider consensus sought from all project participants.</td>
</tr>
</tbody>
</table>
| Reference:              | Indicates the reference of the issue. Serves (among other things) the following purposes:  
- Credit to earlier work  
- Sources for more information on the topic  
Particular attention to earlier European HTA projects, as well as to international standards, such as the ICF (International Classification of Functioning, Disability and Health). | Free text. | Each team within their domain. |
| Relations:              | Some (perhaps most) of the elements are in some related to other elements in the whole model. For instance issues within the topic "quality of life" may be discussed both in the context of "effectiveness" as well as in the context of "economic evaluation". This field provides a means to express such relations. In the current version relations are expressed in free text. In an electronic version of the model, relations may be expressed through direct links between elements. | Primarily a list of Element IDs Free (explanatory) text allowed as well. | All teams, including the general design team. |
| Status:                 | Indicates whether the element belongs to the HTA core or a wider HTA framework. See chapter "Inclusion in the core"  
Elements that clearly do not belong to the core are not described in their respective cards in such a detailed manner as all the other elements. | 3 categories: Core Borderline Not core | Initially within each team in collaboration with WP5. Wider consensus sought from all project participants. |

Displaying the assessment elements are cards fits better electronic formats and resources. To prevent an excessively large paper report, key information regarding each card has been
collected into a table format within each domain. These tables are available in respective chapters (see "Assessment elements" within each domain).

**Inclusion in the core**

The model defines a common core for HTA that can be used in multiple countries or regions. Not all elements defined in the ontology belong to the core. In this model, the inclusion of an element in the core is a function of two basic characteristics of the element: its importance and transferability.

Transferability is an obvious factor in such consideration, as any information that is very specific to a particular context (e.g. region, country, health care system) is most likely not useful in other settings. On the other hand, if the information is fully or partly transferable, it may provide valuable input beyond its original production location.

Importance is included in the consideration to ensure that the core is robust enough, i.e. that it contains information that is really significant from the viewpoint of HTA. The importance considered here is not equal to relevance of information for a particular policy question. It is assumed, however, that issues perceived important from the viewpoint of HTA are often useful when making decisions on health care policy.

Importance and transferability are not necessarily dependent on each other. There may be issues that are very important to consider from the viewpoint of HTA, but that contain data that is only partly transferable to other settings. Likewise, there may be data on other issues that are very easy to transfer from one setting to another, but that are not so significant from the viewpoint of HTA.
The inclusion in the core is defined according to the following core matrix:

<table>
<thead>
<tr>
<th>Transferability</th>
<th>Importance</th>
<th>Optional</th>
<th>Important</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>Borderline -&gt; Not Core</td>
<td>Core</td>
<td>Core</td>
<td></td>
</tr>
<tr>
<td>Partially</td>
<td>Not core</td>
<td>Borderline -&gt; Core</td>
<td>Core</td>
<td></td>
</tr>
<tr>
<td>Not</td>
<td>Not core</td>
<td>Not core</td>
<td>Borderline -&gt; Core</td>
<td></td>
</tr>
</tbody>
</table>

Category "borderline" was included in the matrix during the project period, but it was to be removed from the final version of the Model. The table above indicates our proposed final version at this stage, but further testing will be required to confirm the selections.

It should be emphasized that the inclusion or exclusion of an element into or from the Core is driven by usability of the information across national borders of other contexts. Not belonging to the core does not mean that an element would be unimportant, insignificant or not worth considering in an HTA. On the contrary, important assessment elements (that are not transferable) are excluded from the Core by definition (see Core matrix above). Such elements are likely to provide useful or even critical information to guide decision-making and need to be addressed locally by individual HTA agencies.

In the current version of this document the importance and transferability of each element - and hence their status regarding the Core - has not always been considered enough. Therefore any judgements should be regarded as tentative. Further testing, that will take place after the project period, will provide more accurate values.
Working method

The HTA Core Model was built by several working groups (called "teams") within WP4. Each team focused on one domain. The teams were first requested to agree on a definition of the domain they work on. This definition focused the efforts and provided some indications of possible overlaps with other domains. After this, the teams were requested to define lists of topics and issues within the topics. Hence various teams had created a number of assessment elements. Finally, the importance and transferability for each element was considered and other data on the element were included in an element card. The results of this process are presented in a table within each domain chapter (under heading "Assessment elements"). For practical reasons individual cards are not included in this report.

It is important to acknowledge at this phase of the core model development that the two key characteristics assigned to elements, i.e. their importance and transferability, are a result of a consensus process. Various teams aimed at finding a consensus on the category assigned to each element. Hence the category suggested here does not necessarily reflect a unanimous rating of importance and transferability of each element by the team members. Neither should the ratings suggested here for each element's importance and transferability be seen as final judgements. Further testing may affect the status of each element.

The current version of the model was discussed also in two workshops organized by WP4 Lead Partner in September 2006 and January 2007.

From HTA Core Model to Structured HTA information and Core HTAs

The HTA Core Model can be utilized in two ways for conducting HTA.

Core HTAs are comprehensive assessments that take into account the multidisciplinary nature of health technology assessment. When producing a Core HTA, one should consider all the domains of the Core Model (see the process in more detail below). A Core HTA also contains a summary of the findings of each domain, drawing together evidence gathered in the multidisciplinary process. It should be emphasized that the Core HTA - including its summary - refrains from giving recommendations of the use or non-use of technology.

The second type of use is a more "liberal" selection and use of various assessment elements, perhaps from only one or few of the domains.

Both the Core HTAs and other type of information created through the process explained below constitute a collection of Structured HTA Information that can be utilized in multiple ways when performing local HTAs.
**Process**

The detailed characteristics and breadth of an HTA depends on the technology to be assessed. These differences are taken into account when applying the core model to a single HTA. In that process topic-specific judgements and adjustments need to be made on two levels.

First one needs to consider whether a particular element is relevant for the technology to be assessed. If it is relevant, an answer to the issue question should be found within the core HTA. If the model suggests an issue that is not relevant, finding an answer may be omitted. This exclusion, however, should be recorded in the report, as it may provide useful information for report users who are not necessarily able to make such judgements themselves. For instance issues related to mortality are most likely quite relevant in the context of technologies such as drug eluting stents or gamma knife, but not equally relevant in the context of e.g. mild cortisone creams.

The second adjustment converts the issues into actual research questions. Many of the issues defined in the model are too general to be used as research questions without modifications. The issue within the model only presents the problem on a general level; each research group needs to translate the issue into a research question or several of them. The core HTA should find answers to these questions.

The model guides researchers in selecting which aspect of technology or its use they could (or should) study. Research tradition and guidelines within each scientific domain guide the process in which questions are formulated. In clinical research it is often useful to apply the PICO principle (patients/population, intervention, comparison, outcomes) at this phase.

The element cards provide guidance on how to conduct research, i.e. how to answer the actual research questions. Particularly the field "Information sources" in the cards may contain useful hints, recommended research methodologies or even common research standards (if so desired).

**Table 2. Examples of hints, recommendations and standards in element cards**

<table>
<thead>
<tr>
<th>Content of field &quot;Information sources&quot;</th>
<th>Nature of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Database X can be used</td>
<td>Hint</td>
</tr>
<tr>
<td>Use of Database X is recommended.</td>
<td>Recommendation</td>
</tr>
<tr>
<td>Database X shall be used to check Y.</td>
<td>Standard</td>
</tr>
<tr>
<td>A systematic literature review may be useful</td>
<td>Hint</td>
</tr>
<tr>
<td>A systematic literature review is recommended</td>
<td>Recommendation</td>
</tr>
<tr>
<td>A systematic literature review shall be conducted</td>
<td>Standard</td>
</tr>
<tr>
<td>A systematic literature review shall be conducted using the methodology described in the Cochrane Handbook for Systematic Reviews of Interventions</td>
<td>Standard with detailed requirements regarding methodology</td>
</tr>
</tbody>
</table>
Notice that the information intended to be used in the cards is available in the chapter "Assessment Elements" within each domain (see particularly the tables). Actual cards are not included in this version, as those are more suitable for databases in online environment.

**Reporting**

The model also provides the assessment with a common structure for presenting the findings. Various domains, topics and issues can be used as headings for the report when writing a "traditional" paper report. In the structure of the core HTA, issues can also be replaced with research questions - as we will do in the first core HTA on drug eluting stents. The structure also enables the storage of the assessment in electronic databases and other applications where the results of assessments can be combined and analysed.

**Table 3. Examples of how issues defined in the core model are translated into research questions.**

<table>
<thead>
<tr>
<th>CORE MODEL</th>
<th>CORE HTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the technology reduce the severity of symptoms of disease?</td>
<td>Do drug eluting stents reduce chest pain in patients with angina pectoris?</td>
</tr>
<tr>
<td>Can informed consent be received?</td>
<td>Are stroke patients able to provide informed consent for anticoagulation treatment?</td>
</tr>
<tr>
<td>Does the technology challenge cultural values?</td>
<td>Is screening for fetal malformations accepted by all subgroups in the population?</td>
</tr>
</tbody>
</table>
Examples of element cards

Example 1: Empty element card

<table>
<thead>
<tr>
<th>Element ID:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Domain:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health problem and current use of technology</td>
</tr>
<tr>
<td>Description and technical characteristics</td>
</tr>
<tr>
<td>Safety</td>
</tr>
<tr>
<td>Clinical effectiveness</td>
</tr>
<tr>
<td>Economic evaluation</td>
</tr>
<tr>
<td>Ethical analysis</td>
</tr>
<tr>
<td>Organisational aspects</td>
</tr>
<tr>
<td>Social aspects</td>
</tr>
<tr>
<td>Legal aspects</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Topic:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Issue:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Clarification:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Importance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
</tr>
<tr>
<td>Important</td>
</tr>
<tr>
<td>Optional</td>
</tr>
</tbody>
</table>

Specific requirements for importance:

<table>
<thead>
<tr>
<th>Information source(s):</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Transferability:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
</tr>
<tr>
<td>Partially</td>
</tr>
<tr>
<td>Not</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Relations:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Status:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core</td>
</tr>
<tr>
<td>Borderline</td>
</tr>
<tr>
<td>Not Core</td>
</tr>
</tbody>
</table>
Example 2: Element card on Mortality

<table>
<thead>
<tr>
<th>Element ID:</th>
<th>00001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain:</td>
<td>□ Health problem and current use of technology</td>
</tr>
<tr>
<td>Topic:</td>
<td>Life expectancy</td>
</tr>
<tr>
<td>Issue:</td>
<td>What is the direct effect of the technology on the mortality of patients?</td>
</tr>
<tr>
<td>Clarification:</td>
<td>Use of technology may have a direct impact on patients' life expectancy. It is an important part of effectiveness.</td>
</tr>
<tr>
<td>Importance:</td>
<td>Explanation:</td>
</tr>
<tr>
<td>Specific requirements for importance:</td>
<td>None</td>
</tr>
<tr>
<td>Information source(s):</td>
<td>Typically studied by conducting a systematic literature review.</td>
</tr>
<tr>
<td></td>
<td>Preferred study type: randomised controlled trial.</td>
</tr>
<tr>
<td></td>
<td>If adequate data is not found in the literature, conducting relevant primary research should be considered.</td>
</tr>
<tr>
<td></td>
<td>Health care registers may provide useful data on mortality.</td>
</tr>
<tr>
<td>Transferability:</td>
<td>Explanation:</td>
</tr>
<tr>
<td></td>
<td>In most cases data on mortality is transferable from one population or setting to another.</td>
</tr>
<tr>
<td></td>
<td>The following factors should be considered when using information produced in other countries or settings:</td>
</tr>
<tr>
<td></td>
<td>- patient characteristics (age, gender, race)</td>
</tr>
<tr>
<td></td>
<td>- comorbidity</td>
</tr>
<tr>
<td></td>
<td>- co-interventions</td>
</tr>
<tr>
<td>Reference:</td>
<td>Mortality is discussed in several sources.</td>
</tr>
<tr>
<td>Relations:</td>
<td>Mortality is considered also in the context of quality of life.</td>
</tr>
<tr>
<td>Status:</td>
<td>Explanation:</td>
</tr>
</tbody>
</table>
### Example 3: Element card on Approval

<table>
<thead>
<tr>
<th>Element ID:</th>
<th>00002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain:</td>
<td><img src="true" alt="Health problem and current use of technology" /></td>
</tr>
<tr>
<td>Topic:</td>
<td>Regulatory status</td>
</tr>
<tr>
<td>Issue:</td>
<td>Has the technology been approved by relevant authorities in the EU?</td>
</tr>
<tr>
<td>Clarification:</td>
<td>The use of many health technologies requires authorization by relevant bodies either on international or national level. Data on possible approval defines also the legal status of the technology and often provides information on safety.</td>
</tr>
<tr>
<td>Importance:</td>
<td><img src="true" alt="Critical" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Important" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Optional" /></td>
</tr>
<tr>
<td>Specific requirements for importance:</td>
<td>Critical if the technology requires approval by an authority (such as drugs and medical devices). Medical and surgical procedures do not always require authorisation.</td>
</tr>
<tr>
<td>Information source(s):</td>
<td>EMEA, national authorities</td>
</tr>
<tr>
<td>Transferability:</td>
<td><img src="true" alt="Complete" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Partially" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Not" /></td>
</tr>
<tr>
<td>Relations:</td>
<td>See also relevant elements within safety and legal aspects. <em>LIST OF THOSE ELEMENTS NEEDED HERE</em></td>
</tr>
<tr>
<td>Status:</td>
<td><img src="true" alt="Core" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Borderline" /></td>
</tr>
<tr>
<td></td>
<td><img src="false" alt="Not Core" /></td>
</tr>
</tbody>
</table>
Example 4: Element card on Working life

<table>
<thead>
<tr>
<th>Element ID:</th>
<th>00003</th>
</tr>
</thead>
</table>
| Domain:     | □ Health problem and current use of technology  
□ Description and technical characteristics  
□ Safety  
□ Clinical effectiveness  
□ Economic evaluation  
□ Ethical analysis  
□ Organisational aspects  
☑ Social aspects  
□ Legal aspects |
| Topic:      | Working life |
| Issue:      | What kind of changes can the implementation of the technology mean in the working capacity/life of a person? |
| Clarification: | |
| Importance: | □ Critical | Should always be considered in an HTA  
□ Important | Should be considered in most HTAs  
□ Optional | May provide useful information |
| Specific requirements for importance: | |
| Information source(s): | Search or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted. |
| Transferability: | □ Complete | Data/findings are context independent  
☑ Partially | Data/findings are not directly transferable from one setting to another. Adjustments are needed.  
□ Not | Data/findings are not transferable from one setting to another without serious difficulties. |
| Unemployment and social security benefits may vary across countries. Consider particularly the criteria for benefits and the amount of benefits. |
| Source: | ICF, Activities and participation, Chapter 8 Major life areas, Work and employment: d840-859. |
| Relations: | Effectiveness, organisational aspects. |
| Status: | □ Core | Belongs to core.  
☑ Borderline | May belong to core. (Comment: need to discuss whether this category is needed).  
□ Not Core | Does not belong to core. Part of wider HTA framework. |
Example 5A. Element card on utilisation (followed by the same card filled within an HTA)

<table>
<thead>
<tr>
<th>Element ID:</th>
<th>00030</th>
</tr>
</thead>
</table>
| Domain:    | ☒ Health problem and current use of technology  
            □ Description and technical characteristics  
            □ Safety  
            □ Clinical effectiveness  
            □ Economic evaluation  
            □ Ethical analysis  
            □ Organisational aspects  
            □ Societal aspects  
            □ Legal aspects |
| Topic:     | Utilisation |
| Issue:     | Are there variations in use across countries/regions/settings? |
| Clarification: | Quantitative differences of the utilisation of the technology in question |
| Importance/relevance: | Explanation:  
                        ☒ Critical  Should always be considered in an HTA  
                        □ Important  Should be considered in most HTAs  
                        □ Optional  May provide useful information |
| Specific requirements for importance: | |
| Information source(s): | Utilisation reviews, Audits  
                          Studies on praxis-variation  
                          Own primary analysis of: Disease Register, Procedure Register, Device Register, Administrative Data (DRG, Discharge Databases, Reimbursement Claims Database) |
| Transferability: | Explanation:  
                      ☒ Partially  Data/findings are not directly transferable from one setting to another. Adjustments are needed.  
                      □ Not  Data/findings are not transferable from one setting to another without serious difficulties. |
| Source: | |
| Relations: | Related Topic “Life Cycle” of this domain and to domain “Organisational” |
| Status: | Explanation:  
           ☒ Borderline  May belong to core. (Comment: need to discuss whether this category is needed).  
           □ Not Core  Does not belong to core. Part of wider HTA framework. |
Example 5B. Filled element card on utilisation (all medical data included for example only). Illustrative example only. The future electronic version of the Model will use somewhat different structure.

<table>
<thead>
<tr>
<th>Element ID:</th>
<th>00030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain:</td>
<td>☑ Health problem and current use of technology</td>
</tr>
<tr>
<td></td>
<td>☐ Description and technical characteristics</td>
</tr>
<tr>
<td></td>
<td>☐ Safety</td>
</tr>
<tr>
<td></td>
<td>☐ Clinical effectiveness</td>
</tr>
<tr>
<td></td>
<td>☐ Economic evaluation</td>
</tr>
<tr>
<td></td>
<td>☐ Ethical analysis</td>
</tr>
<tr>
<td></td>
<td>☐ Organisational aspects</td>
</tr>
<tr>
<td></td>
<td>☐ Societal aspects</td>
</tr>
<tr>
<td></td>
<td>☐ Legal aspects</td>
</tr>
<tr>
<td>Topic:</td>
<td>Utilisation</td>
</tr>
<tr>
<td>Issue:</td>
<td>Are there variations in use across countries/regions/settings?</td>
</tr>
<tr>
<td>Research question(s):</td>
<td>Are there variations in use of DES across European countries, and within single countries across regions?</td>
</tr>
<tr>
<td>Result:</td>
<td>The proportion of DES among the total number if implanted stents varies across European countries (see Table).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug Eluting Stents % of all Stents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Spain</td>
</tr>
<tr>
<td>2002</td>
<td>4,1%</td>
</tr>
<tr>
<td>2003</td>
<td>20,2%</td>
</tr>
<tr>
<td>2004</td>
<td>36,5%</td>
</tr>
<tr>
<td>2005</td>
<td>-</td>
</tr>
<tr>
<td>2006</td>
<td>-</td>
</tr>
</tbody>
</table>

* End of Year

Regional variations of the use of DES have been also described within the same country. In Spain the proportion of DES varied from 23.1% to 55.9% in 2004. Three regions used DES in more than 50% of stent implantations, whereas four regions used DES in less than 25% of stent implantations. In Sweden the use of DES varied from 12% to 92%.

Importance/relevance:  
☑ Critical  
☑ Important  
☐ Optional

Explanation:  
Should always be considered in an HTA  
Should be considered in most HTAs  
May provide useful information

Specific requirements for importance:

<table>
<thead>
<tr>
<th>Information source(s):</th>
<th>Literature and internet search for publications reporting data from interventional cardiology registers.</th>
</tr>
</thead>
</table>

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Transferability:

- Complete
  - Data/findings are context independent
- Partially
  - Data/findings are not directly transferable from one setting to another. Adjustments are needed.
- Not
  - Data/findings are not transferable from one setting to another without serious difficulties.

The finding that there are national and regional variations can be transferred. The data (% of DES, range of DES use across regions) are not transferable to the own setting.

Source:

Relations:

Status:

- Core
  - Belongs to core.
- Borderline
  - May belong to core. (Comment: need to discuss whether this category is needed).
- Not Core
  - Does not belong to core. Part of wider HTA framework.

References


Health problem and current use of technology

Marcial Velasco Garrido, Bo Freyschuss, Marta Lopez de Argumedo, Leonor Varela Lema, Alberto Ruano Ravina, Monika Reesev

Domain description

This domain of an assessment deals with the health problems targeted by the technology under assessment (target conditions, target groups) and with the availability and patterns of use of the technology in question. Some of the topics considered relevant for this domain of the assessment have generally been called “Background Information” in previous European projects or recommendations for conducting assessments\(^1\),\(^2\),\(^3\).

Topics within this domain include the epidemiology of the target health problem, the burden – both on individuals and on the society – caused by the health problem, the alternatives to the technology in question, the regulatory status of the technology and the requirements for its use.

The description of the current status of a health technology provides a baseline description of the situation of the technology which is useful to put the results of other parts of the assessment (e.g. clinical effectiveness) in the own geographical context or in the own setting. It also provides information relevant for the construction of economic and/or organisational models in order to assess the impact of, for example, the introduction of a technology, the promotion of its utilisation, etc. It is thus an important part of a health technology assessment report.

Dealing with the issues included in this domain at the early stages of an assessment is also needed in order to refine the research questions (e.g. choosing relevant outcome parameters) and to formulate the methodological approach to be taken in other domains of the assessment (i.e. identification of information sources, formulation of selection and appraisal criteria, etc.). Some elements of this domain will thus overlap to some extent with elements of the effectiveness domain (e.g. issues of outcomes measured and alternative intervention), economic evaluation domain (e.g. costs of target health problem), organizational domain (e.g. conditions for implementation, patterns of use) and legal domain (e.g. regulatory status). Thus, the elements described in this section of the core model are not to be understood as obligatory chapters of an assessment. They represent information pieces which are needed when conducting an assessment. How this information is presented in an HTA-report (i.e. whether it gets located in an specific chapter or whether it is spread among several chapters) will depend on the report structure of each agency. However the information can also be provided in the card form (as explained in the Chapter on “General Design of the Model”) in order to allow an easier exchange and sharing of information among HTA-agencies.
Methodology

The elements included in this domain are heterogeneous. There is no one single methodological approach which can be applied to all elements. For some of the elements there may even be several possible approaches in order to give appropriate answers to their questions. The approaches can be divided into two groups: either analysis of published scientific literature or analysis of primary sources of information or data (including both own primary data collection or analysis of available data collected for other purposes than the assessment). In principle both approaches can be used to study any issue. However the validity of the results for a single issue may differ considerably between the two approaches. For example, one might try to obtain information on the approval status of a technology by doing a literature review for this element. Even if there are scientific papers which have studied this issue (i.e. policy studies) they are likely to be rapidly outdated. The information obtained by directly inquiring the relevant approval agencies will be more reliable (e.g. via telephone interview).

The choice of the most appropriate source of information depends thus mainly on the element in question. However, the resources given in a specific assessment project also play a limiting role on the choice: It is not always possible to analyse primary sources or to collect and analyse primary data (even in a situation when these were the best approaches for a given issue) because of time and money constraints faced by nearly all institutions conducting HTA.

We present here the principal aspects of both methodological approaches. More detail referring to the types of sources to be used in each assessment element is given in the brief descriptions of the single issues.

Independently from which approach is chosen for each assessment element, these should be explained clearly and the findings referred to sources in order to enhance the transparency of this part of HTA reports.

Literature analysis

Ideally, the analysis of literature should always follow the principles of systematic reviews as they have been stated elsewhere:\(^4\):

- Formulation of an answerable question (i.e. the element question)
- Formulation of selection and appraisal criteria
- Searching the relevant literature databases using sensitive search strategies.

Theoretically it is possible to apply this approach to all issues. The issue itself is a question which can be considered to be the research question, i.e. the starting point, for the systematic review. Each issue will require different criteria for the selection of the relevant scientific literature. The most appropriate study design to be included varies according to each question, thus a general recommendation of the best study design cannot be given here.
Practically, the conduction of a systematic review of primary studies is probably not feasible to assess each one of the issues for which this approach is appropriate. In some cases – for example in the assessment of alternative interventions – it is more realistic to focus on existing systematic reviews. An acceptable approach for the identification of relevant literature can be to snowball references from papers identified in a first search or after contacting experts in the field.

Nevertheless any kind of literature (be it identified through a comprehensive literature search, through snowball references, from talks with experts) included in the assessment of any issue should be appraised. The appraisal criteria should reflect the widely accepted set of assessing the validity or quality of research (i.e. assessing risk of bias), assessing reporting, and assessing relevance/transferability.

The choice of the databases to be used in the search for relevant scientific literature is also determined by the element itself. The combination of different databases enhances sensitivity of the literature search. Each database will provide different possibilities to build more or less elaborated systematic search strategies.

Scientific literature object to this systematic approach can be both “primary” (experimental or observational studies) or “secondary” (i.e. systematic reviews, guidelines).

**Analysis of primary sources of information or data**

In general this approach is preferred when it can be expected that an analysis of published scientific literature will not deliver reliable results. Some of the issues included in this domain can be answered more straightforward when the HTA-researchers draw on information and/or data from primary sources as when they try to conduct a systematic literature review. There are several sources of information which we consider here as “primary”.

**Registers**

The information provided by registers can be useful to answer some of the issues in this domain. Mainly two types of registers relevant to this domain exist: technology registers and disease registers.

Technology registers gather information on the use of a single technology, for example a register on knee total endoprosthesis. A new case is registered in the database every time the technology is used (i.e. a procedure is done, an intervention takes place).

Information of the same person can be coded several times since a technology might be applied several times in the same person (e.g. both knees replaced). When appropriately designed technology registers allow the assessment of the use of different types of the technology (e.g. endoprosthesis types, materials) and even explore long-term outcomes of the application of the technology in the real world (including safety and effectiveness issues).

Disease registers gather information on the natural history and/or on the management of single diseases. A new case is registered in the database every time a diagnosis of the target disease is made. Some conditions may occur several times in life (i.e. heart attack), thus a
single person might be represented several times in the register. When appropriately designed, disease registers allow assessment of the diffusion of different strategies/technologies for the management, the quality of care of persons with the condition or even to explore variations in the outcomes of different interventions. The quality of registers should be appraised carefully considering the following questions:

- How representative is the register? (European, National, Regional, Local?) What are the inclusion/exclusion criteria?
- What is the quality of information?
- How complete is the coverage?
- What kind of information is coded?

Data access is an important aspect when working with registers. Own analysis of the data may require previous authorization. It might be impossible for institutions other than the ones managing the register to analyze the raw data, however some registers would conduct customized analyses (i.e. according to the needs of the HTA-researcher).

However, relevant results might be available for the public in the form of grey literature or in the internet (for example the German transplantation register\(^6\) or the Swedish PCI Register\(^7\), or results may even have been published in the scientific literature.

**Routine collected statistics**

Several sources of routine collected statistics exist which can be used to assess the incidence, prevalence or the burden of disease (e.g. life-years lost). These statistics are usually available in aggregated form (increasingly available through the internet). National or regional statistics offices and international initiatives (like EUROSTAT or Health For All Database) are examples of sources of this kind. The use of these sources has several limitations. The reliability of the diagnosis varies and usually it is not possible to differentiate between different stages of the disease. Even the validity of the coding of causes of death may be variable, and in some countries it is known to be very limited.

Routine collected administrative data can be useful too, when available. For example sickness funds collect great amounts of information which could be used to analyse utilisation of technology etc. However, analysis of this kind of data might be very time consuming, since data need to be “prepared” before analysis. By definition, these data has been collected for other purposes than research and they can not be used to answer scientific questions without previous processing. This might not be feasible in the context of an HTA project, due to resource constraints. As with data from registers, own analysis of administrative data often requires authorization from the data owner.

**Regulatory institutions**

Regulatory institutions can be approached to get information on the regulatory status of technologies. Some of these institutions have internet-based searchable databases which are regularly updated. Alternatively key officials/civil servants can be contacted directly with specific questions.
Manufacturers

Manufacturers can be used as primary sources of information too. The information provided by them might be limited by issues of confidentiality and marketing. This source can be useful in order to answer questions concerning the requirements for use of the technology, development status or forthcoming innovations of the technology. Manufacturers may also provide information on ongoing research and on scientific literature which has not been published yet.

Collecting own primary data

For some questions it might be necessary that the HTA researchers conduct own primary research. This approach should be considered very carefully since it may be very time-consuming and costly. For many agencies it is not feasible to conduct primary data collection, even if this would provide very valuable information.

When performing primary research, investigators should minimize the risk of bias, maximize validity and relevance and use the most appropriate methods (i.e. crosssectional survey, focus-groups, etc.) depending on the question to be answered.

Assessment elements

Initially we identified around 30 issues potentially belonging to this domain (see previous versions of the core model). However some of them have been judged to be better placed in other domains (most of them in the organisational and in the description of the technology domain).

At the end 20 issues remain in this domain. Those are summarized in the following table.

Thirteen of the issues have been considered to belong to the Core and seven have been considered to be borderline. Overall many of the issues considered to belong to the core were judged to have a critical importance but to be only partially transferable.
<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
<th>Topic</th>
<th>Issue</th>
<th>Clarification</th>
<th>Importance</th>
<th>Transferability</th>
<th>Information sources</th>
<th>Reference</th>
<th>Relations</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>A0001</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>Which disease/health problem/potential health problem will the intervention target?*</td>
<td>Definition (naming) of the condition, health problem, disease for which the technology is intended.</td>
<td>3</td>
<td>3</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis. Descriptions of the technology (e.g. provided by developers, manufacturers) on the potential targets and what they expect/claim from the technology</td>
<td>Group deliberations and Burls et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Choice of &quot;Patient&quot; component of the PICO for effectiveness assessment</td>
<td>3</td>
</tr>
<tr>
<td>A0002</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What, if any, is the a precise definition/characterization of the target disease? Which diagnosis is given to the condition and according to which classification system (e.g. ICD-10)?*</td>
<td>Characteristics of the condition which allow a precise diagnostic and differentiation of the indication for the use of the technology</td>
<td>3</td>
<td>3</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis.</td>
<td>Group deliberations and Burls et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Choice of &quot;Patient&quot; component of the PICO for effectiveness assessment. Subgroups or indications are also considered under Clinical Effectiveness</td>
<td>3</td>
</tr>
<tr>
<td>A0003</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What are the symptoms of the disease?*</td>
<td>Self-explaining</td>
<td>2</td>
<td>3</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis.</td>
<td>Group deliberations and Burls et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Choice of outcome component of the PICO for effectiveness assessment.</td>
<td>3</td>
</tr>
<tr>
<td>A0004</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What are the consequences of the condition?*</td>
<td>Qualitative description of the burden of disease for the individual (e.g. disability, pain)</td>
<td>3</td>
<td>2</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis.</td>
<td>Group deliberations and Burls et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Choice of outcome parameter for effectiveness assessment (PICO). Disease path can be used to construct economic models</td>
<td>3</td>
</tr>
<tr>
<td>ID</td>
<td>Domain</td>
<td>Topic</td>
<td>Issue</td>
<td>Clarification</td>
<td>Importance</td>
<td>Transferability</td>
<td>Information sources</td>
<td>Reference (was: &quot;source&quot;)</td>
<td>Relations</td>
<td>Status</td>
</tr>
<tr>
<td>------</td>
<td>---------------------------------------------</td>
<td>------------------</td>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>-----------</td>
<td>-----------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
<td>-----------</td>
<td>--------</td>
</tr>
<tr>
<td>A0005</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>Which are the known risk factors for acquiring the condition?*</td>
<td>Self-explaining</td>
<td>2</td>
<td>2</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis.</td>
<td>Group deliberations and Burts et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Identification of alternative (i.e. preventive) approaches</td>
<td>2</td>
</tr>
<tr>
<td>A0006</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What is the natural course of the condition?*</td>
<td>For example stages of the disease which can be object of different interventions.</td>
<td>3</td>
<td>3</td>
<td>Medical Literature, at the best (Systematic) Reviews on mechanism of disease, risk factors, course and prognosis.</td>
<td>Group deliberations and Burts et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Choice of outcome parameter for effectiveness assessment (PICO). Disease path can be used to construct economic models</td>
<td>3</td>
</tr>
<tr>
<td>A0007</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>How many people belong at the moment (will belong) to the specific target group (describe according to sex, age)?</td>
<td>Incidence and/or prevalence of the target condition or the indication for use of the technology</td>
<td>3</td>
<td>1</td>
<td>Literature: Systematic reviews of epidemiological studies such as Cross-Sectional Studies (Prevalence), Cohort-Studies (Incidence) Routine Statistics Own analysis of: Disease Register, Administrative Databases (discharge databases, reimbursement claims databases)</td>
<td>Group deliberations and Burts et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Data can be used when constructing models, however only if they are really generalisable/transferrable</td>
<td>2</td>
</tr>
<tr>
<td>A0008</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What is the burden of disease (mortality, disability, life years lost)?</td>
<td>Disease-specific mortality Prevalence of disability or disabling symptoms caused by the condition Prevalence/Incidence of early retirement due to the condition</td>
<td>3</td>
<td>2</td>
<td>Literature: Systematic reviews of epidemiological studies such as Cross-Sectional Studies (Prevalence), Cohort-Studies (Incidence) Routine Statistics Own analysis of: Disease Register, Administrative Databases (discharge databases, reimbursement claims databases)</td>
<td>Group deliberations and Burts et al. 2000¹, Busse et al. 2002², Liberati et al. 1997³, Imaz-Iglesia et al. 1999⁸, Kristensen et al. 2001⁹</td>
<td>Data can be used when constructing models, however only if they are really generalisable/transferrable</td>
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<tr>
<td>A0019</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Target Condition</td>
<td>What aspects of the burden of disease are targeted by the technology, i.e. are expected to be reduced by the technology?</td>
<td>The application of the technology may target only one aspect of the burden of disease, e.g. disability but not mortality. Or mortality but not symptomatology</td>
<td>3</td>
<td>3</td>
<td>Proposed by reviewers</td>
<td></td>
<td></td>
<td>3</td>
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<tr>
<td>A0009</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Utilisation</td>
<td>How much is the technology being used?</td>
<td>Self-explaining</td>
<td>2</td>
<td>1</td>
<td>Utilisation reviews, Audits Studies on praxis-variation Own primary analysis of: Disease Register, Procedure Register, Device Register, Administrative Data (DRG, Discharge Databases, Reimbursement Claims Database)</td>
<td>Group deliberations and Burls et al. 20001, Busse et al. 20022, Liberati et al. 19973, Imaz-Iglesia et al. 19998, Kristensen et al. 20019</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>A0010</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Utilisation</td>
<td>Describe the variations in use across countries/regions/settings, if any?</td>
<td>Self-explaining</td>
<td>2</td>
<td>2</td>
<td>Utilisation reviews, Audits Studies on praxis-variation Own primary analysis of: Disease Register, Procedure Register, Device Register, Administrative Data (DRG, Discharge Databases, Reimbursement Claims Database)</td>
<td>Group deliberations and Burls et al. 20001, Busse et al. 20022, Liberati et al. 19973, Imaz-Iglesia et al. 19998, Kristensen et al. 20019</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>A0011</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Current Management of the Condition</td>
<td>How is the disease/health condition currently being managed?</td>
<td>Self-explaining</td>
<td>3</td>
<td>1</td>
<td>Surveys, utilisation reviews, (How is it managed) If such information is lacking: Expert Surveys / Expert Interviews</td>
<td>Group deliberations and Burls et al. 20001, Busse et al. 20022, Liberati et al. 19973, Imaz-Iglesia et al. 19998, Kristensen et al. 20019</td>
<td>Findings can be used to assess whether technology could add anything in the management of the disease. Findings can be used when constructing CE-Models comparing to alternatives</td>
<td>2</td>
</tr>
<tr>
<td>ID</td>
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<td>Transferability</td>
<td>Information sources</td>
<td>Reference</td>
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<tr>
<td>A0012</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Current Management of the Condition</td>
<td>According to published algorithms/guidelines (if any), how should the condition be managed?</td>
<td>An assessment of this and the above element allow to draw conclusions on how far the current management is optimal</td>
<td>3</td>
<td>2</td>
<td>Review of Clinical Guidelines, Recommendations (How should it be managed) If such information is lacking: Expert Surveys / Expert Interviews, textbooks</td>
<td>Group deliberations and Burts et al. 2000(^1), Busse et al. 2002(^2), Liberati et al. 1997(^3) Imaz-Iglesia et al. 1999(^8), Kristensen et al. 2001(^9)</td>
<td>Findings can be used to assess whether the technology could add anything in the management of the disease.</td>
<td>3</td>
</tr>
<tr>
<td>A0013</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Current Management of the Condition</td>
<td>How are the differences in the management for different stages of disease, if any?</td>
<td>Identification of practice variations which point out differences in the quality of health care</td>
<td>2</td>
<td>2</td>
<td>Surveys, utilisation reviews, (How ist is managed) Review of Clinical Guidelines, Recommendations (How should it be managed) If such information is lacking: Expert Surveys / Expert Interviews</td>
<td>Group deliberations and Burts et al. 2000(^1), Busse et al. 2002(^2), Liberati et al. 1997(^3) Imaz-Iglesia et al. 1999(^8), Kristensen et al. 2001(^9)</td>
<td>2</td>
<td></td>
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<tr>
<td>A0014</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Current Management of the Condition</td>
<td>What are the other evidence-based alternative interventions, if any?</td>
<td>Self-explaining</td>
<td>3</td>
<td>2</td>
<td>Clinical Guidelines, Recommendations (How should it be managed), Systematic Reviews</td>
<td>Group deliberations and Burts et al. 2000(^1), Busse et al. 2002(^2), Liberati et al. 1997(^3) Imaz-Iglesia et al. 1999(^8), Kristensen et al. 2001(^9)</td>
<td>Choice of comparator for effectiveness assessment (PICO) Choice of comparator for cost-effectiveness assessment</td>
<td>3</td>
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<tr>
<td>A0015</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Life-Cycle</td>
<td>In which phase is the development of the technology (experimental, emerging, routine use, obsolete)?</td>
<td>This is related to the question whether there is enough evidence or experiences on the use of targeted technology on the condition.</td>
<td>3</td>
<td>2</td>
<td>Literature Horizon Scanning Databases, Ongoing research databases Information from Manufacturers</td>
<td>Group deliberations and Burts et al. 2000(^1), Busse et al. 2002(^2), Liberati et al. 1997(^3) Imaz-Iglesia et al. 1999(^8), Kristensen et al. 2001(^9)</td>
<td>Status determines the kind of information which can be expected on other domains (specially in long-term safety, effectiveness)→ Uncertainty grade</td>
<td>3</td>
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<tr>
<td>A0016</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Regulatory Status</td>
<td>Which approval status has the technology in other countries, or international authorities?</td>
<td>Self-explaining</td>
<td>3</td>
<td>3</td>
<td>Drugs: EMEA, FDA, National Authorities Devices: CE-Approval, National Authorities Manufacturer: Manufacturers should be contacted in order to identify which steps have they taken/ are they planning to take concerning Market-Approval</td>
<td>Group deliberations and Burfs et al. 2000, Busse et al. 2002, Liberati et al. 1997 Imaz-Iglesia et al. 1999, Kristensen et al. 2001</td>
<td>Legal Domain</td>
<td>3</td>
</tr>
<tr>
<td>A0017</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Regulatory Status</td>
<td>Has the technology been included in / excluded form the benefit basket of any country? How is the coverage of the technology across countries? (e.g. full-coverage, co-payments, coverage under special circumstances/conditional coverage?)</td>
<td>Are there co-payments, to what extent?</td>
<td>2</td>
<td>3**</td>
<td>Lists of benefits/services of the National Health Services/Sickness Funds, inquiry of technical officers from MoH Manufacturers Literature on Benefit Basket (Comparative policy studies)</td>
<td>Group deliberations and Burfs et al. 2000, Busse et al. 2002, Liberati et al. 1997 Imaz-Iglesia et al. 1999, Kristensen et al. 2001</td>
<td>Legal Domain</td>
<td>3</td>
</tr>
<tr>
<td>A0018</td>
<td>Health Problem and Current Use of the Technology</td>
<td>Other</td>
<td>Who manufactures the technology?</td>
<td>Self-explaining</td>
<td>2</td>
<td>2</td>
<td>Group deliberations and Burfs et al. 2000, Busse et al. 2002, Liberati et al. 1997 Imaz-Iglesia et al. 1999, Kristensen et al. 2001</td>
<td>Related to Organisational or Social domain</td>
<td>Related to Organisational or Social domain</td>
<td>2</td>
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* These issues are very closely related. Depending on the condition in question the separation proposed here might be more or less feasible and may be merged when writing the topic.

** Per definitionem this is international comparative information. The transferability rating does not refer to the model of coverage itself (i.e. the decision on the inclusion in the benefit basket).
**Target Condition**

A Core HTA should provide a brief description of the disease or health problem for which the technology has been designed/is intended to be used. The characterization of the target health problem considers both qualitative and quantitative issues.

**Qualitative Issues**

The qualitative description of the target condition refers to its underlying mechanism(s) (pathophysiology), its natural history (i.e. course of disease), its prognosis and its consequences, as well as risk factors for acquiring the disease. If necessary – i.e. when the technology does not target the whole condition - a description of subgroups or special indications within the disease should be included.

These issues are usually addressed at early stages of any assessment and are generally taken into account in the formulation of the research questions for the the domain of effectiveness. They are also likely to be important in other parts of the assessment (social domain, economic domain, etc).

Since research questions for effectiveness are basically formulated following the PICO model (see chapters on General Methodology and on Definitions) – which itself is the basis for establishing selection and appraisal criteria for the scientific literature – the information provided by the issues described here can be considered to be essential for the formulation of the criteria to be followed in other parts of the assessment (that is mainly for the “P” and the “O” of the PICO model).

Knowledge on the natural course and on the consequences of the health problem is essential for the construction of decision analytic models which reasonably fit the reality. In addition parts of the information can contribute to feed the economic model (e.g. transition probabilities from one stage to another, probabilities of different presentations). It is also important to know whether the health problem and the target population for which the technology is intended can be clearly defined. If this is not the case the appropriate use of the technology may be rightfully challenged.

The issues to be considered here can be assessed using the medical literature. An effective approach can be to use information from existing systematic reviews, (i.e. on risk factors, on prognosis) or to conduct one. Commonly, the types of studies which can be expected to provide this type of information are cohort and case control studies to identify risk factors.

**Quantitative Issues**

As stated above this topic has several issues which can be considered quantitative in nature. The importance of these issues is given by the fact that they quantify the burden of disease. They deal with the incidence and the prevalence of the target condition, as well as with the incidence and/or prevalence of the consequences of the condition (i.e. mortality, disability, sickness leave, retirement, etc.). In addition the burden of diseases for the society can be assessed by addressing the cost of illness, i.e. the economic burden of disease.
Besides systematic reviews of the literature (i.e. of cross-sectional surveys, cohort studies), primary data sources can be used (or even should be used) to assess these quantitative issues. Routinely collected statistics can be used to obtain information on incidence or prevalence of some conditions.

In addition, cause-specific mortality rates are also available from routine statistics. Depending on their scope, registers can also be helpful to estimate some measures of disease frequency or to estimate how many people belong to different subgroups.

The data gathered concerning these elements can be used in other parts of the assessment (e.g. for economic models), or provide a kind of baseline for the assessment of the potential impact of a technology.

Depending on the disease these issues may widely vary between different geographical contexts (e.g. infectious diseases). A Core HTA could however provide available information from different countries (or at least European estimates), which can be used by other assessors when adapting the Core HTA, especially when information from their own geographical context is not available.

**Utilisation**

These issues refer to the evidence on how much the technology is being used in the country where the assessment is being conducted. In addition the issues address variations in utilisation at the national level (regional variations) or the international level (inter-country variations) which may be an indication for under- or overuse of the assessed technology. Studying these issues may allow an estimation of the effort necessary in order to increase or reduce its use, depending on the outcome of other domains of the assessment. These issues are quantitative and probably difficult to transfer although important for “local HTA”. Their relevancy for Core HTA seems not to be given (both qualified as borderline issues).

The sources of information for these issues might be the literature (e.g. utilisation surveys) or the analysis of data provided by registries (depending on their scope and completeness).

**Current management of the condition**

The issues within this topic ask how the disease is being currently managed (alternative treatments, which they are, etc.) and whether there is a consensus on the management of the condition in the form of evidence-based clinical practice guidelines. It is also important to assess whether (and if possible to what extent) current practice differs from these guidelines.

This information is useful to assess whether current management is optimal or not. If the current management of the disease is not in accordance to evidence-based recommendations, the public may have the impression of the need for new technology – which might be costly and not more effective than older ones. In such a situation it would perhaps be more appropriate to improve guideline compliance than to add a newer technology of similar effectiveness or higher costs. In addition it is also useful to assess whether the technology in question will/should add to an existing path of treatment/prevention or might substitute other technologies. Both types of information can also be used when assessing the organisational domain.
Also under the scope of this topic is the issue of potential alternatives for the technology. It is useful to formulate PICO questions for comparative assessment of effectiveness and cost-effectiveness. The available options for treating the disease (or the same subgroup) should be described here. However these may vary from country or region to another. (i.e. not all options might be available everywhere). A presentation of available options worldwide in a Core HTA might, however, be helpful for assessors to identify technologies whose introduction could be alternatively considered.

Information sources for the issues in this topic might be studies on the current management of condition (i.e. cross-sectional surveys, audits, etc.). In addition an overview of guidelines should be given, synthesizing the main recommendations. Guidelines can be searched in both medical literature databases (i.e. Medline) since they are frequently published in indexed journals, or in special databases (i.e. GIN database). They might be also available via internet from the relevant professional associations.

**Life Cycle**

This topic has only one issue concerning the position of the technology in its life cycle.

The overall information concerning most of the domains of an assessment can be expected to be very limited when the technology is at the beginning of its life cycle.

To assess whether a technology is to be considered as emerging (other experimental) or not Horizon Scanning initiatives (i.e. EUROSCAN) can be consulted. In addition contact to manufacturers can be initiated, since these stakeholders can have relevant information concerning the development status of the technology in question.

It is difficult to predict whether a technology has already reached the summit of its utilization, whether it is on the way of reaching it or whether it will be rapidly abandoned.

**Regulatory status**

The issues of this topic aim at providing a comparison with health systems other than the own one.

For decision-makers it is probably useful to know whether the technology in question has been evaluated to some extent by other state bodies or international institutions - and what was the outcome of those evaluations. Since it is expected that no great variations between countries in the issue of approval are observed in Europe (i.e. central approval for pharmaceuticals in Europe), the main interest lays probably on the issues concerning the reimbursement (i.e. coverage) status. However, in some cases it may be of interest to compare approval status with non-European countries (i.e. USA, Australia, New Zealand, etc.) This kind of information may have a great impact on the outcome of the decision-making process, since decision-makers often take into consideration what is being done in other systems or in other countries\(^\text{10}\). This may be particularly important when the estimation of the harm-benefit-costs equation is inconclusive.

To assess these issues the most appropriate approach is to consult primary sources of information, since the published literature may rapidly be outdated. The market approval status can be reviewed by contacting the institutions responsible for this. Some of them have internet-based search engines
which allow quick consultation (e.g. EMEA). Alternatively key officials can be contacted directly with specific questions.

The assessment of the coverage status in other countries (i.e. inclusion in the benefit catalogue, levels of co-payment, etc.) is often difficult. This kind of information is not easy to retrieve and usually requires deep knowledge of the health-care system in order to identify adequate and usable information sources. A comprehensive assessment of this issue may not be feasible during a given HTA project.

The Core HTA should attempt to elucidate the market approval status in supranational authorities and if necessary in European national authorities as well as the coverage status across Europe.

The need for assessment of the market approval status depends on the kind of technology since not all technologies require approval: this concerns mainly drugs and devices. The need for assessment of the coverage status refers also to other types of technology such as medical or surgical procedures.

**Other**

This topic refers to issues which cannot be placed under any of the other topics. Currently we have only an issue here, concerning the manufacturers of the technology. The group considered this issue as being borderline to the core. Knowing who manufactures the technology is relevant in order to identify potential sources of information (e.g. on ongoing developments, ongoing trials).

**References**

6. German Transplantation Register at www.dso.de
7. Swedish Coronary Angiography and Angioplasty Register at www.ucr.uu.se/scaar
Description and technical characteristics of technology

Marjukka Mäkelä, Marcial Velasco Garrido, Pekka Kuukasjärvi, Antti Malmivaara

Domain description

The aspects considered in this domain describe the technology to be evaluated in an HTA and its technical characteristics. These need to be described in a manner that is detailed enough to separate it from related technologies, using concepts that allow for persons unfamiliar with the technology to get an overall understanding on its functioning and use. Different types of technologies will need their own approaches. The chapter may overlap somewhat with the chapters on Current use of Technology and Organisational Aspects.

The introduction tells what the technology is, when it has been developed and for what purpose(s), who is or will be using the technology in what manner, and at which level of health care it is meant to be used. This brief description of the technology may include pictures, diagrams, videos, or other visual material, in order to facilitate understanding for persons who are not experts in the field.

Methodology

Previous work in the area has not covered this domain in much detail; some of the issues relevant for this part of the assessment have been discussed in “Background Information” in previous projects (Busse et al. 2002, Liberati et al. 1997). There is an overlap in several issues with the domain "Current use of the technology". In a WP4 workshop in September 2006, a brainstorming session was used to identify some elements of interest for this domain. The current draft will be tested using several different types of interventions to see if there are elements lacking or if more detail is needed.

The numbers for importance and transferability of the technology (available in the table below) are first suggestions and have not been agreed on within the working group. They are therefore in parentheses and should be used with caution. Any feedback on the structure and details is welcomed.

The information concerning most of the issues of this domain may be obtained from manufacturers of the technology, clinical experts in the use of the technology but also from the literature (i.e. descriptive publications).
Assessment elements

So far 15 issues in this domain have been identified. Eight of them are tentatively considered to be both important and transferable, and would therefore be among core issues. Only one issue seems to be neither transferable nor critical. The table summarizing the elements is below. The numbers on Importance, Transferability, and Status are in parentheses as the final discussion is still lacking.
| ID   | Domain                                                                 | Topic                                                                 | Issue                                                                 | Clarification                                                                                                                                                                                                                                                                                                                                                                                                           | Importance | Transferability | Information sources                                                                 | Reference                                                                 | Relations                                                                 | Status |
|------|------------------------------------------------------------------------|----------------------------------------------------------------------|----------------------------------------------------------------------|                                                                                                                                                                                                                                                                                                                                                                                                                       |           |                 |                                                                    |                                                                             |                                                                            |        |
| B0001 | Description and technical characteristics of technology                | Features of the technology                                            | What is this technology?                                             | Provide a short technical description: Type of device, operation, imaging, etc. Biological rationale and mechanism of action of the technology.                                                                                                                                                                                                                                                                                                                                                     | 3          | 3                | Manufacturer, effectiveness studies, clinical experts, studies in basic science, textbooks                                                                 | Current use                                                                 |                                                                             |        |
| B0002 | Description and technical characteristics of technology                | Features of the technology                                            | Why is this technology used?                                         | Describe the aim of using the technology: How is it expected to be an improvement as compared to previous technologies used for the same health problem?                                                                                                                                                                                                                                                                                                                        | 3          | 2                | Manufacturer, effectiveness studies, clinical experts                                                                 | Current use                                                                 |                                                                             |        |
| B0003 | Description and technical characteristics of technology                | Features of the technology                                            | Phase of the technology: When has it been developed or introduced in health care? | Is it a truly novel one, or has it been used earlier for this or some other purpose? Is the technology fully developed or in its early stages? Most technologies will be introduced at approximately the same time in several countries. If an HTA has been done more than a few months before using it, the technology might have been studied in more detail and moved into another phase (with more published trials, for example). | 3          | 2                | Manufacturer, effectiveness studies                                                                 | Current use                                                                 | Effectiveness                                                                |        |
| B0004 | Description and technical characteristics of technology                | Features of the technology                                            | Who are the users of this technology?                                | What types of professionals (nurses, doctors, other professionals) or patients (all with a certain disease, narrowly defined groups) will be using this technology?                                                                                                                                                                                                                                                                                                                             | 3          | 2                | Manufacturer, effectiveness studies, clinical experts, legislation National or local judgement                                                                 | Current use, Organisational                                                                                           |                                                                            |        |
| B0005 | Description and technical characteristics of technology                | Features of the technology                                            | Where? Place and context for utilizing the technology                | At which level(s) of health care (self-care, primary, secondary, tertiary) will the technology be used?                                                                                                                                                                                                                                                                                                                                                                                | 3          | 1                | Manufacturer, effectiveness studies, clinical experts, legislation National or local judgement                                                                 | Current use, Organisational                                                                                           |                                                                            |        |
| B0006 | Description and technical characteristics of technology                | Features of the technology                                            | Are there any special features relevant to this technology?         | Any points where this technology is different from its predecessors (other technologies used for similar purposes); new aspects that need to be considered when applying it.                                                                                                                                                                                                                                                                                                           | 3          | 2                | Manufacturer, effectiveness studies, clinical experts                                                                 | Effectiveness, Safety                                                                                                    |                                                                            |        |
| B0007 | Description and technical characteristics of technology                | Investments and tools required to use the technology                   | What material investments are needed to use the technology?         | Devices, machinery, computer programs, etc. Those parts of the technology that need to be purchased (and often installed) by an organization in order to use the technology. Includes need for back-up investment to cover for breakdowns in use.                                                                                                                                                                                                                                                                                          | 3          | 2                | Manufacturer, applicability studies, clinical experts, user information National or local judgement                                                                 | Current use, Organisational                                                                                           |                                                                            |        |

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<tr>
<td>B008</td>
<td>Description and technical characteristics of technology</td>
<td>Investments and tools required to use the technology</td>
<td>What kind of special premises are needed to use the technology?</td>
<td>Many technologies require purpose-built premises within organizations, such as radiation-secured areas, Faraday cages, etc. Typical premises in primary or secondary care may differ markedly from country to country. A clear description of necessary facilities, training etc. is needed instead of lump statement (e.g. to be used in hospitals only).</td>
<td>3</td>
<td>2</td>
<td>Manufacturer, applicability studies, clinical experts, user information National or local judgement</td>
<td>Current use Organisational , Legal</td>
<td>(3)</td>
<td></td>
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<tr>
<td>B009</td>
<td>Description and technical characteristics of technology</td>
<td>Investments and tools required to use the technology</td>
<td>What equipment and supplies are needed to use the technology?</td>
<td>Syringes, needles, medicines, fluids, bandages etc. All disposable items necessary for using the technology</td>
<td>3</td>
<td>3</td>
<td>Manufacturer, applicability studies, clinical experts, user information National or local judgement</td>
<td>Current use</td>
<td>(3)</td>
<td></td>
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<tr>
<td>B010</td>
<td>Description and technical characteristics of technology</td>
<td>Investments and tools required to use the technology</td>
<td>What kind of records are needed to monitor the use of the technology?</td>
<td>What kind of data needs to be collected about the use of this technology regarding care processes, professionals involved, patients and their health outcomes?</td>
<td>3</td>
<td>1</td>
<td>Clinical experts, administrative experts, legislation National or local judgement</td>
<td>Current use Organisational , Legal</td>
<td>(2)</td>
<td></td>
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<tr>
<td>B011</td>
<td>Description and technical characteristics of technology</td>
<td>Investments and tools required to use the technology</td>
<td>What kind of registers are needed to monitor the use of the technology?</td>
<td>Are there existing registries that should be used, or should a registry be established, to collect the necessary data?</td>
<td>3</td>
<td>1</td>
<td>Clinical experts, administrative experts, legislation National or local judgement</td>
<td>Current use Organisational , Legal</td>
<td>(2)</td>
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<tr>
<td>B012</td>
<td>Description and technical characteristics of technology</td>
<td>Training and information needed for utilizing the technology</td>
<td>What kind of training is needed for the personnel using or maintaining the technology?</td>
<td>Training materials: writing and/or translation, other adaptation? Personal training: individual and/or group sessions, number and length of sessions, number and qualifications of trainers</td>
<td>3</td>
<td>2</td>
<td>Manufacturer, effectiveness studies, observational studies, applicability studies, clinical experts, user information National or local judgement</td>
<td>Current use Organisational , Legal</td>
<td>(3)</td>
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<tr>
<td>B013</td>
<td>Description and technical characteristics of technology</td>
<td>Training and information needed for utilizing the technology</td>
<td>What kind of training is needed for the personnel treating or investigating patients using this technology?</td>
<td>Training materials: writing and/or translation, other adaptation? Personal training: individual and/or group sessions, number and length of sessions, number and qualifications of trainers. If the technology requires a specific skill that is developed over a period of time using the technology, the training is provided in a stepwise manner.</td>
<td>2</td>
<td>1</td>
<td>Manufacturer, effectiveness studies, observational studies, applicability studies, clinical experts, user information National or local judgement</td>
<td>Current use Organisational , Legal</td>
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<td>Training and information needed for utilizing the technology</td>
<td>What kind of training is needed for the patients receiving or using this technology &amp; their families?</td>
<td>Training materials: writing and/or translation, other adaptation? Personal training: individual and/or group sessions, number and length of sessions, number and qualifications of trainers</td>
<td>3=critical 2=important 1=optional</td>
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<td>B0015</td>
<td>Description and technical characteristics of technology</td>
<td>Training and information needed for utilizing the technology</td>
<td>What information do patients outside the target group and the general public need on the technology?</td>
<td>Training materials: writing and/or translation, other adaptation?</td>
<td>3=critical 2=important 1=optional</td>
<td>3=complete 2=partially 1=not</td>
<td>Manufacturer, effectiveness studies, observational studies, applicability studies, clinical experts, user information, patient organisations National or local judgement</td>
<td>Current use, Organisational, Ethical, Legal</td>
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<td>(2)</td>
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References


Safety

Nicholas Hicks, Marta Lopez de Argumedo, Alberto Ruano Ravina, Nieves Sobradillo, Alison Price, Antti Malmivaara

Domain description

An HTA should include an assessment of the adverse events resulting from the use of a health technology to benefit both individual patients and to inform policy makers. This will help provide a balanced assessment of the relative benefit and harm arising from the use of the health technology as in some circumstances the ‘costs’ of the adverse events may even outweigh the benefit of the technology.

The definitions and the terminology of safety used in HTA have not been standardised and it has been suggested that the term ‘harms’ should replace the use of the word safety and terminology should be standardised. The Cochrane Handbook proposes some definitions for safety, adverse event and adverse effect which provide helpful clarification of the differences.

The diversity of types of health technology means that there are many different types of safety issues and there can be legitimate differences in the way an assessment of “safety” may be undertaken. The systematic assessment of every potential harm of a technology can be time consuming. The authors of a Core-HTA report should select those safety issues that are significant for patients or most likely to be important in guiding the decision of health care providers and policy makers. The following harm categories may help identifying and classifying assessment elements for the Safety domain.

- A technology may have direct harm affecting; mortality, morbidity or disability due to e.g. toxicity or invasiveness
- Safety issues may arise in relation to the use of the technology when there are problems with the application of the technology or in patient selection. These harms may be operator (there may be a learning curve) or setting dependent and can be modified by changing the users’ knowledge, skills or behaviour. These types of issue may also be dealt with in other domains (effectiveness, organisational).
- Harms are typically graded into four classes of severity: mild, moderate, severe, and life threatening. Severe and life threatening harms should always be reported. The more serious the harms are, the less frequently are these likely to occur. Mild harms should be considered if they are of importance for patients, particularly when the benefit of the use of the technology is limited.
- Alternative ways to classify harms are in relation to their dose relatedness, time relatedness or patient susceptibility.
As well as the potential to cause harm directly to a patient, the use of a technology may result in harm through indirect effects to their family or carer, health care professionals, the public or the environment.

This domain does not consider health technologies that have not been licensed or certified for use and are still in a developmental phase. The more serious the harmful effects resulting from the use of a licensed or certified health technology, the less frequently are these likely to occur. This has implications for the types of study and the type of evidence that may have to be used to inform the assessment of harms for a health technology.

It is recommended that whenever possible the overall effect of the harms needs to be quantified, as a QALY or DALY as well as information on the frequency of occurrence, relative risk or number needed to harm (NNH).

It should also be made clear in the scope of the HTA whether adverse events that are an indirect effect of the use of the technology should be included or excluded from the assessment.

The safety domain has potential overlaps with the domains of clinical effectiveness, current use of the technology, organisational and costs/ economic evaluation. It may also be an issue considered in the legal domain.

There are six topics within this domain:
- Identification and assessment of harms
- Quality of evidence for assessment of harms
- Summary of impact (outcomes) of harms
- Minimisation of harms
- Comparison with alternative technologies
- Environmental safety

**Methodology**

**Overview of methodological issues**

A structured and systematic approach is required in the assessment of safety (harms) and the methods adopted for identifying, extracting, synthesising and interpreting data on safety (harms) include all those used in HTA.

At the commencement of work the particular safety issues (harms) to be investigated should be defined and the outcome measures of interest specified. The demographic characteristics of the population in which the technology is to be used should be defined for later comparison against the populations in which safety data has been identified.
The amount of safety (harms) data available for assessment will depend on a number of factors; the type of technology, the timing of the report in the lifecycle of the technology, the number of patients ‘utilising’ the technology and the severity and frequency of occurrence of the specified ‘adverse events’. There are also particular difficulties that arise in the identification of suitable data as a result of inadequate reporting and inconsistent terminology and indexing of harms data.

For these reasons the types of data sought may be of ‘lower quality’ than that usually accepted for HTA reports and a qualitative summary of harms should be undertaken before deciding whether a quantitative assessment of harms can be made.\(^1\)\(^-\)\(^5\) A brief summary of the strengths and weaknesses of different study designs that may be included in a systematic review of harms is given by Jefferson and Demicheli.\(^6\)

The infrequent occurrence of many adverse events makes it unlikely that they will be detected in clinical trials involving relatively small numbers of patients and, as some adverse events are of late onset these may not be detected during the relatively ‘short’ follow up periods of most RCTs. In many situations, case reports, cohort studies, registries, pharmacovigilance systems and post marketing surveillance will by necessity provide the sources of evidence.\(^7\)

As a result the methodological approach used in identifying literature on harms can vary and the approach adopted will lead to different estimates of harm.\(^7\)\(^,\)\(^8\)
Sources of evidence on safety (harms)

The sources of information to be examined should be clearly stated. Potential sources of information include:

- Published peer reviewed literature and grey literature
- Manufacturers product data sheets or applications for a product license
- National or international safety monitoring systems (databases) of adverse events which may be managed by a national statutory body or by a supranational body, i.e. WHO.
- Disease or technology registries of patients receiving treatment which may be organised at an international, national or regional level and managed by a government agency, professional body or the manufacturer.
- Spontaneous adverse event databases and periodic safety reports
- In some cases routine statistics from hospital, primary care or health system funders may be available and provide suitable information

Specific enquiries to manufacturers, regulators or professional bodies may help identify additional sources of information.

Search strategies for safety information for HTA

The search strategy should be clearly defined and a number of papers discuss the types of issue to be considered when undertaking a systematic search for ‘safety (harms)’ information. There is usually a ‘trade off’ between comprehensiveness and quality and the Cochrane Handbook provides the most comprehensive overview. Generally a wide range of sources may be accessed: (published and grey literature, manufacturers, regulators and registries) and a range of study types should be considered for inclusion in the search.

A number of predefined search strategies have been created to overcome the difficulties resulting from the varied terminology and limited inclusion of ‘harms’ related key words in the titles of papers or on searchable databases.

If the information identified for the HTA being undertaken is inadequate, consideration should be given to undertaking a full systematic review of the harms for the technology under assessment.

Extracting evidence

Standard approaches to data extraction can be used when necessary. An appropriate quality assessment should be made for this step of the process.
Synthesizing and analysing evidence

Standard approaches to data synthesis and analysis can be used when necessary. An appropriate quality assessment should be made for this step of the process.

Interpreting evidence

The interpretation of evidence should clearly state qualitative and quantitative limitations of the sources, searches, data and methods used for the analysis.

Comment should be made about the generalisability of the findings to the population for whom the HTA may be used.

Checklists & recommendations about the identification & assessment of quality of safety (harms) data for HTA

## Assessment Elements

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<tr>
<td>C0007</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>What is the scope of the harms to be assessed?</td>
<td>Are the harms intrinsic to the technology (primary effect) or application dependant (secondary effects) or an unrelated event consequent on its use?</td>
<td>3</td>
<td>2</td>
<td>The scope should be specified in the plan for each HTA</td>
<td>Ref 1, 2, 4</td>
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<tr>
<td>C0008</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>What types of harms are of interest for the assessment</td>
<td>The types of harm will be different and depend on the type of technology, i.e. biological agent/ drug/ procedure/ diagnostic test / system of care, e.g. screening programme. The harm may be a predictable consequence of use or an unpredictable or idiosyncratic harm</td>
<td>3</td>
<td>3</td>
<td>Manufacturers/ medical literature/ grey literature/ registries/ national or international safety monitoring systems</td>
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<td>C0009</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>Are there estimates of the incidence of the harms?</td>
<td>Types of harm will be different dependant on type of technology</td>
<td>3</td>
<td>3</td>
<td>Manufacturers/ medical literature/ grey literature/ registries/ national or international safety monitoring systems</td>
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<tr>
<td>C0010</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>What is the timing of onset of the harms, i.e. immediate, early or late onset?</td>
<td>The onset of the harm will be different dependant on the mechanism of action and type of technology. Some harms may not be detected because the duration of follow up is not sufficiently long.</td>
<td>3</td>
<td>3</td>
<td>Manufacturers/ medical literature/ grey literature/ registries/ national or international safety monitoring systems</td>
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<td>C0011</td>
<td>Safety</td>
<td>Identification</td>
<td>What is the harm may be of short or</td>
<td>The harm may be of short or</td>
<td>3</td>
<td>3</td>
<td>Manufacturers/</td>
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<td></td>
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<td>and assessment of harms</td>
<td>duration of the harm and is its severity constant?</td>
<td>3=critical 2=important 1=optional</td>
<td>3=complete 2=partially 1=not</td>
<td>medical literature/ grey literature/ registries/ national or international safety monitoring systems</td>
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<td>C0012</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>Is the incidence of the harms likely to change over time?</td>
<td>For some technologies the occurrence of harms may change over time and be dependant on the experience or training of the operator?</td>
<td>3</td>
<td>2</td>
<td>Medical literature/ grey literature/ professional societies/ registries</td>
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<td>C0035</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>Are there susceptible patient groups?</td>
<td></td>
<td>2</td>
<td>3</td>
<td>Research articles, manufacturers’ product data sheets, safety monitoring databases</td>
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<td>C0036</td>
<td>Safety</td>
<td>Identification and assessment of harms</td>
<td>Is there evidence that harms increase or decrease in different settings?</td>
<td></td>
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<td>3</td>
<td>Accuracy and effectiveness research, epidemiological risk research</td>
<td>Current use, Accuracy</td>
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<td>C0018</td>
<td>Safety</td>
<td>Summary of impact (outcomes) of harms</td>
<td>Is there a qualitative and/or quantitative summary of the impact of harms on individual patients?</td>
<td>Are the effects of the harms on morbidity, mortality, disability and quality of life specified?</td>
<td>3</td>
<td>2</td>
<td></td>
<td>Effectiveness/ legal aspects</td>
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<tr>
<td>C0019</td>
<td>Safety</td>
<td>Summary of impact (outcomes) of harms</td>
<td>Is there a qualitative and/or quantitative summary of the impact of</td>
<td>Are the potential effects of the harms on requirements for health and social services assessed?</td>
<td>1</td>
<td>2</td>
<td></td>
<td>Organisational aspects</td>
<td>2</td>
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<tr>
<td>ID</td>
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<td>C0020</td>
<td>Safety</td>
<td>Summary of impact (outcomes) of harms</td>
<td>Is there a qualitative and/or quantitative summary of the impact of the harms on the overall clinical and cost effectiveness of the technology?</td>
<td>Are the effects of the harms on the cost effectiveness/utility (QALY/DALY) specified?</td>
<td>2</td>
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<td>Effectiveness/costs, economic evaluation</td>
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<td>C0021</td>
<td>Safety</td>
<td>Minimisation of harms</td>
<td>What can be done to minimise the occurrence or consequence of the harms?</td>
<td>Is there a requirement for specific training, use of a protocol or guideline or restricting use to specialist centres, providing patient information, etc. may all reduce the occurrence or severity of harm.</td>
<td>2</td>
<td>2</td>
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<td>Organisational aspects</td>
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<tr>
<td>C0022</td>
<td>Safety</td>
<td>Comparison with alternative technologies?</td>
<td>A comparative assessment of harms (outcomes) of this technology against current practice or comparators</td>
<td>Relative impact of harms comparative to alternative treatment(s) for individual patients, populations, service delivery &amp; cost effectiveness</td>
<td>1</td>
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<td>Other HTA reports or systematic reviews of main comparators, Manufacturer or regulators information</td>
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<td>Safety</td>
<td>Environmental safety</td>
<td>Is there evidence of environmental harms?</td>
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Clinical effectiveness

Antti Malmivaara, Pekka Kuukasjärvi, Chris de Laet, Hans Van Brabandt, Regina Kunz

Domain description

Definition of efficacy and effectiveness

The efficacy of a health technology refers to its performance under ideal circumstances, i.e. what are the health benefits under carefully controlled conditions. Effectiveness refers to the performance of a technology in regular clinical practice, i.e. what are the health benefits in day-to-day clinical practice.

Randomised controlled trials are usually executed under ideal conditions and provide data on the efficacy, e.g. answer questions about how well this intervention can work. The challenge is to obtain answers on the effectiveness, i.e. how well will this intervention work under ordinary circumstances. Pragmatic RCTs, that have enrolled patients from routine practice to a routine health care process, aim to provide answers about the effectiveness of an intervention in the particular health care setting where the trial has been performed. In order to assess applicability of these data to other health care settings, judgement will be needed. If all trials concerning a technology have been performed under ideal conditions, i.e. explanatory trials one will have to make assumptions about the magnitude of effectiveness based on the available efficacy data.

Methodology

PICO

The first step in the assessment process is to specify the questions of the review following the so-called PICO structure where the letters stands for

- Population / patients with the disease of interest
- Intervention(s), i.e. the technology under assessment
- Comparison(s), that should serve as reference
- Outcomes which encompass the endpoints for assessing effectiveness and safety

Key questions based on PICO will drive the evaluation in the domain of clinical effectiveness, and the same applies often to the domains of safety and economics.
Population, intervention and comparison will generally be the same, only the outcomes will be different. In some cases, however, a subpopulation may be of specific interest in a certain domain due to specific details of safety or efficacy/effectiveness.

Scope of the HTA

Domains
- Current Use
- Technical details
- Safety
- Effectiveness
- Economy
- Ethics
- Organisation
- Legal issues

Systematic review of literature

Ideally systematic reviews on RCTs are the basis of knowledge of effectiveness of an intervention. The principles on how to conduct a systematic review are nowadays widely agreed upon and most of the methodologies published by different organisations vary only in details. The most widely used methodology applies the principles and instructions of the Cochrane Collaboration. The same principles and procedures can be applied to systematic reviews of non-randomised comparative study designs or observational studies if there are no or only a few randomised controlled trials to answer the HTA question.

This chapter describes the structure of the clinical effectiveness domain of the EUnetHTA core model for medical and surgical interventions. The objective is to facilitate the transfer of HTAs conducted in one health care setting to another setting (within a country or across countries). For this purpose, we offer an explicit guidance on how the report should be structured, what items should be covered, how information should be presented and advise on certain formats, rules etc. that might help achieving the goal of transferability. We base our guidance on publications from organisations and expert groups that have shaped the field and that have gained broad consensus: the Cochrane Handbook for Systematic Reviews, the CRD guidance for systematic reviews, statement from methodological expert groups such as the CONSORT statement or the QUOROM statement for reporting of systematic reviews, the checklist for HTA reports by INAHTA and the GRADE Working Group recommendations for grading quality of evidence and strength of recommendations.

The chapter intends to provide a structure for a systematic assessment of interventions. It is not a hands-on textbook on how to perform a systematic review – for this we refer...
readers to an extended list of further readings which we found helpful in writing the chapter and which covers those issues in much more detail.

We have aimed at a pragmatic guidance for a health technology report on clinical effectiveness including all the phases from stating the question to the interpretation and judgements about the evidence, and even to stating the recommendations, the latter for those organisations that provide recommendations to policy makers as part of their HTA-report.

**How to plan and conduct a systematic review on effectiveness?**

**Background work**

In the process of conducting a systematic review to assess the effectiveness of a technology, it is wise to check whether others have already published HTA-reports and / or systematic reviews covering the same intervention. There are a number of valuable databases in the Cochrane Library, such as the Cochrane Database on Systematic Reviews and the Health Technology Assessment Database provided by the NHS Centre for Reviews and Dissemination (CRD). The latter is available also online as an independent database. With a bit of luck one may identify a systematic review on the topic of interest, which is sufficiently comprehensive, satisfies the requirements on methodological quality, and meets the research questions. If the report is judged to be transferable to one's own health care system and the local setting, then the work might end right here.

If not, one might need to execute a full systematic review of clinical efficacy / effectiveness. The following paragraphs provide a more detailed guidance for this task.

**Phrasing the problem as focussed and standardised questions**

The first step for the review is to translate the health care problem into focused, structured and searchable questions that capture the essential facets of the health care problem and the benefit one may achieve with the use of the technology. To accomplish this it can be necessary to break down the problem into several research questions that follow the PICO-structure as described above: It is necessary to identify the study population to which the intervention may be applied, i.e. provide details about the patient characteristics including the health care setting, describing the intervention and one or several comparative interventions that are currently in use to deal with the health care problem, and define the outcomes that are regarded as relevant for drawing a conclusion of whether the intervention is beneficial or not. This would be the time to translate all the relevant “critical” and “important” outcomes (= issues) that describe the 5 topics into practical research questions. The authors and the users of an HTA-report would like to see those questions addressed for their judgement about the benefit of this intervention.

Finally, the reviewers need to define the study design(s) they are willing to consider for their review. Following the hierarchy of study designs, reviews on efficacy / effectiveness are generally limited to randomised designs, but it may be necessary to
broaden the inclusion to other designs, if data from randomised trials are not available or are insufficient (Figure 1). Sometimes it might be helpful for reviewers and users of the reviews to explicitly state which aspects of a healthcare problem were not considered in a review. Carefully defined and clearly focused questions will guide the reviewers when doing the review and will help the users of the review to compare the objectives of the review with their own healthcare problem, and to make decisions about the generalisability and transferability of the findings to their own healthcare settings.

Reviews should follow an *a priori* defined protocol, and possible deviations from the protocol should be described.

**Locating and selecting studies**

The focused, structured and searchable question will drive the literature search. The literature search should be comprehensive and transparent. A large variety of sources are available: general medical databases (such as Medline, Embase, Cochrane Controlled Trials register), specialised databases for specific questions (such as CINAHL, PSYCINFO, ASSIA, SOCIOLOGICAL ABSTRACTS) and trial registers (such as Current Controlled Trials [http://www.controlled-trials.com/] or Clinical Trials [http://www.clinicaltrials.gov/], hand searching of journals and abstract books, and the so-called “grey literature”. Performing an additional search in SCI-search of the included articles is a valuable complementary approach. Additional information can be collected from contacts with manufacturers and consultation with experts (domestic and foreign) and agencies. The resources (staff time and cost) required for a comprehensive search can vary considerably for individual sources. Restrictions in locating studies should be given (year, language, population etc). For searching systematic reviews the following databases are suggested: HTA, DARE, NHS EED, CDSR, and Cochrane CENTRAL.

The process of identifying the relevant information should be explicitly described including the search strategy (which may be presented separately as appendix) and the inclusion and exclusion criteria (see also 'Presenting and analysing results').

The selection process is iterative and includes two or more phases: first the selection of potentially relevant titles and / or abstracts, then the selection of full papers that are considered as potentially relevant, then the selection of the final set of studies. At the end of the review, a general update of the most recent literature should follow the same steps. Since some of the decisions in the selection process will always remain subjective, engaging two or more reviewers in this process will improve transparency and objectivity, especially when the report presents information about the degree of agreement or disagreement among reviewers and how disagreement was solved (e.g. consensus after consulting a third researcher).

Using a flow chart to display the process of study selection as recommended by the QUOROM group has been proven to be very informative. The flow chart describes the number of citations and studies identified at each step as well as the number excluded, with reasons for exclusion at each stage ending at the final number and types of studies included.
Assessing study quality

A thorough assessment of the methodological quality of the included studies is crucial to any systematic review. In randomised controlled trials, concealed treatment allocation, blinding of health care provider, patient and outcome assessor to the allocated intervention (experimental or control) and (close to) complete follow-up are the minimum items that need to be looked at when assessing the potential for bias of individual studies. Depending on the research question, however, it might be warranted to look at additional features where bias could enter the study design, or where the results might get distorted.

The body of checklists for assessing the methodological quality of randomised controlled trials is considerable, most of them are variations (e.g.\textsuperscript{15}) of the structure suggested in the User’s Guides to the Medical Literature\textsuperscript{16}, the Consort Statement\textsuperscript{7,9,17} or the criteria suggested in the Cochrane Handbook\textsuperscript{4}.

The discussion and agreement on the methodological criteria for non-randomised trials and observational studies is considerably less. However, a recent methodological HTA-report by John Deeks provides a good overview of available instruments to assess non-randomised intervention studies\textsuperscript{18-21}.

Having reviewed the methodological quality of the individual studies, researchers attempt to capture the overall quality of the body of evidence. The concept of the GRADE Working Group captures the currently most comprehensive approach\textsuperscript{1,13}. Besides looking at the quality of the individual studies, they also include in their judgement of the quality the consistency or heterogeneity of the results, they consider the directness of the comparisons (i.e. to what degree does the identified literature directly address the questions of our HTA-report (regarding the population, the intervention and comparators and the selected endpoints), they comment on imprecision of the available data (number of total events and width of the confidence interval) and provide an estimate about the likelihood of the presence of reporting bias. Deficiencies in any of those considerations can lower the methodological quality of the entire body of evidence. On the other hand, the overall judgement about the methodological quality of the evidence can be raised in the presence of strong and plausible associations between intervention and outcome or an obvious dose-response gradient – in the absence of bias.

Collecting data from individual studies – Evidence summaries

A high degree of reliability and transparency are conditional for the transfer of HTA reports from one setting to another. Comprehensive and informative evidence tables about the methodology and the content of the individual studies are the best guarantor for transparency and reliability. They should allow a judgement of the similarities and differences of the included studies and should provide the basis for the conclusions of the review. Therefore, they should be a compulsory part of each HTA report.

The majority of HTA organisations produce tabulated evidence summaries that follow the PICO structure (ideally with an additional cell for comments on issues that are not captured by the PICO cells but that could have an impact on the results). Although the
items reported in each cell will always be driven by the questions of the review, they
follow some core considerations. A description of the data extraction process including
the number of reviewers involved always assures objectivity and reliability of the results.

**Presenting and analysing results**

**A) Effect measures and confidence intervals**

A meaningful presentation of the study results is the next crucial step for an informative
and transparent report whose findings should be transferable to other settings.

A number of effect measures are in use for describing the treatment effect. For binary
data, common measures are relative effect measures such as risk ratio (= relative risk),
odds ratio, and relative risk reduction, or absolute effect measures such as risk difference
(= absolute risk reduction), often converted into number needed to treat (NNT) or events
per thousand patients to allow for a comparison across studies. Since both relative and
absolute effect measures carry important complementary information, recent approaches
such as the GRADE profiler (www.gradeworkinggroup.org) encourage a presentation of
both measures.

Continuous data are often more difficult to summarize. Commonly used effect measures
that allow the summary of treatment effects are “standardised mean difference” or
“weighted mean difference”. Unfortunately, both measures are difficult to interpret in a
clinical context.

A more recent statistic, the ratio of means, reports the percentage reduction of continuous
data such as proteinuria, which allows a meaningful interpretation to clinicians. For
more details about effect measures and their calculations, we refer to the comprehensive,
user-friendly description of common measures in the Cochrane handbook.

Often studies on the same topic report their findings in very different ways which hinders
meaningful comparisons across studies and a fair / appropriate interpretation of the body
of evidence. Reviewers are encouraged to try and convert (re-calculate) the results to a
joint effect measure and attempt a meta-analysis when the data allow a summary of the
results. However, sufficient clinical homogeneity of the studies is a prerequisite for a
meta-analysis.

Although the nature of the data can forbid pooling for a summary estimate and
researchers can provide only a qualitative summary of the data, it might nevertheless be
worthwhile to display the results in a forest plot, but omitting the summary.

It goes without saying that the presentation of a measure of precision for the estimate of
the treatment effect (confidence interval) is compulsory for the interpretation of the data
and must not be omitted. Researchers need to report if the primary studies lack this
essential information.

**B) Further exploration of the data: Homogeneity and heterogeneity, sensitivity
analysis and publication bias**
Reviewers need to provide statements about the presence of clinical homogeneity / heterogeneity of the studies and the homogeneity / heterogeneity of the results. While homo-/ heterogeneity in the clinical data is often a matter of judgement, there are good statistical tests available to help assessing the presence of statistical heterogeneity which should then be further explored and considered in the discussion. Sensitivity analyses based on clinical or methodological issue could allow further exploration of the stability of the data. Researchers should always consider the presence of publication and reporting bias and explore this either graphically using a funnel plot (provided the number of included studies is large enough) or make a plausible judgement about the likelihood of these biases.

If the data allow no pooling and no quantitative analysis, researchers are encouraged to address the same questions to their data and explore the stability and plausibility of their findings in a qualitative way.

The adverse effects of the intervention(s) in comparison with the comparator(s) should be presented. More details to safety issues will be provided in the domain “Safety”.

Interpreting results

It is possible to make only a preliminary interpretation of the results based on effectiveness data only. A global and balanced interpretation of the benefits and harms of a technology requires also the results of other relevant domains, e.g. safety / harm or economic issues.

Which steps are required?

- Rating the body of evidence as being of high / moderate / low quality (following the GRADE methodology) clarifying (e.g. in footnotes) the reasons for up-/down-rating.
- Interpreting the clinical relevance of the findings:
  - Deciding of the size of the treatment effect (independent of its statistical significance): What would be the minimal clinically important effect size?
  - Considering the importance of the outcomes for clinical decision making (distinguishing between a critical and an important outcome as done when formulating the question)
- Identifying knowledge gaps by calibrating the research questions (including the predefined outcome) with the available evidence.

Primary research

If the data retrieved from current body of evidence through a systematic review does not provide enough adequate information on the effectiveness of a technology, new primary research may be warranted in the form of e.g. a randomised controlled trial. Describing the design of clinical trials, however, is beyond the scope of this report. It should be noted
though, that the issues described in the assessment elements may be answered through primary research if so needed.

**The transfer of data on effectiveness**

To allow transfer of data across countries, HTAs have to be sufficiently transparent and distinguish between evidence (“facts”) and judgements (including values and preferences). Value judgements and preferences (of individuals or of health care systems) have to be labelled as well as the anticipated influence in transferring the result from one health care system to another. There will be situations where only the body of evidence [“evidence summary”] of an HTA can be used, but the data need to be interpreted in the context of the health care system and the prevailing values (as could be the case for HTA-reports on screening). For this reason, reviewers have flagged context-sensitive outcomes (=issues) when formulating the questions and have documented the underlying values that were driving certain decisions.

**Global interpretation**

Once the assessment on effectiveness, safety, economics and other relevant issues is done, the results have to be put together for a joint consideration, balancing the results. Researchers might find it helpful to put their findings in a tool like the GRADE profiler which provides them with a one page summary of their key findings that helps them to look at the entire body of evidence at a time.

If an HTA report is expected to provide recommendations regarding the use of a technology in a health care setting, it would be useful to follow e.g. the methodology of GRADE providing strong or weak recommendations in favour or against an intervention.

**Assessment elements**

Our objective was to identify generic issues that apply to a broad range of technologies, ranging from drugs to medical devices (such as radiotherapy) and complex treatment strategies (such as stem cell transplantations or physiotherapy) to name a few. When we explored our task we identified 4 topics within the effectiveness domain - mortality, morbidity, function/QoL and patient satisfaction - that were sufficiently general to be applied across a broad range of technologies, and at the same time sufficiently specific to capture all relevant areas of interest to individual patients and decision makers in the health care system. The topics are further divided into 18 issues in this domain.

We also explored the relevance of issues in the context of various technologies using a heterogeneous sample of disease-technology pairs¹, and concluded that different technologies require different issues to be considered. This emphasizes the need for

¹ We explored the generic issue approach on technologies such as PUVA therapy in psoriasis, chondrocyte implantation for osteoarthritis, cancer treatment, physiotherapy, use of Viagra, biologicals for rheumatoid arthritis; organisational structures such as stroke units and could not identify a minimum set of common issues that would be relevant across all disease-technology pairs.
considering the relevance of each assessment element and the translation of relevant elements into research questions in the context of each HTA, as explained in more detail in the chapter "General design".
<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
<th>Topic</th>
<th>Issue</th>
<th>Clarification</th>
<th>Importance</th>
<th>Transferability</th>
<th>Information sources</th>
<th>Reference (was: &quot;source&quot;)</th>
<th>Status</th>
<th>Relations</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0001</td>
<td>Effectiveness</td>
<td>Mortality</td>
<td>What is the effect of the intervention on overall mortality?</td>
<td>Use of technology may have an impact on patients' life expectancy.</td>
<td>3=critical</td>
<td>3=complete</td>
<td>Systematic reviews of RCTs (Randomised controlled trials) or CTs (controlled trials), if not available RCTs or CTs itself. If these not available, non-controlled studies and respective systematic reviews. Health care register data.</td>
<td>Several sources, see the Reference list.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0002</td>
<td>Effectiveness</td>
<td>Mortality</td>
<td>What is the effect of the intervention on the mortality caused by the target disease?</td>
<td>Use of technology may have an impact on mortality caused by the target disease.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0003</td>
<td>Effectiveness</td>
<td>Mortality</td>
<td>What is the effect of the intervention on the mortality due to other causes than the target disease?</td>
<td>Use of technology may have an impact on the mortality due to other causes than the target disease.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0004</td>
<td>Effectiveness</td>
<td>Mortality</td>
<td>What is the mortality related to the intervention studied?</td>
<td>Use of technology may have an impact on mortality related to the intervention studied.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td>Safety</td>
</tr>
<tr>
<td>D0005</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>How does the intervention modify the severity and frequency of symptoms and findings?</td>
<td>Use of technology may have an impact on patients' symptoms.</td>
<td></td>
<td></td>
<td>Systematic reviews of RCTs (Randomised controlled trials) or CTs (controlled trials), if not available RCTs or CTs itself. If these not available, non-controlled studies and respective systematic reviews.</td>
<td>See above.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0006</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>How does the intervention modify the progression of disease?</td>
<td>Use of technology may have an impact on course of the illness.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0007</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>How does the intervention modify the recurrence of symptoms and findings?</td>
<td>Use of technology may have an impact on course of the illness.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0008</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>What is the morbidity</td>
<td>Use of technology may have an impact on course of the illness.</td>
<td></td>
<td></td>
<td></td>
<td>See above.</td>
<td></td>
<td>Safety</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
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<th>Status</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>related to the intervention?</td>
<td>impact on morbidity related to the intervention.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0009</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>What other treatments do patients need?</td>
<td>Use of technology may have an impact on morbidity related to the need for other treatments.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0010</td>
<td>Effectiveness</td>
<td>Morbidity</td>
<td>How does the intervention modify the need for hospitalization?</td>
<td>Use of technology may have an impact on morbidity related to the need for hospitalizations.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>D0011</td>
<td>Effectiveness</td>
<td>Function / HRQL (Health-related quality of life)</td>
<td>What is the effect of the intervention on global improvement of function?</td>
<td>Use of technology may have an impact on functional ability</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0012</td>
<td>Effectiveness</td>
<td>Function / HRQL</td>
<td>What is the effect of the intervention on health-related quality of life?</td>
<td>Use of technology may have an impact on quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0013</td>
<td>Effectiveness</td>
<td>Function / HRQL</td>
<td>What is the effect of the intervention on disease specific quality of life?</td>
<td>Use of technology may have an impact on quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0014</td>
<td>Effectiveness</td>
<td>Function / HRQL</td>
<td>What is the effect of the intervention on return to work?</td>
<td>Use of technology may have an impact on working ability.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0015</td>
<td>Effectiveness</td>
<td>Function / HRQL</td>
<td>What is the effect of the intervention on return to previous living conditions?</td>
<td>Use of technology may have an impact on ability to return to previous living conditions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0016</td>
<td>Effectiveness</td>
<td>Function / HRQL</td>
<td>How does the intervention affect activities of daily living?</td>
<td>Use of technology may have an impact on ability to perform daily activities.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0017</td>
<td>Effectiveness</td>
<td>Patient satisfaction</td>
<td>Was the intervention worth it?</td>
<td>Patients overall assessment of the worthiness of the intervention.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D0018</td>
<td>Effectiveness</td>
<td>Patient satisfaction</td>
<td>Would the patient be willing to have the intervention again?</td>
<td>Patients overall assessment of the worthiness of the intervention.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
If only a limited number of poor quality RCTs can be identified, other study designs can be considered. In some cases, even if RCTs are available, studies of other types should be reviewed by the authors, e.g. to identify long-term effectiveness and/or rare or long-term adverse effects.

Undertake a detailed qualitative review of individual studies, i.e. detailed tabulation of study characteristics, assessment of quality and results.

Homogeneous means there is limited clinical heterogeneity in trials, as assessed by their included populations and interventions, plus the absence of evidence of statistical heterogeneity.

Undertake a short, non-detailed review of individual reports, i.e. brief overview, including general characteristics and conclusions.

This may be a systematic qualitative review of trial results without pooling. Qualitative reviews should highlight clinical heterogeneity (differences in participant characteristics, interventions, outcome measures), methodological heterogeneity (study design and quality) and heterogeneity, with respect to results. Tables are useful to describe populations, interventions, settings, outcome measures, etc. It may also be possible to pool results using a random effects model.
References


Costs and Economic evaluation

Kersti Meiesaar, Pirjo Räsänen, Irina Cleemput, Henrik Hauschildt Juhl, Monika Reesev and Harri Sintonen

Domain description

Rising health-care costs and limited resources have become issues of paramount importance over the past two decades. A rapid technological development also implies a conflict between technological possibilities and economic possibilities. Clinical investigators have begun to recognize the importance of performing economic evaluations alongside RCTs. It is not enough to get information just about efficacy and effectiveness when evaluating new technologies, information about costs and outcomes are also needed. Economic evaluation is an important part of health technology assessment.

The main aim of the costs and economic evaluation domain is to provide information to improve decision-making in the health care sector with respect to priority-setting between different health technologies, both emerging, new and existing ones (Kristensen 2007). An economic evaluation identifies, measures, values and compares the costs and outcomes of a technology with its relevant comparator. Its aim is to inform value for money judgements about an intervention (Guidelines for the Economic Evaluation of Health Technologies: Canada, 3rd edition, 2006).

Central to this area of economics are the concepts of opportunity cost and incremental change. In publicly funded health care systems limited resources mean that every available intervention cannot be provided in every situation for all who need or want it. Choices must be made among effective health care interventions, and the decision to fund one means that others cannot be funded. (Guidelines for the Economic Evaluation of Health Technologies: Canada, 3rd edition, 2006)

An economic evaluation should provide decision makers with information that is useful, relevant, and timely. The economic evaluation component of a HTA should be conducted within a common methodological framework that consists of a well-defined research question depicting a specific health policy problem or question, a perspective and scope of analysis, and a set of alternatives to be assessed comparatively (Liberati 1997). It is important to describe the alternatives in detail so that study users can assess the relevance to their own setting. Current practice may vary over time and from country to country. Other elements that are important for the economic evaluation may vary from country to country as well. Therefore, transparency in reporting of economic evaluations is of utmost importance to allow an assessment of the applicability and relevance of an economic evaluation performed in the context of a HTA for its own setting.
Study frame and scoping of the economic evaluations

A coherent and manageable economic analysis needs a framing or scoping of the analysis that defines the following aspects of the analysis:

- **Target population**: The population or patient group that the intervention is aimed at.
- **Intervention**: The technology being studied.
- **Comparators**: The alternative technologies that the technology is being compared to (often including, but not limited to, current practice or “no intervention”).
- **Outcomes**: The positive or negative health outcomes that are included in the analysis.
- **Time frame**: The time frame during which cost and outcomes are assessed.
- **Perspective**: The perspective from which costs and outcomes are assessed.

Some of these aspects are further discussed in the methodology section.

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2 This section of framing and scoping of the economic analysis is placed in the economics chapter in the current version of the model because it is definitely needed here. Testing of the core model may show that the framing and scoping of the analysis needs to be defined as a separate domain or otherwise rewritten.
Methodology

In the following condensed Table 1 (Modification from Drummond) we will review the four main types of economic evaluation which can be part of HTA. The difference between them is based on how health outcomes are measured and valued. The choice between the different types of economic evaluations for answering a specific question depends on the purpose of the evaluation, the availability of specific data and potentially the guidelines for economic evaluations that are to be followed in a specific context.

Table 1. Types of full economic evaluation.

<table>
<thead>
<tr>
<th>Type of economic evaluation</th>
<th>Valuation of costs</th>
<th>Valuation of outcomes</th>
<th>The question to be answered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost-minimisation analysis (CMA)</td>
<td>Monetary units</td>
<td>None</td>
<td>Which intervention is the least costly?</td>
</tr>
<tr>
<td>Cost-effectiveness analysis (CEA)</td>
<td>Monetary units</td>
<td>Natural units</td>
<td>What is the intervention’s incremental cost per additional unit of outcome as compared to its best alternative?</td>
</tr>
<tr>
<td>Cost-utility analysis (CUA)</td>
<td>Monetary units</td>
<td>QALYs, HYEs</td>
<td>What is the intervention’s incremental cost per additional unit of outcome as compared to its best alternative?</td>
</tr>
<tr>
<td>Cost-benefit analysis (CBA)</td>
<td>Monetary units</td>
<td>Monetary units</td>
<td>What is the economic trade-off between different activities that matter for society?</td>
</tr>
</tbody>
</table>

The basic idea behind economic evaluation is to improve allocative efficiency in health care, i.e. given the resources available optimize the health of the population.

Perspective

The perspective of the economic evaluation is a key element in defining which costs and outcomes should be included in the analysis. For instance short stay at hospital may be cost-effective from the
perspective of the hospital but it may be more costly to society if the cost of home care is taken into account.

In the ideal situation the economic evaluation is conducted from the broadest possible perspective. The most comprehensive perspective is societal and then all relevant costs and outcomes of the technologies have to be identified, measured and valued, no matter whom these costs and outcomes fall on (Drummond 2005). Other possible perspectives are the health care sector’s perspective, third party payer’s perspective, hospital perspective or patients’ perspective. The perspective chosen ultimately depends on the purpose of the economic evaluation. If the purpose is to inform societal resource allocation, the societal perspective should be taken. For hospital HTA, the hospital perspective may be more appropriate.

Costs

The costing procedure can be divided into three phases: identification, measurement and valuation of resource use. First of all the relevant resources used have to be identified, then the volume or number of units of the resources uses has to be measured and finally these volumes have to be valued.

Direct costs are all costs directly related to a disease or technology. They include costs borne inside the health care sector (e.g. materials, equipment, personnel, tests – direct health care costs) as well as outside the health care sector (e.g. patients’ travel time – direct non-health care costs).

Indirect costs include the patient’s temporary absence from work due to illness, reduced working capacity due to illness and disablement, or lost production due to an early death. The lost production can be measured either by means of the human capital method or the friction cost method. Lost production is most often reported separately and not integrated in the cost estimate used for the calculation of the incremental cost-effectiveness or cost-utility ratio. Its valuation is made only in situations where it is judged to be relevant. The concept of lost production should not be confused with a transfer payment like sickness benefit.

Physical units or volumes of resources used should be reported separately from the unit costs of resources to allow decision makers to assess the applicability of resource use estimates to their own setting. In addition it is recommended to report direct costs separately from indirect costs.

Outcomes

Health outcomes of interventions can be measured by natural units of health (e.g. deaths, life years gained (LYG)), valuations of health states or utilities, or in monetary terms (Table 1).

If the intervention affects both the length and the quality of life, a composite outcome measure, such as Quality-Adjusted Life Years (QALYs) or Healthy Years Equivalent (HYEs) should be used. The QALY-approach and similar approaches are useful in policy analysis and program decision-making because they are generic and consequently allow broad comparisons between interventions and across diseases. They can in principle be estimated for any population, any disease, any intervention, and can be used to compare across diverse programs, assuming that studies use the same methodology. Health-related quality of life (HRQoL) refers to aspects of quality of life that are related to health. There are different tools to measure HRQoL and there is no single measure
which has been accepted as the gold standard. Patient outcome measures that extend beyond traditional measures of mortality and morbidity, to include physical, social, and emotional aspects that are relevant and important to an individual's wellbeing can be assessed using a disease-specific, generic, or a preference-based instrument. However, for economic evaluation an index measure is at least needed. To be able to compare outcomes in different disease areas, a generic measure should moreover be used.

Incremental cost-effectiveness ratio (ICER)

To be able to conclude which health technology is cost-effective, both the total costs and the effectiveness of at least two interventions have to be compared. The comparison may lead to nine different situations, as described in the decision matrix below.

Table 2. The cost-effectiveness decision matrix (Kristensen 2007)

<table>
<thead>
<tr>
<th>A new technology compared with an old one</th>
<th>Less effective</th>
<th>Same effectiveness</th>
<th>More effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less costly</td>
<td>1. No clear decision non-dominance =&gt; Incremental analysis needed</td>
<td>4. Adopt the new technology the new dominates the old (weak dominance)</td>
<td>7. Adopt the new technology the new dominates the old (strong dominance)</td>
</tr>
<tr>
<td>Same costs</td>
<td>2. Keep the old technology the old dominates the new (weak dominance)</td>
<td>5. The technologies are equal</td>
<td>8. Adopt the new technology the new dominates the old (weak dominance)</td>
</tr>
<tr>
<td>More costly</td>
<td>3. Keep the old technology the old dominates the new (strong dominance)</td>
<td>6. Keep the old technology the old dominates the new (weak dominance)</td>
<td>9. No clear decision non-dominance =&gt; incremental analysis needed</td>
</tr>
</tbody>
</table>

In situations described in cells 1 and 9 incremental analysis is needed to decide, which technology is preferable. For that purpose an incremental cost-effectiveness ratio (ICER) has to be calculated. It is a ratio of the difference in costs of interventions to the difference in outcomes. The ICER indicates the costs of achieving one extra unit of health benefit when switching from one alternative to another. The new intervention is cost-effective if the society is willing to pay for the additional benefits (cell 9) or if the society considers that the cost savings compensate for the lower effectiveness (cell 1).

Threshold cost-effectiveness and net benefit approach

Whether an intervention is cost-effective depends on its relation to the maximum willingness-to-pay for a unit of outcome, or the so-called ICER threshold. If the ICER of the intervention is lower than the threshold, the intervention is considered cost-effective (i.e. improving efficiency in health care). If it is higher than the ICER threshold, the intervention is not considered cost-effective and resource allocation to this intervention would not increase efficiency in health care.

The ICER seems to be most popular method but the ratio gives no idea of the size or scale of the interventions being considered. The net benefit approach is an alternative summary measure of the
value for money. Net monetary benefit (NMB) and net health benefit (NHB)) will be used to overcome problems with cost-effectiveness ratios. Both NMB and NHB are functions of the threshold cost-effectiveness ratio (Drummond 2005).

Modelling

There are several reasons for carrying out an economic evaluation with modelling, for example in a situation where economic and clinical data are missing or when there is a need for extrapolation of short-term clinical data to the long run. Decision trees and Markov models are the most frequently used types of models.

Sensitivity analysis

Economic evaluation is often based upon estimates of variables that are characterised by a specific distribution. Besides parameter uncertainty, economic evaluations –and more specifically economic models- are often based on assumptions about the relationship between parameters which are also uncertain. It is important to take this uncertainty into account in the evaluation, either parameter or model uncertainty. Sensitivity analysis will show the decision maker, how robust (trustworthy) the results and conclusions of the economic analysis are. Deterministic and/or probabilistic sensitivity analyses should always be a part of an economic analysis (Guidelines for the Economic Evaluation of Health Technologies: Canada, 3rd edition, 2006; Guidelines for pharmacoeconomic evaluations in Belgium: Brussels, 2008). Especially in economic models it is very important to conduct a complete sensitivity analysis for all uncertain model inputs to determine the impact on the results. Omission of any model input from the sensitivity analysis should be justified. Different methods to handle uncertainty are presented by Briggs et al 1994 and Briggs et al 2006.

Discounting

Cost and outcomes in the economic analysis that occur in the future should be discounted. Discounting, or calculating the present values of future costs and consequences, makes it possible to compare health technologies in an economic analysis whose costs and outcomes do not occur at the same time. Discounting should not be confused with inflation.

Transferability of resource utilization and unit cost elements

Costs of technologies are generally not transferable from one country to another. However, transferability of individual elements of data differs. Table 3 contains our assessment of transferability for each element. Although the resource utilization and unit cost elements are only partially transferable or not transferable at all, they are all essential parts of an economic assessment. The relevance of economic evaluations cannot be judged without information on these elements. Moreover, data on types and amounts of resources used in one country are often valuable information for researchers performing a HTA in another country.
Table 3 Transferability of resource utilization and unit cost elements

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Transferability</th>
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<tbody>
<tr>
<td>What types of resources are used when delivering the assessed technology and</td>
<td>Partially transferable. In most cases types of resources are completely transferable, but this should be tested, if appropriate.</td>
</tr>
<tr>
<td>its comparators?</td>
<td></td>
</tr>
<tr>
<td>What amounts of resources are used when delivering the assessed technology and</td>
<td>Partially transferable. It is a well-known fact that resource utilization when delivering a specific technology can differ between countries, e.g. the</td>
</tr>
<tr>
<td>its comparators?</td>
<td>average number of hospital days for a specific procedure may vary considerably. Other types of resource utilization may vary little between countries.</td>
</tr>
<tr>
<td></td>
<td>Transferability for this issue is an empirical question that needs to be addressed carefully.</td>
</tr>
<tr>
<td>What are the unit costs of the resources used when delivering the assessed</td>
<td>Not transferable. Although some unit prices are comparable between countries, it cannot generally be assumed that unit costs are transferable.</td>
</tr>
<tr>
<td>technology and its comparators?</td>
<td></td>
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Assessment elements

The costs and economic evaluation domain consists of five topics: resource utilization, unit costs, indirect costs, outcomes, and is the technology cost-effective when compared to the most cost-effective alternative procedure(s). In each topic there are one to two issues, together six issues.

The following is a listing of elements that are specific to economic evaluation. In addition to these elements most economic evaluations will employ one or more outcome elements from the effectiveness and safety domains in order to specify positive and negative health outcomes in the economic analysis. The only exception to this is the case where all effectiveness and safety outcomes are equal for the technology and all comparators, in which case a cost-minimization analysis is relevant.
<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
<th>Topic</th>
<th>Issue</th>
<th>Clarification</th>
<th>Importance</th>
<th>Transferability</th>
<th>Information sources</th>
<th>Reference</th>
<th>Relations</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>E0001</td>
<td>Costs and economic evaluation</td>
<td>Resource utilization</td>
<td>What types of resources are used when delivering the assessed technology and its comparators (resource use identification)?</td>
<td>In order to do an economic evaluation all types of resource utilization must be identified. The study perspective determines what kinds of resource utilization must be identified. A societal perspective implies identifying all kinds of resource utilization irrespective of who pays for the resources. If a health care provider perspective is applied, then resource utilization paid for by the patient is not relevant.</td>
<td>3</td>
<td>2</td>
<td>Health care registers, RCT’s with resource utilization data, reimbursement databases, micro-level costing studies/ABC-costing studies</td>
<td>Guidelines for economic evaluation of Health Technologies: Canada, 3rd edition, 2006, Guidelines for Pharmacoeconomic Evaluations in Belgium, 2008</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>E0002</td>
<td>Costs and economic evaluation</td>
<td>Resource utilization</td>
<td>What amounts of resources are used when delivering the assessed technology and its comparators (resource use measurement)?</td>
<td>For all types of resource utilization the amounts of resources used when delivering the assessed technology as well as when delivering the comparator technologies must be measured</td>
<td>3</td>
<td>2</td>
<td>Health care registers, RCT’s with resource utilization data, reimbursement databases, micro-level costing studies/ABC-costing studies</td>
<td>Guidelines for economic evaluation of Health Technologies: Canada, 3rd edition, 2006, Guidelines for Pharmacoeconomic Evaluations in Belgium, 2008</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>E0003</td>
<td>Costs and economic evaluation</td>
<td>Unit costs</td>
<td>What are the unit costs of the resources used when delivering the assessed technology and its comparators?</td>
<td>Ideally unit cost estimates should be (proxies for) opportunity costs. By the opportunity cost is understood the (lost) health gains that could have been achieved from an alternative technology, which, however, cannot be introduced or retained, because the resources e.g. manpower, are used on the new technology. Market prices are often used as proxies for opportunity costs.</td>
<td>3</td>
<td>1</td>
<td>Market prices, companies, hospital accounting systems, reimbursement databases, micro-level costing studies/ABC-costing studies</td>
<td>Guidelines for economic evaluation of Health Technologies: Canada, 3rd edition, 2006, Guidelines for Pharmacoeconomic Evaluations in Belgium, 2008</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>E0004</td>
<td>Costs and economic evaluation</td>
<td>Indirect Costs</td>
<td>What is the impact of the technology on indirect costs?</td>
<td>Indirect costs include costs to society of lost production. This can be due to patient’s temporary absence from work due to illness, reduced working capacity due to illness and disablement, or lost production due to an early death</td>
<td>2</td>
<td>2</td>
<td>The data are available from different registers e.g. register on sick leave, sickness allowance, patient administration systems/clinical databases, earlier studies, cost diaries.</td>
<td>Kristensen 2007</td>
<td></td>
<td>Overlap with societal domain.</td>
</tr>
<tr>
<td>E0005</td>
<td>Costs and economic evaluation</td>
<td>Outcomes</td>
<td>What are the incremental effects</td>
<td>The calculation of an incremental cost-effectiveness ratio requires the estimation</td>
<td>3</td>
<td>2</td>
<td>Estimation of the incremental effects</td>
<td>Overlap with effectiveness</td>
<td></td>
<td></td>
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<tbody>
<tr>
<td></td>
<td>evaluation</td>
<td></td>
<td>what is the incremental cost-effectiveness ratio?</td>
<td></td>
</tr>
<tr>
<td>E006</td>
<td>Costs and economic evaluation</td>
<td>Cost-effectiveness</td>
<td>The result of the economic analysis will most often be an incremental cost-effectiveness ratio eg. costs/QALY if quality-adjusted life years is used as the main outcome indicator. The incremental cost-effectiveness ratio does not in itself determine that a technology is desirable. Decision makers need – implicitly or explicitly – to weigh the benefits of a technology against the costs. The concept of a cost-effectiveness threshold is one way of expressing decision-makers willingness-to-pay for health benefits. If other types of economic evaluation is chosen, eg. cost benefit analysis, other types of measures are used to express results of the analysis, but most current economic analysis within HTA’s are done within the cost-effectiveness/cost-utility framework.</td>
<td>3</td>
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References:


Ethical analysis

Samuli Saarni, Ilona Autti-Rämö, Dagmar Lühman, Björn Hofmann, Marcial Velasco-Garrido, Marta Lopez de Argumedo, Marco Marchetti

Domain description

Definition

Prevalent morals, values and behavioural models of the society relevant for health technology assessment are considered in ethical analysis. These values, moral principles and social rules (norms) form the basis of social life as well as national laws and consequently it is important to understand them. These factors play a key role in shaping the context in which health technologies are used. The moral rules of the society reflect the values of the society and the values may be weighted differently in various societies. Evident cultural (e.g. religion) and economic (e.g. gross national product) differences have also a major impact on the moral value of the consequences that the implementation of a technology can have. In the context of HTA, ethical analysis is useful in examining the context for technology use, but also in highlighting that HTA is a value-laden process, and should not be considered as a purely technical tool for maximising the health-economic benefits of technology.

Place and significance of ethical analysis

Within an HTA project the ethical analysis appraises the ethical questions raised by the technology itself and by the consequences of implementing / not implementing a health technology as well as the moral and ethical issues that are inherent in the HTA process. Although ethical analysis may be practically approached as a separate domain of the HTA process, moral issues are relevant to all HTA domains and the methods of ethical analysis should take this into account. The ethical analysis should be performed as an integral part during the entire HTA process. It is not a "one session" task. Instead, the various topics and issues described in the assessment element have to be dealt with in different phases of the assessment process. The analysis starts by identifying the technology specific ethical questions and ends in the formation of an HTA report that integrates the results of ethical analysis in such a way that the report can be used for its ultimate purpose: to assist decision making.

Appraising evidence and making decisions on the use of health care resources is never a straightforward, value-free technical process. Moral and social values and various consequences of implementing a new technology play an important role throughout the process and influence the final decision. For example, the choice of certain evaluation criteria and their weighing reflect the underlying values. An ethical analysis aims to provide thorough understanding of value-related aspects that need to be taken into account during the HTA and in the decision making process. Values are inseparable from HTA, so the question is whether to address them explicitly or implicitly. The relative weight placed on the ethical analysis and the selection of methods depends heavily on the technology being evaluated. In general, the more “extraordinary” the technology
appears the more emphasis should be placed on the ethical analysis. Such situations arise e.g. when the technology presents new, severe or fundamental value conflicts, or challenges everyday norms or beliefs. Methods and significance of integrating ethical analysis in HTA have been developed and actively advocated in recent years by the INAHTA ethics working group, whose work has greatly benefited this paper (Andersen et al 2005).

HTA organisations differ in their resources and mandate for decision-making: while some only provide synthesis of evidence, others conduct appraisal of evidence and formulate recommendations or produce clinical practice guidelines. Hence the available methods, weight and ways of reporting an ethical analysis might vary accordingly. For example, the more guiding authority the HTA organisation has, the more weight should be devoted to a balanced explication of the normative valuations underlying the recommendations. If the HTA organisation is clearly separated from decision-makers, it may be enough to describe the different values, attitudes and arguments that should be considered by the decision-makers. The “first” ethical question – which topics to conduct a HTA on – might also be outside the scope of some HTA organisations. Furthermore, a successful integration of ethical analysis into the HTA process depends on recognising its importance within the entire HTA organization: analysing ethical aspects should be conducted and developed through the entire HTA organization, and not as an add-on to selected HTA projects (ten Have 2004).

The ethical analysis is a natural place to go beyond the limits of the PICO approach (patients, intervention, comparison, outcomes, see chapter "Effectiveness"). Strictly applying the PICO model to ethics implies that the comparison technology is ethically problem-free and that, if there are no ethically relevant differences between the technologies, applying the new technology is equally ethically problem-free. As it is unlikely that a thorough ethical analysis has been conducted on the comparison technology, it is important to consider also this issue – in order not to overlook essential moral issues only because they also affect the comparison technology.

Integration of ethical analysis may take various forms in HTA organizations. Some methods align well with the more traditional approach to conducting HTA, e.g.: hiring a bioethicist to conduct a separate chapter on ethical analysis, or conducting meetings for HTA researchers to reflect on the issues raised by their HTA project. Other initiatives are more challenging to the traditional HTA culture, e.g. developing “interactive” or “constructive” HTA processes that involve stakeholders’ participation.

**Methodology**

Although there is wide consensus, that ethical analysis should be a mandatory element of HTA, there is no generally accepted, structured method for performing ethical analysis. The methods must be tailored to suit the HTA organisation, the topic under study as well as the local culture and health care system. Local variation of methods and procedures is not necessarily problematic as long as transparent documentation is provided. The locally most suitable method must be chosen to suit the resources available, HTA topic, position of the HTA organization in the health care system of the country and the competencies of those performing the ethical analysis. The relative weight placed on the ethical analysis and the selection of methods depends also on the technology being evaluated.

Identifying and defining the various methodological approaches for integrating ethical analysis into HTA has been initiated and conducted by the INAHTA ethics working group. Short descriptions of
the various methodological approaches used by HTA agencies that were identified by INAHTA ethics working group and complemented by the EUneHTA ethics working group are included next. Presenting concrete examples of how to apply these methods is beyond the limits of this document. All these emphasise the need to consider issues extending past utilitarian maximisation of (cost) benefits of technology.

**Casuistry**

Casuistry means solving morally challenging situations ("cases") by referring to relevantly similar "paradigmatic" cases for which an undisputed solution has been found (Jonsen 2001, 2005, van Willigenburg 2005, Giacomini 2005).

The methodology of casuistry comprises three steps. First, the case at hand is sorted to a broad category of problems, "topics" (e.g. medical indications, patient preferences, quality of life, contextual features). Details should be described in a standardised way (who, what, where, when, why, how, by what means). Second, common sense moral rules, "maxims", related to the case are explored (e.g. "the wish of the patient has to be respected"). If the maxims are contentious, the moral principles that underlie them in the case at hand are explored. Third, the case at hand is compared with a set of paradigmatic cases on the same topic that have been solved in agreement previously. Comparing the details of the case at hand, including the underlying maxims and principles, with the details of the paradigmatic case then may suggest a solution for the current problem (Neitzke 2005).

In HTA, especially for coverage decisions, a casuistic approach (precedence method) is suggested as at least a part of the ethical analysis. It means first establishing an inventory of past coverage decisions. The aim is to generate a typology of paradigmatic, covered technologies, which would represent the basic moral principles that underlie decision-making in the respective health care system. Next, the relevant qualitative and quantitative characteristics of the new technology are identified, and the technology is compared to similar, preceding paradigmatic cases. Ideally their solution may then be applied to the new technology. However, in addition to applying the solutions of past precedents to current cases, it is also necessary to reflect on the possibility that the value base has changed since the paradigmatic decisions were made. It may be that this reflection leads to a need to reconsider previous decisions.

In pure casuistry, cases are approached without referring to ethical principles, norms or theories. The process might resemble coherence analysis in that coherence between solutions to similar cases is searched for, or interactive approaches that aim for consensus of relevant stakeholders. A pragmatic, "moderate" form of casuistry as described above can include an element of principlism in that referring to ethical maxims and principles is done if comparison to previous cases does not provide clear enough solution. It also includes an element of wide reflective equilibrium, in that applying past precedents to new cases might reveal a need to reconsider previous decisions.

**Coherence analysis (CA)**

The main idea of CA is to reflect upon the consistency of ethical argumentations or broader theories on different levels, without prescribing which facts, arguments or principles are prima facie relevant. It is a procedural, pragmatic approach, i.e. describes a procedure of approaching moral
issues without claims of providing direct answers on “right or wrong”. CA can be compared to test-reliability and internal consistency of tests in empirical research. It cannot ensure validity: an immoral system can be as coherent as a morally justified one. (Grunwald 2004, Musschenga 2005).

CA considers the logical (possibly also emotional or intuitive) consistency of facts, norms and arguments relevant for the HTA. Thus CA is critically dependent on the material input, i.e. the comprehensive identification of facts, values and principles the coherence of which is to be considered.

Some kind of consideration of logical coherence is necessary for any ethical analysis of HTA. The more “extraordinary” the technology under evaluation is, the more useful a formal CA can be.

For CA the evidence can be summarized in regard to

1. society’s normative framework relevant to the technology (legislation, practice norms and guidelines, decision making procedures)
2. society’s, patients' and scientists' expectations regarding the impact of the technology (fears, expectations)
3. society’s general objectives and visions (concepts of justice, autonomy, reasonable development and other ideals)
4. Interpretation of the past and present `biography´ of society or parts of it (deeply held, fundamental values and views central to individuals and societies self-image)

CA can be conducted by one expert or by a group. It is a reflective procedure (internal monologue / group discussion) trying to help achieve a logically consistent HTA. The identification of inconsistencies should lead to attempts to solve these (using, for example, discussions, wide reflective equilibrium, interactive technology assessment, normative approaches based on common principles etc.). Higher consistency of the whole is the norm, on which conflicting ideas are evaluated, edited and possibly abandoned. Thus and in contrast to interactive approaches (see below), opinions of important stakeholders can but need not be taken into account.

Reaching consistency might not succeed, so the end result might as well be identification of incommensurable beliefs or values, or contradictions between empirical claims, normative frameworks, or scientific and societal understandings and needs.

In conclusion, CA does not provide an unequivocal normative “ethical recommendation”, but CA is an essential part of all ethics analysis. It may be especially useful early on in the HTA process, to help identify central issues in need of further scrutiny.

**Interactive, participatory HTA approach (iHTA)**

iHTA aims for intersubjective consensus on ethically problematic issues, reached through real discourse. It integrates patients, professionals and other stakeholders’ perspectives into HTA. It is a procedural approach (like coherence analysis) meaning that it describes a procedure to approach ethical problems, not any ideal solution to these problems. In contrast to coherence analysis, however, iHTA also aims to improve the validity of the whole HTA process through empowering and involving the stakeholders to participate. Although iHTA aims for consensus, this may not always be reached together with the stakeholders. It may also be decided that the conclusions are

The iHTA process begins by asking what kind of values are at stake, whose values they are, who are the important stakeholders and what values of theirs are at stake. Second, an interactive procedure to clarify these values is chosen, depending on presumed severity of value conflicts and the resources available. For example, the Delphi procedure, citizen juries, focus groups or deliberative polls could be used. The results of the interactive process inform the HTA process, i.e. help to identify relevant questions and relevant parameters to assess the (health) effects of the technology, but can also be reported as such.

iHTA informs, but does not dictate, the normative ethical conclusions needed in reporting the results of the HTA. The iHTA can bring into the expert group important opinions and values that may otherwise have been ignored. Ethical conclusions can not, however, be directly derived from any naturalistic population consultation: it is not possible to deduce how things ought to be from how things are. But the description of possibly differing valuations of different stakeholders, discovered with the iHTA process can be important for the application of the results.

**Principlism**

Principlism is based on the idea that there are principles, rooted in society, that are based on a common morality. These principles form a core dimension of all morals occurring in the world, and are presumed to be shared by every serious moral person. Principlism does not imply a specific method of reasoning, but describes a specific content of ethics: the principles form the essence of considered judgments. Principlism considers the validity of ethical analysis. (Beauchamp and Childress 2001, Vieth 2002).

Principlism recognises that there are several ethical principles, in contrast to foundational theories like utilitarianism or Kantian deontology that recognise only one supreme principle. The most influential principlist approach to bioethics (Beauchamp & Childress 2001) comprises four principles, representing clusters of practice norms:

- **Respect for autonomy**: a norm of respecting the decision making capacities of autonomous persons,
- **Non-maleficence**: a norm of avoiding the causation of harm,
- **Beneficence**: a group of norms for providing benefits and *balancing* benefits against risks and costs - also referred to as the `proportionality principle`, highly relevant for HTA and research ethics and
- **Justice**: a group of norms for distributing benefits, risks and costs fairly.

These norms are assumed to form a comprehensive analytical framework for bioethics. The principles are `prima facie` binding, meaning that they are always important in every situation, but they are not absolute, because they can conflict. Highly relevant for HTA is, for example, the conflict between autonomy and beneficence for single persons on the one hand, and the just distribution of resources and beneficence for society on the other.
In practice, as the principles are abstract, they must always first be specified according to the current context. Then, if all principles can not be realised fully (as is most often the case), the specified principles must be balanced with each other. A principle should only be overridden if:

- Better reasons can be offered to act on the overriding one,
- The moral objective which justifies the infringement must have a realistic chance of being achieved,
- The infringement must be the only way to realize one principle at the cost of the other,
- The form of the infringement must be commensurate with achieving the primary goal,
- Any negative effects of the infringement must be minimized and
- The decision must be impartial in regard to all affected parties.

The major advantage of principlism is that it delivers a comprehensive, normative framework for ethical analysis, in contrast to procedural, non-normative approaches like CA, iHTA, wide reflexive equilibrium and casuistry. Conversely, normativity is also the main problem of principlism, as not all ethicists agree in that these and only these principles are universal. If so, the normative framework of four principles might not be valid for every technology and every population.

Explicit principlistic considerations are useful for increasing the transparency and transferability of the ethical analysis. To balance the principles in a context-sensitive manner in practice, WRE (see below) or participatory methods can be useful.

**Social shaping of technology**

The social shaping of technology (SST) approach (Rip 1995, Clausen 2004, Reuzel 2004) views technology as the product of societal processes (within industry, research institutes, governmental bodies, and society at large) rather than an independent artefact that has a certain, measurable impact on its target. The aim is to understand what technology is and how its development is interwoven with its social context (e.g. the engagement and strategies of various actors, and the way various problems are defined and resolved).

Assessing the role, merit, and value of technology becomes important. The social shaping perspective also implies an opportunity to manage technology through its social context. If technology in fact is technology-in-context, then both technology and its context can be influenced or adjusted to improve the outcomes of using technology. The societal processes underlying technology development can be explained to some extent by the values relevant in different contexts.

From the ethics point of view, the SST approach emphasizes

a) reflexive focus on the range and values of relevant actors and their conditions of involvement
b) considering how technology can influence society and how technology can be best managed by society
c) the inadequacy of evaluating a technology without considering the local social environment.
Within this framework, many of the other methodological approaches to ethical questions in HTA can also be applied (e.g. participatory approaches such as iHTA).

**Wide reflective equilibrium (WRE)**

The WRE (Rawls 1971, 1993, Daniels 1979, 1996) is an ideal, perpetual goal of justification in modern philosophical inquiry. It is based on pragmatism and social constructivism, which claim that ethical truths can not be revealed or directly experienced, and that there are no static, fundamental a priori valid universal principles. On one hand, the normative framework of society may change over time. On the other hand, humans need stability, cognitive coherence and some degree of reconciliation of individual and social norms and values. WRE is a central methodological part of the ‘four principles’ approach, discussed above (Beauchamp & Childress 2001).

When using WRE, the reflection starts from the most considered judgments and moral feelings that have a prima facie credibility. This has to be done behind a ‘veil of ignorance’ (i.e. imagining we do not know which position we would have in the society our decisions concern) to try to be as impartial as possible. To approximate WRE, all possible situations, arguments, and judgments need to be taken into account and brought into a coherent whole through rational reflection (see coherence analysis above). This might entail that some of our primary considered judgments have to be adjusted.

WRE is an important political and philosophical goal of coherence analysis and discourse ethics in regard to decision making. However, it is an ideal goal of a theoretical procedure, which may be difficult to apply in real-world HTA processes. As a goal emphasizing individual and intersubjective consensus, WRE may also neglect true conflicts between incommensurable arguments. Essentially, WRE emphasizes open, honest and impartial discourse, conducted by rational, sensible actors in democratic, pluralistic societies who want to reach consensus through finding the most validity of claims.

**Examples of local approaches**

**AETMIS: Promoting context-specific, integrated approaches to analysing ethical issues in HTA**

At AETMIS the ultimate objective is to integrate a context-sensitive ethical inquiry right from the beginning of the HTA (Caron 2005, 2006). Several approaches were developed for different HTA needs that apply at different times in the process of HTA:

- “Start-up” meetings, which is an institutional process to promote context-based, ethically-informed HTA projects. These are conducted at the very beginning of selected HTA projects;
- The “comprehensive” ethical approach, where ethical inquiry is an integral part of the evaluative framework. This means that ethical inquiry is “active” throughout the entire HTA process. Such approach is only used for specific HTA reports (e.g. genetic testing); and
• The more traditional ethical analysis, which refers to the write up of a separate section on ethical issues in an HTA report. Such “add-on” ethical inquiry is usually performed by an ethical expert in collaboration with the assessors.

Integration of ethical analysis throughout the entire HTA process is achieved by teaming a bioethicist with the assessment team responsible for the project. The assessment team can also be advised by a technology-specific advisory committee (e.g. for genetic testing). An “integrated” ethical inquiry involves a reflection on value-laden choices at all levels of the HTA process, namely in: a) defining the scope of assessment, b) performing literature review and primary research to document the experience of patients and their families as well as the context of service delivery, c) establishing a framework for appraisal of technologies and modes of intervention, d) conducting the appraisal of those strategies, e) highlighting specific ethical and social issues, and f) formulating recommendations. In addition to literature review, primary research can be conducted to better document the situation in the local jurisdiction, and to explore the perspectives of different stakeholders on the various issues linked with technology use. Ethical and social considerations pertaining to technology use are also documented in a specific section of the HTA report.

The eclectic approach of FINOHTA

In Finohta, each HTA report is produced in co-operation with the methodological experts from Finohta and clinical experts from health care organizations (Autti-Rämö and Mäkelä 2007). Professional ethicists are included either during the HTA or peer review process depending on the technology to be evaluated.

General and technology specific ethical issues and consequences for various stakeholders are identified during the HTA process by the content experts, through literature search and (when possible) by stakeholder hearing. For each stakeholder, a) possible consequences of proceeding with or b) refraining from the implementation of the technology (as compared with other options) are listed. Including patient representatives is an option in this process.

A repetitive exchange of opinions and weighing different values has been the core of a successful ethical discussion and when making a summary of the evaluation process. New moral issues often emerge during the HTA process and novel aspects have come up even at the final comment round. Ethical evaluation is written as a separate chapter in Finohta reports, but its main aspects are interwoven in the discussion chapter so that evidence is balanced against ethical consequences.

Value analysis of NKCHC

This method is used at the Norwegian Knowledge Centre for Health Services (NKCHC) and it is based on value analysis (axiology) developed with regard to technology, according to which technology is a part of human activity that is related to values in different ways (Hofmann 2002, Hofmann 2006):

• Function (value-ladenness, e.g. visualizing extracorporeal structures by ultrasound for a diagnostic ultrasound machine)
• Purpose (primary value of technology use, e.g. knowledge gained by diagnostic ultrasound)
- Intention (secondary value of technology use, e.g. possible actions as a result of diagnostic ultrasound)
- Intention (social values attributed to technology, e.g. social and professional status of diagnostic ultrasound)

Values come to play in many ways with regard to the implementation and application of health technology, such as:

- general moral issues (consequences, autonomy, integrity, human rights, dignity),
- issues related to stakeholders (professionals, users, industry, patient organisations, assessors),
- issues related to methodological choices (end points, level of evidence)
- issues related to technology assessment (selection of technology to be assessed) (Hofmann 2005a)

A Socratic approach has been applied in this framework through a set of questions which are applied to highlight the value issues at stake in the different areas. (Hofmann 2005b) In the Norwegian context the method has been normatively open, i.e. the value analysis has not resulted in explicit normative advice, but only outlined the important normative issues. This restrictive use is due to the context and not due to the method.

The method has been applied to a series of HTA reports by the NKCHC, such as proton therapy, treatment of CFS/ME, intracytoplasmic sperm injection, palliation of cancer patients, transfusion versus other methods at blood loss, effects of snuff use, methods for age estimation in asylum seekers, methods for removing amalgam fillings, benzodiazepines treatment for drug-dependent subjects, palliative surgery for cancer patients, and use of hemopoietic stem cells from cord blood. As the technologies are different, so are the values involved. Accordingly, only a subset of the questions is applied in each HTA.

The “triangular model” for ethical analysis based on human person-centred approach

The triangular model is centred on a substantial conception of human person. It considers the man as reference-value in the reality, around which all the ethical judgements are coordinated. Based on a cognitivist approach to the ethics, this model considers that it is possible to get some truths, concerning man and his/her praxis, recognizable by everyone through a rational activity. (Sgreccia 2007).

The methodology of the triangular model comprises three steps of analysis: 1. data collection; 2. anthropological aspects, 3. ethical-normative evaluation. The first step, “scientific moment” consists of an in-depth study of all facts/data, including qualitative and relational ones. The second step, “anthropological moment”, consists of the anthropological understanding of facts; in other words, the analysis of eventual values at stake, related to human life, integrity and dignity. According to this analysis it is possible to find values which should be promoted and defended, and norms which should guide human action on individual and societal levels. The third, “ethical-normative” step consists of evaluation of practical choices that should be made.
This model highlights a triangular connection between bio-medicine, anthropology and ethics, settled on two levels: the explanation of a certain topic (descriptive step), followed by a normative phase, in which we can get conclusions within a debate of the meta-empirical perspectives i.e. relating to the steps 2 and 3 described above. It is evident that such an ideal process needs all three theoretical steps in order to be possible.

This model presumes a normative framework for ethical analysis (Sacchini et al. 2005, Sacchini & Refolo 2007). It consists of four principles of reference: 1) the defence of human physical life as a whole, and its integrity, 2) the principles of freedom (capability of the human will) and responsibility (an intra- and inter-subjective evaluation of subject’s own acts and will) 3) the therapeutic principle, according to which the human person has to be treated as a whole of body-mind reality, 4) the principles of sociality and subsidiarity, according to which public or private authority is called to intervene and to help the person only if he is not able to manage, to promote or safeguard him/herself (Sgreccia 2007).

The process of producing the core of ethical analysis

For each HTA project a person within the HTA team needs to be defined to be responsible for facilitating and reporting the ethical analysis. For a successful ethical analysis, it is necessary that it is always done together with the content experts and is not seen as an add-on that can be conducted by separate ethicists alone. A purely philosophical approach may ignore the broader context in which the ethical and moral arise. Ethical analysis is an ongoing process that lasts throughout the HTA project. Ideally, many of the ethical and moral issues should be considered early on while analysing other aspects of the technology and, vice versa, the ethical analysis is dependant on the results and insights gathered for the other domains. However, if the only alternative is to do an “add-on” ethical analysis (for example, by asking an ethicist who is not involved in other domains to answer the questions alone) this is most likely better than no ethical analysis at all. For clarity, within HTA the reflection of ethical aspects relates to two broad areas:

a) Questions related to the HTA process (selection of topic, outcomes, methods, evaluating the importance of ethical analysis and planning it)

b) Questions related to implementing or not implementing the technology

The choice of methods to conduct a formal analysis of ethical aspects depends on a number of interacting factors:

a) The type of technology being assessed. Technologies with strong "prima facie" moral implications (like genetic testing or aggressive cancer therapies in children), technologies concerning diseases with strong interest groups involved (for example cochlear implants) or other “extraordinary” new technologies that appear to challenge commonly held values or everyday beliefs (like home care nurse robots) require more emphasis on the ethical analysis.

b) The role of the HTA organisation and the intended purpose of the assessment especially in relation to national decision making and bodies providing guidance;

c) Prevailing methodological expertise and experience with ethical analysis.
d) Time and resource constraints for the assessment.

Every HTA process should be performed considering general moral issues that have been stated in the introduction chapter. Preferably, ethical considerations should be introduced as early as possible in the process. The person responsible for the ethical analysis should ensure that the moral issues are considered by the whole group during the entire process.
Defining the focus of the overall assessment

The focus within the topic, the specific questions to be answered, the study inclusion criteria and the primary outcome points for the analysis of the consequences of implementing a technology (e.g. efficacy, safety, effectiveness, cost implications) are defined by the entire working group. These choices are value laden and they need to be carefully scrutinized before proceeding to literature review as they can have a major impact on the content and conclusions of the HTA report.

It is important to consider, whether there are issues of potential ethical significance related to the disease or health problem as such – i.e. even before any factual considerations about the effectiveness or consequences of implementing / not implementing a technology. For example, some conditions might be considered “self-inflicted”, and issues related to embryos are likely to raise fundamental questions about the value of life and autonomy, and conflicts of interest (interest of embryo, of mother, of father).

Identification of all stakeholders

The perspective of all relevant stakeholders should be involved in the process. The view of the stakeholders is optimally acknowledged already during the process (e.g. stakeholder hearing meetings) and not first during the external peer review process. It is usually fairly easy to identify the primary stakeholders for each technology - patients, clinicians, patient organizations, industry, providers etc. It is as important to identify also those stakeholders who can be indirectly affected if the technology/change is being implemented (e.g. change in the use of resources at emergency units may have a large impact on other patient groups); this may include the HTA agency itself. Making HTA project plans public as early as possible and allowing for public consultation may help identify relevant stakeholders and their fears early in the process.

Answering the core set of questions

Ethical evaluations can be conducted very differently depending on the resources in the HTA organization and the technology in question. It can, however, be conducted in a transparent way so that process is clearly defined and the objectivity of the analysis can be acknowledged.

The core set of questions to be considered within an ethical analysis are presented at the end of this chapter. This approach is strongly influenced by the work of Hofmann (see above Value analysis of NKCHC). All questions are not relevant for all technologies and thus do not need to be answered every time. Nor are the questions in order of importance, or need to be answered in the same order as presented. Some issues deal with direct consequences of the implementation (simple facts, e.g. can the technology harm the patient). Many issues deal with questions that need careful consideration that will provide a thorough overview of the value-laden aspects that need to be taken into account when deciding on implementation (e.g. balance between benefit and harm). A minority of issues cover areas that lead to clear conclusions (e.g. whether legislation is fair and adequate).
The evaluation of the principal questions about the technology and consequences of implementing/not implementing a new technology are based on the information received from following sources:

- The ongoing assessment of efficacy, safety, effectiveness and cost-implications.
- Discussions among the working group. Discussions with experts are effective in identifying key issues and topics related to the questions, and help in planning the rest of the information gathering. Structured questions presented in the issues list need to be discussed but additional content specific ethical aspects may also be identified during the discussions.
- Literature search focused only on the technology in question may seldom give access to articles relevant to the ethical evaluation. A natural starting point is to include keywords related to ethics to the literature search needed to cover the other areas of the HTA process, to do a hand-search of published HTA reports (ethical considerations are often integrated in the reports), and an internet search for reports, proceedings and books etc. To perform a systematic literature review that will cover all of the ethical and moral issues identified during the process is, however, challenging. Ethically relevant issues are identified during the entire HTA process, and the literature searches thus commonly repeated when new ethically relevant issues are identified. The extended literature search should not be focused only on the technology in question but cover other related technologies with similar ethical challenges (see casuistry above). The detailed literature search should include all relevant sources on ethical aspects of the technology in question. A suggestion for databases and MeSH terms that can be useful has been identified by Droste et al (Droste et al 2003)
- Qualitative analysis of the expectations and fears of various stakeholders may reveal questions that cannot be identified by the content or methodological expert group or from the literature review. This information can be reached through stakeholder meetings or conducting primary studies.
- Philosophical analysis of the logic and coherence of the argumentation.

Information for answering the questions is gathered from several sources, and using several procedures. There is no clear starting point, but the information gathering can be seen as circular process where previous phases identify new needs and questions then answered by other sources (Figure 1). Thus, it may be useful to repeat some phases following new insights.
Figure 1. Process of ethical analysis

**Process of core ethical analysis**

- Efficacy, safety, effectiveness etc. results
- Literature search on ethical issues
- Stakeholder hearings
- Discussions among the working group
- Philosofical analysis of arguments
- Answering the core questions

**Presentation of the ethical analysis and evidence in a balanced fashion**

The morally relevant issues and moral conflicts have to be synthesized and reported transparently so that they can be considered when deciding upon implementation of technology. No single solution to every moral problem exists; neither is it possible to list moral issues according to a commonly agreed weighted value. Answers to the core set of issues may also reflect the wide variety in personal morals and values within the society. The methods described above in the methodology part can be useful tools for eliciting information, but they are probably more useful for analysing, processing and balancing the information and insights gathered during the ethical analysis. The core set of questions is intended especially for identifying ethically relevant issues.

The synthesis of ethical analysis has to be performed in an open way so that the interests of various stakeholders are kept as "unweighted" as possible, or the weighing is done transparently i.e. describing the procedure and participants of the analysis. Ideally, the decision on "whose values are to be weighted" need to be in the hands of the decision makers. The decision makers can be different within the same country between technologies and / or institutions and also between countries. Thus the ideal way to present the synthesis of the analysis may vary accordingly.

Ethical analysis on the consequences of implementing/not implementing the technology may be handled using an open framework (Autti-Rämö and Mäkelä 2007). The possible consequences of proceeding with or refraining from the implementation of the technology can be listed separately for each stakeholder in an open table as the answers for various parties may differ largely (table 2). The identified issues are not valued-weighted against each other but the table offers a transferable list of aspects that need to be appreciated in the final decision making process.
Table 2. Example of a framework for ethical analysis

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Benefits when proceeding with implementation</th>
<th>Adverse consequences when proceeding</th>
<th>Benefits when refraining from implementation</th>
<th>Adverse consequences when refraining</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td></td>
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<tr>
<td>Family</td>
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<tr>
<td>Care Providers</td>
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<tr>
<td>Other patient groups within the specialty</td>
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<td></td>
</tr>
<tr>
<td>Primary Health care providers</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Secondary Health care providers</td>
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<td></td>
<td></td>
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<tr>
<td>Tertiary health care providers</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Payers</td>
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<tr>
<td>Society</td>
<td></td>
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<tr>
<td>Producers/Industry</td>
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<tr>
<td>Decision makers</td>
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<tr>
<td>HTA organisation</td>
<td></td>
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</tbody>
</table>

It is important to identify also those areas where values may differ significantly between various professions (e.g. attitude towards the care of patients with nontreatable diseases or towards treatments of extreme cost). It is important that areas of ethical disagreement are clearly stated in the final document.

Ethical analysis is usually reported as a separate chapter, in order to assure transparent reporting of value issues. The ethical implications of implementing or refraining from the implementation of technology need, however, to be discussed in a balanced way so that the health policy makers have a wider view on all possible consequences of their decision. The open framework as presented in table 2 can be a helpful tool in this process. The decision to implement a new technology requires careful decision on the balance between benefit and harm, cost-effectiveness, reallocation of resources etc. Discussing the context-specific moral issues within the respective chapter (e.g. effectiveness, safety, and costs) may thus also help the decision makers to identify various scenarios and find the best for the common good.

Transferability of ethical analysis

The ethical analysis and its outcome have to be described in an open way in order to judge their transferability. Many of the ethical implications are common to various nations but some value laden issues are likely to be country specific. Analyses relating to ethical principles, coherence or paradigmatic cases are likely to be more easily transferable than argumentation based on interactive approaches relying on local values, stakeholder attitudes and available health care resources.

Overlap with legal and societal evaluation

Ethical analysis can not be separated from the evaluation of legal and societal aspects. These domains overlap the ethical analysis, though the angle of evaluation may differ. The legal
framework forms a basis for professional ethics (e.g. abortion, prenatal screening, and euthanasia). The societal consequences of implementing a technology may differ largely from those of primary outcomes at patient level (f.i. avoidance of death at patient level, avoidance of impaired working ability at societal level). The implementation of new technology will not only have an effect on health, functional abilities and psychosocial well-being but also on social networks and need of support.
## Assessment elements

<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
<th>Topic</th>
<th>Issue</th>
<th>Clarification</th>
<th>Importance</th>
<th>Transferability</th>
<th>Information sources</th>
<th>Reference</th>
<th>Relations</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0001</td>
<td>Ethical analysis</td>
<td>Principal questions about the ethical aspects of technology</td>
<td>Is the technology a new, innovative mode of care, an &quot;add on&quot; to a standard mode of care or a replacement of a standard?</td>
<td>The consequences of totally new models of care are likely to be more difficult to predict than the consequences of replacing an old technology (for individual values, attitudes and expectations as well as for health care systems). Novel, innovative treatment modes may require extra emphasis on ethical analysis, although the literature and research base on the topic may be narrow.</td>
<td>3</td>
<td>2</td>
<td>Literature search Expert opinion</td>
<td>Mitcham 2004</td>
<td>technology description, organizational</td>
<td>Core</td>
</tr>
<tr>
<td>F0002</td>
<td>Ethical analysis</td>
<td>Principal questions about the ethical aspects of technology</td>
<td>Can the technology challenge religious, cultural or moral convictions or beliefs of some groups or change current social arrangements?</td>
<td>It is important to identify those groups within the society for whom the use of the technology may pose serious challenges due to their beliefs, convictions or current social arrangements (e.g. need of blood transfusion adjunct to the use of the technology, contraception). Identification of these conflicts and finding other, acceptable possibilities to treat the condition in these groups is important. Identifying the conceptions behind the beliefs and values may help put them in perspective, when considering the overall acceptability of the technology. Technology may also change generally accepted social arrangements by challenging traditional conceptions (e.g. assisted reproductive technologies have separated the concept of genetic, biological and social motherhood).</td>
<td>3</td>
<td>2</td>
<td>Literature search Expert opinion Stakeholder hearing</td>
<td>Ogletree 2004</td>
<td>Social</td>
<td>Core</td>
</tr>
<tr>
<td>F0003</td>
<td>Ethical analysis</td>
<td>Principal questions about the ethical aspects of technology</td>
<td>What can be the hidden or unintended consequences of the technology and its applications for different stakeholders.</td>
<td>In addition to intended use, the technology may be used for other purposes and have side-effects in addition to those following from the intended use. Unintended consequences are obviously difficult to predict, but the intended purpose and uses of the technology should be evaluated against the likely uses and consequences of the technology in the real world. New technologies tend to lead to new areas of inventions and give rise to new ethical questions (e.g. IVF and development of genetic testing has led to questions of preimplantation genetic diagnostics (PGD). As presymptomatic and prenatal genetic tests have become available, the health care system has to be prepared to handle moral issues raised by true positive and false negative findings.) Many treatments have indirect effects also on relatives.</td>
<td>3</td>
<td>2</td>
<td>Literature search Expert opinion Stakeholder</td>
<td>Ogletree 2004, Hofmann 2002b, Hofmann 2002b</td>
<td></td>
<td>Core</td>
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<tr>
<td>ID</td>
<td>Domain</td>
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<td>Issue</td>
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<tr>
<td>F0004</td>
<td>Ethical analysis</td>
<td>Autonomy</td>
<td>Does the implementation or use of the technology challenge patient autonomy?</td>
<td>Patients have in most cases a right to autonomy, i.e. right to be self-governing agents. This requires the right to decide about things of importance to oneself on one hand, but also relevant information and a capability to understand the information, consider it in relation to personal values and decide accordingly. Thus, technologies and health systems may interfere with patient’s right to autonomy directly or indirectly by influencing the decisional capacity. For example, a technology that does not allow itself to be understandably explained to the patient (e.g. gene therapy for dementia) is potentially problematic, as are treatments that require patients to behave in a certain way (e.g. liver transplants given conditional to not drinking).</td>
<td>3</td>
<td>2</td>
<td>Literature search&lt;br&gt;Expert opinion&lt;br&gt;Stakeholder hearing</td>
<td>Miller 2004</td>
<td>Core</td>
<td></td>
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<tr>
<td>F0005</td>
<td>Ethical analysis</td>
<td>Autonomy</td>
<td>Is the technology used for patients/people that are especially vulnerable?</td>
<td>The right and justification to use the technology for persons who are vulnerable (critically ill or have otherwise reduced decision making capacity, like children, mentally retarded, patients that have due to their illness/state limited decision making capacity, pregnant women etc) has to be clarified. Who has the right to balance the benefit against possible harm in these situations? On what grounds can these decisions be made? Is the technology so valuable, as to justify its use on people who cannot give informed consent to it?</td>
<td>3</td>
<td>3</td>
<td>Literature search&lt;br&gt;Expert opinion&lt;br&gt;Stakeholder hearing</td>
<td>Miller 2004</td>
<td>Core</td>
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<tr>
<td>F0006</td>
<td>Ethical analysis</td>
<td>Autonomy</td>
<td>Can the technology entail special challenges/risk that the patient/person needs to be informed of?</td>
<td>Is the common professional practice of discussing the treatments with patients enough, or is special care needed with this technology? The technology to be used in life-threatening situations may have life-threatening side effects (e.g. invasive techniques). Technology used to get exact information may have unexpected severe side-effects (e.g. miscarriage due to amniocentesis).</td>
<td>3</td>
<td>3</td>
<td>Literature search&lt;br&gt;Expert opinion&lt;br&gt;Registers</td>
<td>Miller 2004</td>
<td>Safety</td>
<td>Core</td>
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<tr>
<td>F0007</td>
<td>Ethical analysis</td>
<td>Autonomy</td>
<td>Does the implementation challenge or change professional values, ethics or traditional roles?</td>
<td>Technologies may change the relationship between physician and patient, challenge professional autonomy or otherwise interfere with professional ethics and values. The patient-physician relationship is traditionally based on mutual trust, confidentiality and professional autonomy so that individual treatment decisions can be made in the best interest of the patient. Technologies that interfere with core virtues and principles of medical and professional ethics challenge the professional integrity of the physicians or other health care professionals. Technologies that align with professional ethics are more likely to be implemented successfully.</td>
<td>3</td>
<td>2</td>
<td>Expert opinion&lt;br&gt;Hofmann 2005b&lt;br&gt;Medical Profession alism Project 2002</td>
<td>Organisational Technology description</td>
<td>Borderline</td>
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<tr>
<td>F0008</td>
<td>Ethical</td>
<td>Human</td>
<td>Does the technologies that are applied for persons with reduced</td>
<td>Especially technologies that are applied for persons with reduced</td>
<td>3</td>
<td>2</td>
<td>Literature search&lt;br&gt;Kilner 2004</td>
<td>Core</td>
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<th>Transferrability</th>
<th>Information sources</th>
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<th>Status</th>
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<tbody>
<tr>
<td>F009</td>
<td>Ethical</td>
<td>Dignity</td>
<td>implementation or use of the technology affect human dignity?</td>
<td>autonomy may violate a person’s dignity (children, mentally impaired, severely ill), i.e. challenge the idea that all human beings have intrinsic moral value, and should thus not be seen as means to others ends.</td>
<td>3</td>
<td>2</td>
<td>Expert opinion, Stakeholder hearing</td>
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<td>Core</td>
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<tr>
<td>F009</td>
<td>Ethical</td>
<td>Human</td>
<td>integrity Does the implementation or use of the technology affect human integrity?</td>
<td>Technology can challenge human integrity by preventing (or even tempting) people (patients or professionals) to live according their moral convictions, preferences or commitments. This is especially important for vulnerable patient groups. Integrity can also be seen as a coherent image or identity of oneself. Thus, for example, prenatal diagnostics might challenge the integrity of people who value new life as gift; cochlear implants are problematic for those, who do not see deafness as a disability. Institutions that discourage honesty or ethical conduct more generally are detrimental to integrity (for example, systems where lying about ones health state might lead to better treatment than being honest).</td>
<td>3</td>
<td>2</td>
<td>Literature search, Expert opinion, Stakeholder hearing</td>
<td>Kliner 2004</td>
<td></td>
<td>Core</td>
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<tr>
<td>F010</td>
<td>Ethical</td>
<td>Beneficenc</td>
<td>e/ nonmaleficence What are the benefits and harms for patients, and what is the balance between the benefits and harms when implementing and when not implementing the technology? Who will balance the risks and benefits in practice and how?</td>
<td>The decision to implement new technology requires careful decision on the balance between benefit and harm, cost-effectiveness, reallocation of resources etc. When this decision has been made the decision on individual patient level rests on both the professional who offers the technology and the patient who autonomously accepts the use of technology in her/his situation. The individual decision has to be based on objective information on possible benefit and risks. Risks are only justified to the extent they are needed to create benefits. If not proven otherwise, the individual patient is generally to be seen as the best judge of risks and benefits for her/himself.</td>
<td>3</td>
<td>2</td>
<td>Literature search, Expert opinion, Stakeholder hearing</td>
<td>Autti-Rämö 2007</td>
<td>safety Effectiveness</td>
<td>Core</td>
</tr>
<tr>
<td>F011</td>
<td>Ethical</td>
<td>Beneficenc</td>
<td>e/ nonmaleficence Can the technology harm any other stakeholders? What are the potential benefits and harms for other stakeholders, what is the balance between them? Who will balance the risks and benefits in practice and how?</td>
<td>Some technologies have the potential to unfold unwanted or harmful effects not only on the patients that the technology is directly applied to but also indirectly on other stakeholders (relatives, other patients, organisations, commercial entities, society etc.) Benefits and harms to individuals must be balanced with benefits and harms that can befall society as a whole (social utility, maximizing public health). These harmful effects may manifest in the physical, social, financial or even other domains of life. For example results of genetic tests may negatively interfere with the family planning and social life of not only the individual being tested but also of his or her relatives. Table 2 in the process description can be used to describe benefits and harms.</td>
<td>3</td>
<td>2</td>
<td>Literature search, Expert opinion, Stakeholder hearing</td>
<td>Autti-Rämö 2007, Beauchamp and Childress 2001</td>
<td>Organisational Social</td>
<td>Core</td>
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<tr>
<td>F012</td>
<td>Ethical</td>
<td>Justice</td>
<td>What are the A new intervention may require reallocation of human resources,</td>
<td></td>
<td>3</td>
<td>2</td>
<td>Literature search, Stakeholder hearing</td>
<td>Sterba</td>
<td>Cost-</td>
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<tr>
<td></td>
<td>analysis</td>
<td>Equity</td>
<td>consequences of implementing / not implementing the technology on justice in the health care system? Are principles of fairness, justness and solidarity respected?</td>
<td>funding and training. A large reallocation of resources may seriously jeopardize other patient groups (e.g. new technology that requires human resources in acute care). How this reallocation affects the existing health care system has to be studied for all stakeholders? Can the technology be applied in a way that there is equal access to those in equal need? How can this be guaranteed? Could potential discrimination or other inequalities (geographic, gender, ethnic, religious, employment, insurance) prevent access? Are specific safeguards needed? How will possible caregivers’ burden and well-being be influenced? Potential inequalities and discrimination should be justified.</td>
<td>3</td>
<td>2</td>
<td>Expert opinion Stakeholder hearing</td>
<td>2004</td>
<td>Daniels  2001</td>
<td>effectiveness Organisational Social</td>
</tr>
<tr>
<td>F0013</td>
<td>Ethical analysis</td>
<td>Justice and Equity</td>
<td>How are technologies presenting with relevantly similar (ethical) problems treated in health care system?</td>
<td>Clearly presenting how relevantly similar technologies are treated in a health care system may help to adopt coherent and just health policies, either by applying past precedents to current cases, or showing that past cases need reconsideration. Similarity is to be defined individually for each technology. The idea is to concentrate only on the similarities relevant for solving the ethical problems found important for the current HTA project. The similarity may be, for example, of medical, technological, economical, ethical, social, organisational or legal nature.</td>
<td>3</td>
<td>2</td>
<td>Literature search Expert opinion</td>
<td>Hofmann 2005b</td>
<td></td>
<td>Core</td>
</tr>
<tr>
<td>F0014</td>
<td>Ethical analysis</td>
<td>Rights</td>
<td>Does the implementation or use of the technology affect the realisation of basic human rights?</td>
<td>Human rights exist both in ethics and legislation, most notably in the United Nations declarations and related statements, like the European Council Biomedicine convention. Basic human rights are universal and consider the most important goods, protections and freedoms. Classes of rights are civil and political rights, social rights, minority and group rights and environmental rights. For HTA, perhaps the most relevant are the rights to equality, non-discrimination, safety, adequate standard of living and health care. For example: -Right to life, liberty and security of person. -Right to a standard of living adequate for the health and well-being of himself and of his family, including medical care and necessary social services, and the right to security in the event of sickness, disability or old age. -Right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health.</td>
<td>3</td>
<td>3</td>
<td>Literature search Law, rules and regulations Expert opinion Stakeholder hearing</td>
<td>Marks 2004</td>
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<td>F0016</td>
<td>Ethical analysis</td>
<td>Legislation</td>
<td>Is legislation and regulation to use the technology may lead to ethical problems that make current regulation inadequate (e.g. ethical reflection is needed when</td>
<td>Technology may lead to ethical problems that make current regulation inadequate (e.g. ethical reflection is needed when</td>
<td>2</td>
<td>1</td>
<td>Law, rules and regulations</td>
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<td></td>
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<td>technology fair and adequate?</td>
<td>considering what kind of regulation is needed. This consideration is done on the basis and in combination with the legal domain. Emphasis should be put on considering the ethically relevant aspects and consequences of current law, needs for legal regulation that have arisen from the ethical analysis, and a global assessment of the adequacy of the legislation based on all available information.</td>
<td>3=critical 2=important 1=optional</td>
<td>3=complete 2=partially 1=not</td>
<td>Stakeholder hearing Expert opinion</td>
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Acknowledgements: We want to thank Tanja Krones, Dario Sacchini, Pietro Refolo, Lorraine Caron, Ingrid Zechmeister and Veikko Launis for their valuable contributions and critical appraisal of the article.

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Organisational aspects

Ulla Saalasti-Koskinen, Juha Koivisto, Camilla Palmhoj-Nielsen, Päivi Reiman-Möttönen, Marcial Velasco Garrido, Marco Marchetti, Finn Børlum Kristensen.

Domain description

In the scope of health technology assessment, organizational issues have not been the visible ones, while the greatest focus has been pointed at the clinical aspects of health technologies (Banta 2003, Draborg 2005). However, organisational aspects are a significant part of HTA, because the focus here is on the delivery modes of technologies. The growing focus in HTA on the delivery modes indicate a recognition that many decisions on resource allocation are made within regional health authorities, hospitals, departments, and in clinical offices, where the organisation of provision of technologies are of crucial importance. Therefore the focus on organisational aspects reflects a need to find ways of influencing the behaviour of a diffuse group of managers and health professionals (Battista, 2006). Also policymakers on the national level need knowledge on organisational aspects when making decisions on the use of technologies. HTA can contribute with analysis of e.g. management, financing and controlling issues. Including organisational aspects in HTA can contribute to clarifying challenges and barriers in implementing health technologies, since the analyses typically include considerations on the unfolding of the respective technologies in health services.

Definition of 'organisation'

Organisation has been defined as a consciously coordinated social unity (Robbins 1987). An organisation has rather clear boundaries and its activities, which target certain goals, are continuous. An organisation is formed in order to assign and carry out special tasks and coordinate these tasks (Schein 1985). The elements that constitute an organisation have been defined in many ways in different approaches, for example the physical structure, social relations, technology and organisational culture. A structure of the organisation defines its assignment of tasks, reporting systems and the mechanisms of interaction and coordination. In addition, other elements of society and its culture have influences on organisation and its function. Different types of organisations exist, e.g. the profit centre organisation, the matrix organisation and the network organisation. (Kristensen 2001)

The complexity of a health care system and especially its processes complicates the assessment of organisational issues. Objectives within an organization are often compromises and they develop over time. Various objectives and criteria may exist. Due to the multiplicity of objectives, organisational HTA-analysis will be less pre-determined and more complicated than for example economic analyses and clinical effectiveness analyses. In addition, the findings are expected to be more context-dependent and less transferable than e.g. in the effectiveness and safety domains of an HTA. The choice of the areas on which the assessment of organisational aspect will be focused should be guided by the information needs of the end users of the assessment (e.g. focus areas
demanded by decision-makers at the level of regional health authorities may differ from those of a hospital manager).

Organisational aspects include the intra-organisational level, inter-organisational level and health care system level. An example of intra-organisational level is how information about the new technology is provided to the patients in the organisation. Co-operation and communications between different organisations is an example of inter-organisational level, and setting down national objectives is an example of health care system level. At these levels, besides staff and patients, there are many stakeholders e.g. payers, providers and suppliers. These groups have usually different aims and expectations of the new technology. For example patients may not accept the new technology because it is uncomfortable, or personnel do not accept it because of safety aspects, or providers do not accept it because of expensiveness.

**Topics**

The organisational domain considers what kind of resources (material artefacts, human skills and knowledge, money, attitudes, work culture, etc) have to be mobilised and organised when implementing a new technology, and what kind of changes or consequences the use can further produce in the organisation. The organisational domain includes issues of work processes (e.g. work flow and patient flow), staff (e.g. training needed), co-operation and communication (e.g. information structures), (de)centralisation (e.g. place of the treatment, accessibility), finances (e.g. payment arrangements), management (e.g. managerial structures), and organisational culture (e.g. acceptance or praxis variation).

The domain might overlap with other domains especially with the domain of current use of technology (e.g. place of the technology), with the economical domain (e.g. finance issues), with the ethical domain (e.g. acceptance and accessibility) and with the social domain (e.g. patient issues).

**Methodology**

*Health care and HTA*

Health care is becoming increasingly complex. This complexity can be seen in the organisational issues of health care. In a complex system the activities of different agents are not always predictable and actions of one agent change the context for the other agents. Furthermore, complex systems typically have fuzzy rather than rigid boundaries. Complexity science suggests that it is often better to use multiple approaches. Through different theoretical frameworks we can understand how various organisational functions operate. For example the collaboration between public health and clinical health can be explained by structuration theory (St-Pierre 2006).

Demands on the way of organizing and delivering health services have become greater. Therefore, health service research has become well-established in some parts of Europe and North America during the last 20 years. Health services research provides answers for example to the following questions: How should services be funded? Who should receive health services? How well are services being delivered? Along with Health Technology Assessment, research of service delivery and organisation (SDO), gives answers to these questions. There is no clearly defined boundary
between HTA and SDO - on the contrary, they complement one another. For example HTA can provide evidence on the cost-effectiveness of one particular intervention and SDO research would be required to determine, where the most cost-effective setting (e.g. primary or secondary care) would be for the delivery of that intervention. (Fulop 2001) Also constructive technology assessment (CTA) - first described in the 1980's - takes into account the dynamics of technology such as e.g. practice organisation and financing and patient reactions (Douma 2007). CTA attempts to influence technological design and implementation to improve the effectiveness of the technology in clinical practice.

Usually, it will be difficult to isolate and measure the output effects of given organisational initiatives. More realistic is to describe the various process dimensions in relationship between a technology and organisational behaviour. The natural starting point of an analysis of change in processes will be to map the current work-flow / patient-flow. Therefore, the methods for data collections may involve qualitative methods such as interviews or observations, or quantitative methods such as surveys. (Kristensen 2001)

Framework

The implementation of new health care technology necessitates changes in the work processes and structures of an organisation. However, the relation between technology and organisation can be tackled in different ways. At least two different and incompatible views on causality and transferability can be differentiated with respect to the organisational (and social) issues that are conducted in HTA. The views are 1) the diffusion model and 2) the translation model which is a version of the loose approach called co-production of technology and its context (Kristensen 2001, Latour 1987).

The diffusion model bases on a linear, unidirectional conception of causality. It assumes a causal order between variables; an independent variable technology with its "effects" (impact) on organisational and other social levels. It considers technology as an exogenous and independent entity which is separate from the social or organisational. It is a given object which stands outside or above the society, its organisations and actors. It supposes that technology stays constant and that it is the same technology which is diffused and transferred from the innovator to the different users, e.g. to hospitals.

The diffusion model assumes that a health technology can "travel" through the society and have an impact on its different levels (see Latour 1987). It supposes that a technology has an inner causal power that can affect and change the individuals (micro-level), the organisations such as hospitals or health care centres (meso-level) or the national and international systems (macro-level).

The Translation model is increasingly utilized in European technology and organisation studies (Kristensen 2001). The translation model sees technology as endogenous, as a part of the organisational and use process. Technology can not be separated from the organisation and its users; it is not an independent and stable entity. The translation model implies a view that technology does not stay constant during the implementation process. This follows from the idea that human activity is a part of the technology in question.

According to the translation model, it can be asked "how many and what kind of resources (material entities, time, money, people, etc.) must be mobilised and organized in order to produce satisfactory
results from a health technology." This means that a technology does not causally affect the organisation and change its social structures, but that the organisation and its work processes and social structures have to be organized so that good results can be produced from the technology. Leavitt's (1965) model of organisational change from the sixties can be seen as early steps towards the translation model, but it may give more ontological autonomy to the different elements of an organisation than the translation model defined by the actor-network theorists (Callon 1991; Law 1992; 1994). Leavitt's model illustrates the importance of aligning task characteristics (autonomy, feedback, identity), structure characteristics (decentralisation, extrinsic rewards), technology environment (access to information technology, information technology use norm, required use of information) and motivational characteristics of people working in the organisation (intrinsic rewards and job variety) in order to effectively bring about change. Technology is broadly referred to as the work performed by the organisation. (Leavitt 1965)

The definition of organizational analysis of this paper is based on the loose approach called co-production of technology and its context and especially on the translation model. Its main thesis is that a technology needs a context or a network to function. In addition to the translation model, other approaches that form the co-production approach are for example constructive technology assessment (Schot 1992; Douma 2007), the systems approach (Hughes 1983) and social construction of technology (Bijker et al. 1987).

Both organisational and administrative perspective can be used in the organisational analysis (Seemann J, Vrangbaek K 2008). Administrative analysis uses a managerial perspective (e.g. decision making, co-ordination and managerial tools) and organisational analysis deals with changes in relation to the executing /producing function (e.g. organisational conditions, change processes). There may be overlapping between these two approaches. Organisational perspective raises from Leavitt's model for organisational change and administrative analysis looks at administrative and managerial structures. In this report, we use mix of both these perspectives. Organisational analysis is used in the topics of work processes, staff, co-operation and communication, (de)centralisation, finances, and culture. Administrative analysis is used mainly in the topic of management, but also in some other topics (e.g. co-operation and communication, (de)centralisation, and finances).

**Research methods**

The complexities of health problems require gathering data by using a broad spectrum of qualitative and quantitative methods. Qualitative methods are more appropriate for certain evaluation questions and purposes, especially in the stage of implementation, in which a technology is getting embedded in the management of certain conditions. Furthermore, qualitative research can contribute to HTA by offering and summarizing the perspectives, meanings, values, and interests the different stakeholders have concerning a particular technology. (Leyes 2003) For example, it has been stated that breast cancer research which includes both qualitative and quantitative methods increases understanding about the organization and delivery of services (Gagliardi 2006).

When qualitative methods are used, the data is gathered in close proximity of a specific situation. Therefore, influences of the local context are taken into account. Because of this, qualitative methods are powerful for studying the meanings of people about events, structures, processes and so on. On the other hand, qualitative research has also been resisted and called unscientific and full
of bias, and qualitative empirical data are judged unreliable, subjective and difficult to replicate. (Leyes 2003).

Qualitative methods include e.g. observation, interviews, content analysis of text, documents and written records, conversation analysis, photographs, and audio- or videotapes. Qualitative research has an interpretative approach which is based on flexible methods of data gathering in order to produce understanding of complexity, detail, and context. Individual approaches include one-to-one interviews, dyadic interviews, case study analyses, the Delphi technique and complaints procedures. Group-based methods include focus groups, concept mapping, citizens' juries, consensus panels, public meetings and nominal group techniques. Validity, reliability, generalisability, objectivity, acceptability to respondents and cost has been identified as the assessment criteria of qualitative methods. (Leyes 2003, Ryan 2001)

Interviews cover a spectrum of enquiry, such as unstructured interviews, interviews based on a theme guide and focus group interviews. Questionnaire or survey methods are tools which provide data by use of questionnaires. The questions could be posed verbally or by using standard interview forms (e.g. telephone interviews) or in written form as postal questionnaires. Prospective studies aim at predicting the users' attitudes and preferences to a new technology. The aim is to create a situation which promotes or renders it possible to make predictions based on collected opinions and preferences. The Delphi method and the Future workshops are examples of the prospective method. (Kristensen 2001)

A range of instruments to measure the culture of health organizations is available, but all of them have limitations in terms of their scope, ease of use, or scientific properties. There is no simple answer to the question of the best instrument. The answer depends on how we define "culture", "measurement" and "organization". Scott et al have reviewed quantitative instruments. They found thirteen instruments with differing characteristics. These adopt either a typological approach, in which the assessment results in one of more “types” of organisational culture; or a dimensional approach, which describes a culture by its position on a number of continuous variables. The choice of instrument should be determined by how organisational culture is conceptualized by research team, the purpose of the investigation, intended use of results, and availability of resources. (Scott 2003)

Triangulation is a way to reduce bias in research, and thus should be done when assessing organisational issues. Triangulation compares the results from either two or more different methods of data collection (for example, interview and observation) or two or more data sources (for example, interviews with members of different interest groups). The researcher looks for patterns of convergence to develop or corroborate an overall interpretation. Triangulation can be seen as a way to ensuring comprehensiveness and encouraging a more reflexive analysis of data than as a pure test of validity. (Mays 2000)

Assessment process

Firstly, the relevant organizational topics relevant for the technology being assessed have to be defined. After that, a theoretical perspective that fits the co-production approach has to be chosen. After identifying the research problems and questions as well as making the study protocol, it's time for selecting the relevant studies. The first step is to make a systematic literature search focusing on
the organisational aspects. If there are no systematic reviews or meta-analysis, primary studies should be used.

To reduce publication bias, it is recommended that a wide range of sources of information should be searched (Bidwell 2003). These should include published literature, as well as grey literature, hand searching of journals, contacting experts and scanning reference lists of relevant papers. It is sensible to allow also studies made in the context of the diffusion model to be included in the assessment of organizational issues, since the co-production approach has not been used in the HTA for a long time and there are not many that kind of studies available. However, the studies made in the context of the diffusion model should be analyzed according to issues defined according to the co-production model approach. One should consider what kind of information can these studies provide and which are their weaknesses.

Organisational studies could be found in different databases. Here are listed the most important databases and other sources of information. The following medical databases are often the most important ones for the organisational domain when conducting a core HTA: Medline, Premedline, Cochrane Library, HTA, DARE, EED, and Cinahl which includes more qualitative studies. General science publishers' databases (browsing databases) such as Emerald Library, that includes administrative studies, could be useful. Science Direct and Ebsco Academic Search Elite are also browsing databases and are useful to check, as well as full-text databases such as Pub Med Central (PMC) and Bio Med Central (BMC). Educational database ERIC and Open Access databases OAIster are sometimes useful, and also the Web of Science database which includes e.g. conference papers. Gray literature can be found e.g. in the databases of Dissertational Abstracts and of Scirus which includes reports of hospital studies and doctoral thesis. HealthSTAR is a Mixed Content database and includes administrative and hospital surveys. Social Science databases (Sociological Abstracts, Social Services Abstracts, Social Care on line / Caredata and SocINDEX) could be informative as well as PsycInfo, but the searches are likely to find many irrelevant studies. The database of GIN recommendations is also an important source of information. Selection of which databases to use depends on the context.

It is crucial to assess the quality of studies. Interpretation of the findings of a study depends on its design, conduct and analyses, as well as on populations, interventions and outcome measures. Quality criteria for assessment of different types of studies have been created (e.g. for experimental, observational and qualitative studies). Whilst the nature and application of procedures to minimise bias in qualitative research may be problematic, it is desirable and theoretically possible to have a structured approach to quality assessment. In qualitative research, many frameworks including a large number of appraisal criteria have been identified, for example the quality criteria made by Popay et al, Mays and Pope and BSA Medical Sociology Group. (CRD 2001)

Registers and international, national and regional routine collected statistics can provide answers to some organisational issues (See chapter Health problem and Current Use of Technology). Also conference proceedings and manufacturers are in some respect important sources of information.

The transferability of the research identified in literature searches, will have to be assessed very carefully, since this domain is in general to be considered highly context-specific. It is possible, that in many cases, the results from the literature review, can be considered to be hypothesis generating, and be useful for planning primary research in the own context.
When necessary, a primary research could be carried out according to the co-production approach, but it will usually be very time-consuming. There are several possibilities of the study methods to choose from, e.g. interviews, questionnaires, observation, an analysis of written material. If the resources available for the assessment project does not allow carrying out own primary research, it can be useful to consult health care professionals or other content experts.

Data extraction can be a subjective process and therefore the design of these forms should be undertaken carefully (Kahn, 2001). The amount of information to be extracted should be directly related to the questions posed. Key components of data extraction (especially of quantitative studies) are identifying features of the study (title, authors, journal, publication details), population characteristics and care setting, methodological quality, interventions, outcomes, length of follow-up, drops-outs, missing data, data of the results, effect measures and notes. Different form may be necessary if there are findings from qualitative studies.

Data synthesis collates and summarizes the results of included primary studies by generating a summary of study results (Khan, 2001). In quantitative data synthesis statistical methods are used to combine the results of the included studies (meta-analysis). The most commonly used graphical approach to express the quantitative results is forest plot. In non-quantitative synthesis tabulation of study characteristics and results are used.

**Assessment elements**

The organisational domain consists of four topics: Processes, Structure, Management and Culture. In each topic there are two to five issues (specific questions within the topic), altogether 11 issues. These topics and issues are probably the most important ones, but the relevance depends on the specific technology and needs to be considered as explained in the chapter "General design". In some technology there might be other more relevant topics and issues and if such are found, the model should be amended.

Different levels of health care (local/regional/national) have been taken into account while defining the issues. Some issues are relevant at all levels (e.g. approval of a new technology) and some mostly in one level, for example issues related to the staff which affect mostly in the hospital level. In addition, different viewpoints have been noticed. There are issues related to the patients in nearly all topics.
## Domain: Organisational aspects
### Process
#### Issue: What kind of work flow and patient flow processes are needed?
A new technology could change current work tasks and processes (including also quality control). Work and patient processes should be described, and it should be explained what kind of activities a new technology might replace or reduce in the target organisation. Patient flow and changes required in patient path should be taken to account when implementing new technology. It is essential to know the change the use of the new technology generates to the performance of care.

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<td>(Current use)</td>
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#### Issue: What kind of patient and relative involvement in treatment or care has to be mobilized?
A new technology may require changes in the distribution of tasks among the people involved in the treatment and care. Patients and their important others may be more actively involved in own care and treatment – or tasks they used to carry out may be taken over by health professionals.

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<td>1=optional</td>
<td></td>
<td>Kristensen 2007</td>
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#### Issue: What kind of staff, training and other human resources is required?
It has to be clarified what kind of staff is needed, and whether the existing staff can be trained or extra staff must be brought in. A new technology can bring along the need for extra staff when extending the ongoing activities in the organisation or when there is a demand for special expert knowledge. It must be considered if there will be a need to increase or decrease the amount of the staff. The implementation of a new innovation can mean change in job satisfaction. It could make some tasks monotonous or bring along new boring job descriptions. It is crucial that there is not just one person familiar with the new technology. If just one person has been trained for a new technology, there is a risk of losing know-how when he/she leaves the organisation (or moves to other tasks).

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<td>2=important</td>
<td>Systematic reviews (and other studies), reports of the hospital or hospital districts and other qualitative research methods</td>
<td>Busse 2002, Kristensen 2001, Kristensen 2007</td>
<td>Description</td>
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#### Issue: What kind of co-operation and communication of activities have to be considered?
The use of technology can presume new co-operation and communication with other parts of the structure (e.g. other units) or outside the structure (e.g. other hospitals, pharmacies). The type of co-operation and communication can change, depending on the type of technology and the work flow of the organisation.

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<td>2=optional</td>
<td>Systematic reviews (and other studies), reports of the hospital or hospital districts and other</td>
<td>Kristensen 2001, Kristensen 2007, Senter för Medisinsk</td>
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<tr>
<td>Organisational</td>
<td>Structure</td>
<td>What consequences the implementation of the new technology will have in respect of decentralisation or centralisation?</td>
<td>The location of use of the technology (primary - secondary - tertiary care) could vary between different countries depending on the system of organisational systems. (De)centralisation could have some economical and qualitative benefits. Centralisation could make a new technology more difficult to access. For example some expensive technologies are centralized to tertiary care units.</td>
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<tr>
<td>Organisational</td>
<td>Structure</td>
<td>What kinds of investments are needed (material or premises)?</td>
<td>The new technology could require many changes in the organisation e.g. premises must be according to the directions of the manufacturer. This could be very costly for the organisation. High costs of the new technology can influence the decision of purchasing the new technology. It is important to know which organisation(s) participate in the investments of a new technology and to what extent the other organisations take part in the running costs.</td>
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<tr>
<td>Organisational</td>
<td>Structure</td>
<td>What is the likely budget impact of the implementation of the technology for the payers (e.g. government)?</td>
<td>When a new technology is introduced, the question about reimbursement quickly arises. Whenever a technology is reimbursed, there will be an impact on the health care budget. Budget impact analysis examines the likely impact of the reimbursement of a new technology on financial outlays from the perspective of the payers (e.g. government).</td>
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<td>1</td>
</tr>
<tr>
<td>Organisational</td>
<td>Management</td>
<td>What management problems and opportunities are attached to the new technology?</td>
<td>The issue concerns the administrative / managerial questions of the new technology: management of resources (e.g. investments), co-ordination (in relation to different levels), establishment of objectives, monitoring and control, evaluation and sanctioning.</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Organisational</td>
<td>Management</td>
<td>Who decides which patients</td>
<td>Procedurals about decisions about the patients who receive care could vary.</td>
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<td>Organisational</td>
<td>Culture</td>
<td>How is the new technology accepted?</td>
<td>Acceptance should be looked at by different perspectives: by organisation, by personnel and by patients. A new technology could consist of elements which don’t suit the image of the organisation. Also, the alternative ways to introduce a new technology into the organisation could influence problems e.g. resistance among staff and dysfunction of processes. Patients are usually very technologically-oriented. However, patients can resist a new technology itself or its implementation. Objective and understandable information on a new technology is important.</td>
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<td>2</td>
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<tr>
<td>Organisational</td>
<td>Culture</td>
<td>How will the other interest groups of the new technology be taken into account in the planning / implementation of the new technology?</td>
<td>It may be useful to know who are the possible stakeholders of the particular technology, as well as what kind of co-operation there has been and what kind of interaction is needed. The stakeholders could be e.g. the pharmaceutical industry and companies offering new technologies, authorities (national / regional), administrative parties, municipalities, policy makers / decision makers, staff groups and patient organisation. One can also ask: Has the patient organisation taken part into the process? Has it been involved from the beginning (in the planning) or in the later stages for example as commentator? Furthermore, it is interesting to figure out what kind of co-operation exists between hospitals and companies offering new technologies and what kind of co-operation is needed.</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
References


Harbers H. Inside the politics of technology: Agency and normativity in the co-production of technology and society. Amsterdam: Amsterdam University Press; 2005.


Social aspects

Heidi Anttila, Charlotte Bredahl Jacobsen, Juha Koivisto, Britta Bjerrum Mortensen, Marie Brandhøj Wiuff, Päivi Reiman-Möttönen, Tuija Ikonen, Ilona Autti-Rämö, Björn Hofmann, Marcial Velasco-Garrido

Domain description

Definition

The social domain takes the patient as a point of departure in its analysis of the manifold social implications of health technology. The focus of the domain is on the diverse social arenas where the patient lives and acts during the period of sickness and treatment. Figure 1 illustrates the scope of social analysis by an example of a patient's itinerary in and outside the health services. A HTA may focus on a specific technology practiced for example in a hospital setting or in general practice, whereas other technologies received from health care may mainly be used and experienced in daily life settings.

The life of a patient takes place in various arenas (hospitals, general practitioner, everyday life, homes, schools, and workplace). The technology moulds and is moulded by all these sites. Irrespective of the site, where a certain technology is used, the implications of its use for a patient may extent far beyond the health care setting, e.g. the hospital or the general practitioner's consultation. The patients may have considerations, worries and experiences both before, during and after the health technology has been put to use. The social analysis is interested in all these aspects that surround the patient and his or her important others.

Figure 1. The scope of social analysis in an example: of patient's itinerary in and outside health care. Circles: Arenas within health care system.
**Why social analysis is important**

Health technologies do not work in a vacuum. People who use technologies give them their specific meanings. Thus health technologies can be said to be used and understood by the people involved in them. This is how they gain their significance. (1, 2) Their perceptions are attached to feelings of hope, fear, or perhaps uncertainty as well as broader norms and values of society (3-5).

The patient is not just a patient but a human being with different roles in different life arenas – a family member, a citizen, an employee, a consumer etc. (1). The use of a new health technology may change these roles, skills and positions in both negative and positive ways. Considerations of power/empowerment/stigmatisation are therefore integral to a patient and social analysis of health technology (6-9).

Irrespective of the technology in question, the use of health technology always requires that the user mobilizes some kind of resources in his or her daily activities (for example some kind of action from him/herself or support from other people) in order to achieve satisfactory results with the technology. The technology does not produce the good results alone. Further, the use of technology always produces some kind of changes or consequences in different spheres of social life, which can be positive or negative, or even unexpected. The different meanings and implications of a technology are dependent on specific sites (10, 11). An assessment of patient and social aspects both in and outside the clinical encounter is therefore necessary. Overall, the social analysis reveals the resources needed when using a technology and the consequences of its use in patients life spheres so that those who will use the technology can anticipate them (12-14).

**Scope of social analysis**

Figure 2 provides a view of different social aspects that are relevant from a patient’s perspective (1). Some of these aspects overlap with other domains in this HTA Core Model, as the patient perspectives are highly relevant to many HTA domains. Thus, figure 2 should be seen as an analytical model with the patient in its centre. The model intends to show and map different patient aspects, which could be considered of relevance for a specific HTA analysis. In practise, patient's experiences of health technologies cannot be seen isolated. Only in an analytical perspective it is possible to narrow the focus to for example communicative topics (1). Having said that, the social domain choose mainly to focus on the individual topics, communicative topics, and topics of major life areas such as family life, work life, and leisure time. These topics are underlined in figure 2. Other topics of relevance for a social analysis such as the patient perspectives concerning ethical/political topics, are mainly considered to be discussed in the ethical analysis domain. Patient-related, patient perspectives on biological/physical topics are discussed in effectiveness and safety domain, and patient-related perspectives on economic topics are included in economic domain. In some situations these three topics could also be relevant to incorporate in the analysis of the social domain. Below there is a short introduction to the content of the different topics.

**Topics of main life areas:** This topic deals with those life areas (e.g. work life, family life, leisure time, cultural, religious etc) that somehow will be influenced by the use of the technology, what kind of support and resources is needed in these areas and what kind of changes the implementation and use of the technology will have for the patients functioning and roles in life.
**Economic topics:** From a patient perspective this topic could deal with what short and long term financial resources the patient need to mobilize in order to use the technology (direct and indirect costs in relation to work, family life, leisure time and life style).

**Individual topics:** This topics covers how patients and important others react and act upon the technology and whether the use of the technology have any positive or negative consequences in that sense.

**Ethical/political topics:** This topic concerns whether the technology from a patient perspective entail ethical and/or political considerations, choices, dilemmas e.g. humiliation, stigmatization, tabooisation etc.

**Communicative topics:** This topic explores the patients and important others knowledge and understanding of the technology, the exchange of information from a patient perspective and limitations and possibilities for patients involvement in decision making.

**Biological/physical topics:** This covers whether, from a patient perspective, the technology leads to or might lead to side effects, pain and temporary or permanently reduced physical functioning.

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**Figure 2.** Social aspects of relevance from a patient perspective in HTA. Modified from (1).
Analytical perspective

The analysis of social aspects can be based on different theoretical perspectives from the social sciences (3, 4, 11, 15-19). The definition of social analysis of this paper is based on the loose approach called co-production of technology and its context (20, 21). According to the approach, technology can include for example the hardware, methods and models used in performing work, the skills and knowledge of workers, and the activities of patients (and other lay people) on which work is performed and who utilize the technologies in their daily life. That is, the humans and their activities constitute and co-create technology as well (22). Technology is a network of human and non-human actors.

According to the co-production approach, it can be asked: "How many and what kind of resources (material entities, time, money, people, skills, knowledge, activities, etc.) must be mobilized and organized in order to produce satisfactory results from a technology?", that is, what kind of network of human and non-human elements has to be established in order for the technology to work. A new technology does not by itself improve the patient's health or quality of life. It is in the hands of the people as to how they use and thereby shape the technology. Among the people using and shaping the technology, one always finds the patient. In that sense patients have a very significant and active role as to how the technology works and what outcomes it brings. Even though a patient might seem very passive in receiving a certain treatment he/she still does a lot of “work” by for example accepting to be treated, indulging pain, managing uncertainty, behaving appropriately (or inappropriately) (23). When a given health technology is assessed it is therefore essential not just to focus on what consequences the use of a given technology might generate for a patients life. It is also important to pay attention to how the patient by his or her way of approaching the technology contributes to its shaping (12).

Core questions

The social analysis includes two kinds of questions. The first set of study questions focuses on what kind of resources (people, support, money etc.) has to be mobilized and organized from the point of view of a patient before, during and after the use of the technology in order to produce satisfactory results from the technology. The task of the assessment is to map and describe the possible resources needed. However, it is evident that there is no predefined combination of resources for a given technology that has to be mobilised.

The other set of study questions focuses on the experiences, actions and reactions of patients with respect to the technologies as well as on the change and consequences that the use of the technologies may further produce, e.g. with respect to a person's working capacity, social relationships, coping with illness and treatment or attitudes towards a person who uses the technology. The task of the assessment is thus to map and describe the possible experiences, actions and reactions towards the technologies and the consequences the use of a given technology may produce. It is again evident that the actions, reactions and consequences vary to some extent between different persons, surroundings, cultures and countries. The assessment should characterize the different and possible actions, reactions and consequences. The more specific questions of social analysis are listed in the assessment elements table.
Transferability

Technologies are not, according to the co-production approach, universally true and thereby applicable wherever. They are constituted by and they work within networks of different human and non-human elements. Thus, to transfer any kind of technology means that the technology and its entailing network — the whole hybrid in fact — have to be re-built in a new place (24, 25). This is equally true for more simple technologies, such as a single drug or a single device, as for complex interventions like disease management programmes.

Furthermore, technologies and patients change over time as people put the technology to use, get accustomed to it, find new ways of using it in combination with other technologies or practices etc. Hence an analysis of social aspects can never foresee the exact social implications and consequences of the use of a given technology. It may however, provide us with important knowledge of aspects that need to be taken into continuous consideration. In short, transferability of the social analysis results requires careful consideration of comparability of the social and cultural circumstances of the compiled data from the literature to the circumstances at hand.

Methodology

Planning and conducting social analysis

For each HTA project a person needs to be defined to be responsible for performing and reporting the social analysis. The social analysis is both theoretically and empirically complex and demanding. Hence, advanced skills in social analysis are required from the person conducting this part of the HTA. Co-operation and interaction between the HTA team members is essential because of complexity of the social analysis. It is recommendable to consult outside experts on the specific theme from within the field of social science.

An assessment of patient and social aspects should not be a separate process within an HTA. Relevant social issues for a technology at hand could be identified together when considering e.g. ethical and organizational aspects. Some issues may also be studied as patient related outcomes (PRO), and may as such be related to effectiveness and safety domains. When these issues are brought into the analysis of social aspects, focus is on the interrelation between biological, individual and social aspects. Patient related outcomes can result in central thematic issues/topics, which should be taken into consideration and which can have major impact on the content and conclusions of a HTA report. For example does a given technology have other patient related consequences than intended?

Overall, the scope of patient related and social analysis of the HTA can be very wide (see Figure 2). During the practical work in designing an HTA, one must single out those topics that are of particular relevance for the technology being assessed, and adjust the work on the social domain with the work being done within the affiliated domains. Figure 2 illustrates the relevant topics that one must consider when designing the social analysis. The assessment elements table contains more specific issues on each topic. These issues can serve as inspiration to study questions for the specific social analysis that is to be conducted.
Preliminary scoping/study framing

The content of the study plan depends on the technology in question. To be able to judge what issues are relevant to a given technology, a preliminary small analysis is required:

1) Define the relevant scope of the analysis:
   - Consider, what is the extension of the technology nationally as well as internationally? How widely is the technology already being used or practised? Information provided by the Health problem and current use of technology domain may provide valuable information.

2) Define the relevant set of research elements:
   - Decide, which topic(s) and issues of the social aspects with respect to the patient and the technology are of particular relevance in the assessment of the technology in question (see figure 1 and Table: assessment elements).

3) Choose the relevant methodological approach:
   - Decide, whether the central questions can be answered based on existing studies or whether there is a need for new primary studies. You may need to conduct some preliminary literature searches.
   - Consider, what would be the specific theoretical perspective within the co-production approach for the analysis
   - Change the relevant assessment elements to precise study questions on the basis of the chosen theoretical perspective

When the scope of the social analysis, exact research questions, and relevant methodologies are clear, you can proceed to write a concrete study plan. The study plan should moreover describe the different phases and strategies of the assessment process.

Answering the core set of questions

Even if the assessment process may differ with respect to each technology, the main phases of the assessment process can be defined. The following phases may need to be gone through in the following order and to the extent that is necessary to find answers to the relevant issues:

1) Search for literature reviews, or if no literature reviews are available
2) Conduct a literature review, or if relevant studies are not available,
3) Conduct a primary study, or if there's no time or other resources for primary study,
4) Consult health care professionals and content experts (proxy informants) for their opinions.

Literature review with thematic mapping

Find out whether there are systematic reviews concerning the social issues in question. Probably you will not find a systematic review on social issues or a large amount of relevant literature may not be analyzed in systematic reviews. This is especially the case with qualitative research. Hence, conduct a systematic review complemented with what may be termed ‘thematic mapping’.
Thematic mapping means mapping out relevant sub-themes for the core set of questions to be investigated and describing each. It further implies estimation of the quantity, quality and applicability of literature existing for each relevant subtheme. Thematic mapping may often begin with the development of a systematic search strategy, but evolve into snowball sampling (citation analysis). It may be time saving to consult experts on the different sub-themes, rather than letting the key person of the social analysis map out all relevant subthemes alone.

Perform searches in psychological/sociological databases such as Psychinfo, Sociological Abstracts and ISI Web of Science, as well as in medical databases such as Pubmed, Medline, Embase, Cinahl etc. The search process is equal to a systematic review practice (cross ref to effectiveness domain), except that studies with different research paradigms will be considered. Since qualitative studies are highly relevant for the social aspects, they should be considered along quantitative studies with various observational designs. All studies, also qualitative studies should be quality evaluated before inclusion. Guidelines for standards on qualitative research vary and are currently debated and developed. For further guidance, see e.g. Malterud et al (26) or Hansen et al (27).

Describe what kind of knowledge is available in the literature, and what questions cannot be answered on basis of the existing literature. Then consider how the included studies can be utilized and what their weaknesses are. Do they give sufficient insight into social processes? The appendix in this chapter provides an example model for data extraction (Appendix A).

In thematic mapping, a thorough description of relevant themes and dimensions is more important than whether all relevant studies are found. Examples of themes may be descriptions of how illness changes family relations, patient roles, people's interaction with technology, unforeseen and unintended social consequences, risk management etc. Such thematic synthesis may be incorporated into the systematic review document or kept apart depending on the nature of studies found. Guidance for making synthesis of qualitative literature can be found in method books (28-30). A critical interpretive synthesis on literature considering access to healthcare by vulnerable groups provides one example (31).

When estimating the applicability of literature found in the systematic review process, it is important to consider to what extent the results can be translated in a valid way. Hence, contextual factors must be taken into account.

**Primary study**

If no relevant studies could be identified, it could be worth while to carry out primary studies concerning the relevant issue/s for the specific technology under assessment. In this case it must always be taken into consideration whether the need is of a primary HTA study, or whether the need of new knowledge has dimensions that speak for a larger research project rather than a HTA. The study design should be based on the ideas corresponding to those described in the domain description. HTA of social issues does not have as its starting point a hierarchy of study methods. The study design has to be structured individually in every primary assessment study. Every kind of study method can in principle be used: interviews, surveys, observation, participant observation, analysis of written material and documents, etc.

The timing of the study of the social aspects must me considered thoroughly. Depending on the specific technology under study, the appropriate time point for assessing the patient experience will
differ. Both ethical and practical considerations must be taken into account when deciding on whether to study people before, during the application or use of technology or ask them of their experience afterwards. This choice may have considerable significance for the results. Any intervention does something to practice, and it must be clear from the social study, whether the effects of the intervention are part of the specific context that the people under study behave in, or whether the social study reflects daily practice.

**Consultation**

If there is not enough time to perform a primary study, the opinion of health care professionals and content experts or other stakeholders can be consulted. However, one needs to be aware of that the health professionals’ knowledge of their patients emanates from the punctual situations of their clinical encounter (narrow context, typically related to the meeting at the bedside or in the consultation). The amount of knowledge on the views of patients which a provider can gather in the clinical encounters is limited by the willingness of the patient and of the provider itself to talk and listen about these aspects. Even when health professionals talk with patients about issues concerning such aspects, the conversation is formed by their positions, power relations, patient’s dependency on doctor’s goodwill, time constraints, etc. Moreover, the kind of knowledge that is most relevant for an analysis of the social aspects often relates to aspects outside the meetings with health professionals. Hence patient’s perspectives are often incompletely represented by health care professionals. Stakeholders may represent patient’s perspective, but often does so with a political agenda.
### Assessment elements

<table>
<thead>
<tr>
<th>ID</th>
<th>Domain</th>
<th>Topic</th>
<th>Issue</th>
<th>Clarification</th>
<th>Importance</th>
<th>Transferability</th>
<th>Information sources</th>
<th>Reference</th>
<th>Status</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>H0001</td>
<td>Social aspects</td>
<td>Major life areas</td>
<td>Which social areas does the use of the technology influence?</td>
<td>Map the major life areas of the patient and the important others (family life, day care, school, work, leisure time, lifestyle, or other daily activities), where the technology is going to be used or where its use may have a direct or indirect influence.</td>
<td>3</td>
<td>2,1</td>
<td>Search for or conduct a literature review or, if relevant data is not available, conduct a primary study; if there's no time for primary study, the opinion of health care professionals and content experts can be consulted.</td>
<td>(1)</td>
<td>2</td>
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<tr>
<td>H0002</td>
<td>Social aspects</td>
<td>Major life areas</td>
<td>Who are the important others that the use of the technology may affect in addition to the patient?</td>
<td>Describe who are the important other people that are involved in the use of technology in addition to the patients (parents, children, friends, people at work place etc)</td>
<td>3</td>
<td>2,1</td>
<td>See above</td>
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<tr>
<td>H0003</td>
<td>Social aspects</td>
<td>Major life areas</td>
<td>What kind of support and resources are needed or might be released as the technology is put to use?</td>
<td>This issue is about any kind of support and resources (practical, physical, emotional, personal social, nurturing, financial etc.) that need to be mobilized, and organized - or might be released - in order for the patient to use the technology with satisfactory results. It covers all arrangements or adjustments that may be needed in the major life areas (e.g. alteration of special tasks, working time, adjustments in the physical environment, emotional support).</td>
<td>3</td>
<td>2,1</td>
<td>See above</td>
<td>ICF(32) environmental factors: support and relationships (chapter 3: e310-399); activities and participation, chapter 6: d698, structural arrangements of patient's environment (10, 12, 13)</td>
<td>Organisational</td>
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<td>H0004</td>
<td>Social aspects</td>
<td>Major life areas</td>
<td>What kinds of changes does the use of the technology generate in the patient's role in the major life areas?</td>
<td>This issue is about the patient's social roles and ability to manage and maintain relations with other people in a socially appropriate manner in major life areas.</td>
<td>3,2</td>
<td>2,1</td>
<td>See above</td>
<td>ICF(32) activities and participation, interpersonal interactions and relationships (chapter 7, d710-779), community, social and Ethical Effectiveness, safety</td>
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<tr>
<td>H0005</td>
<td>Social aspects</td>
<td>Major life areas</td>
<td>What kind of changes does the implementation and use of the technology mean for the patient's physical and psychological functioning in his or her major life areas?</td>
<td>This issue is about the physical and psychological consequences the use of the technology may generate in the patient’s main life areas e.g. on person's body functions and structures, activities on daily living, or performance at work, school, home or leisure time. This issue covers whether, from a patient perspective, the technology leads to improvements or harms (a cross reference to effectiveness, safety domain issues), or generates any other unexpected effects on functioning.</td>
<td>3</td>
<td>2,1</td>
<td>See above</td>
<td>civic life (chapter 9:d910-d999), (5, 7, 33, 34)</td>
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<tr>
<td>H0006</td>
<td>Social aspects</td>
<td>Individual</td>
<td>How do patients and important others react and act upon the technology?</td>
<td>This issue is about the patients and her important others' attitudes, perceptions, preferences, satisfaction and relations to the technology. This covers whether, from a patient perspective, any positive or negative issues arise as a consequence of using the technology e.g. feelings of unity or empowerment and existential experiences (e.g. insecurity, worries, hope, anxiety, stigmatisation, person's value as a human being or social status, courage to face life, satisfaction, changes in self-conception).</td>
<td>3,2</td>
<td>2,1</td>
<td>See above</td>
<td>ICF(32),body functions: mental functions (chapter 13:b110-b199) environmental factors: attitudes (chapter 4; e410-499), (3)</td>
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<tr>
<td>H0007</td>
<td>Social aspects</td>
<td>Communication</td>
<td>What is patients' and important others' knowledge and understanding of the technology?</td>
<td>This issue explores the patient's and important others' understanding of the technology in order to describe and decide what guidance and help (e.g. patient information leaflets, counselling processes, need of follow up consultation or help from other professional(s) they need before, during and after the use of the technology.</td>
<td>3,2</td>
<td>2,1</td>
<td>See above</td>
<td>Current use</td>
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<tr>
<td>H0008</td>
<td>Social aspects</td>
<td>Communication</td>
<td>How is the information regarding the use of the technology?</td>
<td>This issue is about the exchange of information from a patient's perspective.</td>
<td>3</td>
<td>2,1</td>
<td>See above</td>
<td>Organisational</td>
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<td>technology processed and exchanged?</td>
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<td>What are patients' and significant others' questions? How do they receive answers? How is information provided and received?</td>
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<tr>
<td>H0009</td>
<td>Social aspects</td>
<td>Communication</td>
<td>What are the consequences in decision making?</td>
<td>This issue clarifies the possible implications from the patient's perspective to decision making e.g. limitations (dependent, passive user) and possibilities (empowered, active user) as a consequence of using the technology.</td>
<td>3</td>
<td>2,1</td>
<td>See above</td>
<td>Organisational Ethical</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
References


31. Dixon-Woods M et al.: Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC Medical Research Methodology 2006;6:35.


### Appendix: Data extraction sheet for social domain

<table>
<thead>
<tr>
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<td>Nature of the study: aims/objectives, user/carer involvement in the design/conduct of study, country, site (setting, key characteristics of the context), details of theory/conceptual model.</td>
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<tr>
<td>Methods: study type and design, study date and duration, sampling/recruitment, methods of data collection, data collector, used research tools (if any), analysis methods</td>
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<tr>
<td>Participant characteristics: gender, age, ethnicity, types of practitioners, policy makers or patients</td>
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<tr>
<td>Features the studied intervention (when applicable): aim of the intervention, intervention process (description of how was the intervention/service delivered)</td>
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<td>Outcomes and results: outcome measures, details of findings, strengths/limitations of the study, author's conclusions.</td>
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<tr>
<td>Reviewers' comments: e.g. remarks of quality issues</td>
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</table>
Legal aspects

Laura Walin, Marco Marchetti, Inger Norderhaug, Nick Royle

Domain description

Legal issues have not traditionally been considered as standard part of health technology assessment in most countries. However, as the norms of professional ethics are continuously codified into statutes and as European Union is producing ever more health technology related legislation, the legal issues may form a substantial part of the assessment in the future. Moreover, as the patients and health care professionals are allowed free movement within Europe, some evolution in harmonisation of legal regimes is likely to occur in the health care sector. At the same time one must bear in mind the national characteristics of legal and health care systems and be sensitive to the limits of exportation of health technology assessment from one country to another.

Already today proper knowledge of relevant legal questions has significant consequences for the decision making in the health technology assessment process, often perceived as part of sociological issues or so called socio-legal issues (Decker 2004, Møldrup 2002). The consideration of legal issues as an independent domain of health technology assessment helps to focus the scrutiny to relevant legal sources, which may vary according to the nature of the technology in question.

The systematic consideration of legal aspects is also expected to contribute to the implementation of HTA results across the Europe. At the very least it will help to identify the (often) legal barriers which hinder the export and import of HTA results (Drummond & Weatherly 2000, Henshall et al. 2002, Hofman 2005, Terry 2004). Bearing in mind that policies are renewed via regulations, at its best the study of legal aspects during a HTA process will give insight into the areas of health care legislation where harmonisation is needed, and will provide tools for legislative and policy reforms.

The questions that arise in the legal domain can be roughly divided into four categories which operate at different levels in health care:

   i) the issues directly related to the patient and his/her basic rights and freedoms, such as issues of autonomy, informed consent, privacy and confidentiality
   ii) the issues related directly to the technology in question such as proper authorisation, patent/license issues, price and reimbursement regulation, and product safety, guarantee and liability issues
   iii) the issues related to the process of acquisition of the technology, and finally,
   iv) the issues related to the health care policy either at the local, national or European level.

The weighing of the importance of different legal aspects varies depending on technology in question.
One reason why legal issues have not been considered elemental to HTA might be that the issues at stake overlap with e.g. ethics, societal aspects and safety. What separates the legal domain from these (and possible others) is, however, that matters within the legal domain are always codified in national, international and/or supranational legislation or has been agreed on in international conventions or is implicitly or explicitly agreed upon by the manufacturer (or seller) and buyer of the technology. In other words, for an issue to be considered a legal one, one must be able to point the legal source (stipulation, convention or agreement) that makes the issue legally relevant.

Methodology

The study of law is, both as an academic discipline and as a societal conduct, by its nature interpretation and argumentation. From methodological viewpoint it is relevant to recognise the compulsory legal sources that form the basic interpretative framework for any given question. As the outcome of legal argument is basically “the best argument wins”, different other sources (whether legal or not) may then be used to convince the audience. This section will outline those sources that can be considered as important in the context of health technology assessment. The aim is not, and indeed cannot be, a binding legal solution to a given question, but to guide the assessing organisations/personnel in recognising the legal questions at the time when decisions about using the technology are made. Furthermore, directions to the relevant legal sources are given.

The study of health technology related issues in the legal domain requires knowledge on the relevant legal sources on at least four different levels. As the reading of the court decisions as well as the knowledge of national and supranational statutes requires legal expertise, research on the legal issues domain of the core model is most efficiently done by a person with legal training, the best result probably obtained by a team with both legal and medical experts. The different levels to be studied are

The European Union

Whereas doctor-patient relationship does not directly fall under the authority of the Union, it may, however, issue health care related legislation regarding e.g. patient safety and free movement of (health care) goods and personnel. Hence, a search of relevant EC legislation is needed. This can be easily done via the internet database EurLex (http://eur-lex.europa.eu/). Furthermore, the decisions of the European Court of Justice may be relevant and need to be checked. Of special importance are the so called ‘references for preliminary rulings’, which are judgements where the Court interprets the specific point of Community law as requested by a national court.

An example of ECJ judgements which may be relevant for national HTA is a recent case C-6/05. The question to be answered was formulated by the Court as follows: “the national court asks, essentially, whether under the general principles of Community law applicable to tendering procedures, a contracting authority which has initiated such a procedure with a view to purchasing medical devices may directly exclude a tender for products for reasons relating to the protection of public health although those products bear the CE marking as required by the specifications of the invitation to tender, or whether that authority is required first to apply the safeguard clauses provided for in Articles 8 and 18 of Directive 93/42.” Some other examples are given in the model, but novel searches should be conducted regularly. The search form is available on the internet (http://curia.europa.eu/jurisp/cgi-bin/form.pl?lang=en). In general, one must pay attention to using relevant terms of EU law when searching for cases. Among others, such terms as ‘state aid’,
‘marketing authorisation’, ‘personal data’, ‘essentially similar product’, ‘advertising’, ‘free movements of services’, ‘medicinal products’ and ‘medical device’ may be of relevance.

**The Council of Europe**

All countries of the European Union are also members of the Council of Europe. The most important legal document related to health care issues is ‘the Convention for the protection of Human Rights and dignity of the human being with regard to the application of biology and medicine’ (ETS 164), hereafter referred as Biomedicine Convention, with its Additional Protocols, specifying the provisions of European Human Rights Convention in the field of modern biomedicine. Also various recommendations given by the Parliamentary Assembly or Committee of Ministers may need to be considered. These are referred to at the relevant sections of the text. Importantly, it may be necessary to investigate whether the European Court of Human Rights has given a relevant decision on the matter. New court decisions arise in constant manner, and information of these needs to be updated regularly.

**National legislation**

As most of the EC legislation is given in a form of directives, it is necessary in each country to know the relevant national legislation in order to evaluate the exact manner of implementation. Also much of the health care related EC legislation is given as minimum directives and hence a stricter national control may apply. Moreover, any given country may have health technology related purely national regulation, which may cause divergence among European countries and will impede the implementation of HTA procedure across Europe. Also precedents of national Supreme Courts may be of relevance and need to be checked.

**Agreements with and documentation provided by the technology supplier**

These will influence the division of risk and liability between the buyer (health care unit) and the supplier and are hence of economic importance to the health care unit in question. It seems unlikely that any uniform standard agreements emerge and the scrutiny of these documents is most reliably made by a legally educated person.

In addition to these, a survey on legal literature may be conducted, for the legal concepts and their interpretation is also developed within legal science. At the European level such journals as e.g. European Journal of Health Law; Health, Economics, Policy and Law; Medical Law International; Medical Law Review and Medicine and Law may be scrutinised. Also national libraries’ electronic databases can be used to search for relevant international and national monographs and articles on the technology/issue in question. Some literature is given in the references of this chapter, but the list is by no means comprehensive. Moreover, as legal doctrines evolve over time, literature search should be updated every time the model is used. An up-to-date textbook (e.g. Mason & Laurie 2005, Hervey & McHale 2004) is a good starting point for a literary review.

In the following table the *importance* of an issue is evaluated from the point of view of the current medical law researcher community in Europe. The *transferability* of an issue is roughly assessed as a function of the proportion of the national provisions over all regulation (national + supranational + binding international regulation).
### Assessment elements

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<tr>
<td>I0002</td>
<td>Legal aspects</td>
<td>Autonomy of the patient</td>
<td>Can future patients understand the implications of using/not using the technology?</td>
<td>It is important to provide information on the (evermore complex) technologies in such a manner that the patient can truly understand it.</td>
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<tr>
<td>I0003</td>
<td>Legal aspects</td>
<td>Autonomy of the patient</td>
<td>Are there relevant optional technologies that future patients should be allowed to consider?</td>
<td>The concept of informed consent includes also the possibility to consider other therapeutic options, if these are available.</td>
<td>3</td>
<td>2</td>
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<tr>
<td>I0004</td>
<td>Legal aspects</td>
<td>Autonomy of the patient</td>
<td>Is it possible to give future patients enough time to consider their decisions?</td>
<td>It is usually advised that the patient is given some time to think over the treatment decision, especially if the decision involves assimilating complex technical information or a tough weighing of risks and benefits of the procedure. It should be assessed beforehand if a given technology allows such time for consideration.</td>
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<tr>
<td>I0005</td>
<td>Legal aspects</td>
<td>Autonomy of the patient</td>
<td>Is it possible to obtain an advance directive on the use of the technology?</td>
<td>If it is expected that the technology may be used in an emergency situation in the future it is advised that the patient is consulted beforehand and her opinion is recorded to the medical file as an advance directive on the use of a given technology.</td>
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<td>ID</td>
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<tr>
<td>I0009</td>
<td>Legal aspects</td>
<td>Privacy of the patient</td>
<td>Can the access to the patient data secured properly?</td>
<td>At the era of computer-based patient records it is crucial that the health care unit has taken appropriate measures to secure the patient databases. Negligence may lead to liability.</td>
<td>2</td>
<td>1</td>
<td></td>
<td>Directive 95/46/EC</td>
<td>Organisational aspects</td>
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<tr>
<td>I0010</td>
<td>Legal aspects</td>
<td>Privacy of the patient</td>
<td>What levels of access to which kind of patient information exist in the chain of care?</td>
<td>During the therapeutic process many people may either need to get access or semi-accidentally get access to the personal medical data of patients. The delicacy of the information depends on the technology in question. Health care unit must be organised so that it minimises the number of people having access to patient data. Also other measures to minimise the risk of information leakage from health care unit must be taken.</td>
<td>1</td>
<td>1</td>
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<td></td>
<td>Organisational aspects</td>
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<tr>
<td>I0011</td>
<td>Legal aspects</td>
<td>Equality in health care</td>
<td>Is the technology equally accessible to all needing members in a given society?</td>
<td>This topic operates both at national and international level. In general, equality in health care is spoken out in the EU Charter of Fundamental Rights and it is also one of the central principles of the Biomedicine Convention. In many Constitutions equality of citizens covers also access to health care.</td>
<td>3</td>
<td>2</td>
<td></td>
<td>EU FR Charter Art 35, Biomedicine Convention Article 3, CM Recommendation (2006) 18</td>
<td>Societal aspects</td>
<td></td>
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<tr>
<td>I0012</td>
<td>Legal aspects</td>
<td>Equality in health care</td>
<td>Is the technology subsidized by the society?</td>
<td>Governmental interventions or the lack of them may affect to the expected number of patients.</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td>Societal aspects, organisational aspects, economical aspects</td>
<td></td>
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<tr>
<td>I0013</td>
<td>Legal aspects</td>
<td>Equality in health care</td>
<td>Is there a wide variation in the acceptability of the technology across Europe?</td>
<td>Varying legal regimes may lead to health-care tourism across the borders, especially if the technology in question is controversial.</td>
<td>3</td>
<td>3</td>
<td></td>
<td>Europe-wide legal comparison</td>
<td>Societal aspects</td>
<td></td>
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<tr>
<td>I0014</td>
<td>Legal aspects</td>
<td>Equality in health care</td>
<td>Is health-care tourism expected from/to other</td>
<td>Varying legal regimes may lead to health-care tourism across the borders.</td>
<td>2</td>
<td>3</td>
<td>C-158/96 (ECJ), C-372/04 (ECJ), Europe-wide legal comparison</td>
<td>Societal aspects</td>
<td></td>
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<td>ID</td>
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<td>Issue</td>
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<tr>
<td>10015</td>
<td>Legal aspects</td>
<td>Authorisation &amp; safety</td>
<td>Has the technology national/EU level authorisation?</td>
<td>Patient safety as expressed in product safety is one domain of health care technology assessment which clearly falls under the mandate of the European Union</td>
<td>3</td>
<td>3</td>
<td>Safety aspects</td>
<td></td>
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<tr>
<td>10016</td>
<td>Legal aspects</td>
<td>Authorisation &amp; safety</td>
<td>Does the technology need to be listed in a national/EU register?</td>
<td>A European database of medical devices (EUDAMED) is under construction.</td>
<td>2</td>
<td>2</td>
<td>Safety aspects</td>
<td></td>
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<tr>
<td>10017</td>
<td>Legal aspects</td>
<td>Authorisation &amp; safety</td>
<td>Does the technology fulfill product safety requirements?</td>
<td>The implication of findings in the safety domain should be discussed against the relevant European or national legal frameworks to ensure patient safety from using the technology:</td>
<td>3</td>
<td>3</td>
<td>Directive 93/42/EEC, Directive 95/2001/EC</td>
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<tr>
<td>10018</td>
<td>Legal aspects</td>
<td>Authorisation &amp; safety</td>
<td>Does the technology fulfill tissue safety requirements?</td>
<td>Many novel health technologies may utilise human cells or tissue (so called advanced therapy medicinal products). These products must fulfill the safety requirements issued by EC Directive 2004/23/EC.</td>
<td>3</td>
<td>3</td>
<td>COM 567 (2005) final</td>
<td>Directive 2004/23/EC</td>
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<tr>
<td>10019</td>
<td>Legal aspects</td>
<td>Ownership &amp; liability</td>
<td>Does the technology infringe some intellectual property right?</td>
<td>Issues in this topic are to be considered by the health care unit when considering the acquisition of a new technology. The wording of acquisition contract may affect liability sharing between the manufacturer and health care unit.</td>
<td>2</td>
<td>3</td>
<td>Manufacturer, patent data bases</td>
<td>EPO Web site, European patent convention, national legislation</td>
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<tr>
<td>10020</td>
<td>Legal aspects</td>
<td>Ownership &amp; liability</td>
<td>Does the introduction of the technology presume some additional licensing fees to be paid?</td>
<td>As novel technologies build up on existing knowledge, the use of the technology may involve the payment of some additional fees to additional patent holders etc. In principle, the manufacturer should be able to clarify this to the health care unit/health care system in question.</td>
<td>2</td>
<td>2</td>
<td>Manufacturer, patent data bases</td>
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<tr>
<td>10021</td>
<td>Legal aspects</td>
<td>Ownership &amp; liability</td>
<td>What are the width, depth and length of</td>
<td>The terms of the manufacturers guarantee are of importance to the health care unit as well as to the society’s health care sector</td>
<td>3</td>
<td>3</td>
<td>Manufacturer</td>
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<td></td>
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<td>Legal aspects</td>
<td>Ownership &amp; liability</td>
<td>Is the user guide of the technology comprehensive enough?</td>
<td>3</td>
<td>3</td>
<td>Manufacturer</td>
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<td></td>
<td></td>
<td>Legal aspects</td>
<td>Regulation of the market</td>
<td>Is the technology subject to price control?</td>
<td>3</td>
<td>2</td>
<td>C-317/05 (ECJ), C-283/03 (ECJ)</td>
<td>Directive 1989/105/EEC</td>
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<td></td>
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<td>Legal aspects</td>
<td>Regulation of the market</td>
<td>Expensive technology is subject to acquisition regulation.</td>
<td>3</td>
<td>2</td>
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<td>Directive 2004/18/EC</td>
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<td></td>
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<td>Legal aspects</td>
<td>Legal regulation of novel/experimental techniques</td>
<td>Is the technology so novel existing legislation was not designed to cover its regulation?</td>
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<td></td>
<td></td>
<td>Legal aspects</td>
<td>Legal regulation of novel/experimental techniques</td>
<td>Modern biomedical sciences produce novel technologies which may not always be unambiguously covered by existing provisions.</td>
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<td></td>
<td></td>
<td>Legal aspects</td>
<td>Legal regulation of novel/experimental techniques</td>
<td>How the liability issues are solved according to existing legislation?</td>
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<td></td>
<td></td>
<td>Legal aspects</td>
<td>Legal regulation of novel/experimental</td>
<td>Are new legislative measures needed?</td>
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<tr>
<td></td>
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<td>techniques</td>
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<td>introduction, whereas at the level of the society it implies a need to use resources for preparing new laws.</td>
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<tr>
<td>10029</td>
<td>Legal aspects</td>
<td>Legal regulation of novel/experimental techniques</td>
<td>Is the voluntary participation of patients guaranteed properly?</td>
<td>Use of experimental technologies may not compromise patient safety. Patients must not be pressured into such treatments.</td>
<td>3</td>
<td>1</td>
<td></td>
<td>Biomedicine Convention Article 16</td>
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Descriptions

For each issue it is indicated whether it is of relevance in direct doctor-patient relationship (DP), for the health care unit (HCU) or at the level of national health care policy (HCP).

Autonomy of the patient

The Nuremberg trial codified the principle of informed consent in biomedical research, and it was further strengthened after the Helsinki Declaration of the World Medical Association in 1964. Today the informed consent principle, being a central expression of the patient autonomy, is widely recognised also in everyday doctor-patient relationship. The paternalistic relationship has transformed into a discursive one where both parties are to express their opinions. The essential elements of informed consent can be summarised as follows

i) the patient has given it without any external pressure
ii) the consent is based on adequate information of the procedure, its benefits, risks, and options
iii) the patient has had enough time to consider her decision.

Patient autonomy does not mean that doctor-patient relationship is a completely equal one, for the physician always acts as an educated expert when giving opinions and advice. The final decision on the use of any technology must not, however, be made against the expressed will of the patient. The issues in this topic mainly concern the direct doctor-patient relationship, but depending on the legislation, also the health care unit may be liable of infringement of patient autonomy.

- Can the patient understand the implications of using/not using the technology? (DP)
  As scientific advancements are brought into clinical practise the information for the patient tends to become more complex and hence, more difficult for a layperson to evaluate. Therefore it is essential that each patient information sheet concerning novel technologies is carefully scrutinised in order to evaluate whether it is comprehensible for people not familiar with health care technologies. For the most complex or controversial technologies, person-to-person consulting may be needed in order to realise the patients’ autonomy.

- Are there relevant optional technologies that the patient should be allowed to consider? (DP, HCU)
  Although novel health care technologies may represent the cutting edge know-how in treating patients, established methods may still remain useful. This is especially true if the known risks of the older and newer technology markedly differ, e.g. if the risks of newer technologies are not yet fully evaluated. Hence, in order to appreciate patient autonomy, it may be required to clarify the options and their therapeutic and risk implications to her, specifically comparing them to the technology which the physician is recommending. Again, legal responsibility may take place if relevant options are not discussed with the patient.

- Is it possible to give the patient enough time to consider his/her decision? (DP)
  With complex novel health care technologies with elaborate patient information sheets, it is advisable that patients are given enough time to familiarise with the written material before they need to reach a conclusion on the use of the
technology. Also, patients should have the opportunity to see a specific counsellor (e.g. a trained nurse specialised in patient advising) if they have some detailed questions about the technology. If the decision about the use of technology is likely to be a hasty one, appropriate procedures to ensure maximum possible patient understanding should be prepared beforehand.

- Is it possible to obtain an advance directive on the use of the technology? (DP, HCU)
  Advance directives have their own problems, and the legal ones have been recognised for a long time. These include first and foremost the issues of i) with complex real-life medical situations it is often difficult to formulate such an advance directive that would be indisputably applicable it either being too wide or too narrow in scope ii) the advancement in medical know-how may render the directive useless and iii) as the time between the giving of advance directive and the real situation gets longer it is more difficult to decide whether it expresses the patients will at the situation-at-hand. Recognising these problems, it may still be useful to obtain an advance directive on the use of a given technology, if it is likely that the acute need for the use of technology might be a rushed one or that the patient may be unconscious at the time of decision making.


**Privacy of the patient**

Privacy of the patient, which can also be expressed as a principle of confidentiality, is one of the central and most established principles of medical profession and medical law, dating back to Hippocratic Oath. The measures needed to protect privacy are ever more important in the era of computer-based patient records and increasing knowledge of genetic factors in disease emergence.

- Can the access to the patient data secured properly? (HCU)
  One essential part of the patient privacy today, computer-based patient records being more of a rule than an exception, is the technical security of the patient record files. The level of technical security may affect the liability of the health care unit on any information leakage and following breach of patient privacy.

- How many people in the chain of care need to get access to the patient information? (HCU)
  As the number of people that have access to patient data straightforwardly correlates with the possibility of information leakage it is advisable to keep this number as low as rationally possible. The accuracy of this evaluation may affect the liability of the health care unit on any information leakage and following breach of patient privacy.


**Equality in health care**

Equality in health care is one of the central aims of the Human Rights and Biomedicine Convention of the Council of Europe. Many European constitutions have also established both equality and right to adequate health care as basic rights of all people. However, as new
technologies tend to be expensive the equality in health care is threatened at least on two levels. Firstly, the technology may not be (at least easily) available to all citizens and secondly, the use of an expensive technology in one sector of health care may reduce the resources available to other health care sectors. Moreover, some technologies might be morally controversial, and if a given technology is forbidden in one country, its citizens may migrate to health care units of a permissive country for the treatment. This further induces inequality, as only to patients able to cover for their own expenses can rely on this ‘health care tourism’. Also the equality in the receiving country is threatened if its health care units are crowded with foreign patients.

- Is the technology equally accessible to all needing members of society? (HCP)
- Is the technology subsidized by the society? (HCP)
- Is there a wide variation in the permissibility of the technology across Europe? (HCP, HCU)
- Is health-care tourism expected from/to other European countries? (HCP, HCU)

**Literature:** Hervey 2007, Hoedemaekers & Dekkers 2003, Oliver 2007, SEC (2006) 1195/4

**Authorisation & safety**

Patient and product safety are the two areas of health care technology assessment where the European Union has the authorization to issue legal measures. Hence, the issues in this topic are mostly governed by EU directives. The safety problems are regulated via diverse standards, authorisations, and other administrative measures required. One must bear in mind, however, that directives are always implemented in a somewhat different way in different jurisdictions. Health care related directives may also be so called minimum directives, that is, Member States are entitled enact stricter provisions if they so want. Therefore also the national legislation must be examined.

- Has the technique proper national/EU level authorisation? (HCU)
- Does the technology need to be listed in a national/EU register? (HCU)
- Does the technology fulfil product safety requirements? (HCU)
- Does the technology fulfil tissue safety requirements? (HCU)


**Ownership & liability**

Although patents in biotechnology are controversial in general, also many health care technologies are protected by intellectual property rights. These can increase the actual cost of using the technology in question and can hence affect the acquisition decision of the health care unit. When considering the acquisition of a new medical devise, it is also advisable to pay detailed attention to such things as the manufacturers guarantee and e.g. the comprehensiveness of the user manual, for these may have an impact on the liability allotment between the manufacturer and the health care unit in case of devise malfunction.
• Does the technology infringe some intellectual property right? (HCU)
• Does the introduction of the technology presume some additional licensing fees to be paid? (HCU)
• What are the width, depth and length of the manufacturers guarantee? (HCU)
• Is the user guide of the technology comprehensive enough? (HCU, DP)

Regulation of the market

As use of medical services and technologies is literally vital for most people at some point of their lives, its marketing means to the general public may be restricted by the legislation. Also, to render the technology available for all patients, the state may regulate the price that health care unit is allowed to charge from the patients. These may have an effect on the purchase decision of the health care unit. Complex medical devices may be so expensive that they are subject to either national or EU level acquisition regulation.

• Is the technology subject to price control? (HCU, HCP)
• Is the technology subject to acquisition regulation? (HCU, HCP)
• Is the marketing of the technology to the patients restricted? (HCU, HCP)


Legal regulation of novel/experimental technologies

Due to rapid progress in biomedical sciences, it is likely that novel health care technologies not covered by any specific legislation emerge. When considering the use of such technologies the health care unit must be aware of the legal void and ensure that liability issues are clearly settled beforehand. The use of experimental technologies does not diminish the health care unit’s responsibility of its patients, and appropriate measures to ensure patient safety and their voluntary participation to the experimental procedures must be taken. At the level of society, the introduction of a novel health care technology may call for new legislation.

• Is the technology so novel that no legal rules are directly applicable? (HCP, HCU)
• How the liability issues are solved according to existing legislation? (HCU, HCP)
• Are new legislative measures needed? (HCU, HCP)
• Is the voluntary participation of patients guaranteed properly? (DP, HCU)

Literature: COM 567 (2005) final
References

Literature


**European Union**


Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.


SEC (2006) 1195/4 Consultation regarding Community action on health services.

**Council of Europe**

Convention for the protection of Human Rights and dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine CETS No.: 164.

Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin CETS No.: 186.
Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research CETS No.: 195.

Recommendation R (97) 5 of the Committee of Ministers to Member States on the protection of medical data.

Recommendation R (2006) 18 of the Committee of Ministers to Member States on health services in a multicultural society.

**Web sites**

CURIA (The search page for case law of the European Court of Justice)

EMEA Product Safety Announcements

EMEA Marketing Authorisation Withdrawals and Suspensions

European Medical Devices Database (EUDAMED) homepage
http://eudamed.cec.eu.int/

European Patent Convention

European Patent Office – Search page for European patents

EUR-Lex (The legislation of the European Union)

HUDOC (The search page for the case law of the European Court of Human Rights)
http://cmiskp.echr.coe.int/tkp197/search.asp?sessionid=9831593&skin=hudoc-en

Medical devices homepage of the European Commission
http://ec.europa.eu/enterprise/medical%20devices/index_en.htm