Sundhedsstyrelsen
National Board of Health

Health Technology Assessment

HEALTH TECHNOLOGY ASSESSMENT HANDBOOK

2007

Sundhedsstyrelsen
National Board of Health

Health Techology Assessment

HEALTH TECHNOLOGY ASSESSMENT HANDBOOK

Editors: Finn Børlum Kristensen and Helga Sigmund

DACEHTA – Danish Centre for Health Technology Assessment

Health Technology Assessment Handbook

URL: http://www.dacehta.dk

Key words: method, methodology, handbook, ethics, technology, patient, organisation, economy, HTA, health technology assessment, literature search, literature assessment, synthesis, implementation, quality assurance, presentation, project organisation, problem formulation, policy question, HTA question, stakeholder analysis

Language: English (translated from Danish)

Format: pdf
Version: 1.0
Version date: February 15, 2008

Published by: National Board of Health, Denmark, March 2008
2nd edition

Category: Briefing

Design: National Board of Health and 1508 A/S
Layout: Schultz Grafisk

ISBN (electronic version): 978-87-7676-649-8

This report should be referred as follows:
Kristensen FB & Sigmund H (ed.)
Health Technology Assessment Handbook
Copenhagen: Danish Centre for Health Technology Assessment, National Board of Health, 2007

For more information please contact:
Danish Centre for Health Technology Assessment
National Board of Health
Islands Brygge 67
DK-2300 Copenhagen S
Denmark

Phone: +45 72 22 74 00
E-mail: dacehta@sst.dk
Home page: www.dacehta.dk

The publication can be downloaded free of charge at www.dacehta.dk

Preface

This handbook is a new, updated edition of the *Health Technology Assessment Handbook*, which was issued by the Danish National Board of Health in 2001 as part of the fulfilment of the National Strategy for HTA. This was the first actual handbook relating to HTA in Denmark, designed as a tool for HTA practitioners and use in teaching. Among other things, the book formed the basis for teaching on HTA at summer and winter schools held by the National Board of Health for new project managers.The revision of the handbook should be viewed in light of the developments that have taken place in HTA since 2001. New knowledge and new methods have been added, and a much larger pool of experience is available. This applies not only to Denmark, but also internationally, where many of the European countries in particular have expanded their HTA activities and organisations.

The new handbook presents updated and new scientific methods and approaches to HTA. It deals not only with the analysis elements of Danish HTA, namely technology, patient, organisation, economy and ethics, but also with the steps in the HTA process. Viewed in an international context, it emerges that the Danish approach is closely in line with the trend that is currently (2006-2008) taking place within the European Network for HTA (EUnetHTA) project, to which DACEHTA contributes in many ways. In the light of the current development, the handbook will be updated within a period of two years.

Within the health system, the need for planning and decision-making to have a well-documented basis is growing. For HTA practitioners, this means that HTA results could be supplied within a relatively short production time – but without quality consequently suffering. One way to do this is to use existing studies and data from home and abroad as the basis, which requires good skills in assessing the quality and usability of the material in question. Another way is to increase the cooperation, coordination and sharing of work with HTA organisations outside Denmark, which necessitates an understanding of one another's working procedures and methods. The formulation of an English version of the handbook and close interaction with the work of EUnetHTA is intended to promote such co-ordination.

The handbook is aimed at anyone who takes part in planning and implementing of HTA projects and/or seeks HTA to be carried out, i.e. health professionals, political and administrative decision-makers, interest groups, researchers and others who want to adopt an HTA approach, including teachers and students. In Denmark, the handbook is being published at a time when, as part of the reform of local government structure, major changes are taking place in the health care system and many new HTA actors can be expected on the scene.

The contributions to the handbook have been written by specialists trained and experienced in the specific areas who have links with HTA: as members of DACHTA's Scientific Advisory Board, HTA advisers or teachers. Thanks go to all the authors and thanks to Mogens Hørder and Helle Ploug Hansen for their general comments and contributions too.

DACEHTA – Danish Centre for Health Technology Assessment
December 2007
Finn Børlum Kristensen
Director

List of authors

Editors:

Finn Børlum Kristensen
Director, Adjunct Professor, MD, PhD
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Helga Sigmund
Special adviser, M.Sc. (Technology/Sociology)
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Authors of chapters and sections:

Stig Ejdrup Andersen (member of DACEHTA's editorial team)
Consultant, MD, PhD
Unit of Clinical Pharmacology
Bispebjerg Hospital
Copenhagen NV

Svend Andersen
Professor, dr. theol.
Department of Systematic Theology
University of Aarhus

Birgitte M. Bonnevie
HTA adviser, M.H.Sc.
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Jørgen Eriksen
Adviser, M.Sc. (Psychology)
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Claire Gudex
Consultant, MD, MPH, D.M.Sci.
CAST – Centre for Applied Health Services Research and Technology Assessment
University of Southern Denmark

Dorte Gyrd-Hansen (member of DACEHTA's Scientific Advisory Board)
Professor, research director, M.Sc. (Economy), PhD
Institute of Public Health
University of Southern Denmark and
DSI – Danish Institute for Health Services Research

Helle Ploug Hansen (member of DACEHTA's Scientific Advisory Board)
Professor, anthropologist, PhD
Institute of Public Health
University of Southern Denmark

Mogens Hørder (member of DACEHTA's Scientific Advisory Board)
Dean, Professor, D.M.Sci.
Faculty of Health Sciences
University of Southern Denmark

Malene Fabricius Jensen
Head of Library Services, Librarian DB
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Henrik Jørgensen
Consultant, PhD, D.M.Sci.
Hvidovre Hospital
Copenhagen

Torben Jørgensen (member of DACEHTA's Scientific Advisory Board)
Director, Professor, D.M.Sci.
Research Centre for Prevention and Health
Glostrup University Hospital, Copenhagen Capital Region

Kristian Kidholm
Acting head of department, Health Economist, PhD
Department of Applied Research and HTA
Odense University Hospital

Lisbet Knold
Health consultant, M.A.
City of Copenhagen
Health and Care Administration
Copenhagen Public Health
**Formerly:*
Adviser, DACEHTA – Danish Centre for Health Technology Assessment, National Board of Health

Camilla Palmhøj Nielsen
Special adviser, M.Sc. (Political Science)
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Janne Seemann (member of DACEHTA's Scientific Advisory Board)
Associate professor, M.Sc. (Organisation), PhD
Department of Sociology, Social Work and Organisation
Aalborg University

Peter Bo Poulsen
Outcomes Research Manager, M.Sc. (Economy), PhD
Pfizer Denmark
Copenhagen
**Formerly:*
Associate professor, Institute for Health Service Research, University of Southern Denmark

Rikke Juul Poulsen
Quality, Development and Education Co-ordinator, M.Sc. (Economy)
Department of Medicine
Fredericia and Kolding Hospitals
**Formerly:*
Programme manager, CAST – Centre for Applied Health Services Research and Technology Assessment, University of Southern Denmark

Drea Eskildsen Stenbæk
Librarian
DACEHTA – Danish Centre for Health Technology Assessment
National Board of Health

Karsten Vrangbæk
Associate professor, M.Sc.(Political Science), PhD
Department of Political Science
University of Copenhagen

** The author's position and workplace during the drafting of the contribution to the handbook*

Contents

About the handbook

The present handbook deals with Health Technology Assessment (HTA) and is published in an English and a Danish version. HTA is connected with a systematic, research-based approach, but there is no single method or one delimited research field. Rather, HTA is characterised by an approach characterised as being interdisciplinary and versatile and in which the scientific basis builds upon theories and methods from a number of different research disciplines.

The broad approach in HTA should be viewed in light of the fact that the analyses encompass four very different key elements of technology, patient, organisation and economy. In addition to these elements, ethical aspects may also be incorporated in the analyses.

The course of an HTA consists of many components – some are process-related, while others concern the analyses. They are often interconnected and may be handled in parallel, in an overlapping fashion or related to earlier steps in the process.

The complexity that characterizes HTA is also reflected in the content and structure of this handbook. Twenty-one authors with widely differing backgrounds of specialization have contributed to the development of the book. This multidisciplinary approach is exemplified in a number of methodological chapters, in which two or three authors have contributed to the same overall subject on the basis of their scientific understanding. Regardless of the diversity, however, a common aim is pursued in the context of HTA, namely to seek the highest possible level of evidence.

About the structure

The handbook is divided into eleven chapters. For the purpose of providing clarity, each chapter has a short introduction, followed by *useful advice and suggestions* in bullet form. Chapters covering several subjects set out useful advice and suggestions for the subchapters in question.

The handbook's general approach is to reflect the course of an HTA – alternating between process and analysis oriented chapters. The structure of the book can, in general terms, be broken down into the following key areas:

- An introductory, process-related part describing how an HTA is initiated (Chapter 1)
- A general methodological part, which deals with considerations and methods, which are common to the areas of analyses (Chapters 2, 3, 4 and 5)
- A specified methodological part, which focuses on approaches to the analysis of each of the key elements of technology, patient, organisation and economy (Chapters 6, 7, 8 and 9)
- A final process-related part describing how to formulate a basis for decisions and an HTA report (Chapters 10 and 11).

About the aim of the book

The contents of the handbook are designed with a goal of:

- Highlighting the importance of optimal use of existing studies and data material before any primary data generation – where strictly necessary – is initiated

- Presenting up-to-date, research-based methods within not only the development areas of ethics, patient and organisation, but also the more established HTA elements of technology and economy.
- Supporting the HTA process by focusing on current questions such as:
  - How are decision-makers' questions formulated as HTA questions?
  - How is literature sought and assessed and how can supplementary studies be designed?
  - How can the material be analysed and synthesised with a goal of formulating conclusions that can answer the questions asked and form the basis for concrete guidance?

About the concepts of quantitative and qualitative

HTA is based on several scientific disciplines, namely health science, social science, natural science and the humanities. These each have their own theories and research strategies, but with certain overlaps, e.g. interview and questionnaire methods. Traditionally, natural science is connected to a *quantitative* research approach and the humanities with *qualitative* research, whereas social and health sciences can be considered users of "both".

The method chapters (in particular Chapter 4 on assessment of the literature and Chapter 5 on data generation, analysis and assessment) present method-based approaches from the above-mentioned research disciplines in relation to the concepts of *quantitative* and *qualitative* methods. The term of qualitative method is used in the chapters, whereas the term *quantitative* is not used explicitly. Methods with a quantitative approach in this book can be said to belong to the group conceived of as "*non-qualitative*".

The concepts of qualitative and non-qualitative/quantitative are based on the assumption that it is not actually possible to draw a clear distinction between them. Quantitative studies, e.g. within clinical and epidemiological research, may very well incorporate qualitative aspects when it comes to interpretation. Similarly, generic health status measurements of a quantitative type can feasibly contain qualitative elements. Questionnaire and interview based studies may also be either quantitatively or qualitatively oriented or a combination of both.

It is often appropriate to let quantitative and qualitative methods complement one another. Thus, qualitative methods, e.g. a research interview, may have a basis created in a quantitative questionnaire-based study. Conversely, a qualitative focus group interview may form the starting point for a questionnaire. The essential thing is that answers to the specific HTA questions are sought using the methods considered best for generating knowledge in the field in question.

About validity

Evidence is a shared general value in HTA. The HTA questions are, however, answered on the basis of *different* scientific disciplines and methods. All knowledge incorporated or produced must be assessed carefully. The scientific validity expresses the quality and thus the scientific value of a project or study. Different research traditions employ different criteria with a goal of meeting the validity requirements. It is also apparent that with different research approaches, different meanings or definitions are assigned to terms that are otherwise identical. It also occurs that, even within the same research tradition, there can be disagreement about the definition of the concepts.

Validity is the most common and most frequently occurring concept in this book. Furthermore, the terms *credibility* and *reliability* are used by different authors and in different contexts. In consideration of the mutual disagreement referred to above, no attempts are made in this book to seek unambiguous definitions of the concepts. The main thing is that HTAs are carried out systematically and critically with methods and analyses, regardless of what type of HTA is performed.

1 HTA – Clarifications and planning

By Helga Sigmund, Finn Børlum Kristensen and Birgitte Bonnevie

This chapter provides a short introduction to HTA in general and the Danish HTA model in particular. The initial steps in the HTA process are described as 1) clarifications and pre-analyses, 2) organisation of the HTA project, and 3) formulation of the problem and planning of the course. The chapter illustrates that the steps and activities in the initial phase are crucial for all of the further project course – and ultimately for the quality of the HTA results and for the basis for decisions.

Useful advice and suggestions

- Clarify whether the problem is suitable for an HTA or whether it requires a different approach
- Assess whether the topic is sufficiently important to spend resources on an HTA
- Identify the stakeholders and the target group of the HTA
- Check whether the documentation already available is adequate for an HTA
- Work out the problem formulation in the light of the expected decision situation, and be conscious that it will be of crucial importance for the course of the HTA
- Get hold of the right persons for the project team and reference group and establish clear rules for the interaction of the participants
- Do not initiate own studies before it becomes evident, that existing scientific literature does not answer the research questions of the HTA.

1.1 HTA in general

Health Technology Assessment (HTA) has been a concept in the field of health care since the 1980s, when one witnessed a rapid growth of new medical technologies in relation to limited health budgets. The HTA is a multiscientific and interdisciplinary activity delivering input for priorities and decisions in the health care system in relation to prevention, diagnostics, treatment and rehabilitation.

Why HTA?

Decisions on the use of technology are made at all levels in the health care system. They often include a unification of complicated medical, patient-related, organisational and economic information in a context where there may also be ethical problems. Providing input for the decision-makers is highly dependent of interaction, division of labour and cooperation between professionals of the health care system, the research environment and the political decision-makers and their officials. Decisions must be made on an evidence-based foundation where all relevant circumstances and consequences are systematically illustrated by means of scientific methods.

HTA is relevant in connection with complex problems prior to the establishment of a policy. This may be the establishment of a policy for treatment of e.g. *inguinal hernia* or a joint procedure for treatment of *diabetes* in general practice or in regional hospitals. It may also be health-political decisions on treatment and screening offers, with consequences for the whole country.

HTA does not make complexity disappear but offers a structure for the multifaceted basis for decisions. It is important to emphasise that the decision situation itself is beyond HTA. Besides input from HTA, many other components may form part of

decision-making, for instance regarding other patients or other circumstances in the health care system and in society.

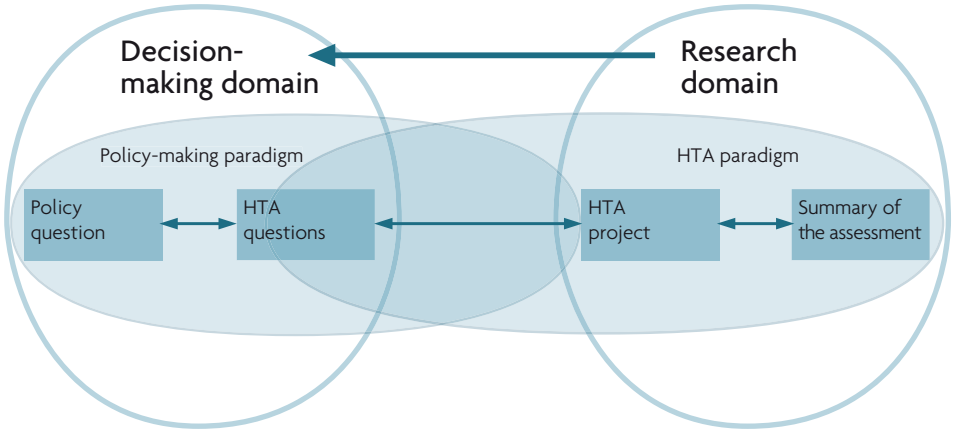
According to the Danish National Strategy for HTA (1), which has been the basis for the development of HTA in Denmark, the HTA should contribute with information for decision-making at *all* levels in the health care system. HTA thus affects political, administrative and clinical decision-makers. Depending on 1) the policy question, 2) the level of decision-making and 3) the time frame, HTA aims to improve the basis for decision-making with results from either broad or more focused types of HTA projects. The HTA framework may also be useful as a "way of thinking", i.e. without major analyses. An example is the mini-HTA providing decentralized decision support, e.g. in hospital departments (see Section 1.2.4).

What is HTA?

HTA is a research-based, usage-orientated assessment of relevant available knowledge about problems in connection with the use of technology in relation to health and diseases. By virtue of its methods, which are based on research, but also in terms of its aiming at decision-making, HTA is related to planning, administration and management.

HTA may therefore be considered as bridging between two domains: a decision-making domain and a research domain (2), cf. Figure 1.1. In order to fulfil such a purpose, the problems in focus of an HTA must be based on the need of the decision-makers (and their advisers) for a documented basis for decisions about the use of health technology.

Figure 1.1. Bridging between decision-making and research domains

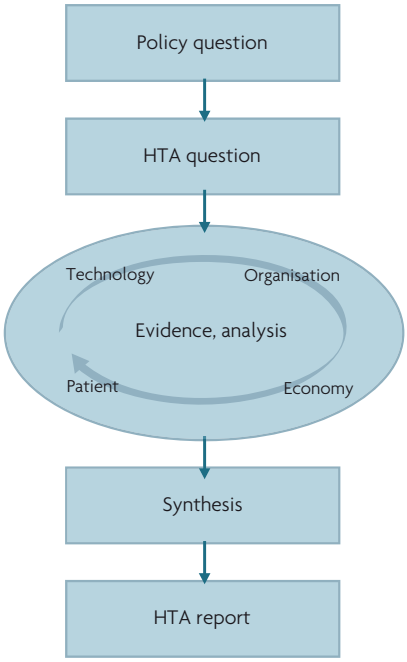


Based on Kristensen FB et al. 2002 (3).

HTA is thus defined in terms of its purpose and not as a specific method (4). At a more specific level, HTA is a comprehensive, systematic assessment of the preconditions for and the consequences of using health technology. In an HTA context, health technology is defined broadly as *procedures and methods of prevention, diagnostics, treatment, care and rehabilitation, including equipment and medical drugs* (5). Supportive systems and organisation within the health care system may furthermore be regarded as health technology. HTA comprises analysis and assessment of various areas where the use of health technology may have consequences. These areas may be grouped under

four main elements in order to ease the overview: *the technology, the patient, the organisation and the economy*, cf. Figure 1.2 (5). The main elements are overlapping to a certain extent. Ethics, which is traditionally attributed to the patient element, cannot for instance be separated from the technology analysis, just as ethics may constitute the framework for analysis across the elements (6). Also legal issues may be included transversally to the elements.

Figure 1.2. The Danish HTA model



As it appears in Figure 1.2, the four main elements are located as the middle step in the HTA process – also called the "horizontal" axis of the HTA model. The analysis within the main elements involves various methods, theories, scientific disciplines and research approaches, each of which must be used with a goal of high scientific quality. The analyses within the single elements are, however, in no way performed separately; on the contrary, there is an exchange of data and results between the elements. Partly because one element may depend on the other knowledge-wise; partly because the elements are analysed within the same an HTA project framework. A typical example is the interaction between the organisational and economic elements.

The "box model" with the four main elements has been criticized and amendments have been made. The Danish National Board of Health has, however, maintained the structure and considers it a "pedagogic" model providing a practical structure for what should be remembered if a decision is to be made on the basis of HTA. In addition, the box model is a good interpretation of the international understanding of HTA and it is an excellent basis for the planning of a specific technology assessment. The model is not to be followed slavishly and an HTA is not devalued by concentrating on the elements that are relevant in the specific situation – provided that possible choices by exclusion have been carefully explained.

However, thorough analysis is in itself not sufficient to make an HTA of a good quality. It is equally important to ensure a valuable HTA process where every step is based

on circumspection, knowledge and competence. The process-related steps are referred to as the "vertical" axis of the HTA model. Similar to the elements of analysis on the horizontal axis, the boxes on the vertical axis are not separate steps in the HTA process, but interwoven. An example is the interaction between the problem formulation and the synthesis (cf. Sections 1.4 and 10.1.2). Successful HTA work thus requires that the structure and the process form a synthesis.

Evidence and HTA

It is important to remember that even though HTA is intended for practical use, it must be on the basis of scientific methods. For many years, "evidence" has been a key word in HTA. The concept of evidence was introduced in connection with "evidence-based medicine" which is a clinical discipline integrating the best scientific results from systematic research in clinical work (7,8). It dates back to the clinicians in Paris in the nineteenth century, and the line goes via the critical clinical school from the 1960s to evidence-based medicine (9).

Connected to evidence-based medicine, the Cochrane cooperation was developed in parallel. Its products are international well-reputed literature overviews. The pivotal point in Cochrane reviews is an evidence assessment of clinical studies according to a pre-determined method. In connection with HTA, systematic Cochrane reviews constitute an important basis of documentation for the assessment of the effects and side effects of technologies (10).

In the mid-1990s the concept of evidence was broadened, leading to the development of an "evidence-based health care system". This indicates that an effort should be made to acquire a rational, well-documented basis for decisions in the health care system in general – not just in a clinical context, but also concerning prioritisation, planning, regulation, management and practice at all levels (9). At the same time, this shows the close relationship between evidence and HTA.

In connection with non-clinical decisions, it will not always be possible to maintain the rational evidence-*based* approach. This has led to the formation of the modified concept: evidence-*informed* decision-making. This concept implies that one looks at evidence and includes it, but at the same time accepts that there is room for other important factors to be part of decision-making.

Internationalization of HTA

In light of the development of HTA, practitioners of such all over the world have organised a number of networks, each of which is strengthening the HTA effort via cooperation and knowledge sharing. Four international organisations, three global and one European, are outlined briefly in the following:

European Network for HTA (EUnetHTA) is a three-year project aimed at establishing a formal European HTA network. EUnetHTA was initiated by the EU and was launched in 2005 with its secretariat function in the Danish National Board of Health. The project comprises 27 European countries of which 24 countries are members of the EU. EUnetHTA is intended to ensure a more efficient utilization of the resources that are used for the assessment of new health technologies, and to enhance the quality and validity of decisions on the application of technologies. These objectives are to be achieved through increased coordination, division of labour and knowledge sharing at a European level. Models and method development aimed at utilizing common knowledge and reducing duplication in relation to specific HTA projects are applied. The

work of EUnetHTA is structured in eight "work packages" each of which involves several participant countries. The network is expected to be made permanent at the end of the project in 2008.

Health Technology Assessment International (HTAi) is an international society for the promotion of HTA based on individual membership. HTAi serves to promote the development of HTA in terms of methods, expertise, quality and application. The task is sought to be approached by an interdisciplinary, international effort, in which timely and effective presentation of international HTA results has high priority. Other core focus areas are support for HTA education and research. HTAi hosts an annual international conference (HTAi Annual Meeting) and is responsible for the publication of the International Journal for Technology Assessment in Health Care (IJTAHC). From 1990 until the establishment of HTAi in 2003 these tasks were handled by a similar society with the name International Society of Technology Assessment in Health Care (ISTAHC).

International Network of Agencies for HTA (INAHTA) was established in 1993 and is presently (2007) a cooperation of 45 HTA organisations in 23 countries. The purpose of INAHTA is to create a forum for exchange of information and cooperation focusing on the joint interests of the member organisations. Together with NHS Centre for Reviews and Dissemination INAHTA is the host for a comprehensive international HTA database, located in York, UK. The database comprises information about completed and ongoing HTA projects, HTA publications as well as articles about HTA. For more information about the database, please visit HTA Database.

International Information Network on New and Changing Health Technologies (EuroScan) has existed since 1997 and is a cooperation between 15 HTA organisations from 9 European and 3 non-European countries about early warning of new technologies. The cooperation concerns the identification and prioritising of new technologies. For the purpose of mutual exchange of technology EuroScan hosts a database with information about new and potentially interesting technologies and overviews of published "technology warnings" to which all member countries contribute to and make use of.

1.2 Introductory clarifications

In connection with the HTA model (cf. Figure 1.2) it was mentioned that the "boxes" in the diagram should not be seen separately, but as interacting with one another. The same applies to the steps and activities in the early phase of an HTA project described in the following sections: They are presented separately, but will often be interconnected in practice and to be handled parallel in an overlapping way.

1.2.1 HTA or an alternative approach?

Planning and policy-making related problems in connection with health technologies give reason for considerations, whether it would be relevant to initiate an HTA.

Firstly, however, it is important to clarify whether an HTA is the *right* tool to use for the problem in question, or whether another approach is better suited.

Different approaches to clarification of a problem:

- An HTA
- A quality-assurance project (if one knows what the right thing to do is in a specific organisational context – but, what is actually done, is not the right thing)
- A basis for decisions prepared in a usual administrative setting (for instance, if a national or regional HTA is available)
- An assessment (if one wants to know whether recommendations, programmes, etc. have been carried out)
- Clinical guidelines or a reference programme (if guidelines are to be given based on evidence)
- Traditional expert- and/or stakeholder-based committee work (if the stakeholder aspect is very important, if certain experts' assessments are in demand, or if only a short period of time is available)
- Exclusively a systematic literature review, possibly a meta-analysis, in order to clarify the efficacy or effectiveness of the technology
- An economic analysis (if sufficient knowledge about the clinical efficacy or effectiveness1 of the technology is available and there are no specific organisational questions, e.g. of many drugs)
- A (primary) research project (if there is a lack of documented knowledge, especially about the clinical efficacy).

If a project type other than an HTA is selected, it is still a good idea to apply an *"HTA way of thinking*" as far as it is possible. This will lead the line of thought into relevant clinical, patient-related, organisational, economic and ethical areas. This ensures greater versatility to counteract decisions being made on an otherwise insubstantial foundation.

1.2.2 HTA topics and target groups

The number of HTA projects completed annually does in no way correspond to the numerous technologies that continuously gain a footing in the health care system – not to mention perhaps obsolete, older procedures that could also be the objective of an HTA with regard to possible discontinuation. There is an endless number of topics to choose from. Thus, appropriate focusing, selection and prioritisation of topics are crucial for HTA projects' fulfilling their ultimate purpose: to contribute to quality and efficient resource consumption within the health care system.

Is the topic sufficiently important for resources to be used on an HTA?

When implementing an HTA it is essential that an assessment has been made on whether the problem is sufficiently important for resources to be set aside for the project. Typically, it is necessary to prioritise between various potential HTAs or other project types.

The prioritisation can be approached in many different ways in different countries. However, a formal HTA organisation often has principles for prioritisation between potential HTAs (11,12). This is, for instance, the case at the national level in the Danish National Board of Health, but also in the contexts of department, hospital or region, it is necessary to give the resources for HTA projects in order of priority. It is in any case necessary to argue in detail for the importance and feasibility of the individual HTA.

1 For further details of the terms, please read Section 6.5.1.

Prior to implementing an HTA it is necessary to assess whether there is a decision problem. In case of an affirmative answer, it is important to clarify the nature of the decision, the context of which it is part and when the decision is expected. Is the HTA to contribute to the basis for decisions of *whether* something is to be done, or *how* it is to be done?

Who sets the agenda for the HTA-topics?

The targeting towards the decision-makers does not necessarily mean that they specifically demand an HTA for a given problem, although this really should be the case – and is the case to an increasing extent. In case of a specific demand, the ”initiator” is rather the planners (“policymakers”), who are to prepare a possible basis for decisions in case a policy is to be established for the area.

In many cases it is the institution or the local professionals who are to prepare HTAs who put topics on the agenda. This takes place based on a more or less formal analysis of requirements and possibilities for an HTA – and in expectation of the HTA results being requested prior to making a decision. Some HTA organisations or programmes, for instance the English one, has a formal system for continuously obtaining suggestions for HTA topics.

What is the organisational basis for an HTA?

Organisational basis for an HTA:

- Health policy/planning
- National/regional/local
- Day-to-day operation
- Research/development.

The organisational basis may have a decisive influence on what will be the target group of an HTA. Whether or not there are specific initiators, the primary customers of the HTA should be identified. If an HTA is prepared in a centre or a department, its management is the primary target group. In the same way, the planners in a region are the primary target group if the HTA is carried out within the regional administration. When the HTA is prepared in a research/development institution, thorough consideration of the target group is necessary, especially if there is no external initiator. An HTA should not be prepared without anchoring.

Who is the target group?

An essential initial task is the clarification of the primary target group of a possible HTA. This is crucial for the formulation of the problem as w ell as for the preparation of the final report.

Primary target groups:

- Politicians and officials at national or regional level
- Planners at regional and hospital level as well as municipality level
- Management at hospital and department level
- Organisations and companies
- Clinicians in the health care system and the primary sector
- The general public.

1.2.3 Pre-analysis

Is adequate documentation available for an HTA?

It only makes sense to carry out an HTA if sufficient – however, not necessarily complete – documented knowledge is available, especially of the clinical effect of the technology. If this is not the case, original (primary) research should be implemented to obtain such knowledge, and the decision-making has to be based on expert assessments until a better documented basis becomes available. Too often, little effort is made to systematically search for and assess available results of research already carried out. Consequently, primary research is implemented which may be unnecessary (13), or expert assessments are used that are not based on a systematic literature review. Those experts who can document that their advice is given following a systematic review of relevant literature should be the strongest contenders in the advising role. However, often there may be a need for data collection, for instance to illustrate epidemiology and organisation (see Chapters 6 and 8).

A complete, solidly documented basis is only rarely available at the start of an HTA. Things are often missing, for instance the elucidation of the patient/user aspect or organisational factors. To clarify such circumstances, initially, one should take advice from professional experts in the area and, at the same time, carry out a preliminary literature search for HTA reports, review articles and health economic analyses (see also Chapter 3). As a supplement to such a literature search, it may, in some cases, be of relevance to look for and visit places where the technology in question is in operation.

Clarifying literature search

As soon as a technology/an area/a problem is identified as a possible topic for an HTA it should be clarified whether the necessary basis for such a project exists. Is there sufficient existing knowledge in the area, and is this knowledge available?

The following questions should be answered in the initial literature search:

- Is there sufficient documentation of effect – in the form of meta-analyses or reviews?
- Alternatively, is there a sufficient number of clinically controlled studies of good quality?
- Are there already HTAs or other types of reports available nationally or internationally?
- Are published studies available nationally or internationally in some of the areas of the suggested HTA?

The following searches are recommended:

- HTA-database
- INAHTA website: briefs, check lists as well as the database of current projects
- Cochrane Library
- Websites from local HTA units in Denmark:
  - DSI, Danish Institute for Health Services Research
  - CAST, Centre for Applied Health Service Research and Technology Assessment
  - Department of Applied Research and HTA, Odense University Hospital (in Danish)
  - HTA and Applied Health Service Research, Central Jutland Region (in Danish).

1.2.4 Different types of HTA products

HTA is based on a systematic, scientifically based work method which can be time consuming as well as resource consuming. At the same time, the HTA information is expected to be relevant, well-documented and, importantly, available at the"right time" in relation to the subsequent decision-making or planning processes. Therefore, different types of HTA, including HTA-related products, have been developed both internationally and in Denmark.

To clarify which product type would be the most appropriate in a specific situation, the following factors play an important part: 1) basis of evidence, 2) problem, 3) decision situation, 4) life cycle of the technology, and 5) time- and resource frame.

Nationally, there is a distinction between the following types of HTA:

- "HTA"
  - with a broad approach
  - with a focused approach
  - regarding cancer drugs
- HTA products integrating foreign work
  - Foreign HTA with comments
  - "Core" HTA (where different parts of the HTA is carried out in different countries)
- HTA-related products
  - Mini-HTA
  - Early warning of new technology (incl. foreign early warning with comments).

Clarification of the term "HTA"

The increasing demands by the decision-makers for shorter production times for HTA reports during recent years have led to a number of foreign HTA environments having developed and introduced a short form of HTA, called Rapid Assessment or Rapid Review. In Denmark as well, Rapid Assessment development was initiated. At the same time, however, the appropriateness and feasibility of differentiating between a normal HTA and a rapid HTA was problematized, especially concerning HTAs at a national level. It had become apparent that the so-called Rapid HTAs could not always be completed within a short period of time of, for instance, six months. The main reason was that neither the HTA user nor the HTA preparer were interested in producing a product of lower quality in terms of methods than the well known HTA. (Some perceive "rapid" as "quick and dirty").

The term "Rapid HTA" thus did not fit the product required, either in terms of time or quality. The term is consequently no longer part of DACEHTA's product catalogue. Instead an "HTA" is prepared with either a *broad* or a *focused* approach according to the type of problem and the time frame. The type of HTA which is tailored to the assessment of new cancer drugs and which DACEHTA prepares at the request of the Danish "Cancer Steering Group" also belongs to this group. The cancer drug HTAs are closest to what is elsewhere – for instance abroad and decentralized in Denmark – referred to as Rapid HTA.

Short description of DACEHTA's HTA products

HTA

HTA – broad	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link/examples:	Based on complex problem or, for instance, area of disease. Broad and general approach; may include alternative technologies. Input for political-administrative and clinical decisions at all levels. 1½ – 2½ years External peer review 200 pages DACEHTA. Publications: "Type 2 diabetes"
HTA – focused	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link/examples:	Based on delineated problem; focus on one technology. Input for decisions as above provided they can be made within a short time frame. 1 year External peer review 100 pages DACEHTA. Publications: "Reduction in the risk of cervical cancer by vaccination against human papillomavirus (HPV)"
HTA – cancer drugs	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link/examples:	Based on delineated problem; focus on one technology. Input for decisions as above which are to be made within a very short time frame. 3 months Expert consensus 4 -15 pages New cancer drugs: "Tarceva", "Avestin"

HTA products which integrate foreign work

Foreign HTA with comments	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link/examples:	Based on foreign HTA report which is related to Danish conditions. Input for decisions in the health care system within a short time frame. 3-6 months Expert assessment 10-25 pages of summary and comments DACEHTA. Publications "Chronic paradontitis" (in Danish)
Core HTA	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link:	Based on problem which is of current interest in several European countries. Input for decisions in the health care system within a short time frame. 6 months Undecided 50 -100 pages Still in the development phase as part of the EUnetHTA project

HTA-related products

Mini HTA	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link:	Based on question framework with HTA questions. Prepared internally within the individual hospital (operational-orientated tool). Input for decisions at local level (department, centre and hospital level). Concerns proposals for new treatments, changes, etc., in relation to the cost. Only completion of questionnaire: 5-15 hours; incl. literature review: 1-2 months No peer review 3 -5 pages mini-HTA
Early warning*	Characteristics: Aim: Time frame: Quality assurance: Extent of report: Link/examples:	An information system which early on in the "life cycle" of the technology warns decision-makers of future technologies that may have to be introduced. Input for decisions and planning nationally as well as locally in hospitals. 2-4 months Expert assessment 4 pages Technology alerts

* "Early warning/technology alerts with comments" is a foreign early-warning product which is related to Danish conditions and presented with supplementary Danish summary and comments.

1.2.5 Stakeholder analysis

The stakeholder analysis is to be carried out early in the HTA process. The results of this analysis are important for the composition of the project organisation as well as for the possible acceptance and application of the HTA results. The stakeholder analysis includes two steps: 1) to clarify who the stakeholders are; 2) to assess which stakeholders are the most important to include, and to which function to assign them to in the context of the project (14).

Identification of stakeholders

Stakeholders are defined as groups which, to a marked degree, have influence on or are influenced by the possible changes in a given HTA. To identify stakeholders, the following questions can be asked (15):

- Who is the initiator?
- Who are the users of the results?
- Who has to accept the results?
- Who pays for the work and the results?
- Who is affected: Who benefits/profits/has drawbacks/risks or is inconvenienced by the results?
- Who has the knowledge and resources, or contributes?

The answers to these questions will produce a list of stakeholders comprising both individuals and institutions: for instance, public authorities, professional groups and interest groups, managements and staff groups within the health care system, experts and researchers in the relevant areas, etc. The list forms part of the further planning of the project organisation and the HTA process. It is primarily the project manager who assesses which stakeholders are the most relevant to involve.

Inclusion of the stakeholders

To ensure the most efficient project course, special attention should be paid to any conflicts of interest within the group of stakeholders. The occurrence of disagreement and conflicts is best prevented by a good balance within the project organisation, between representatives from the various special interest groups.

The stakeholders can be involved in different ways – adapted to the need within the individual project. However, it may be problematic to include stakeholders with obvious opposed interests in the actual project team, as this group is expected to be very labour-intensive and focused. In this case an organisational position in a *reference group* would be more appropriate. In a reference group the stakeholders would be able to follow the project as well as to contribute to it in the form of comments based on their specific point of view (see also Section 1.3 regarding project organisation).

In addition to the main stakeholders being represented in the project organisation it is important to anchor the project amongst those stakeholders who – at the completion of the project – will be close to the decision or planning processes and who can assist in implementing the results and recommendations of the HTA. Information and a certain communication during the project are the best means of making sure that the decision-makers understand that there is a need for the results of the HTA, so that they expect them and will make use of them.

1.3 Project organisation

Problems in connection with project organisation

In building a project organisation there are various problems to face. It is important to ensure that the project is based on sufficient authority, insight and working capacity in order to complete the task within the project organisation. A solid cooperation must be established between the persons that are to deliver an active performance. In relation to the project, there will be a number of stakeholders with different interests. These will become obvious when carrying out the stakeholder analysis mentioned above. Arising conflicts are to be handled in the project organisation, and it must be clarified how this is to be done. To control the organisation, there must be a competent project manager with distinct authority in relation to the project "owner". An organisation is built that comprises a statement of composition (who) and distribution of work (what). The organisation has to be adjusted to recognise persons who are willing to participate and contribute with a (considerable) performance (15).

Establishment of a project team

The formulation of the problem determines which areas, bodies and professional groups should be part of the project team – and not a professional tradition for those who usually take part. One should be aware that an HTA does not necessarily restrict itself to a project within one's own department but may be based at local, regional or national level. Consequently, the entire context of the technology has to be taken into account – across disciplines as well as across sectors. Regarding involvement, strategy and planning of the course of the project, it is important that all relevant bodies are involved from the beginning.

If the project team is too big, it can be an advantage to establish subgroups, each working with specific elements of the HTA. However, if this work form is chosen, it requires that the project team meetings are held with a high degree of coordination and control in order to ensure that all topics relevant for the team are discussed. There are thus more demanding requirements to the management of the project when subgroups are established.

To ensure the completion of the project in relation to manning, economy, fundamental and political decisions which the project manager cannot make, it is important to have a project owner (who is responsible). The same applies to implementation of HTA results.

Project management
Project management comprises four management responsibilities:

- Management of the task; create results that are relevant to the surroundings
- Control and administration of activities; insight into the task; follow-up and proactive reaction in relation to the solution of the task
- Internal management; coordinate the work in the project team; be in charge of meetings and inspire the project team members
- External management; contact with project-responsible manager and stakeholders, including the reference group.

It is important that the project manager is conscious of leading the process – in order not to be involved with too much work himself. This applies especially in relation to the clarification of boundaries in a project or when the completeness of the results is to be ensured.

Reference group
In certain connections, it is advisable to supplement the project team with a reference group, which during the project period can contribute with response, advice and guidance. This is especially important in connection with the problem formulation and synthesis phases (see Section 1.4 and Chapter 10). The reference group participants will often include stakeholders in relation to the particular health technology, for instance administrative representation as well as representatives from professional organisations and patient groups. An effort must be made to ensure that the reference group completely understands the project team's proposals and their consequences. The aim of a reference group is not to achieve a joint decision but rather to register the different viewpoints of the stakeholders. It is important to balance expectations in relation to the role of the reference group to guarantee that this is clear from the start.

The joint work basis of the project team
The project team should constitute itself with a project manager and prepare a project description/a "mandate" for the task which is approved by the project owner.

To create the basis for a good and rewarding cooperation it is important initially to agree on:

- Problem formulation and delineation – what is the main question (the policy question) and what do we want to study (HTA questions)?
- Clarification of the alternatives to be studied
- Strategy regarding information search – what is available and how is its evidence?
- Establishment of time schedule/meeting plan for the project period
- Planning of the work phase – who does what and when?
- Planning of the completion – how, in which form and to whom are the results to be presented?
- Planning of the implementation – if changes are to take place, then, how do we do it?
- Strategy regarding follow-up and problem solving of derived questions.

Work patterns of the project team

Meetings are one of the most important communication patterns in the project work. However, as such meetings are resource-consuming, most of the actual project work will take place outside the meetings. Consequently, the objective of the meetings will be to:

- control the project; work group status, distribution of tasks and joint decision-making
- make the participants feel co-responsible for the project and create understanding and acceptance of the different occupational backgrounds.

Thus, constructive meetings and, ultimately, a good outcome require good cooperative behaviour with trust and high work ethics among the project participants. The meetings are led and coordinated by the project manager.

1.4 Problem formulation: Policy and HTA questions

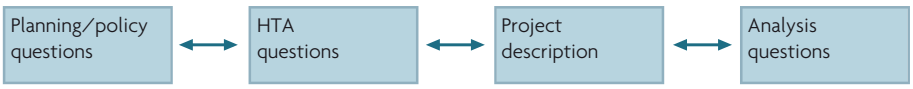
The formulation of the problem is crucial for the project course of the HTA. The formulation takes place in the light of the expected decision situation, i.e. based on the knowledge of decision-makers, target group and stakeholders as well as the results from the pre-analyses. The problem formulation is normative for choice of method, delineation and further project planning. Important factors in the problem formulation process are assessment of the project's benefit and consideration of possible implementation later on.

The starting point of the problem formulation could be, for instance, a technological innovation, the position of which must be clarified in relation to the currently applied technologies in the area (examples: CT-colography and bariatric surgery) (16,17). Another starting point could be the uncertainties about the basis of a current technology in connection with a clinical problem (example: Observation for cerebral concussion, SBU) (18).

Specific problem formulation and specification of answerable questions

The problem formulation phase is a circular process, i.e. it may take place several times. Although this may require considerable resources, it will pay off to use the

necessary time. A team that possesses a combination of professional knowledge of the field, administrative insight and knowledge of HTA will be in the best position to make a useful problem formulation. The steps towards a specific project description can be illustrated schematically.



In accordance with the applicational direction of the HTA method, the problem formulation must be specific and only direct itself towards actual problems. For instance, if there are no ethical or organisational problems, questions and resources should not be wasted trying to procure and illustrate them. Early on, however, a broad and open review should be made of the main problem – one cannot beforehand exclude one or several HTA elements, and reasons should be given for any delineation. In order to ensure the application of the final work, great weight should be attached to the information needed by the decision-makers.

Formulation of the planning and policy questions

Prior to starting the formulation of the project description, it is advisable – in accordance with the idea of HTA – to clarify the planning or policy questions[2], which the HTA contributes towards answering for the basis of decision.

Policy questions are the basis with regard to the contents for HTAs. In a very simplified form, policy questions can be formulated as follows: Is there a considerable health effect or other benefit; what are the requirements on staff and organisation; what are the costs; other factors to be aware of?

Policy questions are not only aimed at general political and administrative decision levels. If an HTA is carried out locally, for instance within a department, it may be the department management's questions that are to be answered. In such a framework it is obvious that the policy questions should be formulated in close dialogue with the management based on the HTA idea. An HTA expert should be involved in the final formulation in order to ensure a systematic HTA process.

Examples of planning/policy questions prior to an HTA:

- If a public offer of vaccination against HPV is requested, who should receive the offer, how should it be organised, with what effects and costs? (19)
- How can the health care system's diagnosis of colo-rectal cancer be organised around suitable clinical strategies – with what effects and at what cost. (20)

Formulation of the HTA questions

Where the policy questions are aimed at the decision situation, the derived HTA questions must be phrased in such a way that their answers will more specifically fulfil the information needed by the decision-makers or the target group. The formulation of HTA questions should be done carefully, since these questions determine the choice of analysis areas and methods and thus the planning of the entire further project course.

2 In this HTA connection, the concept "policy" should be understood as expression for a process, which leads to formulation of policies within a certain area. Decision-making is an element of this process.

The HTA questions must be:

- clearly formulated
- clearly defined
- answerable
- manageable in number.

The HTA questions, which – see above – are of an analytical nature, can be classified in the current four main elements in Denmark: *technology, patient, organisation and economy* as well as any ethical aspects – to ensure that the problem is thoroughly discussed in all phases. Other structures are used abroad. The EUnetHTA project, for instance, uses nine domains that previously were defined in the EUR-ASSES project (4).

New questions often appear during the project period. It is usually advisable to maintain and complete the problem agreed on at the start and only subsequently supplement this with new questions. In the specific completion of the HTA analyses it may be necessary to redefine the HTA questions, for instance in the form of analytical or descriptive research questions – see the following chapters.

Examples of derived HTA questions – HPV:

- What are the effects and side effects of HPV vaccination?
- Are there any interactions with other vaccines in the childhood immunisation programme?
- What influence has choice of vaccination age on acceptance of the vaccination?
- Are there any ethical problems in relation to the HPV vaccination?
- What organisational consequences will different vaccination strategies have?
- What are the benefits compared with the costs for different models of the vaccination programme?

Examples of derived HTA questions – colo-rectal cancer:

- What is the status of current diagnostic methods and strategies?
- Are there any alternative methods and strategies?
- What are the organisational consequences of alternative strategies?
- What are the patient-related aspects of the problem?
- What are the consequences in terms of resources?
- How will a possible screening influence organisation and economy?

Connection between problem formulation and synthesis

During the synthesis process at the end of the HTA project, it is important to look back at the policy or planning questions of the problem formulation. The analytical HTA questions of the project and the analyses carried out must be "captured" and summarised for the final product, which is to be passed on to the decision-makers so that it can form part of the basis for decisions that may be needed in the area (see Section 10.1).

Connection between problem formulation and utilization of HTA

It can never be ensured in advance that an HTA is used as basis for a decision. The likelihood can, however, be increased substantially by including considerations about the use of the HTA in the early planning phases of the project. Important prerequisites are that the target group for the HTA is defined and that the target group considers the problem of the HTA as relevant in connection with its decision-making. In some cases this is ensured by the decision-makers themselves "ordering" an HTA by asking for analysis of a specific problem. In other cases the request for an HTA does not initially come from the decision-makers themselves. In such a case it can be appropriate to enter into a dialogue with the decision-makers (or their representatives) to ensure that the problem reflects their need. In this way, the problem formulation can be specified before the project is started. It is also important that the decision-makers are informed that the project is started. That makes them aware that a basis for decisions, which they can use, is underway. Finally, it may be necessary to enter into a dialogue with the decision-makers on the duration of the project so that the time frame for the HTA can be planned in the best possible way in relation to the requirements of the decision-makers (see Section 10.2).

Connection between problem formulation and indication of "perspectives"

The results of an HTA should point forward, i.e. to the other side of the decision situation. Indication of "perspectives" means that – based on the problem formulation as well as on the conclusions and recommendations (if any) of the HTA – an attempt is made to pinpoint possible development tendencies in the longer term and/or any barriers that could obstruct an appropriate development.

Connection between problem formulation and follow-up evaluation

Similar to perspectives (based on problem formulation, conclusions and recommendations) it should be outlined how the implementation of HTA results into practice within the health care system could be evaluated. It should be considered in which way or in which areas a follow-up evaluation could best document changes in health care as a result of a specific HTA.

1.5 Project and method planning

Project description

The practical planning of the ongoing project course consists of preparing a detailed project description or in extending and clarifying an already existing draft. A project description should, if at all possible, be prepared in close cooperation with the persons that are envisaged to participate in the project. Project descriptions must comprise a number of mandatory pieces of information. There are templates for project descriptions that can be used as a basis.

As a minimum a project description must include the following main elements:

- Background
- Target group/stakeholders
- Objective
- Method
- Analytical framework
- Presentation
- Project organisation

- Time frame
- Budget.

To ensure the completion of useful professional analyses, the project description should comprise precise work descriptions for the completion of the analytical work. Thus, a work description/protocol should be prepared for each part element to be studied in the HTA.

Clarifications in relation to selection of method
The detailed planning of the analytical part requires that the following questions are clarified:

- which research questions/hypotheses should be answered concerning the individual HTA element
- whether the relevant competencies to carry out a literature review in a specific area are at hand
- whether the literature review identifies valid and relevant research results in the area or in adjacent areas
- whether the literature review should be carried out as systematic reviews, meta-analyses and/or as syntheses of qualitative research
- whether primary research has to be carried out.

If the literature review identifies that results are available in the area, it is important to assess the scope and validity of:

- the methods applied for data generation
- the methods applied for analyses and interpretation
- the knowledge of "the studied topic" generated by the literature review.

Only then is it decided whether primary research is necessary.

If primary research is to be implemented, it is important to assess:

- the data generation methods to be used
- the analysis and interpretation methods to be used
- whether the required competencies to carry out primary research are present in the project team
- whether the exploration gives rise to specific ethical questions
- the position of the individual element in relation to the remaining three elements in the given HTA (technology, patient, economy, organisation).

Every HTA project requires that international factors are also considered. The inclusion of relevant knowledge and experience from other countries increases the possibility of rational utilization of resources and should be an integral part of the project work. The importance of this is increasing from year to year.

1.6 Literature for Chapter 1

(1) Health Technology Assessment Committee of the Danish National Board of Health. National strategy for health technology assessment. Copenhagen: National Board of Health; 1996.

(2) Battista RN, Hodge MJ. The development of health care technology assessment. An international perspective. Int J Technol Assess.Health Care 1995 Spring;11(2):287-300.

(3) Kristensen FB, Matzen P, Madsen PB, the Colorectal Cancer Health Technology Assessment Project Group. Health technology assessment of the diagnosis of colorectal cancer in a public health service system. Seminars in Colon & Rectal Surgery 2002;13(1):96-102.

(4) EUR-Assess Project. EUR-Assess Project Special Section Report. Int J Technol Assess Health Care 1997;13:133-340.

(5) Danish Institute for Health Technology Assessment. Medicinsk Teknologivurdering. Hvorfor? Hvad? Hvornår? Hvordan? [Health Technology Assessment. Why? What? When? How?] Copenhagen: Danish Institute for Health Technology Assessment; 2000.

(6) Andersen S. Etiske aspekter ved MTV [Ethical Aspects of HTA]. In: Kristensen FB, Sigmund H (eds.): MTV, sundhedstjemesteforskning og klinisk praksis. [HTA, health science research and clinical practice.] Copenhagen: Danish Health Science Research Board and Danish Institute for Health Technology Assessment; 2000. p. 51-57.

(7) Evidence-based medicine. A new approach to teaching the practice of medicine. Evidence-Based Medicine Working Group. JAMA 1992 Nov 4;268(17):2420-2425.

(8) Kleijnen J, Chalmers I. How to practice and teach evidence-based medicine: role of the Cochrane Colaboration. Acta Anaesthesiol Scand Suppl 1997;111:231-233.

(9) Kristensen FB, Sigmund H, editors. Evidensbaseret sundhedsvæsen. Rapport fra et symposium om evidensbaseret medicin, planlægning og ledelse. Rapport fra et symposium om evidensbaseret sundhedsvæsen. [HTA, health service research and clinical practice. Report from a symposium on evidence-based health service.] Copenhagen: DSI-Institute for Health Services Research;1997. DSI-report 97.02.

(10) Bhatti Y, Hansen HF, Rieper O. Evidensbevægelsen udvikling, organisering og arbejdsform. En kortlægningsrapport. [Development of the evidence movement, organisation and work method. A mapping report.] Copenhagen: AKF-Forlag; 2006.

(11) Goodman C. Introduction to health care technology assessment. National Library of Medicine: National Information Center on Health Services Research & Health Care Technology (NICHSR); 1998.

(12) Oortwijn WJ, Vondeling H, van Barneveld T, van Vugt C, Bouter LM. Priority setting for health technology assessment in The Netherlands: principles and practice. Health Policy 2002 Dec;62(3):227-242.

(13) Chalmers I. Up-to-date systematic reviews and registers of controlled trials. Prerequisites for scientific and ethical trial design, monitoring and reporting. In: Sigmund H, Kristensen FB, editors: MTV, sundhedstjenesteforskning og klinisk praksis. Rapport fra et symposium om evidensbaseret sundhedsvæsen. [HTA, health service

research and clinical practice. Report from a symposium on evidence-based health service.] Copenhagen: The Danish Institute for Health Technology Assessment; 2000.

(14) Vrangbæk K. HTA, Administration and Organisation. In: Danish Institute for Health Technology Assessment: Health Technology Assessment Handbook. Copenhagen: Danish Institute for Health Technology Assessment; 2001.

(15) Mikkelsen H, Riis JO. Grundbog i projektledelse. [Introduction to project management.] 6th ed. Rungsted: PRODEVO ApS; 1998.

(16) Pedersen BG, Arnesen RB, Poulsen PB, Adamsen S, Hansen OH, Laurberg S. Tyktarmsundersøgelse med CT-kolografi – en medicinsk teknologivurdering. [Colonoscopy with CT colonography – a health technology assessment.] Copenhagen: Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects.]; 2005;5(3).

(17) National Board of Health, Danish Centre for Health Technology Assessment. Kirurgisk behandling af svær overvægt – en medicinsk teknologivurdering. [Surgical treatment of severe obesity – a health technology assessment.] Copenhagen: 2007;9(3).

(18) Borg J, Emanuelson I, af Geijerstam JL, Hall P, Larsson, E.M. et al. Hjärnskakning – övervakning på sjukhus eller datortomografi och hemgång? [Concussion of the brain – monitoring at the hospital or CT scanning and discharge?] Stockholm: SBU- Swedish Council on Technology Assessment in Health Care; 2006;180.

(19) National Board of Health, Danish Centre for Health Technology Assessment. Reduction of the risk of cervical cancer by vaccination against human papilloma virus (HPV) – a health technology assessment.] Copenhagen: 2007;9(1).

(20) Danish Institute for Health Technology Assessment. Kræft i tyktarm og endetarm. Diagnostik og screening. [Colorectal cancer. Diagnostics and screening.] Copenhagen: 2001;3(1).

2 Ethical considerations

By Svend Andersen

This chapter concerns ethical considerations in relation to a given HTA issue. The chapter has been written in acknowledgement of the increasing importance of ethics in an HTA context. Thus, ethical aspects, if any, should be identified early in the HTA process and assessed carefully in relation to a possible ethical analysis. An example of the involvement of a professional ethicist in a specific HTA has been included.

Useful advice and suggestions

- An ethical analysis is required when a technology is ethically controversial but is also appropriate in many other instances
- The ethical analysis should include all aspects of the technology; not just the patient aspect
- The involvement of an ethicist or an HTA practitioner trained in ethics should be considered.

2.1 Introduction

The introduction of new technology in the health care system will often give rise to ethical questions. Should screening be offered which implies a risk of treatment of discovered cases? This and similar issues make it natural to incorporate an ethical component in HTA.

In the Danish HTA model, ethics do not hold a clearly defined place. In the descriptions so far of the four elements of the model (cf. Section 1.1), ethics have been included under the element *the patient* (1,2). The reason must be an assumption that potential ethical issues are found in relation to the patients affected by a specific health technology. This is in continuation of a classical understanding of medical ethics which is linked to the doctor-patient relationship. In international method description ethics are on the other hand defined as an independent domain: in EUR-ASSESS ethics constitute one of a total of nine domains (3).

The Danish view up until now may certainly be questioned, but the only two circumstances reaching beyond the doctor-patient relation are pointed out here.

Firstly, it is obvious to distinguish between two types of technology when considering health technology from an ethical point of view. One type could be called *ethically uncontroversial* technology, but the use may nevertheless give rise to certain ethical issues, for example endoscopic surgery in the abdominal cavity. This raises some well-known questions regarding informed consent etc. The other type of health technology is *ethically controversial* technology (2). Such technology is for instance Preimplantation Genetic Diagnosis (PGD) (4).

Secondly, the presence of technology means that an ethical analysis will be more complicated than is otherwise often the case. Usually, the basis of an ethical analysis is that the object of the analysis is *persons* and the *actions* of such persons. A typical example is a doctor informing a patient of the result of an examination. It may seem obvious to consider technologically based procedures in the same way and for instance say that PGD is merely part of a doctor's examination of a woman. In that way, decisive technology features are, however, overlooked. Technology is not an isolated item in terms

of a traditional tool, but is always a complex phenomenon consisting of a large or small amount of sub-elements. PGD thus includes both In Vitro Fertilisation (IVF) and genetic testing as sub-technologies. Furthermore, technology is constantly developing. This means that it is not enough to subject the current application to an ethical analysis. As part of a technology assessment the ethical analysis should include the possible development of a specific technology in the future (5).

It is therefore obvious to consider ethics an interdisciplinary dimension in HTA related to many different elements of the technology under assessment (6). In recent years, people have been engaged in developing a more comprehensive way of integrating ethics in HTA – also internationally. INAHTA (cf. Section 1.1) has thus set up a working group preparing a report on the integration of ethical analysis in HTA. The working group was to consider a number of questions, amongst others whether ethics should be part of an HTA at all, whether ethics may play different roles and when it is the best time of including ethics in the development of a technology.

2.2 What are ethics?

The word "ethics" is used in connection with assessing the actions, behaviour and way of life of people in relation to the difference between right and wrong. Here, *wrong* means that an action etc. injures or offends others, and thus *right* means the opposite, i.e. an action benefits and respects others. The ethical assessment may for instance be that it is *wrong* of a doctor to tell the truth to a patient beyond recovery or that it would be *wrong* to legalise active euthanasia. The two examples show that ethical issues may arise in different connections or contexts. Three contexts should be emphasised:

- The *personal* context concerns the right thing to do for the individual in relation to his/her personal matters. Is it wrong not to see a doctor?
- The *professional* context is defined by the specific responsibility of a certain profession. Health care providers are an obvious example.
- The *political* context concerns the ethics on which the organisation of society is based and which are typically manifested in certain kinds of legislation. In Denmark, the health care system with equal access to health services are for instance based on ethics which may be characterised by concepts of justice and solidarity.

The medical profession probably has the longest tradition of ethics. This is due to the fact that the professional action of a doctor has a particular effect on other people's lives. Often, it is simply decisive for life or death. As mentioned, traditionally the doctor-patient relationship has been the subject of medical ethics; however, in recent years other ethical issues have emerged in connection with the health care system and medical science.

One issue is the use of patients or healthy people as subjects. This concerns *ethics in research and science* in the field of health care. In Denmark, this area has been regulated for several decades in terms of the scientific-ethical committee system.

The other issue is that health technology apparently is developing in a transcendent way. Especially within reproduction and genetics, interventions are possible which give rise to basic (and new) ethical questions. PGD for instance implies that one or more "healthy" fertilized eggs are selected while others are discarded. Is it a responsible way of treating human life? Is it at all possible to speak of human life in connection with a

few days old fertilized egg? A very popular area giving rise to ethical issues of this kind is stem cell research. Such ethical issues are also regulated in Denmark and are prepared by the Danish Council of Ethics.

2.3 Theory

The ethical analysis differs from the other parts of an HTA, i.e. the parts relating to health science, economy and other social science. The most important difference may be formulated in terms of a *normative* element of the ethical analysis. When explaining this it should be noticed that the notion ethics is characterised by an important duplicity. Firstly, ethics may mean the norms or values according to which people act in their private and professional lives. In this case it is a question of *employed ethics*. Secondly, ethics are also an *academic discipline* traditionally associated with philosophy and theology. As an academic discipline ethics are not a model of moral values, but rather a scientific study of employed ethics.

The ethical understanding may be subjected to empirical studies, e.g. surveys or qualitative, e.g. anthropological studies. Such studies will *describe* (analytically/theoretically) ethical attitudes i.e. they will not determine whether or not they are well-founded. Academically practised ethics may usually be characterised as a philosophical study. Often such a study consists of a conceptual analysis and an analysis of the quality of the arguments (e.g. as to consistency or inconsistency). When such analyses are carried out within ethics they may also be referred to as descriptive, in the sense that they do not include an attitude to the validity of ethical assessments. An ethical analysis may also include such an attitude and in this case it concerns *normative ethics*. Normative ethics are thus a philosophically (or theologically) based perception of the right way of acting.

In ethics as an academic discipline it is widely held that *norms* and *principles* play an important role. Norms and principles are rules of action on which the ethical assessment is based. They differ as regards generality: norms are specific rules, e.g. "always tell the truth", whereas principles are more general, e.g. "never hurt others". Principles may also be called basic rules.

Here, a basic ethical difference concerns whether it is possible to formulate one or a few fundamental principles. This variance is e.g. manifested by the frequently described difference between so-called virtue ethics and so-called duty ethics. According to virtue ethics (utilitarianism) the norms of ethics may be traced back to one single basic principle: "Always act in such a way that you obtain the best possible balance of happiness (well-being, wish fulfilment) and unhappiness (pain, suffering) for all parties affected".

According to duty ethics, dating back to the German philosopher Immanuel Kant (1724-1804), the basic principle of ethics is on the other hand "Act so that you treat humanity, both in your own person and in that of another, always as an end and never merely as a means". Such philosophical notions of the basis of ethical attitudes are called *normative ethical theories*. There are, though, many normative attitudes in moral philosophy that do not fit into the distinction between duty ethics and virtue ethics (7). For the different aspects of the notion of ethics, please refer to Andersen 2003, Chapter 1 (8). For ethical methods and theories, please refer to Klint Jensen & Andersen 1999, Chapters 8, 9 and 10 (9).

2.4 The four principles

An ethical assessment which is to be part of the basis for decisions of the health care system of course cannot be based on one specific ethical theory alone. It is therefore necessary to search for an ethical basis of evaluation which may be widely accepted. In normative ethics it seems that the chance of consensus is at its highest when dealing with *middle-ranked principles*, i.e. principles between overall principles and concrete norms. Probably the most influential suggestion for the formulation of such principles in medical ethics has been offered by T. Beauchamp and J. Childress (10). They operate with the following four principles:

- Respect for autonomy
- Non maleficence
- Beneficence
- Justice.

Whereas the three first principles are relevant to the direct doctor-patient relationship (but not just here), the principle of justice concerns the relationship between several persons and possibly groups of people. The question of the distribution of resources in the health care system is, for instance, typically a question of justice.

The four principles are neither the invention of the two authors nor an expression of their personal opinions. These are some of the most basic ethical norms which reappear in most ethical theories and models of moral values. For instance, beneficence cannot be perceived as the non-religious (secular) edition of benevolence. Beauchamp and Childress present the principles as expressive of the widely accepted "common morality" among those who consider ethical issues seriously. Without going into details, it could probably be said that the four principles play a decisive role in a democratic society such as the Danish and the Danish health care system.

The following contains a detailed presentation of each principle.

Autonomy

Autonomy means self-determination and the principle concerns

> *the decisions of the individual regarding his/her life must be respected.*

The prerequisites of self-determination are freedom from intervention from others but also avoidance of misunderstanding and other inhibitory factors. Therefore, the respect for self-determination also includes a positive commitment to provide the necessary information, and support autonomous decisions on the whole. Obviously, not everybody is capable of making autonomous decisions which give rise to a number of ethical problems. When it comes to the health care system, autonomy first and foremost has to do with the individual patient's right to decide on whether to receive treatment. As understanding is an important prerequisite for an autonomous decision, autonomy also includes the right to information. The most important term as regards the respect for autonomy in the health care system is *informed consent*.

Non-maleficence

This principle concerns

> *a duty to avoid causing harm intentionally.*

Harm is a wide notion. But in the context of the health care system the most important types of harm are pain, handicap and death. The principle therefore makes the basis for more specific rules such as:

- Do not kill
- Do not cause pain or suffering in others.

The two rules may very well conflict with each other, i.e. when a patient beyond recovery is in great pain and agony. Those in favour of euthanasia will say that if the patient so wishes (autonomy), the liberation from suffering may outdo the prohibition of killing.

Beneficence

As mentioned, the principle of beneficence may be considered as a temporal version of the Christian commandment "You shall love your neighbour as yourself". Beauchamp and Childress consider the difference important (10). They do not consider the principle as a claim for doing good against everybody (general beneficence) but rather a claim to be applied under special circumstances (specific beneficence). According to them the principle concerns

> *doing good and encouraging good life and balancing the possible benefit of an action against the possible harmful effects.*

Being a limited duty appears from the clarification below.

A person X has a certain duty to beneficence towards person Y if and only if the following conditions are met:

- Y risks a considerable loss or ruining of life and health or loss in relation to other important interests
- X's action is necessary (alone or with others) to prevent this loss
- X's action has high probability of preventing it
- X's action does not imply decisive risks, costs or burden to X
- The benefits of Y may be expected to counterbalance all damage, costs and burden which X will most likely incur.

Apparently, it does not really differ from the principle of non-maleficence as beneficence consists of preventing negative events. In addition to this, the word beneficence primarily implies the positive aspect of contributing to making somebody else's life a good life. It is a difficult issue: "a good life". But in the context of the health care system one could say that good life is at least a life in good health. After all, the overall objective of the health care system is to provide people with the blessing of good health.

However, in the definition of beneficence it is clear that conflicts may easily arise between this principle and autonomy. If the doctor suggests a treatment from which he rightly expects a beneficial effect but the patient refuses, the respect for self-determination forces the doctor to act against the principle of beneficence. The same naturally applies to non-maleficence where a typical example is Jehovah's Witnesses' refusal of blood transfusions.

Justice

Justice may have different meanings: In case of justified punishment it is a question of retributive justice. However, Beauchamp and Childress talk of distributive justice, i.e. a principle of "how social burdens, benefits, and positions ought to be allocated" (Beauchamp & Childress 2001, p. 225) (10). The two authors do not provide a final formulation of a principle of justice. But the principle presented by them aim at

ensuring a fair distribution of all basic benefits and burdens.

Fair means that it does not depend on undeserved properties if a person receives social benefits or is denied receiving them. It is not fair if children are excluded from education because of the colour of their skin.

The principle of distributive justice, however, raises many questions: What are basic benefits and what is a fair distribution? Most people will agree that health/medical care are basic benefits and the same applies to education. But what is fair: A completely fair distribution, a distribution according to needs, dignity, one's deserts or market forces?

In relation to the health care system the claim for distributive justice emerges in two different ways: Firstly in terms of the question of the organisation of the health care system. As the health care system is mainly a public, tax-financed system with equal access, it may be justified on grounds of justice in terms of equal right to necessary treatment. Secondly, there is the question of justice in connection with prioritising of resources. Everybody has access to health care services. But if these services do not comprise treatment of a rare disease, is it then fair to the people suffering from this disease?

It is important to realise that the four principles are not a complete and closed system to be used more or less mechanically. Even though it is maintained that it concerns the most basic ethical principles, it cannot be ruled out that other principles should be included. In the bioethical discussion, referral is often made to the human dignity principle and it may be discussed, if it is an independent principle not included in or covered by the four principles.

The wording of such a principle of dignity is, as mentioned, already expressed by Immanuel Kant. The basic idea is that the human being preserves a dignity in his own person which is not to be belied. Reification of human beings, e.g. slavery or traffic in human beings, is a typical violation of such a principle of dignity. Dignity is often considered the basis of human rights. In a modern version, these rights have been formulated on the basis of the Nazis' "crimes against humanity". An example of these crimes was the doctors' use of concentration camp prisoners for medical experiments. The dignity of the prisoners was violated as they were treated as experimental animals.

Furthermore, it should not be ignored that the wording of the principles is not final. An important part of a concrete ethical analysis is to find an adequate wording in the specific situation. This is discussed in detail under Method (Section 2.6).

2.5 Ethics and economy

One of the overall issues arising when introducing ethics in HTA in a comprehensive way is the relationship between the ethical and economic analysis. This appears from the mentioned draft INAHTA report – "What is the role of the economic models that are applied in the calculations of cost-effectiveness?" (Andersen 2003, p. 10) (11).

The ethical analysis may include an element of balancing or calculation. As it has appeared, Beauchamp and Childress' principle of beneficence implies that the positive consequence for the opposite party must outweigh any negative consequences for the one showing beneficence (10). The more such a balancing resembles a direct quantitative comparison, the more the ethical analysis resembles an economic way of thinking.

A strong tendency as regards the economic aspect lies in the notion *quality of life*. This notion is characterised by a certain paradox. Originally, it was introduced as a counterweight to a quantitative, materialistic perception of life. Offhand, quality seems to be a counter notion to quantity, nevertheless quality of life is increasingly used as a measure. In a way the notion quality of life replaces the classical ethics of good life or happiness. As the meaning of a good and happy life becomes more and more individual and subjective, the issue of a common goal for the good life emerges. The idea is that no matter how the individual defines good life, it may be assessed as a measure of quality of life and compared to the lives of others (cf. Section 5.4.1).

An actual quantification is available with the so-called QALY (Quality Adjusted Life Years, see Section 9.6.2): Numerical values are applied to the "benefits" of a certain treatment in terms of gained life years with a given quality of life. It thus becomes possible to perform an assessment of the most effective use of resources.

The quantification of quality of life and the use of QALY, however, give rise to basic ethical issues. Is it at all legitimate to quantify good life? It is true that we use the language so that we can say that we feel much better today than yesterday. But it does not necessary mean that we can indicate how *much better* we feel. Does it really make sense to compare one's life with the lives of others and say that one lives a better life? The problem is that good life is interaction between "objective" factors such as materiel prosperity, health, mobility etc. – and the individual's attitude to his/her life. That attitude will depend on view of life, e.g. religious persuasion. If an individual believes that his/her life is "in the hands of God", this person will consider it meaningful almost no matter how miserable life is according to "objective" categories. These questions do not necessarily imply a rejection of the inclusion of quality of life in economic calculations, but may require careful handling.

Another question is whether the most efficient use of resources is always the fairest solution (see Section 2.4).

2.6 Method

After the initial, general introduction to ethics follows a description of what an ethical analysis may look like within the framework of an HTA. Parallels are drawn to some of the phases in an HTA. The main emphasis will be laid on the use of the four principles.

Planning

The ethical issue may be defined so broadly that it does not only concern the use of the assessed technology but also the assessment as such, i.e. the HTA. In the INAHTA report it is emphasised that even the prioritisation of issues for the technology assessment has ethical implications (11). Furthermore, the report includes various examples of questions for the ethical analysis of which the following concern the assessed technology (11):

- What are the reasons that this technology is selected to be assessed?
- What are the interests of the persons participating in the technology assessment?

It is natural to consider these and similar questions during the planning phase, where the HTA project and the HTA group have still not been defined.

In this phase it will also be appropriate to attempt to get a preliminary overview over possible ethical problems with the technology. It should be clarified if it is an ethically controversial technology and it should be decided if an ethicist should be involved.

Initial delimitation of ethics

When the project has been formulated and the group has been set up, a preliminary wording of the ethical issues should be provided. It is an advantage if the group agrees on this wording. The wording may be characterised by an

identification of ethically relevant characteristics.

Ethically relevant characteristics mean the characteristics that give rise to ethical questions and considerations. "Ethically relevant" does not imply an assessment; it is neither positive nor negative, for instance screening for abdominal aorta aneurism. Here, it is relevant that a screening will lead to the detection of a number of cases with a fatal outcome if they remain undetected, but it is also ethically relevant that treatment of detected cases may have a fatal outcome.

The group should agree on how to analyse the problems.

Analysis on the basis of the principles

The actual ethical analysis will make use of the four principles. Firstly, the following should be performed

a presentation of the ethical problems.

The presentation of the ethically relevant characteristics is followed by an explanation of the ethical problems attached to such characteristics. This account is based on the literature on the subject. The presentation is also descriptive in the sense that it describes the problems discussed in the literature.

This is followed by

the ethical assessment.

The last part of the discussion of the ethical aspects is *the ethical assessment.* Here, the four principles really come into the picture.

Beauchamp and Childress mention two important procedures when using the principles in specific analyses: specification and balancing (10).

Specification has to do with the principles being formulated in rather general terms. The principle of not causing harm is a prohibition on several kinds of actions and interventions. Specification implies finding a more adequate wording of a principle covering the specific situation being analysed. The prohibition on killing other people is an example of such a specification. The rule of "avoid causing harm" is another. That

rule in particular shows an important quality of the principles: None of the principles are absolute, they are, all other things being equal, *prima facie*. But if pain cannot be avoided at major life-saving surgery, all other things are not exactly equal. Pain is a minor evil compared to the good result.

Balancing is necessary due to another important characteristic of the principles: They are coordinated. As mentioned, the principles may be conflicting, which necessitates balancing. Balancing means that the different relevant principles are balanced and it is decided which one carries the greater weight under the circumstances. If a doctor has to decide whether a minor of a Jehovah's Witnesses is to have a blood transfusion, the parents' surrogate self-determination conflicts with the principle of beneficence. The child can be saved if the parents' decision is disregarded. If the doctor acts in this way, (s)he considers the principle of beneficence as carrying the greater weight.

It can be discussed if the ethical assessment should result in a concluding attitude to whether the technology in question is ethically justified. An argument against it could be that the HTA should form the basis of a decision of adoption but not as such make the decision. On the other hand, it seems natural that a normative analysis of ethical problems is carried out to a conclusion. Such a conclusion can never be absolute or final. It is impossible if only for the reason that the balancing of the principles is based on discretion.

It may be useful to draw the decision-makers' attention to the problem of justice, which is always connected with the use of economic resources on initiatives in the health care system. The chosen decision is always a choice be rejection of other possibilities.

2.7 Example: Caesarean section without clinical indication

In 2005, the National Board of Health carried out an HTA concerning caesarean section by maternal request which included an ethical analysis besides the conventional areas of analysis (technology, patient, organisation, economy) (12).

The *ethically relevant* part of the problem is that there are usually two different ways of terminating a pregnancy and bringing a child into the world within the framework of the health care system: The traditional "natural" childbirth (vaginal birth) – or caesarean section (birth by surgery). The current opinion and policy of the health care system has been that caesarean sections are only carried out on medical/clinical indication. The question is, however, if caesarean section may be chosen solely on the grounds that the pregnant woman wants it.

For the sake of clarity an ethical analysis of each of the two ways is performed at first.

1) Ethics in the clinical indication
A differentiation can be made between two types of clinical indications for caesarean section; a traditional and "extended" indication. In the traditional clinical indication either the woman or the child is in danger – or vaginal delivery is impossible. In the extended clinical indication there is a health risk for the mother or the child. In both cases the clinical indication for a caesarean section is due to a marked/significant risk for the mother and/or the child in vaginal delivery.

Offering caesarean section in these two types of indications is based on ethics. There is a duty according to the classic medical-ethical principle: *Avoid harm* (non-maleficence). Traditionally, caesarean section is exactly the chosen alternative when the "natural" birth implies a risk of harm to either the mother or the child.

It could also be said that any kind of health service in connection with the termination of a pregnancy is based on the positive principle: *The duty to do good / help* (beneficence). The health personnel and the health care system play the ethical part and there is a general duty to act in such a way that it is of most benefit to the patient. The best solution is chosen on the basis of a balancing of benefits and risks.

It is important to realise that the health professionals have two "patients"; mother and child / children. Furthermore, the child is the weak part.

2) Ethics in caesarean section on maternal request / without clinical indication
As evident from above, the risk of injuries to the child or the mother is decisive for carrying out a planned caesarean section. However, there is a continuous scale of risks which makes it impossible to distinguish clearly between caesarean section as a right and caesarean section on request. In case of caesarean section on maternal request, two different types of situations are essential. One is where there is no medical justification for a planned caesarean section, but where previous birth experiences worries the woman. The risk of physical problems when attempting a vaginal birth is not or only slightly increased compared to normal first-time births. Here it is a question of *non-medical indications for a planned caesarean section.* The other is, where the woman is healthy and has not previously experienced problems with either pregnancy, birth or maternity leave. The risk of attempting a vaginal birth is estimated to be at the same level or less as normal first-time births. Here it is *not* a question of *identifiable indications* for a planned caesarean section.

Ethically it is a question of what is dictated by the woman's *autonomy*. Autonomy means self-determination and implies that the individual has a right to decide in matters concerning her own person and her own life. Self-determination means that the individual is free to decide but this may mean two different things:

- A person makes a free decision when (s)he is not under constraint.
- A person has a free choice meaning that (s)he may choose between two or more possibilities without limitations.

The principle of autonomy is a good example of ethical qualifications in the public health legislation. It appears from the following wordings in the *Danish Act on Legal Status of Patients.*.

Self-determination

Informed consent

Section 6. No action shall be initiated or continued without the patient's informed consent unless otherwise implied in legislation or provisions according to Act or in Sections 8-10. Subsection 2. The patient shall be entitled to withdraw his/her consent at any time according to subsection 1.

Subsection 3. In this Act informed consent shall mean consent given based on satisfactory information from the health care staff, cf. Section 7.
Subsection 4. An informed consent according to this Part can be written, oral or, according to the circumstances, implicit.
Subsection 5. The minister of health shall lay down detailed provisions about the form and contents of the consent.

Section 7. The patient shall be entitled to receive information about his/her health status and treatment options, including risks of complications and side effects.

Subsection 2. The patient shall be entitled to decline information according to subsection 1.
Subsection 3. The information shall be provided on an ongoing basis and shall provide an understandable presentation of the disease, the examination and the intended treatment. The information shall be presented in a considerate fashion and shall be conditioned to the recipient's individual prerequisites in view of age, maturity, experience, etc.
Subsection 4. The information shall include details about relevant prevention, treatment and care options, including details about other medically justifiable treatment options as well as information about the consequences if no treatment is implemented. The information shall be more comprehensive when the treatment involves immediate risk of serious consequences and side effects.
Subsection 5. Is the patient otherwise perceived to be ignorant of circumstances of importance for his/her decision, cf. Section 6, the health care person shall inform especially about such matters, unless the patient has declined to receive the information, cf. subsection 2.
Subsection 6. The minister of health shall lay down detailed provisions about the form and contents of the information.

It appears explicitly that the principle of respect for self-determination motivates two rights of a patient: the right to give informed consent and the right to information about health and possibilities of treatment (13).

The two rights are connected in the way that the second right is a prerequisite for the first right. A distinction is thus made between two elements in the informed consent as an expression of self-determination: the element of information where the understanding of the patient is decisive – and the free decision as such. The emphasising of the importance of information may be interpreted as an expression of a freedom of choice in the health care system, which is not unlimited or unqualified for the patient but rather freedom to make decisions on a somewhat defined basis. One could say that the informed consent is normally authorisation to perform an intervention suggested by the health personnel. Naturally, the informed consent also implies the right to reject such a suggestion or offer.

The important question is whether the right to self-determination includes the right to caesarean section in cases where the risk in vaginal birth is very limited. The question may also be formulated as whether caesarean section should still be considered the type of delivery requiring reasoned justification. If this is the case, the woman's informed consent is of a special nature. She is not to or cannot decide in favour of or against a kind of treatment since she cannot opt out of vaginal birth with good reason. If, however, the perception of caesarean section changes so significantly that it does not require reasoned justification, it is a question of choosing between tow equal possibilities of treatment. In this case, however, the nature of self-determination changes so that it is not a right to make an informed decision on a suggested kind of treatment but a claim for a free choice between to kinds of treatment.

Various circumstances speak in favour of the traditional "precedence" of vaginal birth. In favour of the maintenance of the traditional preference for vaginal birth is the fact that it follows the physiology of pregnancy. Furthermore, for many women the planned vaginal birth will be an experience beyond normal limits – perhaps the greatest experience ever.

There is thus still good reason to consider the planned vaginal birth as the preferred way of terminating a pregnancy. Caesarean section requires a special reason, i.e. that vaginal delivery is linked to an increased risk for mother and child. If this is not the case, we cannot speak of a mother's *right* to a caesarean section, but we can speak of a mother's *request*. Such a request does not itself require the health care system to accommodate it, but health professionals may in the concrete situation agree that the reasons cited for the request make a caesarean section the best choice. If, however, the woman is not able to cite such non-medical indications it would be ethically justifiable to refuse the request.

It is, however, important to maintain the element of information in the relationship between the pregnant woman and the health professionals. The aim must be to make the pregnant woman understand that vaginal delivery is the right choice. No one can guarantee that such an understanding may be obtained. Therefore, it is not possible to answer the question unambiguously, if a woman's request may also be complied with in this type of situation.

The principle of autonomy thus places only a limited amount of the decision competence with the woman when it comes to the choice between vaginal delivery and caesarean section. It is, therefore, very important that the right information is given and that it is given in the right form. The information should be characterised by support from the health personnel. Such support cannot be called paternalism but may on the other hand support a joint decision, e.g. by removing fear and insecurity.

2.8 Literature for Chapter 2

(1) National Board of Health. Medicinsk Teknologivurdering – hvad er det? [Health technology assessment – what is it?] Copenhagen: 1984.

(2) Danish Institute for Health Technology Assessment. Medicinsk Teknologivurdering. Hvorfor? Hvad? Hvornår? Hvordan? [Health Technology Assessment. Why? What? When? How?] Copenhagen: Danish Institute for Health Technology Assessment; 2000.

(3) EUR-Assess Project. EUR-Assess Project Special Section Report. Int J Technol Assess Health Care 1997;13:133-340.

(4) Ingerslev HJ, Poulsen PB, Højgaard A, Andersen S, Kølvrå S, Hindkjær J, et al. Pr æimplantationsdiagnostik – en medicinsk teknologivurdering. [Preimplantation diagnostics – a health technology assessment]. Copenhagen: Medicinsk Teknologivurdering – puljeprojekter. [Health technology assessment – pool projects.] 2002; 2(1).

(5) Reuzel R, et al. Ethics and HTA: some lessons and challenges for the future. Poiesis & Praxis 2004;2:2-3.

(6) Andersen S. Etiske aspekter ved MTV [Ethical Aspects of HTA]. In: Kristensen FB, Sigmund H, editors: MTV, sundhedstjemesteforskning og klinisk praksis. [HTA, health science research and clinical practice.] Copenhagen: Danish Health Science Research Board and Danish Institute for Health Technology Assessment; 2000. p. 51-57.

(7) Birkler J. Etik i sundhedsvæsenet. [Ethics in the health care system.] Copenhagen: Munksgaard Danmark; 2006.

(8) Andersen S. Som dig selv. En indføring i etik [Just like yourself. An introduction to ethics]. 2nd ed. Århus: Aarhus Universitetsforlag; 2003.

(9) Jensen KK, Andersen S. Bioetik [Bioethics]. Copenhagen: Rosinante; 1999.

(10) Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 5.th ed. Oxford: Oxford University Press; 2001.

(11) Andersen S, et al. INHATA's Working Group on Handling Ethical Issues. 2005; Final Report.

(12) National Board of Health. Centre for Evalutation and Health Technology Assessment. Kejsersnit på moders ønske – en medicinsk teknologivurdering. [Caesarean section at the mother's wish – a health technology assessment.] Copenhagen: Medicinsk Teknologivurdering [Health Technology Assessment]; 2005; 7(4).

(13) National Board of Health. Vejledning om information og samtykke og om videregivelse af helbredsoplysninger mv. [Guide on information and consent and on the disclosure of health details etc.] Copenhagen:1998;161.

3 Literature searches

By Drea Eskildsen Stenbæk and Malene Fabricius Jensen

This chapter comprises guidelines on correct literature searches, in which every step in a search is examined closely. Specific instructions and information are provided on data sources. The guidance is provided in general terms, i.e. it applies to all types of studies, both qualitative and quantitative, and concerns all HTA aspects. The later chapters on technology (Section 6.4.1), patient (Section 7.1.2.6), organisation (Section 8.4), economy (Section 9.12) and measurement of health status (Section 5.4.3) provide additional sections with specific information on literature searches concerning the aspect in question.

Useful advice and suggestions

- Use a search protocol
- Formulate focused questions that can be answered
- Involve an information specialist/librarian in literature searches
- Choose relevant databases and information sources
- Draw up search strategies (with a separate strategy for each source)
- Evaluate searches
- Return repeatedly to the question focused on.

3.1 Introduction

A health technology assessment is based, to a great extent, on existing knowledge from published and unpublished studies, with a view on documenting results and substantiating conclusions and recommendations. The incorporation of literature-based documentation is nevertheless conditioned by the literature in question being searched and assessed systematically and the use of internationally recognised methods for searching and assessment.

The systematic approach means that:

- the literature is identified in accordance with an explicit search strategy (Sections 3.2 – 3.5)
- the literature is selected on the basis of defined inclusion and exclusion criteria (Section 3.3.3)
- the literature is assessed using recognised methodological standards (Chapter 4).

3.2 Planning of searches

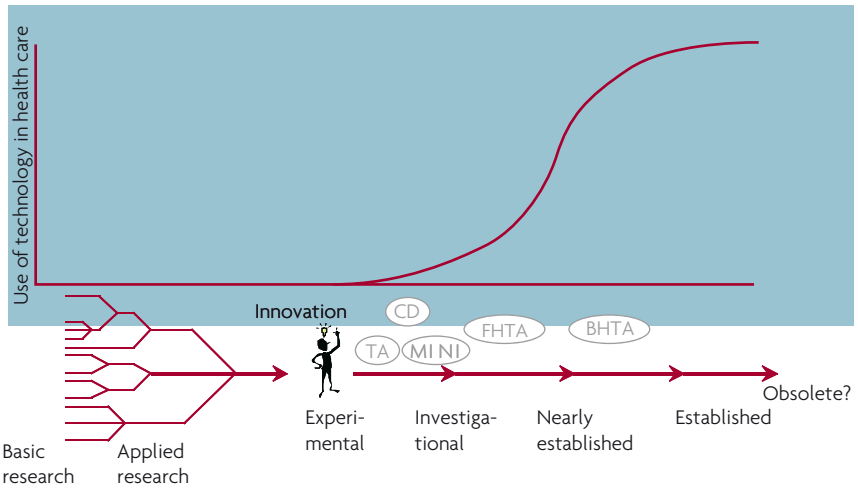
The formulation of problems and the definition of HTA questions are carried out by the project team. Many hospital libraries and university libraries have access to payment databases. The selection of resources for elucidating the question can often be carried out advantageously by an information specialist/librarian who is familiar with the various databases and knows how to search the individual databases. Planning and implementation of the literature search should, however, always take place in close collaboration with the project team.

Before searches of the literature are initiated, the search process must be planned so that the object, scale and time horizon of the search is clear both to the party who is to

undertake the search (the literature searcher) and to the party commissioning the literature search (the project team).

A number of factors concerning the actual HTA are important in selecting literature search strategies, e.g. whether a new or well-known (and used) technology is involved, and in what kind of HTA the search is to be incorporated (Figure 3.1).

Figure 3.1. Life cycles of technologies and HTA products



Note: TA = Technology Alert (early warning); MINI = Mini-HTA; CD = Cancer Drug HTA; FHTA = Focused HTA; BHTA = Broad HTA; (see Section 1.2.4).

Generally, it can be said that the older a technology is the more studies may be expected to be identified by the literature search, and the more resources it will therefore take to examine, select and assess the literature.

Once the choice of HTA products has been made, it is time to consider what kind of studies will probably give the greatest return on the effort made, and in which sources these studies can be identified. The following diagram of HTA products and search approaches (Table 3.1) can be taken as the basis for this.

Table 3.1. HTA products and search approaches

HTA product	Start with search for ...
Technology alert (early warning)	Primary studies*
Mini-HTA	Secondary or primary studies**
Cancer drug HTA	Primary studies
Focused HTA	Secondary studies*
Broad HTA	Secondary studies

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

** In the case of new technologies: start with searching in primary sources. In the case of known technologies with a new indication: start with searches of secondary sources.

An essential part of the planning is the formulation of a search protocol, which is used both during and after the literature search (for documentation).

3.3 Formulation of search protocol

As part of the literature search process, it is a good idea to formulate a *search protocol*.

The search protocol is an explicit, structured plan for the collection of information.

The search protocol is designed to provide an overview and transparency of the process concerning the collection of information.

The search protocol documents in a *detailed and transparent* way *what* is searched for, *where* the search is carried out and *how* searching and selection are undertaken. The search protocol helps ensure consistency in the follow-up/repetition of the search, and must be so detailed that, by following the description, the search can be performed again and the same results obtained. In other words, the search protocol must contain information on not only how *it has been intended to search the literature*, but also how the search has actually *been conducted*.

The search protocol should contain the following elements, cf. Table 3.2:

- Background and presentation of the problem
- Focused questions
- Inclusion and exclusion criteria
- Information sources (databases, internet pages, etc.)
- Search strategy and results for each information source
- Strategy for reviewing and selecting the literature found.

The individual elements are described in more detail in the following sections.

Table 3.2. Examples of search protocols (extract)

Presentation of the problem:
What is the expected impact of early detection of disease in age-related screening of colorectal cancer?

Focused questions:
1) What is the mortality reduction in colorectal cancer from faecal blood screening in adults?
2) What psychosocial factors are important for the rate of participation in a screening programme?

Inclusion and exclusion criteria:
Inclusion criteria: literature from 1990-2005
Exclusion criteria: animal experiment-based studies

Information sources, search strategies and results:
A) What is the mortality reduction in colorectal cancer from faecal blood screening in adults?

Medline (SilverPlatter WEBSPIRS), 26 September 2005:
1) colorectal cancer or bowel cancer or explode colorectal neoplasms/all subheadings (60249)
2) screen? or early detection (46451)
3) mortality or death? or survival (626993)
4) fecal occult blood or faecal occult blood (1208)
5) 1 and 2 and 3 and 4 (91)
6) 5 and (py=1990-2005) (88)

B) What psychosocial factors are important for the rate of participation in a screening programme?

PsycINFO (SilverPlatter WEBSPIRS), 28 September 2005:
1) "Cancer-Screening" in MJ, MN (738)
2) (colorectal cancer or bowel cancer) and screening (121)
3) 1 or 2 (770)
4) explode "Compliance" in MJ, MN (5413)
5) "Client-Participation" in MJ, MN (556)
6) acceptability or acceptance (13769)
7) 4 or 5 or 6 (19520)
8) 3 and 7 (58)
9) 8 and (py=1990-2005) (58)

3.3.1 Background and presentation of the problem

The literature search is based on the individual HTA's presentation of the problem. It is important to remember in this context that the literature search must cover all relevant aspects, and that the sources will differ from one element of an aspect to another.

Questions to be elucidated in the search are clarified – including specification of the starting point for the search (e.g. disease, diagnostic method, treatment), and in what contexts the subject is to be investigated.

An example may be the elucidation of the effects and side effects of a given method of treatment. Another example may be the review of methods for preventing late complications of a given disease.

Often, an introductory search could help specify the presentation of the problem in the actual HTA (cf. Section 1.2.3). The subsequent searches are based on the final presentation of the problem and must also elucidate aspects of the HTA (cf. Section 1.4).

3.3.2 Formulation of focused questions

The starting point for the search is the health problem which the search is intended to enlighten. In formulating the presentation of the problem, it is important that the task is delimited clearly. The questions asked must be clear in terms of number, clearly defined and possible to answer. A well-formulated question is crucial in establishing the best search strategy – the more precise the questions, the more precise the searches (see examples in Table 3.3). In this context, it is important to bear in mind that it is also possible to formulate questions that can be answered in the case of presentations of *non-clinical* problems.

A well-formulated clinical question comprises four elements:

- The population – what kind of patients are involved?
- The intervention – diagnostic testing, pharmaceutical, surgical method, etc.?
- The comparative intervention – what is the alternative to the intervention?
- The result/outcome – what clinical endpoints are involved?

Table 3.3. Examples of well-formulated questions

Technology
- What postoperative complications are observed after laparoscopic hysterectomy compared with vaginal and abdominal hysterectomy in women with benign gynaecological disease?
- What effect does the use of lifestyle consultations in general practice have on preventing the development of lifestyle diseases?

Patient
- What ethical, psychological and psychosocial consequences are associated with screening for cancer of the colon and rectum?
- What factors influence the scale of lifestyle changes that can be achieved in patients with newly diagnosed type 2 diabetes?

Organisation
- How many extra specialists/specially trained nurses will be needed nationally to introduce a screening programme for cancer of the colon and rectum?
- What specialist groups take best care of information, teaching and motivation for treatment and follow-up in relation to more intensive use of pharmaceuticals for type 2 diabetes?

Economy
- How high are the total direct costs of ongoing monitoring and pharmacological therapy of type 2 diabetes?
- What economic costs are associated with preimplantation genetic diagnosis (PGD) compared with prenatal diagnosis (PND) in the diagnosis of hereditary diseases?

The clinical questions can be advantageously drawn up in diagrammatic form, as this example shows, cf. Table 3.4:

Clinical questions concerning status epilepticus: What is the evidence that acute treatment of prolonged isolated seizures or seizure clusters with benzodiazepines reduces 1) the number of casualty ward visits or 2) the frequency of generalised tonic clonic convulsions or 3) the development of status epilepticus?

Table 3.4. Example of diagram concerning focused questions

Population	Intervention	Alternative	Result/ outcome	Search terms
Adults with epilepsy and prolonged isolated seizures or seizure clusters	Acute therapy with benzodi-azepines	No medical therapy	Number of patients with status epilepticus or number of casualty ward visits	Seizure cluster, status epilepticus, benzodiazepines, prolonged seizures, emer-gency room, tonic clonic seizures

3.3.3 Inclusion and exclusion criteria for the search

What criteria should underpin the selection of the studies found, so that they can be included in the HTA? By defining inclusion and exclusion criteria before embarking on searches, a search result that is more precise and clearer in numerical terms can be achieved because criteria can be built into the search strategy (Table 3.5).

Table 3.5. Examples of inclusion and exclusion criteria

- Should only a particular age group be included?
- Are both clinical and animal experimental studies relevant?
- Should only patients with particular courses of disease be included?
- Should only men or women be included?
- Is only literature from a particular period wanted?
- What study design should be included (e.g. randomised clinical trial, meta-analyses, cohort studies)?
- Can literature from particular geographic areas or in particular languages be excluded?

3.3.4 Choice of information sources

Two types of studies are used to answer the questions focused upon, namely *secondary studies* and *primary studies*.

Secondary studies are systematic reviews and assessments of published material, e.g. HTA reports, clinical guidelines and systematic reviews.

Primary studies are the individual scientific primary articles in the form of, for example, randomised clinical trials or cohort studies.

The first step in the literature search is usually to identify the secondary literature, see Table 3.6. If, for example, there are already foreign HTA reports, Cochrane reviews or clinical guidelines which systematically assess the primary literature and synthesise within the relevant area, there is no reason to repeat this large-scale task, which is very demanding in terms of resources.

If the secondary literature cannot answer the questions focused upon, or there is a need to update the literature, the primary literature is searched, cf. Table 3.7.

Table 3.6. Sources for the identification of secondary studies – examples

- The national project database for HTAs and evaluation: www.dacehta.dk
- The HTA Database: http://www.crd.york.ac.uk/crdweb/
- HTA institutions' website, see www.inahta.org
- Cochrane Database of Systematic Reviews. The Cochrane Library can be accessed via: www.Cochrane.org
- Database of Abstracts of Reviews of Effects (DARE): part of The Cochrane Library: http://www.crd.york.ac.uk/crdweb/
- Guidelines International Network (G-I-N): www.g-i-n.net
- National Guidelines Clearinghouse: www.guideline.gov
- Health Evidence Network (HEN): http://www.euro.who.int/hen
- National Electronic Library for Health: Guidelines Finder: http://rms.nelh.nhs.uk/guidelines-finder/
- Turning Research Into Practice (TRIP+): http://www.tripdatabase.com/

Table 3.7. Sources for the identification of primary studies – examples (*=payment database)

The technology

- CENTRAL (Cochrane Central Register of Controlled Trials): part of The Cochrane Library
- Medline free edition (PubMed): www.ncbi.nlm.nih.gov/pubmed
- Embase*
- CINAHL* (Cumulative Index to Nursing and Allied Health Literature)
- PsycINFO*
- PEDro (Physiotherapy Evidence Database): http://www.pedro.fhs.usyd.edu.au/index.html
- AMED* (Allied and Complementary Medicine Database)
- Science Citation Index*
- Pharmaceutical companies' web sites

The patient

- PsycINFO*
- Sociological Abstracts*
- Medline free edition (PubMed): www.ncbi.nlm.nih.gov/pubmed
- Embase*
- Social Sciences Citation Index*
- The Campbell Collaboration: http://www.campbellcollaboration.org/frontend.aspx
- The patient associations' (in Danish): http://www.netpatient.dk/patientforeninger.htm
- The Danish Council of Ethics: http://www.etiskraad.dk/sw293.asp
- Faculty of Pharmaceutical Science: http://www.farma.ku.dk/index.php?id=2
- Article search (bibliotek.dk): http://bibliotek.dk/?lingo=eng

The organisation

- DSI's library catalogue (in Danish): http://www.dsi.dk
- Center for Health Management: http://uk.cbs.dk/chm
- Medline free edition (PubMed): www.ncbi.nlm.nih.gov/pubmed
- The Copenhagen Business School's databases: http://uk.cbs.dk

The economy

- NHS EED (NHS Economic Evaluation Database): http://www.crd.york.ac.uk/crdweb/
- DSI's library catalogue (in Danish): http://www.dsi.dk
- Embase*
- Medline free edition (PubMed): www.ncbi.nlm.nih.gov/pubmed
- HEED* (Health Economic Evaluation Database)
- EconLit*

Searches of the bibliographic databases may often be supplemented with information found in the "grey literature", which covers material that is typically not recorded in bibliographic databases. This concerns, for example, conference abstracts, reports (e.g. from scientific societies, hospitals/wards, pharmaceutical companies and patient associations), unpublished studies (e.g. ongoing clinical trials) and specialist/personal networks.

3.3.5 Formulation of search strategy

Based on the questions focused upon, a search strategy is formulated. In this context, it is important to bear in mind that *the various databases require their own search strategy* as they each have search languages of their own.

Searches of bibliographic databases must be based on a detailed search strategy in which it is defined in advance how the database in question is to be searched: what search terms are to be used, and how these words are to be combined to make the search as precise and comprehensive as possible. All this information is set aside during the process – see Section 3.5 on documentation of the literature search.

To be sure to include all relevant studies, the following must be done:

- use relevant synonyms (search, for example, on colorectal cancer and bowel cancer)
- truncate so that the various inflexions and structures of a word are included (e.g. search on pregnan* to find pregnant, pregnancy and pregnancies). Note that the truncation sign may differ from one database to another
- search on controlled key words (subject headings) in addition to free text (e.g. there are controlled subject headings for colorectal cancer that are identical to "colorectal neoplasms" in the Medline database).

The advantage of searching on controlled key words is that this catches studies employing terms for what one is searching for and not just the ones one could think of. This is because all studies that deal with the same thing (e.g. colorectal cancer) are always assigned the same controlled key words (in this case, colorectal neoplasms), regardless of which term the authors have chosen to employ.

As the controlled key words are built up as a hierarchy with higher-level, lower-level and same-level terms, it is also possible to "explode" a term, i.e. search on the chosen term at the same time as catching studies containing terms at a lower level from the chosen term. If, for example, the term "colorectal neoplasms" is exploded, studies that, for example, deal with sigmoid neoplasms and anal neoplasms are also caught because these terms are at a lower level from colorectal neoplasms. These are studies which are not caught by searching (free text) on colorectal cancer or bowel cancer (unless, of course, these words are also mentioned somewhere in the studies). Note that different databases have different controlled key words.

Once one's search terms have been defined, it is decided how the terms should be combined (AND, OR, NOT, NEAR, NEXT, ADJ, WITH, etc.). It should be noted again that the options differ in the various databases.

Example of structure of a search strategy:

Focused question: what is the mortality reduction in colorectal cancer from faecal occult blood screening in adults?

Synonyms:
colorectal cancer, bowel cancer
screening, early detection
mortality, death, survival
Truncation:
screen*, death*
Controlled key words:
colorectal neoplasms [MeSH]

Combination of search terms:
1. colorectal cancer OR bowel cancer OR explode COLORECTAL-NEOPLASMS/all subheadings
2. screen* OR early detection
3. mortality OR death* OR survival
4. 1 AND 2 AND 3

A number of ready-made search filters for use in various databases are available for searching for certain aspects of a subject, such as diagnosis, therapy and prognosis. This applies also to certain study designs such as meta-analyses, systematic reviews and randomised clinical trials.

The search filters consist of specially formulated search strategies, which can be "linked" to one's subject search so that the result is limited to studies that deal with the desired aspect or meet the requirement of a certain study design (Table 3.8).

Table 3.8. Examples of search filters

- Search Strategies to Identify Reviews and Meta-analyses in MEDLINE and CINAHL (Centre for Reviews and Dissemination (CRD)): http://www.york.ac.uk/inst/crd/search.htm
- The InterTASC Information Specialists' Sub-Group: Search filters resource http://www.york.ac.uk/inst/crd/intertasc/index.htm
- PubMed Clinical Queries: http://www.ncbi.nlm.nih.gov/entrez/query/static/clinical.shtml

3.4 Evaluation of searches

Once a search has been completed, it is checked whether what one has been looking for has been found. If a known (and preferably relatively recent) article on the subject concerned was at hand before the search, this article can be used to check whether what was being sought has been found. If the article is not included in the search result, this may be due to the article being too new, or to the journal not being included in the database in question, and not necessarily to the search being insufficiently precise.

If, on the other hand, the article is in the database (but not in the search result), one must go back and revise one's search strategy. A good method is to use the key words assigned to the "good" article on registration in the database, to adjust one's search strategy.

3.5 Documentation of literature searches

Documentation of searches in sources that have yielded usable information and also sources that did not contain interesting information must be set aside and included in

the search protocol. It is therefore important that information on the following aspects is kept from each search:

- What sources have been used (databases, web sites, etc.)
- What period the search covers
- How the search has been conducted (what search terms have been used, in what fields, how the search terms have been combined)
- Date of the search.

3.6 Updating

Depending on the scale of the project (assessment of a broad or narrow, well-known or new technology) and the time horizon of the project (does the project go on for several years or a few months), the searches may need to be repeated. In some projects, it is sufficient to repeat the searches at the end of the data collection period; in other projects, the searches must be conducted at intervals of a few months. Regardless of how many times the searches are repeated in the course of the project period, it is important that the above-mentioned information is set aside for each search.

For in-depth information, see *E-text on Health Technology Assessment (HTA) Information Resources* (1)

3.7 Literature for Chapter 3

(1) Topfer LA, Auston L. Etext on Health Technology Assessment (HTA) Information Resources. Available at:
http://www.nlm.nih.gov/archive//2060905/nichsr/ehta/ehta.html

4 Assessment of literature

This chapter links up with Chapter 3 regarding literature search, and concerns the assessment of literature that has been acquired and subsequently selected. The chapter comprises a medical scientific as well as a humanistic approach. The first part of the chapter concerns an assessment of clinical and epidemiological studies based on well-known systematic methodology with checklists and evidence grading tables. The second part assesses qualitative studies, including the introduction of a new development area within qualitative research: Syntheses of qualitative studies. This is a tool which will promote the use of existing knowledge within qualitative areas in which primary investigations would traditionally have been initiated. Regarding terms reference is made to the introduction: About the Handbook.

4.1 Assessment of clinical and epidemiological studies

By Henrik Jørgensen

Useful advice and suggestions

- Primarily select the literature with the highest class of evidence
- Use the focused question when assessing whether the article is of relevance
- Use checklists in the review of the individual articles
- Use internationally recognised standards for the assessment of articles.

4.1.1 Why perform a critical literature assessment?

When the systematic and thorough literature search is completed, the result is often an immense quantity of material in the form of systematic reviews, meta-analyses, reviews (ordinary reviews that are seldom systematic), randomised controlled trials (RCTs) and a number of other published studies, with and without control groups. In order not to be overwhelmed by this vast quantity of literature and to avoid spending one's resources inappropriately, it is necessary to use a strict methodological approach to the literature. Even articles published in established journals by highly esteemed authors may contain errors or be misleading from the point of view of one's own requirement. In addition, articles whose heading claims to be a meta-analysis or an RCT may not live up to this and consequently be of inferior quality compared with other articles covering the same subject. It is therefore important to use a method for the assessment of the literature which is relatively objective and which can be reproduced and documented. For that purpose, check lists are a good aid to ensure that the objectives, design and method of the study are of a reasonable standard. It also makes it easier to compare different studies when they produce results pointing in opposite directions. Finally, in connection with the preparation of the report, it is a good tool for getting a quick overview of the literature reviewed (1).

Each article discovered during the literature search should be assessed:

- Is it of relevance to the subject?
- Are the results in the article reliable?
- How good is the quality of the evidence in the article?
- Are the results in the article important in the present context?

Why assess literature with a systematic approach?

- Easy to deselect inferior articles
- Possible to compare different article types (study design)
- Ensures a uniform evaluation in the working group.

4.1.2 The focused question

The focused question is a key concept which, during the entire process of preparing an HTA, helps maintain the right course (cf. Section 3.3.2). The focused question is the reflective clinician's specific problem, and it should include the following four elements: 1) population, 2) intervention, 3) alternative intervention, and 4) endpoint (outcome). In English literature these elements are often abbreviated to PICO: Patient/Problem, Intervention, Comparison and Outcome (2).

The focused question is the foundation of the work and provides the basis for (i) literature search, (ii) initial sorting of abstracts, (iii) the critical reading of the individual article and (iv) the final assessment of the quality of the evidence. With the focused question on the one hand and the individual article on the other, one has to ensure that the article looks as if it may answer the focus question. It is not always directly ascertainable from the heading – instead one has to look at the objective of the study (*aim*). Most journals contain the objective at the beginning of the summary. In the actual article the objective is often described at the end of the introduction just before the chapter about "Method". There is no need to waste time on assessing articles that do not answer the focus question.

The focused question is to be used once again when all relevant articles have been read and the draft has been written. It is important to check that the text confirms the original focused question. If this is not the case, it is necessary to start the literature search over again.

The focused question provides the basis for the following steps:

- Literature search
- Selection of abstracts
- Reading the articles
- Final text assessment.

4.1.3 Dividing the literature

If the literature search has resulted in a large quantity of material, it may be of use to subdivide this into groups according to the presumed quality, i.e. the design used in the article. Initially, the literature can be divided into two groups:

1) *secondary studies* (systematic reviews of previously published articles, i.e. meta-analyses, systematic reviews, Cochrane reviews, evidence-based clinical guidelines and evidence-based HTA reports, position papers, reviews and leading articles in journals) and 2) *primary studies* (the individual scientific articles independent of design. See review in Section 3.3.4).

The primary studies can be hierarchically subdivided into randomised controlled studies, controlled non-randomised studies, cohort studies, case-control studies, descriptive

studies and limited series (Table 4.1). Naturally, this is a broad division, and there may be cases where a large, successful cohort study has to be assessed as better than a smaller RCT (for RCT, please see Chapter 6). It is important to note that a "leading article" for instance, written by a prominent professor or a position paper prepared by a European group of experts are at the bottom of the literature hierarchy since these are seldom supported by a proper quantity of literature references and often are an expression of subjective views.

Table 4.1. Hierarchy of scientific literature

1. Meta-analyses and systematic reviews (amongst others Cochrane reviews)
2. Randomised controlled trials (RCTs)
3. Non-randomised controlled trials
4. Cohort studies
5. Case-control studies
6. Descriptive studies, limited series
7. Position papers, non-systematic reviews, leading articles, expert opinions

4.1.4 Quality assessment of articles

The wide variation in the quality of the articles within the individual literature groups, together with an inevitable subjectivity in different readers, makes it necessary to use a tool to perform a uniform assessment of the articles. For that purpose, different national centres within evidence-based medicine and preparation of clinical guidelines, for instance SIGN, NICE, GRADE and Centre for Evidence-based Medicine, Oxford, have made check lists which can be found on their websites (Table 4.2). The first link in Table 4.2 refers to Centre for Evidence-based Medicine University of Oxford, which has four lists for studies comprising meta-analyses, RCTs, diagnosis and prognosis. These lists are used by DACEHTA.

The website of the National Board of Health has five check lists from the Danish Secretariat of Clinical Guidelines (DSCG) with explanatory notes, so that even an inexperienced person can quickly use the check lists when reviewing an article (see for instance the meta-analysis check list (in Danish: http://www.sst.dk/upload/checkliste_1-2004.doc) (1).

When an important article is to be assessed, it is a good plan to let two readers assess the article independently of each other, and subsequently compare to the check lists, to ensure the objectivity in the hard cases.

Table 4.2. Links to websites with check lists

- http://cebmh.warne.ox.ac.uk/cebmh/downloads/education_resources/diagnosis.pdf
- http://www.nphp.gov.au/publications/phpractice/schemaV4.pdf (also includes lists for economic and qualitative studies)
- http://www.sign.ac.uk/guidelines/fulltext/50/annexc.html
- http://www.nice.org.uk/niceMedia/pdf/GuidelinesManualAppendixB.pdf
- http://www.sst.dk/Planlaegning_og_behandling/SfR/Vejledning.aspx?lang=da (in Danish)

4.1.5 Check list structure

Generally speaking, the check lists from NICE (National Institute of Clinical Excellence), SIGN (Scottish Intercollegiate Guidelines Network) and the DSCG are identical. The three types of check lists and most other check lists are structured in the same way. Usually the check lists are divided into three parts (Table 4.3).

Table 4.3. General check list structure

1. Reliability of the article
   Relevant problem
   Assessment of method
   Statistics
2. Overall assessment of the study
   Can be graduated using ++ / + / -
3. Description of the study
   Outcome, effect, population
   Summary of the study's key areas

4.1.6 Internal validity

It should initially be decided whether the article seems to confirm the focused question and whether it includes a well-defined and relevant problem. Many articles are eliminated in this step.

The method section of the article should give an indication of whether the selected study design is suitable for the one that is to be analysed. Correct choice of design is a very critical parameter and is consequently the next item on the check list (regarding study design, see Section 6.4.2). The selection of a good design ensures the best possible benefit from the study, the reduction of methodological sources of error and the feasibility of the study. Irrespective of the design of the study, methodological errors may occur. The type of sources of error depends on the selected method. Generally, there are three types of sources of error: bias, confounding and random errors.

Bias (influence) occurs when factors other than the actual intervention influence the subject groups to a varying degree, and hence the study outcome. It may be a question of selection bias where a poor design leads to certain types of patients or controls being recruited. It may be that there is a large dropout in a group during the study due to unpleasant side effects. In cohort and case-control studies it may be difficult to define the onset of certain diseases and to exclude the possibility that healthy controls could be ill. Finally, bias may occur due to inaccurate methods of measurement.

In order to reduce the risk of bias it is important that the only parameter differentiating the intervention group from the control group, is the actual intervention being studied. Consequently, there should always be a table at the start of the article indicating whether the two (or more) groups in the study are identical in respect of the selected relevant parameters, e.g. gender, age, disease stage, social status, ethnic origin or any competing disorders. If this is not stated, or if the groups differ, it is necessary to view the result with caution.

Concerning RCTs it is important that the study population has been randomised to e. g. active treatment or placebo. If this is not stated, the article has to be rejected. If it seems that the randomisation is inadequate, the result must been regarded with caution. If possible, patient, health care provider and researcher should be blinded to the allocation to the different groups and the subsequent treatment during the entire study. If the allocation is transparent, the treatment effect can be overvalued by up to 40% (3). If it is assessed that the randomisation is easily seen through, one has to be cautious of the study. A study may be single-blind (the patient is unaware of the intervention), double-blind (patient and health care provider are unaware) or triple-blind (patient, health care provider and researcher are unaware). In general it is said that the higher the level of blinding the lower the risk of bias.

If substantial results are omitted or, if they are not assessed correctly, there is a risk of a biased outcome. It is important that the applied methods of measurement are validated and applied consistently. All methods of measurement contain some uncertainty which should be minimised.

Especially for non-randomised studies (cohort and case-control studies), it is important to ensure that factors other than the intervention do not influence the result (confounding). Confounding may appear if the intervention group has more examinations or appointments than the control group. In studies of occupational or socially related diseases, it is important to take other external factors into account, e.g. environment, medicine, tobacco and other habits that are potential confounders.

The reliability of the study is questionable if a very large number of patients discontinue the study. In general, a dropout rate of 20% is considered acceptable; however, there may be large variations with higher rates in connection with long-term studies. It should be stated *why and how many* patients discontinued.

4.1.7 External validity

Even if the study has been carried out sensibly, there are often problems in connection with the data processing when the effect of the intervention is to be measured and interpreted. It requires much attention to identify such errors.

In many cases, some patients randomised to active treatment, neglect to take the agreed medicine or they leave the study during the course due to side effects, other diseases or other reasons. That way, the randomisation is lost and the group composition is changed. If the groups are still to be comparable following the randomisation, the results *must* be analysed according to the group into which the patients were originally randomised, irrespective of the actual treatment received. This principle is called *intention to treat analysis*.

To ensure that a study can demonstrate, with statistical significance, an actual difference between interventions, the sample size must be calculated.

Data presented in an article must be subjected to relevant statistical methods (4). It may be difficult to determine if this has happened if one has not acquainted oneself with basic knowledge about medical statistics. Comparable data must include confidence intervals. Confidence intervals express the random uncertainty 1) of a sample's representativity and 2) in the measurement of the size of the effectiveness (random error). This is much more informative than a simple *asterisk* indicating a "significant difference".

Even if a study is found to be s*tatistically* significant, it must be considered whether it also is an expression of *clinical* significance. With minor differences between the interventions, it is clearly not always the case that it is of importance for the patients' final outcome (e.g. survival or reduction of complication frequency). A new intervention or diagnostic method may be uneconomic, have many side effects or complications, be unacceptable to patients, or be difficult to implement at treatment centres due to technical obstacles.

Finally, it must be assessed whether the outcome is attributable to the "intervention" of the study, when clinical considerations, evaluation of the method and the statistical strength of the study are taken into account. Further, it must be assessed whether the

result of the study is directly applicable to one's own patient group. See Table 4.4 for a check list example.

Table 4.4. Example of check list for intervention studies

1. Is the problem well-defined and clinically relevant?
2. Were the subjects randomised?
3. Were the intervention and control groups identical at the start of the study?
4. Was the blinding method adequate?
5. Are all relevant endpoints measured in a standardised way and validated?
6. Were the groups treated in an identical way apart from the studied treatment?
7. How big was the dropout in the different groups?
8. Were all subjects analysed according to the randomisation (ITT)?
9. Are there statistical uncertainties (certainty intervals)?
10. When assessing clinical considerations, the method applied and the statistics, are you of the opinion that the outcome is attributable to the study "intervention"?

Essential areas of diagnostic studies

It is essential that the article answers the focused question. It is also important, in order to assess the efficiency of a diagnostic test, that the comparison is made with a reference standard (*Gold standard*), see Table 4.5. The reference standard can be an existing test or a diagnostic method with known and well-defined precision. The standard applied and the evidence of its applicability should be stated (5).

The reference standard and the current test should be used blindly by an independent researcher on the same patients, to compare whether the outcomes are reliable. The study should be rejected if it is not blinded. Blinding also implies that the researcher is not permitted to have knowledge of the result of the previous test (the study test), if a further test (the reference test) is performed.

If it was necessary to start the treatment as soon as the first diagnostic test result was available, this may affect the result of the subsequent test. This may be unavoidable but should be taken into consideration since the risk of bias increases.

It is essential that the test being studied is precise. In order to determine this, its sensitivity and specificity as well as the *likelihood ratio* expressing a measure of its efficacy must be stated (5). The sensitivity is the proportion of persons with the disease who have a positive test result (states how good the test is at identifying anyone with disease). The specificity is the proportion of persons without disease who have a negative test result (states that the test only identifies the actually diseased persons). It is also important that the test result is reproducible when the test is repeated (also by others).

Table 4.5. Diagnostic test and gold standard

		Gold standard	
		Present	Absent
Diagnostic test	**Positive**	a	b
	Negative	c	d

Sensitivity	$\frac{a}{a+c}$	Likelihood ratio for positivt resultat LR+ = sens/(1-spec)
Specificity	$\frac{b}{b+d}$	Likelihood ratio for negativt resultat LR- = (1-sens)/spec

As in other studies it is relevant to assess whether the study is performed in a patient category similar to one's own patients.

Links to centres and organisations working with EBM:

- http://www.nice.org.uk/page.aspx?o=201982
- http://www.clinicalevidence.com/ceweb/about/put_together.jsp.

4.2 Assessment and syntheses of qualitative studies

By Helle Ploug Hansen

Useful advice and suggestions

Literature assessment of qualitative studies

- It is important to reflect on the range and validity of the results based on qualitative methods
- It is important to decide who can/should assess the results based on qualitative methods.

Syntheses of qualitative studies

- can contribute to the decision-makers having the best possible evidence-based foundation to assess, for instance, core patient aspects in relation to a given HTA
- can be used to assess whether there is a need for primary research
- can be used to gain new insight into, for instance, relevant patient and/or organisational aspects
- can be used to make a generalisation
- require in-depth insight into the method prior to use in connection with HTA.

4.2.1 Literature assessment of qualitative studies

In connection with the assessment of literature, it is important to relate to range and validity of the results produced by qualitative methods. See Section 5.1.1 for an in-depth description of qualitative methods.

The researcher has to assess whether, in the selected articles, books, etc., there are:

- arguments for the selection of qualitative method(s) for generation of data
- arguments for the selection of qualitative method(s) for analysis and interpretation of data
- arguments for generalisation
- strict and transparent use of qualitative method(s) for generation of data
- strict and transparent analysis and interpretation of data
- a clear connection between research questions and/or hypotheses and results
- a clear account of the form of knowledge generated on the strength of the qualitative methods for generation, analysis and interpretation of data.

If no literature is available in the requested area, e.g. in relation to patient-related subjects such as patient perception, patient experience and/or organisational topics, it is important to assess whether scientific results within closely related areas are available. If this is the case, it is necessary for the researcher to closely assess whether:

- the socio-cultural circumstances are comparable
- the data material is comparable
- the study/studies in question is/are up-to-date.

In connection with the patient and organisational element, the results transferable to a Danish context on e.g. screening, will often either be produced in another comparable Western society (empiric level) or be comparable at an analytical level.

4.2.2 Synthesis of qualitative studies

4.2.2.1 In general

Within recent years, a request has emerged within the field of health science and health services research to be able to perform syntheses of qualitative studies; and decision-makers and decision-takers today frequently demand an evidence-based foundation to make decisions. A few books have been published on the topic (6,7), and some articles in which syntheses of qualitative studies are described, used and assessed in relation to concrete empiric qualitative studies (8-11). Thus, syntheses of qualitative studies have become a new methodology. The third International HTAi conference in 2006 included for the first time a panel session with the title:"HTA and qualitative research: How to synthesise information" (12). The purpose was to discuss the different methods used for syntheses of qualitative studies and the requirement for development and anchorage of syntheses of qualitative studies in relation to HTA.

Within the National Board of Health and the international HTA institutions, there has been an increasing interest in the use of qualitative research methodology in either primary or secondary research. This interest has emerged, inter alia, because it became obvious that HTA is no longer just a question of effect. HTA is also concerned with why and how different technologies work, ethical questions and dilemmas, how patients, users and the general public relate to a given technology, and technology's requirements for knowledge and skills in the professionals, organisations, etc. Qualitative research methodology (see Chapter 5) has often been criticised for being context-dependent and specific, for including an insufficient number of informants, for being interpretative and for having a low degree of generalisation. The synthesis of qualitative studies is one way of taking this into account, in relation to HTA, and methodological limitations; and the interest in synthesis of qualitative studies has been reinforced by the development within quantitative meta-analyses and the requirement for evidence-based practice (13-16).

Qualitative research methodology is often used in primary research, especially for studies of patient and organisational aspects (see Chapters 7 and 8) in a given HTA. In secondary research, it is mostly necessary to assess the results from several different qualitative studies. Even though HTA literature seldom contains patient aspects (17), it is often possible to find scientific literature on the topic via a systematic literature search. This literature is often based on qualitative research methodology. It is primarily a question of articles published in humanistic, sociological and broad health scientific journals like *Medical Anthropology Quarterly*, *Social, Science and Medicine*, *Culture, Medicine and Psychiatry*, *Anthropology and Medicine*, *Sociology of Health and Illness*.

The use of synthesis of qualitative studies in connection with HTA will make it possible to:

- contribute to decision-makers with the best possible evidence-based foundation to assess, for instance, core patient aspects in relation to a given HTA
- avoid undertaking new, expensive and unnecessary studies
- avoid disturbing e.g. very ill patients with unnecessary interviews, conversations, participant observations, etc.

4.2.2.2 Definitions of syntheses of qualitative studies

From a general perspective, synthesis of qualitative studies can be defined as the use of qualitative methods for generating satisfactory interpretative explanations based on several qualitative studies (18). *Websters 9. New Collegiate Dictionary* presents three definitions of the word "synthesis". Synthesis is:

- a combination of parts to form a whole
- a dialectic combination of thesis and antithesis
- a combination of often diverse conceptions into a coherent whole.

In conclusion one could say that a synthesis is the product of an activity, where some types of parts are combined or integrated to form a whole (Strike 1983, p. 346) (19).

The objective of synthesis of qualitative studies is to:

- gain new insights, i.e. acquire better understanding/knowledge about, for instance, relevant patient aspects in relation to the given HTA
- make generalisations based on a synthesis of results from several qualitative research studies
- reach a level of conceptual and/or theoretical development reaching beyond what is achieved in every individual empiric study:

"This implies that qualitative synthesis would go beyond the description and summarising associated with a narrative literature review and be quite different from a quantitative meta-analysis in that it would not entail the simple aggregation of findings" (Campbell 2003, p. 672) (10).

4.2.2.3 Methods for syntheses of qualitative studies

There are different methods for synthesis of qualitative studies. The two most important are *meta-ethnography* (6,7) and *narrative synthesis* (20). A brief description is given. If one wants to use one of these methods in an HTA, it is necessary to gain an in-depth insight into them.

The ethnologists Noblit and Hare (6) have developed *meta-ethnography*. They argue that any similarity with meta-analyses only consists of a joint interest in synthesising empiric studies. The prefix "meta" indicates their interest in the synthesis phase. They emphasise that synthesis of qualitative studies is about interpreting and translating, perhaps rather merging qualitative studies with each other and not primarily about generalising. Noblit and Hare use almost the same definitions as described above. They argue that a synthesis can be performed in the following ways:

- An approach where the different studies are "put together" – the studies must deal with the same topic (reciprocal)
- If the studies are not about the same topic one can use an approach in which the synthesis is seen as a refutation, i.e. one tries to refute, oppose or break down an interpretation. Refutation syntheses are a specific type of interpretation designed to provoke a new interpretation
- The final form of synthesis concerns arriving at a logical conclusion. This is the type of synthesis for which Noblit and Hare argue. One performs a "lines-of-argument" synthesis, i.e. a reconceptualisation. This is a process of clinical conclusions and/or reasoned theorising.

Thus, meta-ethnography, via the synthesis, seeks to present a new theory to explain the discovered and included research findings. It is a method for reanalysing and comparing text from published studies with a view to producing a new interpretation (21).

Narrative synthesis is a relatively new approach. It can be used for syntheses of both quantitative and qualitative studies. If a synthesis is narrative it indicates a process in which a narrative approach has been chosen contrary to a statistical approach with a goal of synthesising knowledge/evidence from several studies. The purpose is to go beyond merely producing a summary of the research findings and generate new insight, to be more systematic and transparent (Mays 2005, p. 12) (21). In a report it is argued that narrative synthesis is suitable in three situations (20):

- Prior to performing a statistical meta-analysis
- Instead of a statistical meta-analysis in which the included experimental or quasi-experimental studies are not sufficiently identical for this type of analysis
- Where the study/assessment questions are intended to include qualitative studies or a very different research design (qualitative and quantitative).

Synthesis of qualitative studies is thus a new type of methodology that may be a central method in future HTAs. Synthesis of qualitative studies can generate systematic and transparent descriptions, exploration and interpretation of relevant international qualitative studies, especially when it comes to patient and organisational aspects in connection with a given technology.

4.3 Literature for Chapter 4

(1) Reference Programme Secretariat. Vejledning i udarbejdelse af referenceprogrammer [Guide on the preparation of reference programmes]. Copenhagen: SfR, CEMTV, Sundhedhedsstyrelsen; 2004.

(2) Heneghan C, Badenoch D. Evidence-based medicine toolkit. Oxford: Blackwell Publishing; 2006.

(3) Sackett DL, Strauss SE, Richardson WS, Rosenberg W, Haynes RB. Evidensbased medicine. How to practice and teach EBM. Edinburgh: Churchill Linvingstone; 2000. p. 67-95.

(4) Madsen JS, Andersen IB. At skelne skidt fra kanel – kritisk udvælgelse og læsning af evidens. [To distinguish chalk from cheese – critical selection and interpretation of evidence.] In: Andersen IB, Matzen P, editors. Evidensbaseret medicin [Evidence-based medicine]. Copenhagen: Gads Forlag; 2005.

(5) Sox H, Stern S, Owens D, Abrams HL. Assessment of diagnostic technology in health care. Washington: National Academy Press; 1989.

(6) Noblitt GW, Hare RD. Meta-Etnography: Synthesizing Qualitative Studies. Newbury Park, CA: Sage Publications; 1988.

(7) Paterson BL, Thorne SE, Canam C, Jillings C. Meta-study of Qualitative Health Research. A Practical Guide to Meta-Analysis and Meta-Synthesis. London: Sage Publications; 2001.

(8) Smith LK, Pope C, Botha JL. Patients' helping-seeking experiences and delay in cancer presentation: a qualitative synthesis. The Lancet 2005;366(9488):825-831.

(9) Britten N, Campbell R, Pope C, Donovan J, Morgan M, et al. Using meta ethnosraphy to synthesise qualitative research: a worked example. J Health Services Research & Policy 2002:209-215.

(10) Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. Soc Sci Med 2003 Feb;56(4):671-684.

(11) Barroso J, Powell-Cope GM. Metasynthesis of qualitative research on living with HIV infection. Qual Health Res. 2000 May;10(3):340-353.

(12) 3rd Annual Meeting Health Technology Assessment International Handbook. 2nd – 5th July; 2006.

(13) Popay J, Williams G. Qualitative research and evidence-based healthcare. J R Soc Med 1998;91(Suppl 35):32-37.

(14) Green J, Britten N. Qualitative research and evidence based medicine. BMJ 1998 Apr 18;316(7139):1230-1232.

(15) Dixon-Woods M, Fitzpatrick R, Roberts K. Including qualitative research in systematic reviews: opportunities and problems. J Eval Clin Pract 2001 May;7(2):125-133.

(16) Murphy E, Dingwall R, Greatbatch PS, Watson P. Qualitative research methods in health technology assessmet: a review of the literature. 1998; Health Technology Assessment; 2(16).

(17) Draborg E, Andersen CK. What influences the choice of assessment methods in health technology assessments? Statistical analysis of international health technology assessments from 1989 to 2002. Int J Technol.Assess Health Care 2006 Winter;22(1):19-25.

(18) Doyle LH. Synthesis through meta-etnography: paradoxes, enhancements, and possibilities. Qual Res 2003;3(3):321-344.

(19) Strike K, Posner G. Types of synthesis and their criteria. In: Ward S, Reed L, editors. Knowledge structure and use: Implications for synthesis and interpretation. Philadelphia: Temple University Press; 1983. p. 343-362.

(20) Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Roen K, et al. Guidance on the conduct of narrative synthesis in systematic reviews. Draft report from ESRC Methods Programme. Institute for Health Research, University of Lancaster 2004.

(21) Mays N, Pope C, Popay J. Systematically reviewing qualitative and quantitative evidence to inform management and policy-making in the health field. J Health Serv Res Policy. 2005;10(Suppl 1):6-20.

5 Data generation, analysis and assessment

This chapter presents various methods for the generation, analysis, assessment and use of data. These are qualitative methods involving interviews, participant observation and fieldwork and also procedures for questionnaire-based and register studies. The chapter ends with a section on measurement of patients' self-reported health status. Like Chapter 4 relating to review of the literature, this entails descriptions of methods which 1) encompass both qualitative and quantitative approaches, and 2) are related to more than one of the HTA elements. With regard to concepts, the reader is referred to the book's introductory chapter entitled *About the handbook*.

Initiation of primary investigations within the context of HTA, is only considered relevant if the knowledge that can be gained from a prior review of the literature proves inadequate, and if it is of vital importance to generate the basis of knowledge in question.

5.1 Qualitative methods: Interviews, participant observation and fieldwork

By Helle Ploug Hansen

Useful advice and suggestions

- In primary research, it is important to assess whether the use of qualitative methods is appropriate in the exploration of one or more elements in the specific HTA project
- It is important to assess what qualitative methods are most appropriate to use for generating data
- It is important to assess what qualitative methods are most appropriate to use when analysing and interpreting data
- It is important to assess whether it will be relevant to undertake syntheses of qualitative studies
- It is important to assess within what scientific theory and theoretical framework the qualitative methods fit
- It is important to decide who can/should assume the qualitative part of the HTA project.

5.1.1 General aspects of qualitative methods

"Qualitative methods" is a generic term for numerous research methods for generating, analysing and interpreting data developed within the humanities and social sciences, including disciplines such as anthropology, sociology, psychology and education. There are differences in how researchers within the individual disciplines approach, understand and apply various qualitative data generation methods, e.g. individual interviews, participant observation, focus group discussions. Similarly, there are differences in how researchers approach the analysis and interpretation of the data generated. Qualitative methods are therefore more than just various techniques or tools. The choice of qualitative methods must entail theoretical considerations. This makes particular demands of the researcher, who must either assess results arising from a review of the literature or must conduct primary research of his own. Not only qualitative methods, but all methods have been and continue to be developed on the basis of certain science theory-related and theoretical understandings (Ellen 1984(1); Hansen 2002 (2), 2004 (3); Hastrup 2003 (4), 2004 (5); Nielsen et al. (6). This entails, among other thing, an understanding of the following aspects:

- Knowledge, truth and evidence

- Scope for general application and validity
- Research ethics.

The underlying theory of science assumptions of the methods are therefore important for the scope and validity of the knowledge that has been or is produced. The theory of science based understanding argued for in this section is that knowledge is not neutral. Knowledge is always generated from a specific scientific position. There are consequently different ways of understanding a given approach to, for example, screening for breast cancer, i.e. knowledge is created in specific contexts. Thus, it can be said that knowledge is a social construction. Researchers generate data. They are not data collectors. It is only when something is discovered and defined (as data) that data are generated. It is the researcher's theory of science related theoretical and empirical considerations that help determine, what gains the status of data and what does not. *Primary research* is examined briefly below (while, in relation to *literature reviews,* the reader is referred to the previous Chapter 3 and Section 4.2.1). At the end of this section is a list of suggested reading that can provide a further analysis of qualitative methods.

Primary research

Primary research as part of an HTA should *only* be conducted if knowledge is lacking in the relevant field. In planning primary research, consideration should be given to whether qualitative methods are the most appropriate methods to be used in exploring one or more elements of the HTA project. Qualitative methods will often be appropriate for exploring patient-related aspects (see Chapter 7 "Patient"), organisational elements (see Chapter 8 "Organisation") or in exploring the relationships between two or more elements (cf. Chapter 7). Based on the research questions/hypotheses set out in the HTA in question, researchers must decide which qualitative methods are most appropriate, and how they should be interpreted. The main qualitative methods for generating and analysing data are now briefly described. Syntheses of qualitative studies are described in Section 4.2.2.

5.1.2 Methods for generating data

The main qualitative methods for generating data are:

- individual interviews
- focus group discussions and interviews
- participant observation
- fieldwork.

The main quantitative methods for generating data are:

- questionnaires
- surveys.

Individual interviews

Individual interviews are central in exploring patients', users', citizens', etc. *articulated* knowledge, experience and experiences, attitudes, needs and desires, etc. in relation to the technology to be assessed. Interviews can be conducted in various ways. Various kinds of questioning and conversational techniques, semi-structured issue guides or open and unstructured (undirected) interviews, which may take the form of a life history interview can be used (see, for example, Kvale 1998 (7); Malterud 2003 (8); Spradley 1979 (9); Lorensen 1998 (10); Lunde & Ramhøj 2001 (11); Jacobsen et al.

2002 (12)). Whichever interview form is chosen, it is important to point out that answers to questions are not the same as information. People who are willing to take part in a study often also respond willingly and obligingly to questions that are irrelevant to them. As a result, it is always important to reflect on one's own understanding, one's "role" as an interviewer and one's position in the field.

Focus group discussions and interviews

Focus group discussions and interviews can be defined as a semi-structured group process typically involving 6-10 participants discussing a specific defined subject (see, for example, Morgan 1997(13)). The method involves a group dynamic element, which makes it possible to generate data of a very detailed kind from a number of people at the same time. In addition, the group formation process often encourages:

- a more "natural" discussion than an individual interview
- subtle and conflicting statements
- "quiet" individuals to express themselves
- mutual communication and thus the emergence of interesting accounts/stories
- the highlighting of complex aspects of motivation, significance and attitude.

Participant observation

Participant observation is a central method in exploring:

- how patients, such as users of a particular technology, experience the technology in their everyday lives
- the relationship between – in popular terms – what patients say they do in a specific context, and what they actually do in practice
- various forms of knowledge which unfold in a specific practice between, for example, health professionals and patients (see, for example, Nielsen et al 2006 (6); Hansen 2002 (2), 2004 (3); Hastrup 2003 (4), 2004 (5)).

Fieldwork

Fieldwork is actually not a method in itself, but rather a framework for various research methods, of which the most important are participant observation, individual interviews and focus group interviews (see, for example, Nielsen et al. 2006 (6); Hansen 2002 (2), 2004 (3); Hastrup 2003 (4), 2004 (5); Sanjek 199 (14); Ellen 1985 (1)). Fieldwork is an appropriate framework when the HTA in question entails:

- using various qualitative methods on the basis of an anthropological/sociological framework of understanding
- generating data in different contexts over a protracted period (weeks or months)
- exploring relations between the various elements of an HTA (patient, organisation, technology, economy) based on the assumption that health technology is not something in itself, but arises in *relations* between, among others, patients, health professionals, health economics interests and organisational frameworks
- exploring how different players create different knowledge of technological and organisational and economic aspects.

5.1.3 Methods for qualitative analysis and interpretation of data

The main methods for qualitative analysis and interpretation of empirical data generated via qualitative methods are *theory-based analyses* and *qualitative computer-based data programs.* Regardless of whether a theory-based analysis or a computer-based program is chosen, analysis and interpretation of data must lead to *generalisation***.** Generalisation

is meant as an analytical generalisation which arises by virtue of the deep understanding of the data that is achieved (see, for example, Jørgensen 2005, p. 316 (15); Watt-Boesen 2006 (16); Kock & Vallgårda 2003 (17); Hastrup 2004 (5)).

Theory-based analysis and interpretation entail the researcher selecting relevant theory for analysing the data generated. In formulating research questions/hypotheses, the researcher will already, whether consciously or unconsciously, have made certain choices and thus also omissions in relation to subsequent theoretical positioning. It is important that researchers set out explicitly their choice of theory because this opens up scope at any time in the research process for assessing, whether their choice of theory is still appropriate or whether new choices of theory must be made, if the data generated point in a completely different direction.

Qualitative computer-based programs provide another way of analysing and interpreting the data generated. There are currently a number of different computer programs, e.g. NVivo (18). Some are easy to use, whereas others require instruction and plenty of time.

5.2 Questionnaire-based surveys

By Torben Jørgensen

Useful advice and suggestions

- The design of a questionnaire should be in line with the hypotheses and aims of the study in question
- The questionnaire should be adapted to the target group, and the questionnaires should be understood in the same way by all readers
- The questionnaire should be brief and understandable, clear and comprehensive, properly tested and ethically acceptable.

5.2.1 In general

Questionnaires are measurement instruments used to appraise individual characteristics and behaviour. They form an important instrument within areas such as epidemiology and health services research. Questionnaires are indispensable when studying very large groups of people, but can also be used in smaller studies (19).

The requirements associated with a questionnaire are not essentially different from the requirements for all other measuring instruments:

- The questionnaire must measure what we would like to measure, and do so as precisely as possible
- The measurement must be reproducible
- The measurement should preferably be comparable with other studies.

That the questionnaire must measure what we would like to measure is self-evident, but not necessarily straightforward. The questionnaire must distinguish between the sick and the healthy, between those with a certain characteristic and those without, etc. If information is wanted on a disease like angina pectoris (heart pain), it is not enough merely to ask for it. Instead, a number of symptoms are asked about, and it is assumed that people with a certain pattern of symptoms have the condition. The questionnaire must be validated – if possible, against an "objective source" – to identify the proportion of false positives and false negatives. With diseases such as ischaemic heart disease and chronic obstructive pulmonary disease, there is a close match between classification based on questionnaires and the objective measures (exercise ECG and pulmonary function test). On the other hand, there are no equivalent objective endpoints for, say, headache, back pain and quality of life, which is why other validation methods are used. Measurement of reproducibility (the individual responds in the same way when asked the question several times) will be one option here. A person's circumstances may change over time, however, and the individual can often remember the answer from the previous time. The measurements will thus not become independent.

Another method is to get several people (e.g. 5-10) from the target group to complete the questionnaire and then interview them (see footnote 3 to Table 5.2). Despite these difficulties, it must, when drawing up a questionnaire, be assessed how validity and reproducibility can be subjected to testing. Practical experience from combined analyses of a number of population studies have shown that what appear to be small differences in the formulation of the questions, can lead to major problems with the comparability of data. The need for deviation from previously tested "standard" questionnaires should always be considered carefully as this can make it impossible later to compare one's own results with others'.

5.2.2 The questionnaire

When assessing a questionnaire that has been used or when designing a new questionnaire, it must be observed whether certain requirements are met (cf. Table 5.1). The main requirements are that the questionnaire is brief, suitable, adapted to the target group, understandable and clear, does not favour particular answers, and is comprehensive and precise, well-tested and ethically acceptable.

Table 5.1. Requirements for a questionnaire

1. Brief	When possible, avoid long questionnaires. Remove any questions that do not serve a specific purpose.
2. Fit for the purpose	The questionnaire must answer precisely the questions for which answers are wanted. Particularly if questionnaires developed for other projects are used, it is important to ascertain whether they precisely meet the aim.
3. Adapted to the target group	The questions must be adapted to the target group, so that the questions are relevant.
4. Understandable	Use language that is understandable to the target group. Get selected individuals from the target group to comment on the questionnaire.
5. Clear	The questions must mean the same for the person answering the questionnaire as for the person who has formulated it. This usually requires validation of the questionnaire.
6. Unbiased	The questions must not favour particular answers. Avoid, for example, formulations such as "Do you feel that the treatment had a good effect?" – instead, use: "How do you feel the treatment worked?".
7. Comprehensive	Possible answers must be exhaustive, i.e. the person completing the questionnaire must be able to tick at least one option. This can often be achieved with a possible answer phrased as "other".
8. Precise	The options offered for possible answers must as a rule be exclusive, i.e. they must be mutually exclusive so that there is no doubt about which should be ticked (e.g. "How do you rate the effect of the treatment? – particularly good, good, not so good, poor). Sometimes, a question is formulated in such a way that several answers are expected (e.g. "State the three main problems after your treatment" – followed by a number of statements).
9. Easy to code	As a rule, data from a questionnaire must subsequently be input in a PC. It will therefore be an advantage if the questionnaire is prepared for inputting in a data file.
10. Ethical	It must be assessed whether the questions go beyond the target group's boundaries. This may, for example, entail sexual questions or questions about lifestyle for certain ethnic groups.

After Stones DH, 1993 (20).

The size of the questionnaire often grows in an uncontrolled fashion. The cost of this is poorly completed questionnaires and low participation rates. The art of limitation is therefore crucial. The design of the questionnaire must be in line with the study's hypotheses and aims. They must be adapted to the target group, and the questions must be understood in the same way by all readers. Education, social groupings and ethnicity can all influence the interpretation of a questionnaire. Trialling of questionnaires before the beginning of the study is a matter of necessity, and must be undertaken using the target group in which it is to be used, and not among friends and staff. The questions must not provoke irritation or animosity in participants, and must not favour specific possible answers. The possible answers on offer must be comprehensive, preferably with the addition of "other" as an option. The questions should not be any more intrusive for the individual than is necessary for the task in hand.

A number of internationally validated questionnaires exist – e.g. questionnaires about general health (SF36, SF12, cf. Section 5.4.5), stress scales (Cohen's perceived stress scale), depression scales, and personality scales (e.g. NeoPir). Before commencing a study, it is therefore appropriate to search the market.

If existing questionnaires are used, it is important to establish whether they precisely cover the purpose of the study to be launched; if it is wanted to develop questions of one's own, there are a number of criteria that must be fulfilled. Both in assessing existing questionnaires and in drawing up new questions, there are a number of simple aspects that should be borne in mind (cf. Table 5.2).

Table 5.2. Designing a questionnaire – step by step

1. Selecting data	If the object of the study is formulated precisely enough, it will be relatively clear what data are needed.
2. Selecting questions	Draw up a list of the specific matters to be asked about.
3. Designing questions	Are open or closed questions wanted? In closed questions, the respondent must tick the correct answer; in open questions, on the other hand, the respondent has the opportunity of writing his or her answer in free text[1]. If closed questions are chosen, the individual answer categories must be defined. A decision must also be taken on whether the respondent must tick more than one answer.
4. Selecting options for answering	How many options for answering should there be? The more categories, the more subtle the answers achieved; at the same time, however, many answer categories require a lot of material. If the options take the form of a scale (e.g. from good to bad), it must be decided whether there should be an equal or unequal number of possible answers, with the former entailing a neutral possible answer, and the latter compelling the respondent to choose sides (e.g.: very good, good, poor, very poor).
5. Formulating the text	Short clear questions and options for answering. Neither the investigator nor the respondent should be in any doubt about what is meant.
6. Layout	The questionnaire starts with an objective and instructions. Provide examples of correct and incorrect responses to a question. Start with general questions and continue with more specific ones. Start with the most neutral question (e.g. age, sex). The questionnaire must be adapted for subsequent inputting in data files.
7. Pilot testing	Select people from the target group, test the questionnaires and evaluate the answers. Conduct a reproducibility test[2] or a validation exercise[3].

1 In open questions, space is provided for free text. This allows for subtler possible answers, but interpretation can call for qualitative analyses, which is time-consuming, particularly in questionnaire-based studies covering many people. Open response options may, however, be used with reference to rare events. In questionnaires in which a participant chooses an open response, a record of this must be made and kept in the database, so that the relevant questionnaires can later be found and the answers reviewed.

2 In a reproducibility test (test/retest), a group of respondents are asked to fill in the same questionnaire twice at certain intervals (e.g. 15 days). The weakness of this design is that the respondents may remember how they answered the first time or that their symptoms/views have changed in the time between the completion of one questionnaire and the next.

3 A question must be validated against an objective source, if one exists. Otherwise, the question is validated by putting it to a group of respondents, who are then interviewed with a view to discovering whether any questions and possibility for answering are unclear, whether any questions are irrelevant, and whether there are important areas not covered by the questions. Lastly, the respondent is interviewed about his or her actual answer and, if this tallies with the answer agreed upon by the project team, it is assessed whether this is covered by the various answer categories.

Questionnaires are thus a complex discipline, but there are often no alternatives. Smoking habits, alcohol habits and occupational exposure to harmful substances are examples of areas in which information can be obtained only exceptionally in a different way, and measuring quality of life, stress and mental vulnerability is impossible without questionnaires. The questionnaire is in other words an effective and necessary

tool – when used correctly and in accordance with a number of quality requirements. Employed uncritically, the questionnaire is, on the other hand, at best unusable, and at worst damaging to future research (21). Unless the researcher has significant experience in the field, he should seek qualified guidance in making a questionnaire. A large number of epidemiological institutions in Denmark have substantial experience of the use of questionnaire-based studies.

5.2.3 Assessment of existing questionnaire-based studies

Often, a situation exists in which a view must be taken on the value of a questionnaire-based study that has already been conducted. Besides ensuring that validated questionnaires have been used for the study or that the questionnaire used has been designed in accordance with the principles set out above, an evaluation of the actual study must also be conducted. This evaluation must contain the following elements:

- Is it substantiated in the description of the study that relevant selection of respondents has been undertaken? This could be done by having sent the questionnaire to all relevant people or only a representative selection of them. Is it described how the representative selection has been arrived at?
- The participation rate must be described, and a comparison must be carried out between those who answered and those who did not.
- A lack of or deficient answers to individual questions should also be discussed.
- Besides these specific aspects of the actual questionnaire-based study, the report/article must of course be assessed on the basis of the usual methodological scientific criteria.

5.3 Register analyses

By Kristian Kidholm and Torben Jørgensen

Useful advice and suggestions

- Assess whether the quality of the data collected from databases or registers is sufficiently high for the data to be usable as the basis for analyses in HTAs
- Validate and substantiate the results of data analyses by, for example, obtaining discharge summaries or copies of records
- Explain where the data used come from, and what inclusion and exclusion criteria underlie the extract.

5.3.1 In general

Even if there are many studies of a therapeutic effect, literature studies only rarely provide adequate information for a comprehensive HTA report. The literature study may therefore be advantageously supplemented with data from existing registers (cf. Section 6.4.2).

Analysis of register data can be used in the HTA report to quantify a given problem, e.g. the size of a given patient group. Register information can therefore be incorporated in connection with the planning of an HTA. In this context, register data will be included together with other gained knowledge when choosing methods and be a supplement to other data, e.g. interviews and literature reviews.

The use of the following registers, for example, may be appropriate:

- The National Patient Registry (National Board of Health) contains a range of information on admissions and outpatient visits to Danish hospitals, including information on diagnoses, procedures, admission times, discharge methods, deaths, etc. The information is at patient level and may, among other things, be used to estimate the number of patients nationally per annum. It should nevertheless be emphasised that outpatient services are registered only as from 1995.
  Link to the extended version in Danish: Landspatientregisteret
- The Causes of Death Registry (National Board of Health) contains information on causes of death for all deaths in Denmark. The register can be used to identify disease-specific causes of death and supplement the National Patient Register in cases where information is sought on both fatal and non-fatal cases of disease.
  Link to the extended version in Danish: Dødsårsagsregisteret
- The National Health Insurance Service Registry (National Board of Health) contains information at patient level on services provided by general practitioners, dentists, psychologists, physiotherapists and chiropractors with support from the Public Danish National Health Insurance Service. The register can be used to elucidate a patient group's consumption of services in the primary sector and when calculating costs.
  Link to the extended version in Danish: Sygesikringsregisteret
- The Cancer Registry (National Board of Health) lists cases of cancer and notifiable diseases. Information is provided on the time of diagnosis for the notifiable disease, where the notifiable disease to be found and what type it is. The spread of the disease is also recorded in relation to the time of diagnosis, over the first four months, how the diagnosis has been made and what treatment is administered in the first four months after diagnosis.
  Link to the extended version in Danish: Cancerregisteret
- The Pathology Database/Patobank (in Danish) (National Board of Health) is a national database comprising tissue and cell samples from patients. The Pathology Database provides information on earlier pathoanatomical investigations and diagnoses, regardless of where in the country these have been carried out.
- Danish Psychiatric Central Research Registry (National Board of Health) forms part of the National Patient Registry and contains information on all admissions to psychiatric wards. Since 1995, the register has also covered all outpatient contacts and casualty ward visits of a psychiatric nature.
  Link to the extendet version in Danish: Psykiatrisk Centralregister
- Clinical databases (in Danish)
  There are a number of clinical databases that can be used when describing, for example, numbers of patients or treatment activities. A clinical database is a public register concerning a disease group, a specific diagnosis or method of treatment or investigation that forms an established part of quality development. The databases typically contain information at patient level on the individual patient, the disease, the treatment, the organisation and the treatment result. A list of databases supported by the Danish National Competence Centres for Clinical Databases is set out below (Table 5.3). Note that a number of smaller clinical databases, which may hold relevant data, are often to be found at the individual hospital.

Table 5.3. Clinical databases supported by National Competence Centre for Clinical Databases

Underlining = link to the database (in Danish)
Danish Anaesthesia Database (DAD)
Danish Bladder Cancer Register
Danish Crohn's Colitis Database (DCCD)
Danish Biliary Database
Danish Gynaecological Cancer Database
Danish Hernia Database
Danish Cardiac Register
Danish Hysterectomy Database
Danish Knee Arthroplasty Register
Danish Colorectal Cancer Database
Danish Register for Juvenile Diabetes
Danish Rheumatology Database
Database for chronic renal failure
The Danish Database for Chronic Hepatitis B and C (DANHEP)
The Joint Haematology Database
The Cardiac Arrest Database
The Headache Database
Hysteroscopy Database
Karbase
The Clinical Vein Database
National database for geriatrics
National database for myelomatosis
The Polyposis Register
The Sclerosis Treatment Register
AML database
Danish Disk Database
Danish Hip Arthroplasty Register
Danish Liver Database
Danish Transfusion Database
Database for clinical quality in outpatient psychiatric treatment
DECV Cancer Database
The Cataract Database
The Pros Database
Shoulder Arthroplasty Database
BupBasen
Diabetes Database
Danish Lung Cancer Register
Epibase
LYFO
Thrombo-Base

Source: Clinical databases

- Local patient administration systems
  A local patient administration system containing information on patients treated in the hospital, exists at the individual hospital. Data from this become included in the National Patient Registry (NPR). The local patient administration system may, however, contain more information and newer data than the NPR. There may also be local registration systems, e.g. concerning blood banks, that are not included in the NPR and which only exist locally.

5.3.2 Assessment of register data

Denmark benefits from the many central registers and legislation which give researchers the opportunity of using register data for research purposes. The establishing of an arrangement for researchers at the National Board of Health and Statistics Denmark

made it easier to collect registers and obtain qualified guidance on the use of the registers. Some of the registers can only be used within the arrangement of Statistics Denmark. This means that the institution, responsible for the analysis, must establish a contract with Statistics Denmark which allows researchers at the institution to link to Statistics Denmark and conduct the analysis. The results of the analysis will be accessible, but not raw data. Generally, there is good experience in Denmark with the use central registers.

When using register data, a number of aspects must be borne in mind:

- Data are often collected for a purpose other than wanted for an HTA report. Data in the NPR, the National Health Insurance Service Registry, the Causes of Death Registry and the Pharmaceutical Database are all collected for administrative purposes, while data in the clinical databases are collected with a view to measuring the *quality* of a particular treatment. It must therefore be assessed from time to time whether the relevant data exist.
- If data are wanted on a particular disease, it is important to verify whether the nature of the disease is of such that virtually all cases will be recorded in the NPR and the Causes of Death Registry or whether many cases will only be treated in a specialist practice or general practice. An extract from central registers will in these cases mean that only the sickest of the patients are recorded. Sometimes, extra information can be gathered from the National Health Insurance Service Registry. This has been done, for example, in connection with the setting-up of a register for diabetes. If the disease is covered by a clinical (quality) database, it can be an advantage to use this instead of – or in combination with – the NPR.
- There is good experience of using central disease registers for major epidemiological analyses, i.e. at group level data seem to be in order. There are a number of misclassifications, which, in the NPR, are more pronounced for diagnosis codes than for treatment codes. At the same time, it should be noted that, with the introduction of diagnosis-related groups (DRGs) for financial management, a change was made to code practice, not only in the form of subtle changes in diagnoses but also in the form of more thorough registration. Caution should therefore be exercised in interpreting changes in the incidence of a disease over time.
- Validating data from central registers is therefore a big job. Before embarking upon validation, it is therefore important to investigate whether validation already exists. So far as the national clinical (quality) databases are concerned, an annual or more frequent assessment of completeness of data will be undertaken in most cases. For the other registers, there are only sporadic validation studies. National Board of Health holds a number of reports/articles concerning validation of the NPR. If it is wanted to undertake validation of register data in, for example, the NPR oneself, this must be done by comparing a random extract from the register with the information in the patient's medical records or discharge summary. This is a very extensive job.
- The problem with the Causes of Death Registry is that the proportion of cases involving a post-mortem has fallen sharply in Denmark, and so cause of death depends upon what the doctor, who issues the death certificate, knows about the patient's case history. A change in code practice also took place in 2005, with manual inputting being replaced by electronic inputting. This might lead to reduced validity.
- A number of the registers are not fully updated as pruning work is required before data can be input.
- So far as the Pharmaceutical Database is concerned, it should be noted that it is only recorded whether a patient has paid for a prescription – not whether the medication has been taken.

- If it is wanted to estimate the number of new cases of disease (incident cases), the register's start date should be borne in mind. For example, the Pharmaceutical Database starts in 1995, i.e. data cannot be used from the first year(s) to determine, whether incident cases of disease are involved as it is not known whether the patient paid for a prescription in, for example, 1994.

General experience of working with register data is good. This represents a relatively easy and inexpensive way of obtaining data and, unlike questionnaire-based studies, information can be gained on all patients registered. If one does not have experience oneself of using register data, it will be a good idea to contact a research establishment that has this experience.

5.4 Measurement of health status

By Claire Gudex

Useful advice and suggestions

- Instruments for measuring health status may be disease-specific or generic; using both types in the same study can be useful
- Heath status instruments can be further categorised as profile or index measures; the latter can be used as utility measures in economic evaluations
- The choice of instrument is based on patient characteristics, the expected health status consequences of the intervention, the objective of the study, and fulfilment of psychometric and practical criteria
- Besides assessment of patient outcome, it may be relevant to include assessment of the intervention's consequences for the patient's family and/or caregivers
- It is recommended that potential users of a health status instrument consult the instrument's developers or website to obtain an approved (language) version.

5.4.1 Definition of health status

In clinical studies, the primary endpoint for the effectiveness of health technologies is assessed in terms of changes in mortality and/or morbidity, e.g. as survival rates, risk reductions, or elimination or reduction of symptoms. Illnesses and their treatment may, however, also affect patients' physical and mental well-being, often designated as "health-related quality of life" (HRQOL), which is not necessarily captured by mortality and morbidity endpoints. The traditional clinical outcome endpoints are thus increasingly complemented by endpoints that focus on changes in the patient's self-assessed health status that occur as a result of a treatment. Assessment of patients' health status, over and above mortality and morbidity, is particularly relevant in an HTA context where a broad coverage of relevant elements is desirable. Certain diseases and treatments (e.g. dementia) may also affect the patients' families and care providers. In these cases, it may be relevant to include assessment of HRQOL for these patients' families and/or caregivers.

In HRQOL assessment, so-called *health status instruments* can be used to describe patients' health and well-being in terms of clinical, functional and psychosocial dimensions (22,23). These aspects are typically described in domains such as mobility, pain, role function, psychological well-being, etc. When health status instruments are used to assess changes in patients' health status over time (e.g. in a clinical intervention study), *health outcome* is measured.

5.4.2 How is health status measured?

Instruments have been developed for measuring health status within a wide range of disease areas (22,24,25). These instruments can be categorised in relation to:

- The breadth of disease coverage, i.e. whether the instruments are targeted at an individual disease or a specific health problem (*disease-specific* instruments) or whether they are more universal and cover general health aspects which make them relevant for a number of patient groups and allow comparison across disease groups (*generic* instruments)
- The way in which health status is summarised, i.e. whether the instrument retains its multidimensional structure by generating a score for each dimension (*profile measure*), or whether a total score/index can be aggregated over all the instrument's dimensions (*index measure*).

The advantage of using *disease-specific instruments* lies in their focus on a particular disease and thus often greater sensitivity in relation to changes as a result of treatment. For example, instruments have been developed for measuring health status in relation to arthritis, chronic lung disease, diabetes and various forms of cancer; other instruments measure single dimensions, such as pain or depression. The disadvantage of disease-specific instruments is that they can only be used in connection with the specific disease. They are unsuited to comparisons across disease groups.

Generic instruments are those developed for use among a wide range of patient groups and diseases, and are therefore relevant for broader comparisons across disease areas. Certain generic instruments are also index measures and can be used for calculating QALYs in cost-utility analyses (see section below). A disadvantage of generic instruments may be, however, that they are insufficiently sensitive in relation to a specific disease, and that they may not pick up changes over time that are relevant for the patient or health professional. Depending on the objective of the study, it is often recommended to use both a generic and a disease-specific instrument in the same study.

In an HTA context, the assessment of changes in patients' health and well-being form a central part of the patient element. The use of health status instruments gives rise to a number of considerations, which are described below.

5.4.3 Assessment of health status measurement

A number of factors should be taken into consideration when systematic searches and literature reviews of studies of health status measurement are conducted within an HTA (see also Chapter 3 and 4 on literature search and assessment).

Literature searches in databases such as Medline, EMBASE, The Cochrane Library, Cinahl and PsycINFO will identify most publications concerning the health consequences of a disease or treatment. It is often necessary to use several search terms to cover the various expressions used within this area. Besides identifying the disease/intervention, it can be useful to search by expressions such as "health status", "health-related quality of life", "health outcome", "patient outcome", "health status instrument", "preferences" and "quality-adjusted life years". It can be appropriate to search using expressions such as "Activities of Daily Living", "ADL", "depression", "psychological function", "mental health", etc. It may also be appropriate to search for literature that employs specific types of instruments for measuring health status, e.g. "generic", "disease-specific" and the names of particular instruments, e.g. "AIMS" (arthritis) or "Chronic Respiratory Disease Questionnaire".

In reviewing literature that employs health status instruments, one should review aspects related to the health status measure itself (e.g. the choice of health status instrument and its characteristics) and aspects common to all elements in an HTA (e.g. has the health status instrument been used in a suitable and valid manner?). For disease areas in which many different health status measures are available, the instruments that inspire the greatest confidence as health status measures in connection with the disease or intervention under consideration can be identified. Many of the following parameters are described in greater detail in the Cochrane Handbook for Systematic Reviews of Interventions (26).

- *Study design*: Many instruments have been developed with a view to describing patients' health status at a particular time (health status indicator) in a cross-sectional study. Some of these instruments can, however, also be used in prospective studies to assess changes in the state of patients over time (health outcome). Background information about the instrument is important, and an article should describe the purpose for which the instrument was developed (e.g. in the form of references), with documentation about the instrument's ability to measure the relevant changes over time in the disease in question.
- *Number of patients*: The sample size needs to be large enough to allow the identification of significant changes in health status. Changes in HRQOL are not always the primary endpoint, and many studies will be dimensioned to test significant differences in clinical parameters. Whether sample size is large enough to test for changes in health status is an important piece of information, however, as it has implications for the validity of the results. There is considerable variation in clinically meaningful differences for health status measures and the sample sizes needed. This depends, among other things, on the type of responses used in the instrument (e.g. Yes/No answers, Likert scale, visual analogue scale) and the method used for calculating scores.
- *Patient characteristics*: These are crucial for the choice of health status instrument. Many instruments exist in different versions, which are aimed at, for example, adults, children or observers (proxy). The type of disease and intervention determines what dimensions and thus what instruments are relevant; the choice of a generic or disease-specific instrument (or both) also depends upon the purpose of the study in terms of the extent to which different patient groups will be compared, and the level at which the consequences of a particular disease or intervention will be explored.
- *Method of data collection and analysis*: While many instruments are intended for self-completion by the patient (incl. by telephone), the length or complexity of some instruments requires a personal interview. It is also important to check whether data collection has been conducted at times when clinically relevant changes in health status would be expected to be seen. The data should have been analysed and interpreted using relevant statistical methods.
- *Bias*: As with literature reviews in general, checks should be done for i) *selection bias*, i.e. that, apart from the intervention, there are no systematic differences in terms of patient characteristics in the patient groups compared; ii) *drop-out bias*, i.e. any systematic differences between groups in terms of the number of patients who drop out of or are excluded from the analysis (particularly in prospective studies, there can be many patients who do not complete the follow-up questionnaires – perhaps because they feel well again, or alternatively feel unwell even after the intervention); iii) *detection bias*, i.e. how the results are affected by the fact that the person assessing the outcome of the study is not "blind" with respect to which intervention the patient has received); and iv) reporting bias (where results are not presented for some of the study's patient groups or instruments used).

- *Instrument type*: It is often appropriate to assess HRQOL results from generic and disease-specific instruments separately; even if the results from the disease-specific instruments should typically be reflected in the generic instruments, the two instrument types often employ very different methods of calculation and formats for expressing their results. It should also be considered whether all relevant health status aspects have been adequately assessed in the studies identified. An HTA study of an intervention in connection with, for example, arthritis should at least assess patients' physical function, pain, mental well-being and role function. As a rule of thumb, confidence in results from a well-known and broadly used instrument is much greater than for an instrument that has been developed specifically for the individual study; the development of a health status instrument involves many considerations and comprehensive investigation to ensure that the instrument meets psychometric and practical requirements.
- Besides considerations of what dimensions have been assessed, it can be checked whether all the relevant individuals have been involved in assessing the consequences of an intervention. It is often sufficient to assess outcome for the patients only, although in many (particularly chronic) diseases it can be just as relevant to assess the consequences for the patients' families and/or caregivers (e.g. nursing staff in a nursing unit in the case of dementia studies). These people can often complete the same (generic) instrument as the patient; otherwise, there are a range of instruments that measure disease burden, stress levels, etc. experienced by families and caregivers.

5.4.4 Generation of new data on health status

On the basis of the literature review findings, it is decided whether original research is needed to obtain the relevant information about the technology's consequences for health status. If the results from the identified studies can be used in the context of the HTA study (i.e. are relevant and valid for the respective patient groups and interventions and also in a Danish context) and therefore have "external validity", new data do not need to be generated. Where the information is insufficient, however, new data need to be generated.

The choice of health status instrument is based on many of the parameters described in the literature review checklist, e.g. patient characteristics, the intervention's expected health status consequences and the study objective with respect to comparisons across patient groups/interventions. Besides being appropriate in the context of the HTA study, the instrument should meet a number of psychometric and practical criteria, including (internal) validity, reliability, sensitivity to changes over time, patient acceptance and reliable translation (22-24,27).

Validity assesses the extent to which the instrument measures what it claims to measure. This can be investigated in several ways: to what extent are the instrument's items relevant and sufficient in relation to the health dimensions that the instrument measures (content validity); to what extent do the instrument's results reflect the expected (theoretical) relations with other measurements (construct validity), e.g. whether the instrument distinguishes between groups expected to have differing health status (e.g. owing to the severity of the disease, comorbidity), or whether the instrument's scores correlate with scores from other instruments which measure the same health concept (convergent validity) and also other generic/disease-specific instruments, clinical measurements of pain and mobility.

Test-retest reliability assesses how stable the instrument's results are when the measurement is repeated after a relatively short period in people without health changes (e.g.

with stable chronic disease). Good test-retest reliability (over 0.7) makes it more likely that any differences in pre- and post-intervention health status are due to the intervention and not the instrument employed. *Inter-rater reliability* assesses concordance in results from the same test conducted by different observers.

Sensitivity assesses how good the instrument is in picking up "meaningful" changes in health status over time – whether these are meaningful with respect to clinical decisions or the patient's experience of health status changes. Lack of sensitivity in a generic instrument (which is used for other reasons) can thus be remedied with a disease-specific instrument that allows more detailed exploration of the consequences for particular aspects of health status.

Patients' *acceptance* of an instrument is crucial for the success of the measurement; patient burden is affected, for example, by the completion time, the method of administration (postal questionnaire, personal interview) and level of language used. The use of instruments in languages other than the instrument's original language requires a translation process that follows accepted procedures (typically forward and back translation followed by testing on relevant individuals). Potential users should therefore consult the instrument's developers or website to obtain an approved (language) version.

5.4.5 Generic instruments as utility measures

Besides functioning as a profile measure for describing patients' self-assessed health, certain health status instruments can also be used as utility measures in economic evaluations. In this context, the instrument must be able to generate a simple preference-based index score (on a scale of 0-1) for health status, e.g. for various patient groups or treatment alternatives. Table 5.4 presents five generic instruments, which have either been developed primarily as utility measures (EQ-5D, 15D, HUI, AQoL) or aim at this on the basis of broad use as a profile measure (SF-36) (23,24,28). Whereas 15D and AQoL are relatively new, the other instruments are widely used and perform well with respect to validity and reliability.

Table 5.4. Generic instruments as measures of utility

EQ-5D
Description: The EQ-5D classification system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), with each dimension being subdivided into three levels (no problems, some problems and extreme problems); the profile system comprises 243 possible health states. In the EQ-5D questionnaire, the patient describes his or her own current health status in relation to the 5 dimensions and then on a visual analogue scale (VAS) with endpoints of 0 (worst) and 100 (best health state); the information can be compared over time for the same patient before and after treatment, with data from other patients or from the general population (29,30).
Index score: Where EQ-5D is used as a utility measure, patients' responses about their own health over time are collected and then each health state is assigned an index score using population-based preference values for the 243 possible health states. Preference values based on time trade-off and VAS rating methods exist for a number of countries, including Denmark (31).
Use: EQ-5D is self-completed by the patient and takes only a few minutes to complete. The instrument is recommended for cost-effectiveness analysis in both the USA (Washington Panel on Cost Effectiveness in Health & Medicine) and the UK (National Institute for Clinical Excellence, NICE). A Danish version has been translated and validated (32-34). There is no copyright on EQ-5D, but users are expected to register their study on the EuroQol Group's website, which also provides information on the instrument's use, alternative versions (e.g. telephone/proxy versions, translations, child version) and publications; http://www.euroqol.org.

➤

SF-36

Description: SF-36 (MOS SF-36 or RAND 36-Item Health Survey 1.0) was developed as a profile measure and comprises 36 items, which are subdivided into 8 dimensions: physical function, role limitation due to physical problems, bodily pain, general health perception, energy/vitality, social functioning, role limitation due to emotional problems, and mental health (35). The answers to the questions in the original version vary from dichotomous (yes/no) to 6-point Likert scales. Scores are calculated for each of the 8 dimensions, and they can be transformed on a scale from 0 to 100 by summing the answers under each dimension; a higher score indicates a better health status. Scores on the 8 dimensions can be further summed as a physical (PCS, Physical Component Summary) and a mental (MCS, Mental Component Summary) component.

Index score: In a shorter version comprising 12 items – SF-12v2, which also incorporates changes in the instructions and response choices (36) – PCS and MCS are calculated on the basis of weight calculations via a principal component analysis of SF-36. An index measure (SF-6D) has been developed using standard gamble values to describe health status on the basis of six of the original dimensions (37).

Use: SF-36 is self-completed by the patient and takes about 10 minutes. A Danish version of SF-36 (and SF-12) has been translated and validated (38-40). There is copyright on the use of the SF instruments; se http://www.qualitymetric.com.

15D

Description: 15D is a Finnish-developed instrument comprising 15 dimensions (mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity), where each dimension is subdivided into a 5-point scale; the instrument describes approx. 30 billion possible health states (41,42).

Index score: 15D's preference values are based on multi-attribute utility theory, where a weighting for each level in each dimension is calculated using valuations obtained from the general population that have been generated through a combination of rating and magnitude estimation methods; both Finnish and Danish preference values are available.

Use: 15D covers more dimensions than the other generic instruments; it is self-completed by the patient and takes 5-10 minutes. There is evidence (mostly from the Nordic region) for the instrument's validity, reliability and sensitivity in relation to changes; a Danish version of 15D has been translated and validated (43,44). There is no copyright on 15D, but users are asked to register their study on the website, which also describes the instrument's use and alternative versions (e.g. for children, translations) and publications; http://www.15d-instrument.net/15d.

HUI Mark 3

Description: The HUI instruments comprise Health Utilities Index Mark 1 (HUI1, which is rarely used), Mark 2 (HUI2) and Mark 3 (HUI3). HUI2 and HUI3 measure some of the same dimensions, but HUI2 describes seven dimensions with 3-5 levels, and HUI3 describes 8 dimensions with 5-6 levels; even where the same dimension is measured, there can be differences in the terms used. The 8 dimensions in HUI3 are vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain; in total, 972,000 health states are described.

Index score: HUI3 can be used as a utility measure. The scoring system uses multiplicative multi-attribute utility functions (MAUFs), where preference values based on the standard gamble method have been generated among the general population in Hamilton, Ontario (45,46).

Use: HUI3 has been included in all major health studies of the Canadian population since 1990. There is copyright on the use of the HUI instruments; se http://www.fhs.mcmaster.ca/hug/.

AQOL

Description: The Australian Assessment of Quality of Life Instrument (AQoL) comprises 15 questions covering 5 dimensions (illness, independence, social relationships, physical senses and psychological well-being). A revised version (AQoL-2) is under development. Scores from the five dimensions provide a health profile, but the primary purpose of the instrument is to provide a utility index for quality of life (47-49).

Index score: AQoL preference values are calculated without the "illness" dimension and are based on *multi*-attribute utility theory. Within each dimension, each level is assigned a preference value, which is obtained from a random sample taken from the general (Australian) population; these values are then combined in dimension scores, which are also combined.

Use: As AQoL is relatively new, experience with the instrument is limited. Nevertheless, there have been a number of comparative studies of AQoL and other utility measures. Use of AQoL is free of charge; users are asked to register their study; see http://www.psychiatry.unimelb.edu.au/qol/aqol/use_aqol.html

5.5 Literature for Chapter 5

(1) Ellen RF, editor. Ethnographic research. A guide to General Conduct. London: Academic Press; 1984.

(2) Hansen HP. I grænsefladen mellem liv og død. En kulturanalyse af sygeplejen på en onkologisk afdeling [In the boundary between life and death. A cultural analysis of nursing care in an oncology department]. Copenhagen: Munksgaard; 2002.

(3) Hansen HP. Antropologisk opmærksomhed – Refleksioner fra et feltarbejde om kvinder, kræft og rehabilitering [Anthropological attention – Reflections from fieldwork about women, cancer and rehabilitation]. Socialmedicinsk tidskrift 2004;6:504-512.

(4) Hastrup K, editor. Ind i verden [Into the world]. Copenhagen: Hans Reitzels Forlag; 2003.

(5) Hastrup K, editor. Viden om verden. En grundbog i Antropologisk analyse [Knowledge about the world. An introductory textbook on anthropological analysis]. Copenhagen: Hans Reitzels Forlag; 2004.

(6) Nielsen KT, Swane CE, Huniche L, Hansen HP, Johannessen H. Når sundhed, sygdom og helbredelse er mere end ord. Om brug af deltagerobservation i sundehedsvidenskabelige undersøgelser [When health, disease and recovery are more than words. About the use of participant observation in health science studies]. Månedsskr Prak Lægegern 2006;84:1129-1140.

(7) Kvale S. Interview. En introduktion til det kvalitative forskningsinterview [An introduction to the qualitative research interview]. Copenhagen: Hans Reitzels Forlag; 1998.

(8) Malterud K. Kvalitative metoder i medisinsk forskning [Qualitative methods in medical research]. Oslo: Universitetsforlaget; 2003.

(9) Spradley JP. The Ethnographic Interview. Fort Worth: Holt, Reinehart & Winston; 1979.

(10) Lorensen M, editor. Spørgsmålet bestemmer metoden. Forksningsmetoder i sygepleie og andre helsefag [The question determines the method. Research methods in nursing and other health professions]. Oslo: Universitetsforlaget AS; 1998.

(11) Lunde IM, Ramhøj P, editors. Humanistisk forskning indenfor sundhedsvidenskab [Humanistic research within health sciences]. Copenhagen: Akademisk; 2001.

(12) Jacobsen MH, Kristiansen S, Prieu A, editors. Liv, fortælling, tekst. Strejftog i kvalitativ sociologi [Life, narrative, text. Incursions into qualitative sociology]. Aalborg: Aalborg Universitetsforlag; 2002.

(13) Morgan D. Focus groups as qualitative research. London: SAGE; 1997.

(14) Sanjek R, editor. Fieldnotes. The making of Anthropology. London: Cornelle University Press; 1990.

(15) Jørgensen T, Christensen E, Kampmann JP, editors. Klinisk forskningsmetode [Clinical research method]. 2.th ed. Copenhagen: Munksgaard Danmark; 2005.

(16) Watt-Boesen M. Kvalitative analyser. At finde årsager og sammenhænge [Qualitative analyses. Finding reasons and connections]. Copenhagen: Hans Reitzels Forlag; 2006.

(17) Kock L, Vallgårda S, editors. Forskningsmetoder i folkesundhedsvidenskab [Research methods in public-health science]. 2nd ed. Copenhagen: Munksgaard; 2003.

(18) Gibbs GR. Qualitative data analysis: explorations with NVivo. Buckingham: Open University press; 2002.

(19) Jørgensen T. Klinisk epidemiologi [Clinical epidemiology]. In: Jørgensen T, Christensen E, Kampmann JP, editors. Klinisk forskningsmetode [Clinical research method]. 2nd ed. Copenhagen: Munksgaard Danmark; 2005.

(20) Stone DH. Design a questionnaire. BMJ 1993;307:1264-1266.

(21) Rasmussen NK. Faldgruber og vanskeligheder ved spørgeskemaundersøgelser af patienttilfredshed [Pitfalls and difficulties associated with questionnaires of patient satisfaction]. Tidsskr Dan Sygehusvæsen 2005;6:2-9.

(22) Hutchinson A, Bentzen N, König-Zahn C, on behalf of European Research Group on Health Outcomes. Cross Cultural Health Outcome Assessment: A User's Guide: European Research Group on Health Outcomes (ERGHO); 1996.

(23) Fayers P, Hays R, editors. Assessing quality of life in clinical trials: methods and practice. 2nd ed. Oxford University Press; 2005.

(24) Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. 1998 Health Technology Assessment;Vol. 2: No. 14.

(25) Bowling A. Measuring disease: a review of disease-specific quality of life measurement scales. Buckingham: Open University Press; 2001.

(26) Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5. The Cochrane Library Chichester, UK: John Wiley & Sons, Ltd.; 2005.

(27) Aaronson N, Alonso J, Burnam A, Lohr KN, Patrick DL, Perrin E, et al. Assessing health status and quality-of-life instruments: Attributes and review criteria. Qual Life Res. 2002;11:193-205.

(28) Brazier J, Deverill M, Green C, Harper R, Booth A. A review of the use of health status measures in economic evaluation. Health Technology Assessment 1999;3(9).

(29) Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med 2001 Jul;33(5):337-343.

(30) Brooks R, Rabin RE, de Charro F. The measurement and valuation of health status using EQ-5D: a European perspective. Dordrecht: Kluwer Academic Publishers; 2003.

(31) Pedersen KM, Wittrup-Jensen K, Brooks R, Gudex C. Værdisætning af sundhed: teorien om kvalitetsjusterede leveår og en dansk anvendelse [Valuation of health: the theory of quality-adjusted years of life and application in Denmark]. Odense: Syddansk Universitetsforlag; 2006.

(32) Gudex C, Sørensen J. EuroQol: et generisk mål for helbredstilstand [EuroQol: a generic measurement of health]. Månedsskr Prak Lægegern 1998;76(10):1339-1345.

(33) Christensen PM, Brixen K, Gyrd-Hansen D, Kristiansen IS. Cost-effectiveness of alendronate in the prevention of osteoporotic fractures in Danish women. Basic Clin. Pharmacol.Toxicol. 2005 May;96(5):387-396.

(34) Kessing LV, Hansen HV, Bech P. General health and well-being in outpatients with depressive and bipolar disorders. Nord J Psychiatry 2006;60(2):150-156.

(35) McHorney CA, Ware JE,Jr, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Med Care 1994 Jan;32(1):40-66.

(36) Ware JE, Kosinski M, Turner-Bowker DM, Gandek B. How to score version 2 of the SF-12-v2 health survey. Lincoln, RI: Quality Metric Incorporated; 2002.

(37) Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ 2002 Mar;21(2):271-292.

(38) Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, et al. Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. International Quality of Life Assessment. J.Clin.Epidemiol. 1998 Nov;51(11):1171-1178.

(39) Holm T, Lassen JF, Genefke J, Melchiorsen H, Hybel U, Sørensen J. Tværsektorielt samarbejde mellem almen praksis og hospital – shared care belyst ved antikoagulansbehandling som eksempel: en medicinsk teknologivurdering [Cross-sectoral cooperation between general practitioners and hospitals – shared care illustrated through the example of anticoagulant therapy: a health technology assessment]. Copenhagen: Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects] 2006; 6(2).

(40) Peuckmann V, Ekholm O, Rasmussen NK, Moller S, Groenvold M, Christiansen P, et al. Health-related quality of life in long-term breast cancer survivores: Nationwide survey in Denmark. Breast Cancer Res Treat 2007 29.09.2007;Jul;104(1:39-46).

(41) Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med 2001 Jul;33(5):328-336.

(42) Kauppinen R, Vilkka V, Sintonen H, Klaukka T, Tukiainen H. Long-term economic evaluation of intensive patient education during the first treatment year in newly diagnosed adult asthma. Respir Med 2001 Jan;95(1):56-63.

(43) Lauridsen J, Christiansen T, Hakkinen U. Measuring inequality in self-reported health-discussion of a recently suggested approach using Finnish data. Health Econ 2004 Jul;13(7):725-732.

(44) Meyhoff CS, Thomsen CH, Rasmussen LS, Nielsen PR. High incidence of chronic pain following surgery for pelvic fracture. Clin J Pain 2006 Feb;22(2):167-172.

(45) Torrance GW, Feeny DH, Goldsmith C, Furlong W, Zhu Z, DePauw S. A multilinear multi-attribute utility function for the health utilities index mark 3 (HUI3). Medical Decision Making 1998;18:490.

(46) Furlong WJ, Feeny DH, Torrance GW, Barr RD. The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. Ann Med 2001 Jul;33(5):375-384.

(47) Hawthorne G, Richardson J, Osborne R. The Assessment of Quality of Life (AQoL) instrument: a psychometric measure of health-related quality of life. Qual Life Res 1999 May;8(3):209-224.

(48) Hawthorne G, Osborne R. Population norms and meaningful differences for the Assessment of Quality of Life (AQoL) measure. Aust N Z J Public Health 2005 Apr;29(2):136-142.

(49) Richardson J, Day NA, Peacock S, Iezzi A. Measurement of the quality of life for economic evaluation and the Assesment of Quality of Life (AQoL) Mark 2 instrument. Australian Economic Journal 2004;37:62-88.

6 The technology

By Stig Ejdrup Andersen and Finn Børlum Kristensen

This chapter deals with the technology element of HTA. It is described how technology is defined and delimited, and how questions of effect and safety are handled in HTA. Instructions are given as to how different types of clinical studies are assessed with regard to evidence. This links up with Chapter 3 and Section 4.1 about literature search and assessment of clinical and epidemiological studies.

Useful advice and suggestions

- The technology should be precisely defined and delimited so that the type of technology in question becomes clear
- The technology is best described from its material nature, its purpose as well as the degree of dissemination and maturity
- The technology should be compared with alternative technologies in terms of advantages and disadvantages
- The technology is assessed by a systematic literature review, often supplemented by analysis of data from other primary information or data sources
- Usually both positive and negative effects are attached to the use of a technology – it is always important to illustrate the risk scenario.

6.1 The analysis should be linked continuously to the remaining elements of the HTA

What is health technology?
Health technology is a collective term for procedures and methods for examination, treatment, care and rehabilitation of patients, including instruments, drugs and preventive procedures.

Even though the technology will naturally be the pivotal point of an HTA, the technology element can be weighted more or less, dependent on the topic of the HTA. Goodman et al. describes three fundamentally different approaches to health technology assessment (http://www.nlm.nih.gov/nichsr/hta101/ta101_c1.html) (1):

- Technology-orientated HTA
- Problem-orientated HTA
- Project- or organisation-orientated HTA.

The purpose of a technology-orientated HTA is to assess the importance of a specific health technology, e.g. the clinical, social or economic importance of population-based screening for prostate cancer, preventive treatment with anticoagulant drugs in cancer patients or endoscopic surgery of the gallbladder.

The aim of a problem-orientated HTA is to find solutions or strategies for solution of medical problems, for which there are several different alternative technologies available. It may be the planning of dementia assessment, including the development of a basis for clinical guidelines for the use of clinical examinations, neurological assessment and various clinical-chemical and imaging options.

The purpose of a project- or organisation-orientated HTA can be to assess how a specific technology can be fitted into a specific institution, programme or project.

Problems of this nature, which can arise, for instance, when an institution considers establishing an outpatient orthopaedic surgical centre, require, amongst others, an assessment of existing and needed facilities, necessary instrument acquisitions, need for staff training, operation and maintenance.

The three different approaches can overlap and complement each other, and many health technology assessments will include elements from all three approaches.

Apart from a characterisation of the technology and an account of dissemination, application, effectiveness and safety, a description of the medical problem affected by the technology also belong under the analysis of the technology element. It is, however, obvious that the different approaches make widely different demands on the content of the technology analysis. It is therefore impossible to set up a standard check list of the technology components and the data to be included in the technology section of an HTA report. Here, as well as for the other HTA elements, the major *HTA question* (research question) becomes decisive for the content. It is however crucial that the analysis is planned and carried out in connection with the analysis of the remaining elements: organisation, patient and economy (see Section 1.4 and 10.1). Table 6.1 provides examples of questions that can be used for an assessment of the technology element of an HTA.

Table 6.1. Technology description

- At which disease/health problem/potential problem is the technology aimed?
- Has the medical problem been precisely defined and characterised?
- What are the symptoms and stages of the disease (if relevant)?
- How is the natural course?
- What are the consequences of the disease?
- Any prognostic factors?
- Any factors conditioning the acquiring of the disease?
- The number of patients affected by the medical problem?
- The number of patients benefitting from the technology?
- The size of the disease burden (mortality, years of life lost, etc.)?
- The medical problem's economic costs?
- How is the condition treated presently?
- Are there treatment algorithms or guidelines?
- Are the stages of the condition treated differently?
- Are there any evidence-based treatment alternatives?
- What is the material nature of the technology?
- What is the purpose and application area of the technology?
- Is it a future/experimental/tested/established/obsolete technology?
- Does the technology require regulatory approval (for instance, marketing authorisation for medical products) and what is its status for the case handling?
- Are there any special professional or technical requirements for operating the technology?
- Are there factors affecting the application of the technology?

6.2 The medical problem

A health technology assessment should comprise a description of the medical problem at which the technology is aimed as well as an account of the availability, current distribution and use of the technology. Depending on the HTA question, many different methods can be appropriate, however, often a systematic analysis of published literature, collection of primary data from e.g. registers, authorities and producers as well as any own collection of original data, will be required.

The medical problem should be described following common medical tradition (2). The description should comprise, among other things, the aetiology and pathogenesis of the disease, incidence, symptomatology, risk factors, staging, pathways, prognosis and consequences. The qualitative description is supplemented with a more quantitative description which can include:

- the number of patients affected by the technology
- the number of patients that can benefit from the technology
- the actual disease burden (mortality, years of life lost, etc.)
- the economic importance of the medical problem.

It will often be appropriate to add an account of the current treatment of the medical condition, including treatment algorithms and guidelines, treatment of different stages of a disease and special patient groups as well as relevant evidence-based treatment alternatives.

6.3 The technology must be defined and delimited

Prior to describing the technology based on its material nature, its purpose and the degree of dissemination and maturity, the technology must be defined and delimited to make it clear which instruments, techniques, pharmaceuticals and procedures are assessed. The decision-makers, who ultimately have to relate to the available basis for decisions, need a precise description of the technology in order to clarify whether the results of the HTA report will affect the existing practice. A clear definition and delineation is also a prerequisite for being able to search for relevant literature and assess the desired and undesired effects of the technology.

If it is a question of equipment or a surgical instrument, the definition and delineation rarely cause problems. But other technologies are more complex and unformed, e.g. wound care, fast-track surgery or electronic medication. For instance, there is no consensus as to what is understood by an electronic medication system, which, apart from computers and software with designed user interfaces, can include decision support, prescription modules, barcode readers, electronic packaging machines, medicine cupboards, medicine trolleys, training programmes and a large number of procedures. In connection with this type of composite and complex technology it should be the effect of the complete technology that is assessed. The same applies to, for instance, screening programmes. If evidence is only available for the single components, this should be clearly stated in the HTA report.

6.3.1 Technical properties

The HTA question (research question) will always be decisive for how the technical properties of the technology are to be characterised. The necessary content, the structure and the importance of this information will vary from one technology to another. A drug should be characterised completely different than a diagnostic device or a new principle for follow-up home visits to elderly, discharged from hospital.

6.3.2 The material nature of the technology

Health technology comprises more than instruments and equipment – such as, for instance, practical use of knowledge within the health care system. The following broad categorisation can often be used for subdividing health technology:

- *Drugs:* e.g. cytostatic drugs for chemotherapy or drugs for parkinsonism

- *Biological preparations:* e.g. vaccines, blood products and gene therapy
- *Equipment, devices and supplies:* e.g. pacemakers, CT-scanners, diagnostic test kits and elastic stockings
- *Medical and surgical procedures:* e.g. manual therapy, nutrition therapy, medical dementia treatment, cognitive therapy and surgical treatment of myopia
- *Diagnostic procedures and techniques:* e.g. determination of functional capacity, diagnosis of depression and palpation
- *Presentation of knowledge:* e.g. patient schools, preventive health interviews and diet campaigns
- *Support systems:* e.g. telemedicine systems, electronic booking systems, drug selections, clinical laboratories and blood bank
- *Organisational and managerial systems:* e.g. outreach psychosis teams, visiting nurse service, free choice of hospital, vaccination programmes and health-insurance reimbursement for dental treatment.

6.3.3 Purpose and field of application of the technology

Based on the medical problem to be assessed, health technology can also be described by its purpose and field of application:

- *Prevention:* Seeks to protect against a disease by preventing that it occurs, reducing the risk of its occurrence, or limiting its consequences and sequela (e.g. childhood immunisation and infection control programmes in institutions)
- *Screening:* Seeks to detect early signs of disease or risk factors in symptomless persons, to be able to intervene in the disease process (e.g. mammography, blood pressure control or measurement of serum cholesterol)
- *Diagnosis:* Seeks to identify diseases in patients with clinical signs of diseases (e.g. x-ray to detect collapse of the spine, or demonstration of bacteria in the blood)
- *Treatment:* Seeks to maintain good health, cure the sick patient or provide palliation (e.g. antiviral treatment of HIV infection, drug treatment of type 2 diabetes or pain relief in terminal cancer patients)
- *Rehabilitation:* Seeks to restore, maintain or improve well-being or quality of life in patients with physical or mental loss of function.

Some technologies can be placed in more than one category, e.g. mammography which can be used both as a diagnostic method and for screening. Other technologies combine properties from several categories. For instance, stents that are inserted to treat stricture of coronary arteries also release drugs to prevent formation of blood clots, and ultrasound equipment which can be used for both screening and diagnostics.

6.3.4 Maturity and diffusion of the technology

The health technology to be assessed will have a certain degree of maturity and diffusion:

- *Future:* A technology at the conceptual stage or at the earliest stage of development
- *Experimental:* The technology is tested in laboratories, e.g. in animal models or cell cultures
- *Tested:* The technology is tested in clinical studies, e.g. in patients with specific diseases, or applied in a few institutions or in limited parts of the health care system as part of a study
- *Established:* The technology is considered to be standard treatment or routine practice and generally applied in the health care system

- *Obsolete:* New, safer or more effective technologies have surpassed or replaced older technology.

Often the different stages are not clearly delineated. Technologies do not necessarily run a full cycle and a technology is not infrequently experimental or being tested on for certain patient groups, standard treatment for other groups and replaced by other treatment options or principles for still other patient groups. For instance, x-ray examination of the chest is still of great value at assessment of heart and lung diseases but is no longer used routinely for all patients prior to surgery.

When relevant the technology description can furthermore include:

- who is to operate the technology
- technical and professional requirements of the operator
- status of the technology within the medical legislation and its consequences
- requirement for special purchase of spare parts, supplies, machinery, computer programs or utensils, etc.
- prerequisites for application, e.g. relation to special departments or facilities
- whether the technology is a supplement to existing technologies.

The area of indication should always be illustrated thoroughly, both the areas in which the technology is currently applied, based on solid scientific evidence, and those areas in which the technology is expected to become important, but where the scientific basis is still incomplete. It is fairly common that the area of indication for a health technology is expanded gradually so that a technology developed with a view to a specific problem area is gradually applied within other areas.

If possible, factors that influence the application and diffusion of the technology should also be described. This may be the clinicians' expectations, the decision-makers' involvement, lack of alternative technologies, marketing, commercial interests, etc.

6.3.5 Compare with best practice

A review of a health technology must comprise an account of alternative technologies, including both established as well as new alternative ways of solving the medical problem in question. The assessed technology should be compared with alternative technologies, primarily with the best established practice for comparison of advantages and disadvantages of the various methods. Therefore one has to search for studies that compare the technology in question with relevant alternatives.

To which extent a method, a regimen or a treatment practice is more effective than another can only be determined by a direct "head to head" comparison in the same study. When assessing these comparative studies one has to look closely at the selected treatment intensities, dosages, step-ups and step-downs, treatment duration, number of control visits, etc. to ensure that it is an equal comparison. The fact is that there is ample opportunity to plan studies in such a way that the result of a comparison is a foregone conclusion.

Often one will be in the situation that a new treatment or practice has only been compared with one treatment which is not the current standard. Then it may be necessary to carry out an indirect comparison, for instance, by comparing the results of two different placebo-controlled studies. This must be accompanied by considerable reservations. The two different treatments will merely be one of various differences between

the studies: Differences in, for instance, patient populations, the patients' risk profile, study design, or examination circumstances will often by far overshadow differences in treatment effect.

6.4 Evidence

A technology assessment nearly always requires a systematic review of the existing scientific literature (see Chapter 3 and Section 4.1.) and will often have to be supplemented with an analysis of data from other primary information or data sources. The two approaches lead to results of different reliability and validity and it is primarily the HTA question that determines the choice of the most appropriate method (see Section 6.5.1 about efficacy and effectiveness).

A number of medical challenges are handled on a weak scientific basis, and consequently it may be necessary for oneself to collect primary data as part of a health technology assessment. However, own studies are often very time- and resource-consuming and should only be implemented if the existing scientific literature neither wholly nor partly answers the research question. In too many cases studies are initiated in spite of the fact that the literature already contains scientific documentation regarding the problem.

It should also be resolved whether similar studies have been carried out elsewhere. Especially when it concerns randomised clinical studies an increasing number of registers of ongoing clinical studies are available (e.g. CancerNet.gov, CenterWatch.com, ClinicalTrials.gov). By orientating oneself in these registers, superfluous studies are avoided or otherwise the quality of one's own study can be increased.

6.4.1 Systematic literature search regarding the technology

When assessing a health technology, firstly, one should systematise and analyse the knowledge available within the scientific literature.

The literature analysis should always follow the principles for systematic reviews (www.cochrane.org/resources/handbook/) (3):

- Formulation of an actual question which can be answered
- Search in relevant literature databases using explicit search criteria
- Establishing criteria for selection and evaluation of the articles.

In practice it will depend on the question which criteria are used for selection and evaluation of the literature, as well as which study design to include in the analysis (Table 6.2). When it comes to assessing a health technology, clinical and epidemiological studies are of the most interest, but often health services research can contribute significantly. In addition to a critical assessment of the scientific quality of the literature, the transferability of the results should always be discussed. Is it possible to transfer the result informally to the patient group who will be affected by the technology? The assessment is based on the studied patients' age, gender, disease severity, etc. as well as on the framework of the study. It may, for instance, be difficult to transmit results obtained at a highly specialised university hospital to the primary health sector, in which, amongst others, the professionals' competencies and the disease panorama are totally different.

Table 6.2. Preferred study designs for different research questions

Research question	Purpose of study	Preferred study design
Therapy and prevention	Study the effect ("efficacy") of medical or surgical treatment, preventive measures, care methods or other interventions.	A randomised controlled trial.
Diagnostics	Study whether a diagnostic test is valid (can we trust it?) and reliable (same result each time?).	A cross-over study in which both the new test and the standard test (gold standard) are applied.
Screening	Study the value of an examination or a test which to be used in larger groups to identify persons with a disease at an early pre-clinical stage.	A cross-sectional study.
Prognosis	Clarify the course over time in patients with a disease at an early stage.	A cohort study.
Causality	Determine whether a presumed detrimental effect (e.g. air pollution) increases the risk of development of disease.	A cohort or case-control study depending on whether the disease is common or rare.

The literature analysis applied should always be described in detail and the result should be summarised and presented in clear tables, and should be included in a meta-analysis if possible (www.cochrane.org/resources/handbook/) (3).

Literature search and assessment are described in more detail in Chapter 3 and Section 4.1. For in-depth reading, reference is made to two websites with recommendations for the reporting of clinical and epidemiological studies: www.CONSORT-statement.org, concerning randomised controlled studies and www.STROBE-statement.org, concerning observational studies.

6.4.2 Analysis of data from primary sources

Databases and registers

Observational data to illustrate effect and safety are often based on one's own data collections, but can also be based on routinely collected register data. The (Danish) Cancer Registry, National Patient Registry, Causes of Death Registry and Pharmaceutical Database are examples of valuable data sources for epidemiological studies (see Section 5.3).

The number of national and regional clinical databases is increasing and can be a valuable source of data on current clinical quality (Clinical Databases, NHS). The same applies to data from authorities and producers (but may be restricted due to patent protection, competition, marketing, etc.).

Methodological stringency is an absolute necessity when summarising and interpreting such data in order to avoid "over-interpretation". There must be justification in the data for the conclusions, and any restrictions must be stated explicitly. When data from registers or clinical databases are used, it must always be stated how the data are collected and coded, inclusion and exclusion criteria, data quality as well as to what extent the register/database is representative (European, national, regional, local).

When carrying out original studies as part of a health technology assessment, the studies should naturally live up to general scientific standards.

Even where it would be appropriate to supplement a literature review with an analysis of data from primary sources, this is not always possible within the economic scope or time frame of a project. One has to restrict oneself to the evidence that can be provided from literature or other data sources. Encircling areas in which the evidence is weak or lacking altogether can in itself be a useful result of an HTA.

Important study designs

Studies can be designed in many ways and researchers have a large degree of freedom to use particular design variations to study special research questions (Table 6.2). Preparing an HTA is primarily an interpretation of others' research. Therefore one must be able to see through the different designs and take any errors and pitfalls into account.

A detailed review of study designs and research methodology is beyond the scope of this Handbook and reference is made to the large quantity of standard literature available on the topic, e.g. "How to Read a Paper: the Basics of Evidence Based Medicine", BMJ Publishing Group 1997 (www.bmj.com) (4) or "Users' Guide to the Medical Literature. A Manual for Evidence Based Clinical Practice", AMA press 2002 (www.usersguides.org) (5).

Here the principles for the most important study designs are outlined. Advantages and disadvantages of different experimental and observational studies appear in Table 6.3.

Table 6.3. Characteristics of different types of study design*

Egenskaber	**Typer af design**			
	Controlled randomised study	Cohort study	Case-control study	Pre-/post-treament
Quick to perform	(÷)	÷	+	(÷)
Reasonable economy	÷	÷	+	+
Well-controlled confounding factors	+	(÷)	÷	÷
Generalisable results	(+)	+	+	÷
Well-controlled exposure	+	+	÷	÷
Well-controlled outcome	+	+	+	(+)

*Qualitative studies are not included in the table.

Randomised controlled studies

The randomised controlled study, or the randomised controlled clinical trial (RCT) is scientifically the strongest design when evaluating the effect of health technology.

Examples of questions that can be studied in a randomised clinical study:

- Is treatment with SSRIs more efficacious/effective than placebo for mild to moderate depression?
- Is a leaflet superior to oral information when advising patients on choice of treatment for carotic arteriosclerosis?

The principle of an RCT is that patients are randomly selected for two different technologies, the effect of which is to be compared. It may be a question of comparing a treatment with placebo or, for instance, a new technology with a previously applied technology.

Because the patients are allocated by a principle of chance corresponding to "flipping a coin", the patient groups become directly comparable, and known – as well as unknown – risk factors among the patients are considered. Thus, it is possible to create a controlled experimental situation in which the intervention is the only difference between the two groups. Consequently, the variances in the results can be attributed to different effects of the tested technologies.

Ideally neither patients nor researchers should be able to identify with which technology the different patient groups are treated (double blinding). This is relatively easy when the effect of two drugs is compared, but more difficult – or completely impossible – if, for instance, a training programme is compared with psychotherapy. Inadequate blinding leads to risk of misinterpretation of the result (bias).

An RCT presumes the patients' informed consent, and patients who choose to participate are often different from the ones that do not participate. In addition, the inclusion criteria in these trials are often so strict that large parts of the target population are excluded from the trial. This means that the result cannot be transferred to "normal" patients or daily clinical practice.

Pre/post studies

Pre/post studies are intervention studies like the randomised controlled trials. But their design is scientifically less strong than RCTs and more sensitive to bias. A pre/post study makes use of one technology during one period and another technology during a later period within the same population. Finally, the effect from the two periods is compared. The biggest weakness of this design is that both the population and the overall intervention can change during the interval between the two periods. This also applies to other parameters which can influence the result of the intervention, e.g. staff's awareness of a problem or its competencies.

A cross-over study is a special variant of the pre/post study. In this study the individual patients function as their own controls, and each patient is subjected to all the studied technologies. The patients are often randomised to a specific order of intervention. The main weakness is possible interactions between the interventions or what is often referred to as "carry-over effect" (a late effect of one intervention which then influences a later intervention).

Observational epidemiological studies

Cohort studies: In a cohort study, two or more groups are selected based on differences in exposure (vaccine, drug, hazardous influence, etc.). The groups are followed over time to observe whether they develop specific diseases or symptoms.

Examples of questions that can be studied in a cohort study:

- Is it dangerous to live in the vicinity of high-voltage cables?
- How is the development of children with mothers who abused alcohol during the pregnancy?

The result of a cohort study is often presented as a relative risk (however, also more advanced statistical methods may have been applied):

		Survival	
		Yes	**No**
Exposure	Treatment A	a	b
	Treatment B	c	d

As an example, when testing a treatment A for a specific disease *a* patients survive for 5 years, while *b* patients do not survive for 5 years. Among the control cohort treated with treatment B *c* patients survive for 5 years, while *d* patients do not survive for 5 years.

The relative risk (RR) is calculated as $\frac{a}{a+b}$ divided by $\frac{c}{c+d}$

If there is no statistically significant difference between the two fractions (RR = 1), this suggests that there is no difference in effect between the two treatments.

However, if $\frac{a}{a+b} > \frac{c}{c+d}$ or $\frac{a}{a+b} < \frac{c}{c+d}$ (RR is statistically different from 1) treatment A is more effective, less effective, respectively, than treatment B.

This result presupposes that the two populations are basically identical. This is, however, rarely the case. Nevertheless, there are methods which make these populations more comparable in analyses (so-called *matching*).

Since, naturally, a cohort study is not randomised, the groups will be different. When reading cohort studies, one of the most important tasks is thus to assess whether the researchers have systematically tried to identify potential confounders, and next, whether they have analysed the distribution of the potential confounders between the compared groups and taken any biased distribution into account in their analysis (cf. Section 4.1.6).

Case-control studies: An alternative observational study design is case-control. In a case-control study a group is selected with an effect or an outcome (e.g. leukaemia or pulmonary embolus) as cases and compared with one or more groups without disease with

a view to the exposure to which the group has been subjected. For instance, epileptic mothers, who have given birth to a child with *spina bifida*, can be compared with a group of epileptic mothers, who have given birth to normal children regarding taking specific drugs during the pregnancy. It is a principal rule that controls must be selected from a population of persons which themselves are at risk of becoming a case. The controls can be selected and matched with cases in different ways, and when interpreting case-control studies, one has to pay special attention to the selection of controls.

Examples of questions to be studied in a case-control study:

- Is pulmonary embolus a side effect in the treatment with antipsychotics?
- Is the gene variant COL1A1 important for the development of myopia?

The result of a case-control study is often presented as an odds-ratio (however, also more advanced statistical methods may have been applied):

		Cases	Controls
Exposure	Yes	a	b
	No	c	d

The odds-ratio (OR) is calculated as $\frac{a}{a+c}$ divided by $\frac{b}{b+d}$

If $\frac{a}{a+c}$ and $\frac{b}{b+d}$ are equal (OR =1) there is no statistical difference between the two groups. If OR is statistically different from 1 this suggests that the exposure is associated with the disease or symptom of interest.

6.5 Effects, endpoints and outcomes

6.5.1 Effect is more than "efficacy"

Effect means how effective a treatment or the application of the technology is. In English there are two terms for effect: "efficacy" and "effectiveness". "Efficacy" expresses the efficiency under ideal conditions, i.e. under research conditions, whereas "effectiveness" expresses the efficiency under more normal daily practice. Contrary to daily practice, the patient population and treatment conditions in a clinical study are standardised. The patients receive, for instance, detailed, standardised information, the treatment is followed according to a schedule, and patients with competing diseases, poor compliance, great age, etc. are excluded from participation. An "aquarium situation" which is rarely found in the clinical reality. Consequently the results of a successful clinical study can be seen as the maximum achievable.

In Danish we do not have the same linguistic division of effect into "efficacy" and "effectiveness", but when we talk about the effect of a technology in an HTA context, effect is essentially understood as the English "effectiveness", in which we are interested. As a minimum it should be assessed to which extent the effect documented in research framework ("efficacy") is also achievable in daily practice ("effectiveness").

6.5.2 Surrogate endpoints and compound endpoints

Many different relevant objectives of effect can be established, depending on whether the purpose of the technology is prevention, screening, diagnosis, treatment or care. It is not infrequent to use surrogate endpoints. For instance, one measures the change in bone mineral content (but is actually interested in symptom-producing fractures), the prostate-specific antigen in the blood (interested in exacerbation of prostate cancer) and the wall thickness of the neck arteries (interested in cerebral infarction and sudden death).

From a scientific methodological point of view, there can be many reasons for using surrogate endpoints. However, the normal interest would be whether the technology gives the patient increased survival, relief, fewer complications or increased quality of life. Only a few patients would worry about the activity of an enzyme in the blood. When the effects of the technology is described based on surrogate endpoints, it follows that one has to state whether the surrogate endpoint is associated with a relevant, definite endpoint and to what extent a clinically relevant effect can be precisely predicted based on changes in the surrogate endpoint.

Compound endpoints are also used increasingly, e.g. the combination of coronary death, fatal or non-fatal acute myocardial infraction (AMI) and fatal or non-fatal cerebral infarction (apoplexy). Compound endpoints are appropriate in several connections and enable, amongst other things, the carrying out of studies with fewer patients. However, the interpretation can cause problems, especially if the combination consists of endpoints with very different clinical importance. How should one deal with changes in endpoints that combine death and terminal renal failure with a doubling of serum creatinine? The problem is that a decrease in the frequency of double serum creatinine may turn out essentially to represent an apparently beneficial effect on death and terminal renal failure. In this situation it may be a good idea to view each endpoint individually and at the same time remember that this may pose a considerable risk of overlooking an effect.

6.5.3 Effect sizes

Effect size can be expressed in many different ways, for instance as difference in mean blood pressure (continuous endpoint) or difference in mortality (categorical endpoint). Categorical endpoints, especially, such as dead/alive, healthy/ill can be manipulated. The same quantitative effect can be expressed in many different ways, for instance, as relative risk reduction (RRR), absolute risk reduction (ARR), odds ratio (OR) or number needed to treat (NNT). As the example in Table 6.4 shows, the same effect can be expressed as an odds ratio of 0.45, a relative risk reduction of 54%, an absolute risk reduction of 1.6% and number needed to treat of 62.

Table 6.4. Calculation of different endpoints

Data from a randomised study

Treatment	Number of patients	Number of patients with effect	Number of patients without effect
Intervention	4047	56	3991
Control	4029	121	3908

➤

Calculations based on data

Experimental event rate	ERR	56/4047 = 0.014 (1.4%)
Control event rate	CER	121/4029 = 0.030 (3.0%)
Odds for experimental events	OE	56/3991 = 0.014 (1.4%)
Odds for control events	OC	121/3908 = 0.031 (3.1%)
Odds-ratio	OR = OE/OC	0.014/0.031 = 0.45
Relative risk reduction	RRR = 100x((CER-ERR)/CER)	100x((0.030-0.014)/0.030) = 0.539 (54%)
Absolute risk reduction	ARR = CER-ERR	0.030-0.014 = 0.016 (1.6%)
Number needed to treat	NNT = 1/ARR	1/0.016 = 62

The same quantitative effect is expressed as an odds-ratio of 0.45, a relative risk reduction of 54%, an absolute risk reduction of 1.6% and number needed to treat of 62.

It is very important for the subjective perception of the effect size whether ARR or RRR is used. Take as an example, a study in which 1% of the patients in the placebo group and 0.6% of the patients in the intervention group die. ARR for death is 0.4% (1%-0.6%), whereas RRR for death is as much as 40% (100x(1%-0.6%)/1%). Since RRR is a larger number, RRR is naturally often used in abstracts and marketing material. The example shows how easily a moderate absolute reduction in a moderate death of 0.4% can be transformed into a fairly large (convincing!) relative risk reduction of 40%. Both effect expressions are correct and both should be stated instead of just the one.

It is important to note that just because an effect in a study is statistically significant this does not mean that it is of a *clinically* interesting magnitude. Consequently, it is not sufficient to state that a statistically significant effect has been found, or state the p-value. The effect size must be stated. To ensure the best possible transparency the experimental and control event rates as well as ARR should be stated, if possible.

6.6 Risk and safety

Positive as well as negative effects will nearly always be attached to the use of a technology, and the risk scenario should always be examined. In addition to safety data from clinical tests, it can be of interest to search for, for instance, case-control studies, cohort studies, routinely collected safety data, data from clinical databases, the pharmaceutical companies' pharmacovigilance data or the producers' safety information and data sheets. The sources must always be stated, and data should be analysed and interpreted using the same scientific stringency as for data on effect.

The risk analysis should always include both the patients and the staff who are to operate the technology. The following elements can be included:

- Safety requirements for the application of the technology (requirement for licence or certification?)
- Terminology and definitions (how is "safety" defined when it comes to the technology in question?)
- Identification of risks and hazardous effects (which side effects or adverse effects can be expected?)
- Assessment of the hazardous effects of the technology (is it possible to have a total overview of risks? how well are they documented?)

- The importance of the hazardous effects (how frequent and serious are the side effects and negative effects? are they associated with increased mortality and morbidity?)
- Prevention (does the risk scenario change over time? can risk and injury be prevented? work-related precautions? other necessary technology? assistance and backup from experts?)
- Comparison with alternative technologies.

Some hazardous effects are only detected after using the technology for a long time or after systematic observation of a large number of treated patients for a considerable time. An assessment of the risk scenario must include a description of expected injuries that require special attention in the short and the long term. First priority should be on the frequent negative effects (irrespective of severity) and the rare but serious negative effects. In addition, one should consider the acceptability of such side effects. The tolerance threshold for complications is very low when the technology is used for healthy persons (prevention or screening) or for patients with less serious disorders. Finally the risk scenario should be summarised and the adverse effects balanced against the requested effects of the health technology. Where possible a comparison is made with alternative technologies.

6.7 Shortly about diagnostic tests

A diagnostic test can be described using a number of terms (Table 6.5) which collectively express the validity of the test.

Table 6.5. Description of a diagnostic test

		Gold standard	
		Positive	**Negative**
Test	**Positive**	a	b
	Negative	c	d

Expression	**Formula**
Sensitivity	a / (a + c)
Specificity	d / (b + d)
Positive predictive value	a / (a + b)
Negative predictive value	d / (c + d)

When assessing articles describing validation of a diagnostic test there are a number of circumstances to be aware of:

- Is the new test being compared with a relevant gold standard?
- Has the test been studied in a relevant patient population (age, gender, stage of disease, etc.)?
- Were all patients tested using both the new test and the gold standard (workup bias)? And was it blinded (expectation bias)?
- Is the new test valid?
- Have the confidence intervals been stated?
- Is the normal range described (continuous objectives)?

It is also necessary to decide how to categorise the test in a diagnostic sequence. Should an electrocardiogram (ECG) be carried out first, if, for instance, it is a test which is to be used in the assessment of patients suspected of having acute myocardial infarction (AMI)? Is the test to be used on all or only on patients with ECG changes? Etc.

Finally, the diagnostic test should be put into context with health problem – diagnosis – intervention – health result. Although it cannot be a requirement for the introduction of a diagnostic test, scientific documentation should be found which indicates that the diagnostic technology used in normal clinical practice leads to improved treatment results.

6.8 Literature for Chapter 6

(1) Goodman C. Introduction to health care technology assessment. National Library of Medicine: National Information Center on Health Services Research & Health Care Technology (NICHSR); 1998.

(2) Magnus P, Bakketeig L. Epidemiologi [Epidemiology]. 3rd ed.: Gyldendal Norsk Forlag; 2003.

(3) Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5. The Cochrane Library Chichester, UK: John Wiley & Sons, Ltd.; 2005.

(4) Greenhalgh T. How to Read a Paper: The Basics of Evidence Based Medicine. London: BMJ Publishing Group; 1997.

(5) Guyatt G, Rennie D, editors. Users' guide to the medical literature: a manual for evidence-based clinical practice. Chicago: AMA Press; 2002.

7 The patient

This chapter is intended to assist HTA practitioners in clarifying how patient aspects can or should be explored in a given HTA. The research field is presented from a humanistic perspective, and the importance and handling of patient aspects in an HTA context are discussed. Links are made with the general method-related chapters concerning qualitative methods (Sections 4.2 and 5.1). This patient-oriented chapter ends with a section on patient-experienced quality.

7.1 Patient aspects in HTA

By Helle Ploug Hansen

Useful advice and suggestions

- Patient aspects need to be explored when the respective technology, organisation and/or economic aspects concern (affect and influence) people, i.e. (nearly) always
- In HTA contexts, the concept of patient also refers to the concepts of citizen, customer, user and individual
- A thorough review of the literature is needed before primary research is decided upon – this applies generally in HTA, i.e. also to patient aspects
- Reviews of the literature in the form of systematic reviews and any syntheses of qualitative research should be used in preference to primary research, if valid and usable research results are available or can be analysed
- Any research results (the knowledge produced) are always subject to the knowledge being "positioned".

7.1.1 Introduction

This chapter is based *firstly* on the assumption that the health technologies to be assessed in a specific HTA do not exist in a vacuum. Health technologies can be said to be used and understood by the people involved. This is how they gain their significance. It is therefore difficult to consider health technology in isolation from the people (patients, treatment providers, researchers, politicians and decision-makers) who use and understand it, including their social understanding of the technology and the organisational and economic frameworks.

Secondly, this chapter is based on the assumption that any research results implicitly or explicitly entail a specific understanding of knowledge, i.e. whether knowledge is something we *have* or whether it is something we produce and reproduce in different social relations and in different contexts. This means that one's understanding of knowledge will always have implications in relation to the validity and scope of the research results. Exploring patient aspects in a specific HTA therefore entails the researcher bearing in mind that knowledge always arises from certain theoretical/analytical positions (Bruun et al. (1); Hansen 2004 (2)).

The understanding of patient aspects presented in this chapter is rooted in an understanding of Man as a biological, social and cultural being who creates and recreates meaning, and who forms part of a material, practical and linguistic community (Hansen 2002) (3). An individual is therefore at the same time, among other things:

- an individual with specific experiences, thoughts and feelings
- social in a very fundamental sense, as relations are logically social.

7.1.2 Exploration of patient aspects

Patient aspects must be explored in an HTA if technology, organisation and/or economic aspects concern (affect and influence) people. Both nationally and internationally, HTAs have hitherto first and foremost been formulated on the basis of experts' knowledge of a given health technology with the aim of providing the basis for political and/or administrative decision-making and action. In recent years, it has become increasingly important for patients' own experiences, preferences, resources, needs, requirements and assessments generally in respect of initiatives in the health care sector to be taken into account, as part of formalised, systematic quality assurance (4). Patients must have the opportunity of choosing between the health services, with this being manifested in, for example, free choice of hospitals and in the provision of informed consent for diagnosis, treatment and care.

The wish to illuminate a given technology from the perspectives of patients, both in terms of new technological measures and the evaluation of existing health measures, has consequently become more and more dominant[3]. This may entail gaining an understanding of the following aspects:

- patients' knowledge and experiences of a given technology
- patients' preferences, needs and expectations of the technology
- patients' visions and requirements concerning the technology, economic aspects and organisation
- how customs, attitudes and traditions influence patients' experiences, preferences, etc.
- what importance the technology in question has or may have for the patient's everyday life
- how patients' self-care and/or empowerment resources are best exploited, and what opportunities and limitations apply to self-care/empowerment (see, for example, Bridges & Jones 2007 (5); Coulter 2004 (6); Draborg et al. 2005 (7); Lehoux & Williams-Jones 2007 (8); Leggs & Evans 1992 (9)).

It is also important that HTA practitioners think about and decide whether, as part of a planned HTA, they need to produce knowledge from:

- *an individual perspective:* Focus on the individual patient in relation to his or her everyday life
- *a group perspective:* Focus on a group of patients' experiences and assessments of the effect of a given technology on their everyday lives
- *a social perspective:* Focus on patients as citizens, users, consumers and, for example, their assessment of what criteria should underpin the development or introduction of a specific technology, or how different technologies should be prioritised.

This assessment is of central importance, in relation both to reviews of the literature and primary research.

7.1.2.1 Patient, citizen, user and individual

In HTA contexts, the term "patient" also refers to concepts such as *citizen*, *user*, *customer*, *consumer* and *individual*. The actual word "patient" comes from the Latin word "pati", which means *to suffer* and from "patients, patientis", which means *passive* and *suffering*. Nowadays, this understanding is inadequate. Decision-makers, health professionals and many patients consciously and/or unconsciously seek to add new meanings to the patient concept. Patients set up self-help groups, communicate with one another

3 The list of literature contains references to reports in which the patient aspect has been explored either via reviews of the literature or via primary research.

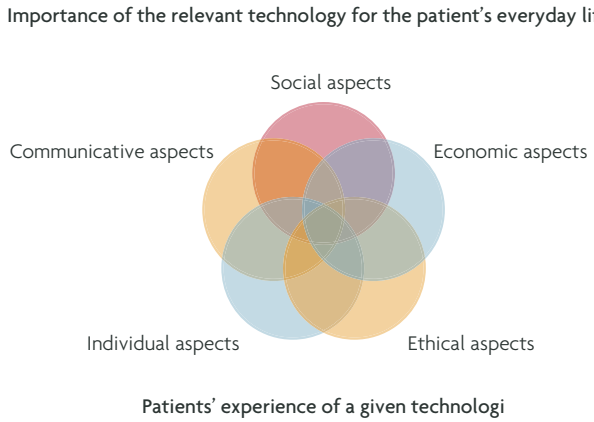
in various internet chat rooms, download scientific articles, etc. They are no longer merely dogged and long-suffering. They want to help determine health promotion, disease prevention, treatment, care and rehabilitation or measures they are offered or would like to be offered. A *patient* is thus also a *citizen* within a state and civil society, a *user, customer and consumer* in a market-based society and an *individual* who may need care and support.

In overall terms, the health care sector is designed to offer health promotion, disease prevention, treatment, care and support, palliation and rehabilitation to people whose health is threatened or who are sick, suffering or dying. This includes a wide range of measures that are not merely or perhaps not even aimed at the traditional understanding of the term ”patient”. Terms such as ”patient education in groups”, ”self-care” and ”empowerment” are used by actors in the health care sector (including politicians, civil servants, researchers and health professionals). These terms are also indicative of a broadening of the patient concept.

7.1.2.2 A model

The analytical model below sets out some of the aspects that previous HTA reports and literature (see, for example, Lee & Seest Sinding 2007) (10) have identified as being relevant in exploring patient aspects (Figure 7.1). Often, such exploration will mean a focus being placed on patients' knowledge and experience of a given technology, patients' resources and the importance of the technology in question for the patient's everyday life.

Figure 7.1. Exploration of patient aspects in HTA



The model is intended to show that the various areas upon which HTA practitioners choose to focus when exploring patient aspects cannot be considered in isolation from one another. Only in an analytical fashion is it possible to focus on, for example, ethical aspects instead of economic ones. Some examples of what one can choose to investigate within each area are set out below.

Social aspects

This covers whether, from a patient perspective, the technology will have or has, for example:

- a direct and/or indirect influence on/significance for
  - work and training

- family life
- leisure time
- lifestyle/quality of life.

Economic aspects (see also Section 9.6.3)
This covers whether, from a patient perspective, the technology entails, for example:

- direct and/or indirect costs in relation to
  - work
  - family life
  - leisure time
  - lifestyle/quality of life.

Ethical aspects (see also Chapter 2)
This covers whether, from a patient perspective, the technology entails, for example:

- ethical considerations
- ethical choices
- ethical dilemmas.

Individual aspects
This covers whether, from a patient perspective, the technology entails:

- existential experiences, e.g. insecurity, worry, hope, anxiety
- patient roles and stigmatisation
- courage to face life
- satisfaction
- use of one's own resources (self-care, empowerment).

Communicative aspects
This covers whether, from a patient perspective, the technology will have or has an influence on:

- exchange of information
- patients' knowledge and understanding of the technology
- modified relations between the patient and health professionals
- involvement in decision-making.

7.1.2.3 Research questions

Based on the model presented, central research questions will therefore typically be aimed at:

- social aspects
- economic aspects
- ethical aspects
- individual aspects
- communicative aspects.

It is nevertheless important to be attentive to preventing that research questions from previous HTA reports and other HTA literature are simply applied to the HTA project in question. In principle, research questions only become clear once work is done on formulating a project description/protocol, including the formulation of a clear defini-

tion of the problem. Good research questions are formulated on the basis of a thorough review of the literature. It thereby also becomes clear whether valid and relevant research results exist in the area concerned, or within adjacent areas.

7.1.2.4 Positioning

Lastly, it is important that HTA practitioners think about how the people/patients included or to be included in the exploration of patient aspects in a given HTA are positioned and position themselves. The positioning of a person as a patient, citizen, user or consumer has an influence on the data generated, and thus, in the final phase of an HTA, on the scope and validity of the results produced. This applies both to primary research and to secondary research (review of the literature). The fact that not only are informants always positioned but that they always position themselves becomes particularly clear in primary research, where the investigator, for example, interviews the same people several times or in fieldwork with participant observation, where the researcher meets the same people in a number of different situations.

Regardless of whether the participating patients have positioned themselves or have been positioned by researchers as citizens, as users, as consumers or as patients, their perspectives on health, disease and suffering will often differ from health professionals' (see, for example, Busch 1997 (11); Kleinman 1988 (12); Hansen 2002 (3), Timm 1997 (13); Svendsen 2004 (14); Montgomery & Fahey 2001 (15); Say & Thomson 2003 (16); Jensen 1997 (17)). Patients' knowledge and experiences of, and attitudes towards e.g. health promotion, disease prevention, illness, suffering, treatment, care, rehabilitation and the health technology in which they are involved are very much linked to everyday life and based on their own actual experiences and/or those of others close to them and on a shared everyday culture.

HTA practitioners who undertake the generation of data are of course also themselves positioned, and are positioned by the participating patients. Merely asking questions, in certain ways and perhaps at certain times during an interview says something about the position or positions that the researcher has consciously and/or unconsciously chosen and thus also about the range of data generated. Open questions are not open, but merely so in a general sense. They are asked from a particular position. This represents a condition. Even if, for example, a researcher starts off by saying: "Will you tell me something about your experiences with …", a choice, and thus also a choice to omit, is made. The researcher wants to hear about certain specific experiences, and not all possible experiences. The researcher is engaged on a particular matter that he/she pursues using his/her chosen research methods and questions.

7.1.2.5 Patient aspects – a separate element of an HTA?

In national HTA reports, patient aspects are usually handled separately, whereas international HTA reports have for the most part regarded the "patient" as part of the technology (10). In this context, however, there is now a tendency to deal with patient aspects individually. When exploration of patient aspects is based on secondary research, i.e. reviews of the literature, and incorporates results from different types of patient satisfaction surveys, investigations of patient preferences and/or qualitative studies of patient needs, desires, experiences, etc., it is often appropriate to address patient aspects separately from technology, organisation and economic aspects.

Where exploration of patient aspects is based on primary research, it is possible to work from the assumption that health technology is not something isolated. Health technologies are used and understood by the people involved in them. Health techno-

logies are of importance only through the people, who use and understand them as, for example, patients, citizens, users, treatment providers, politicians and decision-makers. Even if a patient, doctor, nurse or politician may have the same aim with a given health technology, their knowledge of the technology, their areas of responsibility, ethical obligations, practical duties, etc. differ. It may therefore be appropriate to investigate the HTA in question as a generation of knowledge, i.e. as a social process: *"… in which various players (doctor, nurse, patient, journal) interact and thus exchange various kinds of knowledge, i.e. different ways of understanding the situation, the problem and the solution"* (Willemann et al. 2005, p. 35) (18).

Knowledge thus becomes something that is produced as and should be understood as something social rather than something substantive. An example of an HTA project that has focused on knowledge generation is published in the Danish report *Ward Rounds – an HTA focused on production of knowledge* (18). If the HTA researchers choose this understanding of knowledge, it becomes possible to regard the various elements of an HTA as relationally linked. In a "traditional" form of Danish HTA, the four elements will be investigated separately and followed by a synthesis. If the various elements are regarded as relationally linked, it will be possible to investigate how the patient, technology, economic aspects and structure are linked, and how they affect and influence one another. This form of HTA will be demanding in terms of resources as a closely cooperating team of researchers will be needed, and at least one of these researchers should have skills within this kind of knowledge generation, i.e. within humanities or social science.

7.1.2.6 Patient-specific aspects of literature reviews

Most investigations of patient aspects in an HTA entail to literature reviews. For a general description of searches of the literature, see Chapter 3, and for assessments of the literature, see Chapter 4. The first review of the literature is performed early in the project description phase. This is a necessary part of being able to frame a clear formulation of the problem in a precise language, including posing the research questions to be answered by the investigation, and/or the hypotheses to be confirmed or rejected. It is important that the researcher has drawn up a number of explicit search criteria, e.g. that it must be international, reviewed articles and confined to, for example, meta-analyses, systematic reviews and concept analysis. If the introductory review of the literature does not yield relevant results, it is important to assess whether this is because:

- Patient aspects in the HTA in question have not been explored previously
- The search criteria have been too broad and unfocused
- The search criteria have been too narrow and must therefore be supplemented by new search criteria to be able to assess whether there are valid research results within adjacent comparable areas.

If the review of the literature reveals that valid and relevant research results exist within the area in question or within adjacent areas, it is important to clarify what form(s) of knowledge about the patient the review of the literature has uncovered.

It is necessary to assess what kind of understanding(s) of knowledge the review of the literature has uncovered and not merely concentrate on what one knows. Results from questionnaire-based investigations, surveys, will primarily be found in, for example, HTA investigations, epidemiological studies, quality-of-life investigations, studies of behaviour and attitudes, self-reported health status investigations, patient satisfaction studies and informant studies. Secondarily, the above-mentioned types of study will

reveal results from qualitative studies of patients' experiences, their everyday lives, and the history of their suffering and illness. In a large proportion of both quantitative and qualitative studies, knowledge often appears as something that someone *has*. Patients *have* desires, *have* needs, *have* preferences, etc., which are experienced by the patient virtually independently of the context (ill, healthy, health-threatened, etc.) in which the individual in question found himself/herself when he/she was interviewed or was required to answer a questionnaire. It is important that researchers consider that their understanding of knowledge has a bearing on the scope and validity of the research results. If researchers work from an understanding of knowledge as something that someone *has*, it is disregarded (which may be necessary in the HTA in question) that communication is an active and creative process which takes place in relations in which significance is created and recreated (2).

When searches are performed in more humanistic databases such as Psychinfo, CINAHL, Sociological Abstracts and generally within humanistic health research literature, research results based on a different understanding of knowledge could be produced. Here, knowledge is often concidered as something that is produced in and with a context, and as something which comes about in communication, i.e. the social relations between patients, citizens, users, health professionals, specific objects and organisational frameworks. If an HTA of patient aspects is to be based on results from a search of the literature conducted within humanistic databases, it will probably be necessary to undertake a *synthesis* of certain qualitative studies (see Section 4.2.2). The review of the literature can be used in part to gain an understanding of how a certain area, e.g. screening, can be understood, while it can also help clarify how patient aspects in the planned HTA are to be tackled, i.e. whether primary research is to be conducted.

Selected HTA reports in which patient aspects are addressed:

Boothroyd L, Lehoux P. Home-Based Chemotherapy for Cancer: Issues for Patients, Caregivers and the Health Care System. Quebec: AETMIS. Quebec; 2004. (http://www.aetmis.gouv.qc.ca/site/home.phtml)

Christensen LA, Dahlerup JF, Poulsen PB, Thranholm L. Capsule Endoscopies of the Small Intestine – a Health Technology Assessment. Copenhagen: National Board of Heath, Danish Centre for Health Technology Assessment; 2007. Health Technology Assessment – projects funded by DACEHTA 2007;7(1). English summary: (http://www.sst.dk/publ/Publ2007/MTV/Kapselendoskopi/Kapselendoskopi_en.pdf)

Lassen KØ, Olsen J, Ginderslev E, Melchiorsen H, Kruse F, Bjerrum M. Medicinske patienters ernæringspleje – en medicinsk teknologivrudering. [Nutritional Care of Medical Patients – a Health Technology Assessment] Copenhagen: National Board of Health, Danish Centre for Health Technology Assessment; 2005. Health Technology Assessment – projects funded by DACEHTA 2005;5(4). Report in Danish with English summary: (http://www.sst.dk/publ/publ2005/CEMTV/ernaeringspleje/ernaeringspleje_final.pdf)

Lee A, Sinding LS. A review of organisational and patient-related assessments in HTAs published by INAHTA members. Copenhagen: National Board of Health, Danish Centre for Health Technology Assessment; 2007. Danish Health Technology Assessment 2007;9(2). (http://www.sst.dk/publ/Publ2007/MTV/Litteraturstudie/A_review_of_HTAs.pdf)

Mathiesen TP, Jørgensen T, Freil M, Willaing I, Andreasen AH, Harling, H. Treatment and care as assessed by patients and health care professionals – an analysis based on patients treated for colorectal cancer. Copenhagen: National Board of Health, Danish Centre for Health Technology Assessment; 2006. Health Technology Assessment 2006;8(1). English summary: (http://www.sst.dk/publ/Publ2006/CEMTV/Patient_sundhedsv/Patient_sundhedsv_Summary.pdf)

National Board of Health, Danish Centre for Health Technology. Type 2-diabetes: Health Technology Assessment of screening, diagnosis and treatment. Health Technology Assessment 2003;5(1). (http://www.sst.dk/publ/publ2005/CEMTV/diabetes_uk/diabetes_uk.pdf).

Willemann M, Svendsen MN, Ankjær-Jensen A, Petersen PG, Christensen M. Ward Rounds – a Health Technology Assessment Focused on Production of Knowledge. Copenhagen: the National Board of Health, Danish Centre for Health Technology Assessment; 2006. Health Technology Assessment – projects funded by DACEHTA 2006; 6(1)/DSI Rapport 2006.02. English summary: (http://www.sst.dk/publ/Publ2006/CEMTV/Stuegang/Stuegang_UKsum.pdf)

7.2 Patient-experienced quality

By Jørgen Eriksen and Torben Jørgensen

Useful advice and suggestions

- Quality in the health service is typically subdivided into three dimensions: technical health quality, organisational quality and patient-related quality
- Patients' experience of quality is often inadequately elucidated or severely restricted to communication and information
- A complete picture of quality of diagnosis, treatment and care calls for the use of the patient's assessments of technical, interpersonal and organisational aspects.

7.2.1 In general

The foregoing sections deal with patient-related aspects of HTA, from a humanistic research perspective. It is apparent, among other things, that the *patient* concept in an HTA concept must be conceived of in "broad" terms, i.e. that the person should also be understood to be a citizen, user and individual. But how are patients' experiences elucidated in specific terms? A review of 50 HTA reports from eight countries over the period 2000 – 2005 has shown that clinical studies are usually taken as the basis when patient aspects are discussed – and *not* in terms of the actual effects related to the patient's everyday life or treatment situation (10). This is in spite of the fact that the patient is the only one who experiences an overall course of events, regardless of whether a limited admission situation or the course of a disease is involved in which different sectors and authorities cooperate over a number of years.

In the Danish health service, the concept of *quality* has become a key term. This applies at the political/administrative and clinical level, where quality reform and quality registrations are referred to, and applies not least of all in relation to the perspective of patients. Assessments of the quality of diagnosis, care and treatment can only be satisfactory if the patients' own experiences are included.

Quality in the health care system

Quality can be defined as: *"The entire properties of a service or product which determines the service's or product's ability to meet specified or generally inadequately understood needs and expectations"* (Mainz et al. 2003, p. 8) (19).

Quality can be assessed from various perspectives, and distinctions are therefore typically drawn between three forms of quality, namely *technical quality*, *organisational quality* and *patient-experienced* quality (20). The main parties involved in assessing quality are health professionals, the political/administrative system and the citizen/patient (21). These groups correspond to the three forms of quality listed.

Patient-experienced quality

"*Patient-experienced quality concerns patients' experiences, priorities and assessments in relation to the specific course of events concerning the patient. These experiences may be related to the provision and the result of technical health services.*" (Kjærgaard et al. 2001, p. 26) (20).

In work on elucidating quality in the health service, the technical aspects of diagnosis, treatment and care are often focused on. This means that assessment of quality is often undertaken from a technical health perspective, whereas the patient's experience of

quality is often inadequately elucidated or confined to an assessment of interpersonal relations (21).

The patient is especially well qualified to assess *interpersonal* aspects, including communication and information (21). In principle, however, the patient can contribute information on all three forms of quality. Within the *organisational* dimension, the patient can contribute key information on continuity and coordination. On the other hand, there is disagreement in the literature on whether the patient can assess the *technical* quality of a given treatment. A number of studies indicate that the patient is capable of assessing elements of the technical health service (21). A complete picture of the quality of diagnosis, treatment and care calls for use of the patient's assessments of technical, interpersonal and organisational aspects. When focusing on technical quality, it is consequently important to be alert to what patients can assess, and how this assessment can be used.

7.2.2 Patient's experience in relation to assessments by health professionals

An HTA-related report from 2006 investigates whether patients' experiences reflect technical quality, and whether the professionals' assessments of their own performance match patients' experience (22). There was moderate to substantial concordance between patients' and specialists' answers to *factual* questions, whereas there was only a slight degree of concordance between the groups' answers to more *subjective/assessment-type* questions. In a number of cases, however, the responses were significantly different for both factual and subjective questions (22).

The study provides an ambiguous picture of how well the experience of patients matches that of personnel. Disagreement on assessment-type questions scarcely expresses patients' lack of medical knowledge or misunderstanding of the quality provided: *"A subtler interpretation of the differences observed suggests, however, that patient and personnel evaluations each contribute to a subtle picture of the quality of the health care system"* (Mathiesen 2006, p. 8) (22).

There was also a significant correlation between patients' assessment of technical quality and their interpersonal and organisational experiences during admission – which may potentially lead to bias in the assessment of technological aspects. However, the relationship between cause and effect has not been uncovered, and it is stated in the study that it may in principle be the patient's experience of technical/professional quality that affects the patient's assessment of the other aspects (22).

7.2.3 Measurement of patient-experienced quality

Typically, the patient's experience of quality is measured using questionnaires such as satisfaction surveys or informant studies (21). In recent years, a number of interview-based studies have also been conducted. The disadvantage of questionnaires and structured interviews alike is that there are dimensions and aspects that may be essential for patients that are omitted (21). Chapter 5 contains a detailed review of opportunities for and limitations on qualitative studies and questionnaire-based studies. In terms of choosing methods, it is crucially important to focus on the HTA question and on how this question is defined operationally. At the same time, it is crucial to be alert to the fact that the patient cannot evaluate interpersonal aspects. The patient can make a valuable contribution in assessing both organisational and technical health aspects – from his or her perspective (21).

7.3 Literature for Chapter 7

(1) Bruun JJ, Hanak ML, Kofoed BG editors. Viden og evidens i forebyggelsen [Knowledge and evidence in prevention]. Copenhagen: Sundhedsstyrelsen, Viden- og dokumentationsenheden [National Board of Health, Division of knowledge and documentation]; 2004.

(2) Hansen HP. Evidence-based nursing: must or mantra? In: Kristiansen IS, Mooney G, editors. Evidence-based Medicine. In its place. London & New York: Routledge; 2004. p. 33-50.

(3) Hansen HP. I grænsefladen mellem liv og død. En kulturanalyse af sygeplejen på en onkologisk afdeling [In the boundary between life and death. A cultural analysis of nursing care in an oncology department]. Copenhagen: Munksgaard; 2002.

(4) National Board of Health. Patientforløb og kvalitetsudvikling [Clinical pathways and quality development]. Copenhagen: National Board of Health; 1999.

(5) Bridges JF, Jones C. Patient-based health technology assessment: a vision of the future. Int J Technol Assess Health Care 2007 Winter;23(1):30-35.

(6) Coulter A. Perspectives on health technology assessment: response from the patient's perspective. Int J Technol Assess Health Care 2004 Winter;20(1):92-96.

(7) Draborg E, Gyrd-Hansen D, Poulsen PB, Horder M. International comparison of the definition and the practical application of health technology assessment. Int J Technol Assess Health Care 2005 Winter;21(1):89-95.

(8) Lehoux P, Williams-Jones B. Mapping the integration of social and ethical issues in health technology assessment. Int J Technol Assess Health Care 2007 Winter;23(1):9-16.

(9) Leggs ES, Evans J. Patients' choices and perceptions after an invitation to participate in treatment decisions. Soc Sci Med 1992;11(34):1217-1225.

(10) National Board of Health. A review of organisational and patient-related assessments in HTAs published by INAHTA members. Copenhagen: National Board of Health, Danish Centre for Health Technology Assessment; 2007. Danish Health Technology Assessment 2007;9(2)

(11) Busch HJ. En dialogisk fortælling om diagnose og død [A dialogic narrative about diagnosis and death]. In: Hansen HP, Ramhøj P, editors. Tværvidenskabelige perspektiver på sundhed og sygdom [Interdisciplinary perspectives on health and disease]. Copenhagen: Akademisk Forlag; 1997. p. 9-42.

(12) Kleinman A. Illness as narrative: suffering, healing and the human condition. New York: Basic Books; 1988.

(13) Timm HU. Patienten i centrum? Brugerundersøgelse, lægeperspektiver og kvalitetsudvikling [The patient at the centre? User survey, doctors' perspectives and quality development]. Copenhagen: DSI- Institute of Health Services Research;1997. DSI report 97.06.

(14) Svendsen MN. The Space in the Gap. A study of the Social Implications of Cancer Genetic Counselling and Testing in Denmark. Copenhagen: Institute for Anthropology, University of Copenhagen; 2004.

(15) Montgomery AA, Fahey T. How do patients' treatment preferences compare with those of clinicians? Qual Health Care 2001 Sep;10(Suppl 1):39-43.

(16) Say RE, Thomson R. The importance of patient preferences in treatment decisions – challenges for doctors. BMJ 2003 Sep 6;327(7414):542-545.

(17) Jensen SK, et al. Mellem håb og afmagt. Om ALS-patienter og lægemidlet riluzole [Between hope and despair. About ALS patients and the drug riluzole]. Copenhagen: DSI- Institute of Health Services Research;1997. DSI-report 97.07.

(18) Willemann M, Svendsen MN, Ankjær-Jensen A, Petersen PG, Christensen M. Stuegang – en medicinsk teknologivurdering med fokus på vidensproduktion [Rounds – a health technology assessment focusing on the generation of knowledge]. Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects]; 2006; 6(1)/ DSI Rapport 2006.02.

(19) Mainz J, et al. Sundhedsvæsenets kvalitetsbegreber og -definitioner [Quality concepts and definitions in the health care system]. Denmark: The Danish Society for Quality in Health care; 2003.

(20) Kjærgaard J, Mainz J, Jørgensen T, Willaing I. Kvalitetsudvikling i Sundhedsvæsenet [Quality development in the health care system]. Copenhagen: Munksgaard Danmark; 2001.

(21) Mainz J. Problemidentifikation og kvalitetsvurdering i sundhedsvæsenet [Problem identification and quality assessment in the health care system]. Copenhagen: Munksgaard; 1996.

(22) Mathiesen TP, Jørgensen T, Freil M, Willaing I, Andreasen AH, Hartling H. Patienters og sundhedsprofessionelles oplevelser af behandling og pleje – en analyse baseret på patienter behandlet for tyk- og endetarmskræft [Treatment and care as experienced by patients and health care professionals – an analysis based on patients treated for colorectal cancer]. 2006; Medicinsk Teknologivurdering [Health Technology Assessment] 2006; 8(1).

8 The organisation

This chapter concerns the methods of studying organisational conditions and consequences in relation to an HTA problem. It includes an introduction to the actual knowledge about organisational as well as political-administrative analysis. Among other things, the chapter comprises structured tables about dimensions and criteria that may support the implementation of these analyses.

Useful advice and suggestions

- Think through whether you should include both an administrative and an organisational perspective in the organisational analysis
- Adjust/limit the analysis model to illustrate the most essential organisational objectives in relation to the policy question of the HTA
- Consider which relation the technological and organisational elements have/will have in the organisational analysis
- Consider the level of analysis to be used to illustrate the problem
- Start with a short description of the organisation
- Then carry out the organisational analysis, including the aspects that have been selected by means of the above considerations
- Remember that an organisational analysis never presents a total picture. Explicit choices and delineations, together with their consequences are thus decisive for the usefulness of the analysis results.

The study of organisational conditions in relation to HTA can take place using both organisational and administrative analyses. There may be a certain overlap between the two approaches. However, broadly speaking, the administrative analysis uses a managerial perspective, whereas the organisational analysis deals with changes in relation to the executing/producing function. Typically, the administrative analysis looks at structures for decision-making and coordination across levels (e.g. state, region, municipality, hospital management or department management) and at the managerial tools (planning, financial management, communication and control) used to carry out political decisions, to ensure and control the operation of the health care system. The organisational analysis, on the other hand, typically focuses more closely on organisational conditions and change processes attached to the actual production of treatment services. The overlap appears because the administrative structures are an important part of the external conditions for the producing processes. From an administrative point of view, the overall intention of the organisational analysis is thus – based on the material available and considering uncertainties and various interpretation options – to describe the organisational dimensions of the new technology and some of the most important conditions for its implementation and possible consequences for the organisational structure.

8.1 Organisational analysis

By Janne Seemann

8.1.1 Introduction – no cookbook recipes

Social/behavioural sciences and thus also organisational theory perspectives and analyses may be an unfamiliar world for a health scientific trained HTA project participant to enter. In my experience, many doctors and other research-active health care providers often associate organisational theory with textbooks inspired by management and business economics about how to manage and delegate the many different tasks within

the health care system in the most cost-effective way. Hopefully, this contribution can challenge these assumptions.

In addition, amongst health care providers there is a general demand for *the* organisational model – i.e. the "proper" or "true" analysis model which is able to capture "everything". One hunts for "the one best way". However, the requirement for *the* organisational analysis which: a) can be used independently of organisation and problem, and b) give *the* overall picture, cannot be satisfied.

One has to reconcile oneself to the fact that organisational analyses cannot be introduced like recipes and that they must, to a larger extent than both clinical/medical and economic analyses, be adapted to the individual case or problem. There are several reasons for this.

Firstly, the health care system's organisations are pluralistic since they accommodate several types of objectives and conflicting interests: For instance, at one and the same time fulfil objectives of high treatment quality together with economic efficiency; objectives of flexibility together with control of tasks and activities; objectives of staff participation together with uniform and decisive management. Certain technologies and organisation types can thus favour something and someone rather than something and somebody else. Already for that reason it can be difficult to define precisely and unambiguously what a so-called good and appropriate organisation is. Here one can ask the question: Appropriate for what and whom? Society? Patients? Staff? Day-to-day management? Political/administrative system? Etc.

Organisational objectives as well as certain technologies and organisation types can be seen as an expression of historic development and negotiated compromises or solutions. The health care system's perceptions and discussions of objectives, resources and organisation types are constantly in motion and they are continuously the subject of ongoing negotiations and campaigns. HTA analyses can be seen as part of these campaigns, as HTA analyses choose certain criteria and focus areas. Consequently it should be stressed that when making an organisational HTA analysis, one should realise that one has to choose to illustrate some objectives rather than others.

Secondly, the organisations within the health care system including, especially, hospitals and local health care schemes, are so complex and immense that, at the very start, one has to drop the ambition of capturing "all". There is no simple analytical tool that will provide us with a sort of overall organisational picture. This leads to an urgent need for making explicit choices and delineations in connection with the analysis. In other words, one has to simplify as well as choose. It is thus important for the results of the HTA analysis that one is aware of how the delineation and simplification are done and, not least, how aware one is of the consequences of one's choices. Therefore it is often best to assume a relatively humble role in relation to how wide-ranging conclusions and generalisations can be drawn from the organisational analysis.

When the necessary simplification takes place it does not make sense to reduce or simplify organisations into purely technological systems, formal structures, information systems etc. The organisations of the health care system are social systems in which people act and react (also to the presence of HTA project participants/researchers). Health care providers work, cooperate with and compete against each other and build systems up and down with routines and renewals.

A good technology or solution for a given organisation may thus be inappropriate for another, even though the organisations may otherwise be similar in a number of areas. A solution, e.g. an appropriate technology for the given organisation – or what is interpreted as an appropriate technology – is organisation-specific, since "the appropriate technology" relates to the special conditions of this organisation (Borum & Tryggestad 2001, p. 88) (1).

However, through analysis of selected organisational elements which are considered the most central ones, a qualified basis can be formed with a view to technological options and their (different) consequences.

It is a very comprehensive and difficult task to gain control of the effects of various organisational actions. But, even if one is able to have control of the effects at a given time, the changes in the social system will mean that such knowledge quickly becomes of no (or little) interest. Therefore, a good and realistic ambition in connection with HTA analyses from an organisational point of view is to use the analyses to illustrate different *process* dimensions in the interaction between health technology and organisation. The following therefore gives first priority to this type of analytical approach.

8.1.2 HTA as an ongoing process

Health technologies imply adaptation and influence problems and opportunities that over time mean an ongoing development of organisations. Consequently, organisational HTA analyses cannot be expressed in a meaningful way by use of static "snapshots". Thus, HTA can benefit from being seen as an ongoing assessment process in which one – based on one's analyses – attempts to assess whether a given development seems to move in an appropriate direction.

Such assessments *"can lead to a better awareness and self-reflection within the organisation. Analysis of different measurement indicators can form part of the ongoing self-evaluation. Despite problems with measuring, it may be useful to establish material in terms of values to supplement the qualitative descriptions. Jointly qualitative and quantitative elements can be part of gathering experience and varied/interpretative comparisons across organisations. In this connection a certain option is to establish forums for representatives from the various organisations to exchange experience based on the organisationally specific results and descriptions. This can be developed into more formal "benchmarking" exercises and descriptions of "best practice(s)", although the greatest benefit is probably the ongoing exchange of experience"* (Vrangbæk 2001, p. 83) (2).

8.1.3 Conceptions of technology and organisation

In HTA-project connections there seems to be a widespread belief that a health technology can be unambiguously identified and that it has certain consequences. HTA-project participants often start from the assumption that the technology influences the organisation and its staff and that the importance of the technology is primarily expressed via the tasks. By virtue of this assumption, one will get an appropriate or efficient organisation when it is modelled in accordance with the technology and the characteristics of the tasks, including – especially – requirements of the competencies, learning and coordination of the staff.

In other words, one builds on the conception of an organisation as an identifiable and well-defined social system, which is mutually dependent on another system – the technology. Based on each system's logics and legality, these two *separate* systems have a correlation that results in a functioning organisation. In this connection analyses are thus

carried out with a view to finding and implementing that exact technology which results in a required and well-functioning organisational solution.

The conception of *organisation* and *technology* as two separate systems also expresses the assumption of a causal order between technology as an independent variable that has given effects on organisation as a dependent variable, typically delimited to the organisational dimensions *staff, organisational structure* and *working environment*.

Essential parts of recent organisational theory, however, problematize the assumption of technology and organisation as two separate systems. Instead, technology is seen as part of an organisational process (Nylehn 1997) (3). In this perspective, interest is not centred on analysing given connections between technology and organisation, but on the processes that shape the organisation (Svenningsen 2004) (4).

This is due to the fact that technology has been defined in different ways in the organisational theory and that there is no distinction between technology and organisation as two separate systems. Technology is not seen as an independent variable with certain or given effects on an organisation. The main point is that technology is of great importance via *the way we use technology* within our organisations. Furthermore, technology development is in itself a social process influenced by the organisations generating it.

Various studies show (see Svenningsen 2004, p. 35) (4) that:

- occasionally technology is not used
- technology is drastically adjusted to be usable
- technology is made the subject of negotiation or conflict
- technology is used in completely different ways from that originally planned.

Consequently a technology cannot be seen solely as something constituting important premises to which an organisation has to adjust, and adjustment does not occur only in relation to the given technology. It is at least as important to view technology as a factor for *ways* in which organisations develop and relate to their surroundings.

In organisations technology will thus both *form organisations and be formed by organisations*. Therefore perspectives in terms of organisational theory rather turn the attention to these *forms of interaction* than to defining and understanding connections between two separate systems.

The importance of the process is reflected in the claim that so-called "organisational solutions" cannot, and should not, be seen as autonomous phenomena. The so-called "organisational solution" – for instance the implementation of a health technology – will be a (unique) organisational solution, which reflects what took place in the process, with both the organisation and its staff.

The intention is not, by the use of analysis, to find out how a given organisation within the health care system should be structured, but to form an overview of opportunities and delineations in the processes that can lead to an appropriate organisation.

8.1.4 Analysis of individual organisations

An organisational HTA analysis must include considerations about analysis level(s)/analysis unit. For delineation and clarity reasons, analysis of individual organisations and thus individual case studies of organisations are taken as the starting point[4].

4 See also Ib Andersen 1990 and 1997 (16,17) for an introduction to methods relating to social science and concrete organisational theories. For an introduction into organisational case studies reference is made to Andersen et al. 1992 and Maaløe 1996 (18,19)

This means exclusion of a) comparative studies of two or more organisations, b) field analyses, and c) interorganisational network analyses requiring other types of approaches and analyses[5].

It is difficult, and not unproblematic, to define above opportunities and delineations ex ante, or before a new health technology is put into play in an organisation, especially when it is precisely a question of different opportunities for adaptation and change. Consequently it is beneficial to make a (brief) introductory description of the organisation.

Introductory description of the organisation

An introductory description of the organisation offers a chance for prior insight into the organisation, in which new health technology is to be put into play. This can contribute to a further clarification of the essential and most interesting problems in the "organisational" part of the HTA analysis.

Such an introductory description is not intended to be too comprehensive, but must be usable for generating and clarifying views in terms of:

- whether the problem(s) (processes/forms of interaction) raised in the organisational HTA analysis are still both relevant and interesting or whether the problem needs to be redefined/fine-tuned
- which organisational theories could be used to understand and explain the problem(s) formulated
- whether to retain the purpose of the analysis unchanged, or whether it needs to be adjusted
- which organisational conditions should be at the centre of the organisational analysis, including which organisational conditions to give lower priority or to omit, because they are found to be irrelevant to the problem?

Amongst others and primarily, the introductory description of the organisation should comprise (Jespersen 1991, p. 8) (5):

Organisational history

- Is the organisation old or new?
- Its main development phases?
- Major events that still characterise it?

One should not disparage an organisation's history and development as a good foundation for interpretation, insight into, and explanation for the organisations' present and possible future conditions.

Institutionalising and culture

- Which special or specific competencies are developed within the organisation?
- Which special reaction patterns are characterising the organisation?
- Which myths and standards (including professional standards) are characteristic of the organisation?

5 Depending on the organisation and the chosen problem it may turn out that the organisation's surroundings are more or variously important than assumed and may be understood better based on a field or network perspective.

In a broad perspective the organisational theory uses the concept organisational field, which should not be mistaken for the health services concept. With an organisational field all the organisations and interests that are linked in different ways are included; suppliers, regulatory bodies and related organisations (organisations that can replace or complement each others' services). The organisational field concept is clarified in DiMaggio and Powell 1991, Chapter 3 (20). A concrete field-analytical approach in connection with the Danish health care system is included in P. Kürstein Kjellberg 2006 (21). A comprehensive field analysis of the American health care system (San Francisco Bay Area) appears from W.R. Scott et al. 1998 (22).

In an interorganisational network perspective – as the term suggests – one focuses on what takes place between or across organisations that are directly resource- and task-dependent. The development within several health technologies, including, for instance, socio-psychological procedures, has created new types of interorganisational network systems totally different from traditional organisational hierarchies or pyramidal steering systems. A lot of work is to be coordinated across the primary and secondary health sector, between region and municipalities and across medical specialities and professions. If the "point of impact" of the health technology hits several different organisations at the same time, it is important to focus on these types of interorganisational network solutions, with regard to their problems and opportunities. Interorganisational dynamics are sparsely elucidated in relation to the Danish health care system. Reference is made to Seemann 1999 (23) as well as Seemann and Antoft 2002 (24) as examples of interorganisational studies of district psychiatry and dementia, respectively. A general introduction to interorganisational analysis is found in Alter and Hage 1996 (25), which contains examples from the American health care system.

Internal structures and processes (formal and informal)

- Horizontal and vertical division of labour
- Centralised or decentralised decisions
- Nature of tasks (the possibility of making it a routine, the degree of clarity and unambiguousness, variation)
- Nature of applied technologies (requirement for knowledge and skills)
- Important qualities in staff and management (e.g. views, conflict types, coalition structures).

The surroundings of the organisation

The surroundings can have different meanings for different organisations, especially because of the organisation's variation of external dependencies. Consequently, it is important to pinpoint the surroundings in the introductory description of the organisation:

- The nature of the surroundings? (use, for instance, classical concept pairs, like simple-complex; stable-dynamic; homogeneous-heterogeneous; structured-unstructured, referring to H. Minzberg 1979) (6)
- The relationship with the surroundings? (use, for instance, classical concept pairs, like friendly-hostile; high dependency-low dependency (6)
- The main stakeholders? (professional groups, patient groups, other hospitals, regions, politicians, interest groups, etc.).

The surroundings of organisations usually equal their stakeholders. However, more recent, and especially so-called new institutionalised organisation theory[6], differentiates between technical surroundings (patients and other service customers, suppliers and related organisations) and the institutional surroundings (prevailing standards and norms made with a view to creating and maintaining the organisation's legitimacy, which, for instance, come from the superior authorities, the prevailing sector and professional logics, or trade unions and occupational federations). The institutional concept is used as a description of the phenomena in a given social context which are sufficiently stable not to change rapidly. Institutions are often so well-established that actors take them for granted. Usually, institutions have a long life and can be of great importance for the actions of the organisation's members, precisely because they *are* taken for granted, and consequently their reason for being is not questioned (Kragh Jespersen 2005) (7).

Within the technical surroundings the productivity of the organisation is the centre of attention. However, new institutional organisation theory has suggested that organisational structures are not chosen based on a motive of tasks alone. Organisational structures also include symbolic functions in order to consider pressure from the institutional surroundings (7). In the institutional surroundings it is crucial for an organisation to live up to dominating standards, values and procedural requirements in order to establish legitimacy.

The institutional surroundings are thus not directly stakeholder-supported and for that reason a pure stakeholder analysis is not enough. In an HTA correlation it is consequently necessary to study whether there is existence of institutionalised technologies against which, the new technology has to fight or compete. The existing technologies can be supported by rules in the form of guidelines or standards, in the form of rooted perceptions of what is working. This is not captured by the current stakeholder analysis.

6 New institutional organisation theory has gradually become quite extensive. A relatively brief overview with useful references can be found in P. Kragh Jespersen 2005, Chapter 3 (7).

Such an introductory description of the surroundings can be instrumental in qualifying the basis of the analysis, including whether the technical and institutional surroundings of the studied organisation are more, less or differently important compared with the first assumption.

In Section 8.2, political-administrative analyses are described more closely, since administrative structures are an important condition in terms of surroundings for the organisational processes.

Organisational insight and introductory description of the organisation can often be based on available written material (manuals of the organisation, organisational charts and job descriptions, staff magazine, annual reports or similar). However, available written material is usually insufficient and should be supplemented with introductory interviews with individual key figures selected at different levels of the organisation and/or with external persons with a good knowledge of, or cooperation with, the organisation.

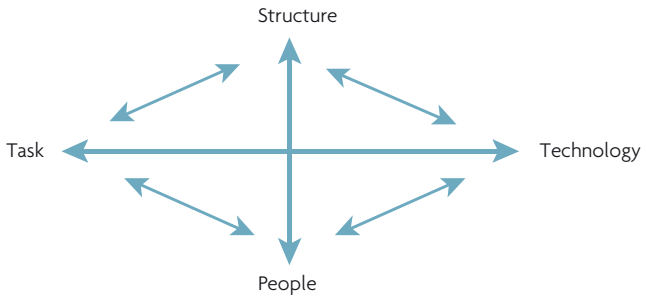
An introductory description of the organisation reduces the tendency to become caught by one's own immediate personal perception or the same in the (typically few) organisation members with whom one has contact when preparing the HTA project.

Leavitt's organisational model

The following is based on an extremely well-known organisational model, with a view to identifying and analysing forms of interaction, including strengths, weaknesses, opportunities and threats in the processes that can lead to an appropriate organisation. The model can be used as inspiration for identifying and selecting the variables that are central to the problem of the HTA organisational analysis.

It concerns the use of Harold J. Leavitt's 1965 (8) model for organisational change where, in an organisation, there is differentiated between structure variables, task variables, technology variables and people variables. In its simplest form the model can be illustrated as shown in Figure 8.1.

Figure 8.1. Leavitt's simple organisational model



A fundamental principle in Leavitt's model is to view different changes and change strategies in a system-oriented and dynamic perspective. In common language, we cannot merely implement health technologies. When health technologies are put into play in an organisation, this will influence organisational structures, tasks and the organisation's staff (people) and vice versa.

As mentioned, the model was originally developed for the planning of change processes (see Borum 1995) (9), but the model can also be used to diagnose organisational problems through analysis of possible problems and delineations in the interaction between the variables[7].

Leavitt's model has been used in a large number of different types of organisational analyses. This is probably due to the fact that the model is relatively simple and clear, as well as being easily understandable. One should, however, not underestimate that the model may be difficult to transfer into practice as one has to "operationalize" the variables oneself.

In addition, it is advantageous if one has some knowledge of (other) organisational theories with a view to utilizing the potentials embedded in the model. As touched upon earlier, it can also be difficult to separate the elements of the model. The decision whether, for instance, with new information technology to maintain technology as an independent variable or rather view it as part of the structure, is debatable[8]. The decision as to where which elements belong should always be made in relation to the actual organisation and consequently what is appropriate in relation to the problem and the specific analysis.

In its original form the model does not capture all aspects of intraorganisational analysis. Leavitt's model has been criticised particularly for not including the surroundings of the organisation. In a health organisation it may be that (new) health technologies are external factors which exert pressure on the organisation. The organisation's tasks, objectives, structures and staff are also influenced by (and influence) the development taking place in the surroundings.

Organisational culture enthusiasts, especially, have furthermore criticised the model for failing to notice organisational cultures, or for not, to a sufficient extent, including organisations' informal structures. It is difficult to differentiate between organisational culture and informal structure – and it is beyond the scope and objective of this chapter to discuss this in detail. In this context we can be content with claiming that organisational culture suggests, or can be seen as, an expression of the informal organisational structure and that the knowledge and views of the staff are co-creators of organisational culture[9].

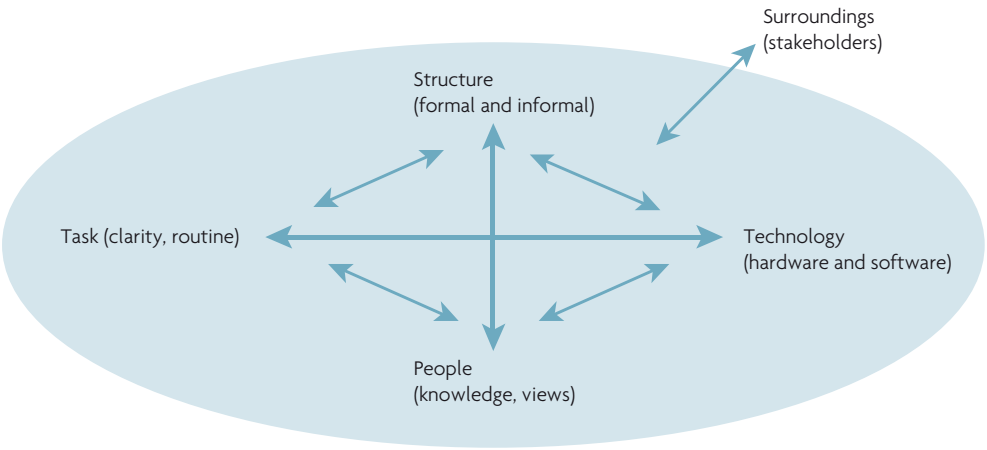
Consequently, the model is typically modified with the inclusion of organisational culture (the informal organisation), staff knowledge and views as well as the surroundings – with a view to analyses of the organisational processes. A modified Leavitt model is illustrated in Figure 8.2.

7 It may be useful to read J. C. Ry Nielsen and M. Ry 2002 (26) with a view to different uses of and modifications/extensions of Leavitt's model. See also Borum et al. 1981 (27) for an analytical description of hospitals using Leavitt's model.

8 "Especially in connection with information technology it becomes more and more clear that it is really not the technology understood as technique which is limiting in relation to choices of organisational models and the problem-solving. The conception of the technique as setting the limits for the organisation disappear and instead it becomes more and more obvious that it is economic and management-strategic considerations that determine the choice of technology, and that the same technique can be used very differently in different organisations" (P.K. Jespersen 1991, p.14) (5).

9 Organisational culture, culture dimensions and different analyses of these can be seen in Schultz 1990 and Schein 1994 (28,29).

Figure 8.2. Modified Leavitt organisational model



Task

All organisations exist to solve one or several tasks. These tasks can vary greatly. Within the health care system the essential core function can in short be characterised as "human treatment". But to perform surgery on a patient is quite different from primary prevention and health-promotion tasks, screening or rehabilitation. One therefore expects that organisations undertaking such different types of task to have different organisational forms. The tasks and their nature are thus important for the internal functioning of the organisation and consequently for the organisation of its work.

The core tasks of the health care system are typically the provision of (intangible) services that are consumed at the same time as they are produced. Services imply a social interaction between producer and patient or user and are typically very labour-intensive. Services can be seen as social processes for which a necessary condition especially is motivated employees, whose standards and values should create commitment and service orientation. Such a condition points to the importance of organisational culture.

Another central question is the possibility of "routinising" tasks. Two dimensions of a task can be suggested to indicate whether or not it can be solved routinely through the possible establishment of fixed systems and rules (Jacobsen & Torsvik 2002) (10):

- To what extent can the task be described explicitly and unambiguously?
- How broad is the task variation?

Even though, a doctor, for instance, can establish a number of routines in his work, there will be obvious limits for routinising and standardising because patients can be difficult to diagnose or have unknown illnesses. In such cases the doctor must search for new information, enter into a discussion with his closest colleagues, forward referrals to other specialists, etc.

Technology

Technology does not only indicate technique, but also routine practices/processes and administrative procedures with relation to the technology. Health technology thus comprises a combination of technique (drug, form of diagnosis, form of treatment and care) as well as a number of behavioural relations relating to the technique (Vrangbæk 2001) (2). *"The technical element can constitute a larger or smaller part of health technolo-*

gy. In relation to all technologies there is an organisational and a behavioural element. In some cases the assessed technology is only an organisational/behavioural change. Here it is especially important to focus on the related dimensions (tasks, structures, people and surroundings, ed.)"(Vrangbæk 2001, p. 70) (2).

Analysis form and options will vary depending on the type of health technology to be assessed. Vrangbæk (2) in this connection exemplifies as follows:
"Is it a matter of an actual treatment (e.g. a new type of medicine or surgical intervention)? Is it a matter of a new treatment programme (e.g. a new type of cancer treatment consisting of several different treatment elements)? Is it a matter of a change in the organisational arrangement of the treatment system (restructuring to outpatient treatment forms, setting up of function-bearing units) or a matter of a broader structural reform (establishing free pricing on treatment, transition to activity-based payment, modification of the role of the counties (presently regions, municipalities, ed.)*?"*

The above examples can be used to stress a higher or lower complexity in relation to a health technology assessment. It is relatively more difficult to assess (radical) changes in organisational arrangements in a treatment system and broad structural reforms than to assess an actual treatment, for instance, a new type of medicine. With the increasing complexity of the technological change, organisational perspectives and assessments come to play a larger part in connection with the HTA dimensions, patient, economy and clinical assessments.

This is also evident in connection with the scope of the health technology. A wide scope means that many other factors are influenced by the given technology even though, for instance, a new type of treatment in itself is not especially complex.

Structure
Organisational structures are usually defined in organisational literature as the relatively stable patterns that can be captured from the actions and behaviour of the players (Bakka & Fivelsdal 2004) (11). This concerns in particular:

- the vertical division of labour (the hierarchy, authority system)
- the horizontal division of labour between different task areas
- communication and cooperation patterns
- the degree of formalisation
- the degree of centralisation
- remuneration and sanction structures.

Essential parts of the structure in an organisation can be identified in available organisational charts and various formal descriptions. This is however insufficient, since innumerable studies show large variations in what is formally committed to writing or prescribed relative to the actual organisational behaviour. One cannot read these so-called informal structures, which capture essential parts of the organisation's culture, out of a book. An organisation's informal structure or organisational culture has to be identified from observational studies and interviews. The informal organisational structure can be identified, for instance, via the organisation's more informal standards and routines, informal communication patterns, informal coalitions, informal authorities and not least through conflicts and conflict patterns.

People

People indicate persons employed in the organisation. Formally, they can be characterised by their number, gender, age distribution, formal training, knowledge and skills/qualifications. At the same time it is essential to include the values, views and motivation of the people; their preparedness in terms of innovation and change as well as their economic and loyalty bonds to the organisation. Since the organisation's employees carry out a number of their actions in collaboration with colleagues and in connection with the organisation's task solutions, it is important to visualise the grouping that takes place via both formal and informal teams as well as network formations. As already mentioned these contribute to creating the organisational culture or forms of organisational subcultures. Precisely in relation to health technology it should be stressed that the interaction between people, groups and not least professionals plays an important part.

Surroundings

Here one typically moves into a (defined) stakeholder analysis. Depending on the nature and complexity of the health technology one has to select the stakeholders that are particularly relevant for, as well as task and resource dependent on, the HTA project. Some typical stakeholder groups would be:

- various professionals in the secondary health care sector (nurses, physiotherapists, physicians, etc.)
- various professionals in the primary health care sector (district nurses, social workers, general practitioners, etc.)
- pharmacies and pharmacists
- municipal and regional players from the political/administrative levels
- managements at various levels (department managements, hospital managements)
- other departments, other hospitals
- stakeholder organisations (unions, patient groups)
- the pharmaceutical industry.

Ask questions like: Who has an interest in the technology? What are the ideas behind this interest? What (conflicting) requirements are set? What is the relative strength between the stakeholders? What are the options for compromise and coalition?

Add to this, as mentioned in the previous section about introductory description of the organisation, the institutional surroundings regarding which, one in an HTA analysis especially has to ask the question: Which institutionalised perceptions will the new technology fight or compete against?

Work flow and patient flowcharts[10]

Usually, the organisational assessments of an HTA analysis should be based on a description of the technology which specifies the actual work process and describes the organisational options and delineations in various parts of the process. Preparation of work flow and patient flowcharts in relation to the existing production process can make a useful foundation for assessments of the changes in which the new technology can result. Below a "check list" with possible dimensions for such an analysis is shown. The list should be adapted to actual requirements. Although it should be stressed again that it is difficult beforehand to assess the consequences of possible forms of interaction in connection with new technology, the table aims at setting up dimensions for ex ante description and assessment. Table 8.1 summarises dimensions for this analysis.

10 The section is a (slightly adapted) reproduction of Vrangbæk 2001, p. 80-82 (2), which in particular comprises a useful "check list" in connection with the preparation of work flow and patient flowcharts.

Table 8.1. Dimensions for description and ex ante assessment of organisational adaptation

Process	Description of the technology via, for instance, preparation of work flow diagram **A) Work flow** How is the technology applied specifically? Describe patient flow and work processes. How is existing patient flow and work processes influenced? How is ongoing control and evaluation ensured? **B) Staff, training and resources** Which players participate, and which resources do they need to apply to the new technology? Is extra staff required? Is other staff or further training required? Who decides which patients are to receive the treatment? On what basis? **C) Interaction and communication** Interaction with other parts of the structure (other treatment units and interdisciplinary functions, e.g. financial management). State consequences for other treatments and other treatment units within and outside the department. Interaction and communication with patients and relatives. State changes and new requirements. Interaction with external actors (other hospitals, general practitioners, municipalities, pharmacies, technical consultants, etc.). State changes. Requirement for change in financial reporting and payment structure? Can potential bottlenecks be identified (staff, funding, knowledge/information) in the work process?
Structure	**A) Centralisation/decentralisation. Dispersal of technology** Where is the treatment located in terms of organisation? Who is in charge and has the responsibility? Where is the treatment physically undertaken? Who decides on dispersal and organisational arrangement? Who is in charge of control and evaluation? **B) Economy** Requirement for changes in payment arrangement, rates, etc.? Does the technology entail an essential additional expenditure to be covered by giving other treatment types lower priority? Which incentive structures (in terms of economy, career, work process, treatment, etc.) are established from use of the new technology, for treatment staff, patients and referring bodies (general practitioners)? Which incentives are established for the individual regions, hospitals, departments and units?
Culture	**Views and standards among staff and patients** Is it likely that the treatment will be accepted or will it meet with opposition? How well does the treatment go with existing routines and traditions in the organisation? Is it necessary to change perceptions and understanding of the treatment situation? Is the technology seen as an advantage or a disadvantage by different staff groups (working conditions and working environment).

The first item about "process" implies a description of work processes and changes in work processes in connection with the new technology; i.e. how the technology works and which resources are necessary to get started? Apart from descriptions of work processes as relevant work method, literature studies on how it has been organised in other places, experience gained, including options and delineations that can be encircled in relation with the new technology, can supplement the descriptions.

The remaining items in the table are an attempt to assess the technology in the interaction with organisational structure(s) and culture(s) as well as in the organisation's relations to its surroundings. In practice there is a certain overlap, since "structural" and "cultural" dimensions will work in close cooperation with "process" dimensions (Bakka & Fivelsdal 2004) (11). For instance, it will be difficult to describe work flow or patient flow without describing elements of the organisational and managerial structure relating to the technology. However, here it can be an advantage to separate the dimensions intellectually.

Organisational dynamics

The urge for attaining a so-called stable organisation or a balanced organisation is embedded in Leavitt's model. Thus the purpose is to get task, technology, structure and people to "form a stable synthesis" in order for a given technology to be in balance with the organisation into which it is implemented when the "correct" adjustment takes place.

There is, however, nothing new in the fact that innumerable organisational analyses have shown that organisational instability is more common than organisational stability and that organisational imbalance is more common than organisational balance – which also applies in relation to the health care system.

Organisational changes, including changes in health technologies, can give rise to quite complex processes in which technical/economic and political circumstances are mixed up with people's emotions and attitudes.

An essential art is to not be content with a static organisational description and analysis. Organisations are dynamic since the organisations themselves and the organisations' actors should be understood as socially acting entities that actively and constantly influence both organisation-internal and external structures, cultures and processes.

It is a difficult task providing organisational analyses with the dynamics they deserve; partly due to the often large number of variables included and partly due to a typically complex interaction in terms of time. It is however an exciting challenge which one constantly has to practise doing – also in connection with HTA.

However, despite an accumulation of theories, models and empiric results it seems *"that we have only taken the initial steps to a deeper understanding of how technology takes part in the organisational life"* (Svenningsen 2004, p. 26) (4).

8.1.5 The devilish detail

Following the above quotation this subsection will be rounded off with an essential core point which could be called "the devilish detail" (FLOS 2004) (12).

With a number of research projects in the period 1999-2004, the FLOS centre[11] has in particular concentrated on work practices and day-to-day organisation within the

11 The Research Center for Hospital Management and Organisation (FLOS)

health care system, which is more than the mere interest in how to rationalise work processes.

When the objective is rationalisation with a view to work routines and organisational routines it is easy to look automatically for the aspects which can immediately be rationalised or which are sufficiently simple to be captured in pre-programmed tables and measurements. It is naturally important to work with improvement, but it is necessary to emphasise that improvements take place *not only* through targeted mapping of activities. Developing best practices and implementing these – which one can claim the health care systems are in the habit of arguing for – is *the* key to change.

The FLOS centre, amongst others, has been particularly interested in everything which otherwise tends to disappear from many analyses of and discussions about the health care systems, i.e.: The everyday life, the details and the practicalities in connection with actual tasks (Vikkelsøe & Vinge 2004) (13).

Quite a lot of valuable knowledge is hidden here. Careful and detailed studies show that the health care systems are more than a mere arena for professional fights and excessive consumption of resources. Generating knowledge about everyday practices can teach us something new and give us more unconventional ideas as to how to organise and improve the health care system. This type of knowledge is needed even though it does not correspond with the prevalent and traditional demand for generalisable survey studies.

Knowledge based on the insight into details of everyday life helps expand the repertoire of action and improvement options. Some studies have been driven forward by a fundamental curiosity to understand working people as social and complex creatures, and working life as an ongoing handling of a large number of divergent tasks and considerations.

If formal work descriptions are taken as the starting point one cannot be sure which real activities are carried out in practice in everyday life. Neither can we, for instance, take for granted that a work activity is unambiguous and well-defined. In the book *Everyday work and organisation in the health care system* (13), among other things, the question is asked, what does it, for instance, mean that a new type of surgery saves *care*? Is it that the patients are hospitalised for a shorter period – and thus reduce the need for the care for patients in a hospital bed – but who on the other hand perhaps need long-term aftercare or another type of *invisible* care to be carried out by relatives or district nurses in the primary sector?

And what is really meant with the statement that the electronic patient record *facilitates the cooperation between the occupational groups*? Do doctors and nurses talk more or less with each other and/or does it mean that the occupational groups perform new tasks together?[12]

The point is that in many cases we have become too accustomed to accepting statements like "save care efforts" or "it facilitates the cooperation across occupational groups". The consequence is that we tend to discuss improvements and changes within the health care system without having sufficient insight into how things have changed *in practice* and what has become different for whom.

12 Read also Svenningsen 2004 (4), which is the first Danish account of how electronic patient records function in practice as well as the consequences in terms of organisation and health care.

There are many tasks – and work areas – in the health care systems where the occupational groups' work in practice pass into others' formal responsibility. This can be seen as problematic from a rationalisation and standardisation point of view. However, on the other hand, in practice it is a question of creating flexibility which makes the work run more smoothly. Consequently, it is important to acquire knowledge about how people in practice enter into relations with each other.

One important key to a successful technological change is thus a deep insight into everyday structures and otherwise invisible connections. This insight can both inspire efficient reforms in micro plan and throw light on unintended (both positive and negative) effects of other reform and technological change projects.

It brings up an interesting but also open question: Whether one can and should plan one's HTA organisational analysis based on anticipated and expected consequences or whether one should take a more unconditional approach and carry out micro studies of the interaction between technology and organisation? In general, HTA analyses are dominated by using anticipated and expected consequences as the starting point. When this open question is included in the conclusion it is in order to inform about and inspire to other organisational studies than the ones prevalent in connection HTA.

8.2 Politically administrative analyses

By Karsten Vrangbæk

8.2.1 HTA from an administrative point of view

Based on a formal assumption, administrative studies deal with the organisation of decision preparation and execution in a political/administrative context. Consequently, the administrative analysis typically looks at structures for decision-making and coordination across levels (e.g. state, region, municipality or region, hospital management, department management) and at the management tools (planning, financial management, communication and control) that are used to carry out political decisions, ensure and control the operation of the health care system. Management tools means intended attempts towards influencing behaviour, so that it to the widest possible extent is brought into agreement with politically/administratively fixed objectives.

Both decision preparation and execution are relevant perspectives in relation to HTA. HTA is prepared as a tool for a more rational decision preparation. The concept is thus that HTA should be part of the administrative work prior to the decision-making about use of technology. To provide an adequate picture such an assessment should also include the possible management structures and processes attached to the use of technologies. Consequently, in addition to the clinical, economic, patient-related and organisational dimensions, in-depth technology assessments should consider the administrative/managerial questions: 1) Which management problems and options are attached to the given technology, e.g. in relation to resource allocation, coordination with other activities, fixing of objectives, monitoring, control and evaluation of the activity and the results, and 2) What are the alternative options for managing the use of the technology and which advantages and disadvantages do alternative management methods represent? How do the management aspects of this technology play together with the existing management structure?

A number of the management dimensions will have been decided in advance as part of the general administrative structure. Others can vary from technology to technology.

An administrative assessment of a technology, and its possible management implications, will add a number of questions and criteria to the HTA analysis – of a broader nature than the medical, economic, organisational and patient-related ones presented above. It is important to consider actively the relevance of the individual questions for the actual HTA.

Before we discuss these questions in detail it is necessary to clarify a couple of general points in relation to administrative analysis. The *first one* concerns *different interests* attached to management structures. A general starting point for politically scientific and administrative analyses is that there are conflicting interests. Certain organisation forms will favour certain groups of people and certain objectives will suit patterns of understanding better with some people than other. Organisational objectives thus often reflect compromise, and there can be many and varying perceptions of both objectives and criteria for success. Similarly, administrative structures and organisational forms reflect compromise and historic development. It is not necessarily a question of optimum structures but of structures established over time in interaction between different and legitimately conflicting interests. One could say that the understanding of administration, organisation, objectives and resources within the health care system is constantly shifting and that arguments for definition are an ongoing feature. HTA analyses will become part of such definition arguments, since one uses the HTA to select certain criteria and focus fields. Therefore one has to bear in mind that, no matter which set of criteria is selected for an administrative/organisational HTA analysis, it only represents one interpretation out of several possibilities, just as the associated selections of measurement methods will represent one selection out of several possibilities.

This means that an organisational/administrative HTA analysis cannot be determined once and for all. It is necessary to select focus field and analysis dimensions in each individual case, and it is necessary to argue in favour of these selections.

The *second* general point concerns *indeterminacy* in relation to *objectives and resources*. In connection with both management relations and organisation there is usually more than one way to achieve the objective. Furthermore, it is necessary to be aware that organisational/administrative arrangements often serve several concurrent purposes (e. g. simultaneously consider treatment quality and economic efficiency; flexibility and control of activities; knowledge development and efficient operation; well-being and staff participation; political legitimacy and popular acceptance; democratic anchoring, effective management, etc.). This also applies to organisational and administrative choices in relation to new technology.

A *third* general point concerns *the analysis unit*. The question of management demands an answer as to who is managed and by whom? In other words, how widely should we focus in relation to the analysis of management organisation? Should one look at individual organisations or network of organisations and people? How large a part of the administrative structure should be included in the individual analysis? Another type of defining question concerns whether the individual initiative (the individual technological change) can be seen in isolation or whether any synergistic effects should be included.

Due to these different circumstances (conflicting interests and perspectives on the organisation, possible indeterminacy in the correlation between objectives and resources, various possible analysis levels and units) organisational-administrative HTA analyses are less precise than other parts of the HTA analysis. Therefore it is much more

important to make explicit selections in the planning of the analysis and to include the specific context in which the technology is to function and the uncertainty that exists in relation to the results. There is also good reason to be more modest in relation to the robustness of the conclusions reached. As a principal rule, it will be difficult to separate and measure output effects of given management approaches. A more realistic but no less important ambition, therefore, has to be to use administrative organisational analyses to illustrate various possible options and their consequences, and especially look at the *process* dimensions in the interaction between technology and organisational behaviour.

In any case, the HTA analysis must be seen as an approach to a "politicised" and interest-driven decision process rather than as an exact science. Seen in this light there is however good reason to continue with organisational-administrative HTA. A technology must be assessed in relation to the way it is used, and it is in the interaction between technology and organisation that the economic as well as the clinical consequences are decided.

Furthermore one has to say that it is far from unusual to have to make decisions on an uncertain basis. Both within public and private sector management many "politicised" decisions are made based on balancing of interests, uncertainty and inadequate information. The ambition of the HTA analysis can be to create more clarity in connection with such options, by attempting to move forward as far as possible by asking qualified questions and by assessing possible consequences of organisational and administrative choices in connection with new technologies.

Bearing these conditions for administrative analysis in mind we can now return to the questions asked initially. The following sections should be seen as a form of catalogue of tools presenting various dimensions which one can choose to focus on in an administrative HTA. The idea is that by analysing selected administrative/management elements it is possible to create a more informed platform for assessing various options and their consequences in relation to the dimensions found to be the core ones.

Question 1: *Which management problems and opportunities are attached to the given technology, e.g. in relation to resource allocation, coordination, establishment of objectives, monitoring, control and evaluation of the activity and the results.*

As mentioned, management can be analysed in relation to several levels. In most local and regional HTA analyses it will be appropriate to start with the management relation between the regional administration and the executing organisations/health care staff. In national HTAs it may be relevant also to include the relations across regulatory levels.

The *first* example of administrative management dimension is *resource allocation*. The question here is, how to organise decisions about consumption of resources for the studied technologies. A differentiation can be made between decisions about investments related to the new technology and decisions about consumption of resources during operation. Investments can be in both hard technology, such as machinery, and soft technology like education and training. The question here is, how and at which levels in such investment decisions can be made. Is it, for instance, at administrative, functional, hospital or department level?

Administrative questions about the operation include setting systems for the technology. Who is to pay for using it and in which way (fixed grant or per activity)? In other

words, the basic problem is to map out the various needs and options in order to organise an administrative structure for handling the consumption of resources in connection with the new technology.

The *second* example of an administrative management dimension is *coordination*. This concerns coordination between different parts of the treatment system to make the given technology work. The question – in other words – is which management or behaviour-influencing tools can be put into use to support the coordination of activities associated with the given technology. The coordination concerns care pathway and information exchange across treatment levels and organisational boundaries.

The *third* example of a management dimension concerns *the establishment of objectives* for the given technology. It can be a question of activity, quality as well as service objectives. The point is that processes for establishment of relevant and realistic objectives with the technology must be included as part of the necessary management structure in relation to given technologies. It has to be considered which objectives can be set for the use of the technology and how to monitor, control and evaluate the process towards these objectives (see next item).

The *remaining* examples concern processes for monitoring, control and evaluation of the activity and the results. It has to be considered which procedures to implement in order to ensure the achievement of the general objectives for the technology.

For all dimensions, ***question 2*** of the administrative/management analysis has to be considered, i.e.: *Which alternatives are there for managing the use of the technology and which advantages and disadvantages do alternative management methods present?*

8.2.2 Administrative and managerial assessments

A number of criteria can be established for the administrative assessment of a technology. The following table (Table 8.2) illustrates the questions mentioned and the associated dimensions and criteria.

Table 8.2. Administrative/managerial assessment

1. Management problems and options associated with the given technology:

Management of resources
- Investment (technology and knowledge)
- Operation (settlement system, systems for ongoing monitoring of cost development)

Coordination in relation to
- Administrative units (e.g. region/municipality or region/region)
- Treatment levels (e.g. primary/secondary, treatment/rehabilitation)
- Organisational units (e.g. acute/follow-up, treatment/service etc.)

Establishment of objectives
- In relation to activity, quality and service
- Who, how and when are objectives established? Who is to follow up?
- At which level are objectives to be established (technology, team, department, etc.)?

Monitoring and control
- Information systems and data collection
- Potential indicators

➤

Evaluation of the activity and the results
- Procedures for ongoing evaluation of results
- Establishment of criteria

Sanctioning
- Procedures for intervention (positive and negative sanctions)
- When to intervene and by whom?

2. Optional criteria for assessment of alternative management tools and their importance for the given technology:

Resource control
- Does the given technology and management model ensure appropriate resource control? Is there a good balance between management cost (effort) and the results?

Transparency and administratively manageable solution
- Does the chosen combination of technology and management model provide transparency and is it practically manageable for the involved parties?

Political legitimacy/acceptance by the general public
- Can the chosen combination of technology and management model support acceptance of the use of the technology by the surroundings?

Equality (consumption and access). Fairness
- Does the chosen combination of technology and management model support objectives of equal access to the technology?

Coordination and interaction
- Which demands does the technology make on the interaction of relations, and is it possible to establish appropriate management tools to support this?

Attracting and retaining staff. Human resource development
- Which demands does the technology make on the personnel competencies? Is it possible to attract and retain personnel for this activity?

Management competencies
- Which demands does the technology make on the management competencies? Are they available at the relevant levels?

Robustness (the system can deal with various degrees of load – no weak links in the chain)
- Are the technology and the different stages of the technology's application sufficiently robust?

Freedom of choice? Flexibility for patients
- Does the chosen combination of technology and management model support freedom of choice?

Planning capacity
- Does the technology restrict the use of resources inappropriately in the coming years? Is it possible to predict the drain of resources or will it fluctuate? Does the chosen combination of technology and management model support planning?

8.3 Generalisation regarding organisational aspects

Another distinction is whether HTA analyses can be made generally for all parts of the system (all organisations or networks), that is to implement a given technology, or whether each individual organisation's choice and adaptation to technology is to be considered as unique. Medical and economic analyses tend to view implementation as

independent of the specific organisation. It is usually assumed that results can be generalised laterally.

Political and administrative analyses would provide a mixed picture. Some dimensions will be of a general nature (assessment in relation to overall objectives, coordination at national level, general economic management principles, etc.). In many other cases general rules are translated and interpreted to suit practice in the various places of the system (Czarniawska & Joerges 1997, Røvik 1998) (14,15). In this way one gets structures and items that are specific for parts of the administration, for individual regions or municipalities. It can be a question of specific types of settlement, agreements, etc., which are based on particular historical, geographical, or other circumstances in different areas. The preferred solution in North Jutland Region may not necessarily be sensible in the Copenhagen Capital Region. Prerequisites in Southern Denmark do not necessarily correspond to prerequisites in Bornholm. Therefore the task can often be formulated as describing possible ways of adaptation and different options as a basis for comparison.

In relation to *organisational* analyses, there is much to be said for viewing each adaptation as a unique result of the given organisation's history, development, relation to its surroundings, etc. This results in many organisation theorists being sceptical in relation to generalisation and comparative assessments for different implementations of technology/organisational combinations.

The perspective is that there will probably be different ways of change. But at the same time there will be a number of dimensions that deserve consideration for all organisations, and that can form the basis for assessments of the development process for the given technology and perhaps over time also for "soft" comparisons, in the form of exchanges of experience, benchmarking, etc. The degree of generalisation of results will, among other things, depend on the type of technology in question. Some will be easier to introduce in all organisational contexts while others to a larger extent would result in changes in the existing organisation.

8.4 Organisation-specific aspects of literature reviews

Organisational analyses should always start with a systematic literature search and review of available literature in the area (see Chapter 3 and 4). It is, however, important to be aware of any delineations in the use of the literature found. Since organisational analyses are context-dependent, it is important to decide whether results and conclusions can be generalised for the context in question. If it is not possible directly to transfer results and conclusions, it is, however, always possible to draw inspiration both in relation to the use of methods in the analysis and for identification of analysis categories to be studied in one's own organisational analysis.

The principles of systematic literature search have been reviewed before in the Handbook (see Chapter 3), which is why only details of relevance for the search of literature regarding the organisational aspect are described here. In addition to the databases mentioned in Chapter 3, it is often necessary to use so-called "grey literature", i.e. literature that is not registered in the current databases. It may include administrative reports, dissertations, theses, etc. These types of literature typically should be sought actively by submitting requests to regions/municipalities/hospitals, etc. and by searches on the Internet. Next one can find further references by looking at literature references in the discovered literature. It is important that this literature is *thoroughly* assessed

prior to inclusion in the organisational analysis as it may not necessarily have been carried out as scientific studies, and consequently it is always especially important to assess whether results and conclusions have been produced in a systematic and transparent way.

8.5 Literature for Chapter 8

(1) Borum F, Tryggestad K. *Organisationen* i Medicinsk Teknologivurdering. Hvorfor? Hvad? Hvornår? Hvordan? [*The organisation* in Health Technology Assessment. Why? What? How? When?] Copenhagen: Danish Institute for Health Technology Assessment, 2001.

(2) Vrangbæk C. MTV, Forvaltning og organisation. [HTA, administration and organisation.] In: Statens Institut for Medicinsk Teknologivurdering, editor. Medicinsk Teknologivurdering. Hvorfor? Hvad? Hvornår? Hvordan? [Health Technology Assessment. Why? What? How? When?] Copenhagen: Danish Institute for Health Technology Assessment; 2000.

(3) Nylehn B. Organisasjonsteori. Kritiske analyser og refleksjoner [Organisational theory. Critical analyses and reflections]. Otta: Kolle Forlag; 1997.

(4) Svenningsen S. Den elektroniske patientjournal og medicinsk arbejde – reorganisering af roller, ansvar og risici på sygehuse [The electronic patient record and medical work – reorganisation of roles, responsibility and risks at hospitals]. Copenhagen: Handelshøjskolens Forlag; 2004.

(5) Jespersen PK. Empiriske organisationsanalyser i enkeltorganisationer [Empirical organisational analyses of individual organisations]. Aalborg Universitet: Institut for Økonomi, Politik og Forvaltning; 1991.

(6) Minzberg H. The Structuring of Organizations. Englewood Cliffs, N.J: Prentice-Hall; 1979.

(7) Jespersen PK. Mellem profession og management [Between profession and management]. Copenhagen: Handelshøjskolens Forlag; 2005.

(8) Leavitt HJ. Applied Organizational Change in Industry: Structural, Technological and Humanistic Approaches. In: March JG, editor. Handbook of OrganizationsChicago: Rand McNally & co; 1965.

(9) Borum F. Strategier for organisationsændring [Strategies for organisational change]. Copenhagen: Handelshøjskolens Forlag; 1995.

(10) Jacobsen DI, Torsvik J. Hvordan organisationer fungerer. Indføring i organisation og ledelse [How organisations work. Introduction to organisation and management]. Copenhagen: Hans Reitzels Forlag; 2002.

(11) Bakka F, Fivelsdal E. Organisationsteori – struktur, kultur, processer [Organisational theory – structure, culture, processes]. 4.th ed. Randers: Handelshøjskolens Forlag; 2004.

(12) Research Centre for Management and Organisation in the Hospital Service (FLOS). Forskning i sygehuse under forandring. Hovedpointer fra fem års studier af ledelse og organisering i det danske sygehusvæsen [Research in hospitals undergoing change. Main points from five years' studies of management and organisation in the Danish hospital service]. Copenhagen: Nyt fra Samfundsvidenskaberne; 2004.

(13) Vikkelsøe S, Vinge S, editors. Hverdagens arbejde og organisering i sundhedsvæsenet [Everyday work and organisation in the health care system]. Copenhagen: Handelshøjskolens Forlag; 2004.

(14) Czarniawska B, Joerges B. Travels of Ideas. In: Czarniawska B, Sevón G, editors. Translating Organizational Change New York: Walter de Gruyter; 1996.

(15) Røvik KA. Moderne Organisasjoner. Trender i Organisasjonstenkningen ved tusenårsskiftet [Modern organisations. Trends in organisational thinking at the turn of the millenium]. Bergen: Fakbokforlaget; 1998.

(16) Andersen I, editor. Valg af Organisationssociologiske metoder – et kombinationsperspektiv [Choice of organisational sociological methods – a combination perspective]. Copenhagen: Samfundslitteratur; 1990.

(17) Andersen I. Den skinbarlige virkelighed – om valg af samfundsvidenskabelige metoder [Reality incarnate – about the choice of social science methods]. Copenhagen: Samfundslitteratur; 1997.

(18) Andersen I et al., editors. Om kunsten af bedrive feltstudier [About the art of conducting field studies]. Copenhagen: Samfundslitteratur; 1992.

(19) Maaløe E. Case-studier af og om mennesker i organisationer [Case studies of and about people in organisations]. Copenhagen: Akademisk Forlag; 1996.

(20) Di Maggio PJ, Powell W, editors. The New Institutionalism in Organisational Analysis. Chicago: University of Chicago Press; 1991.

(21) Kjellberg PK. Klinisk praksisvariation og kliniske redegørelser i sociologisk nyinstitutionelt perspektiv. Ph.d. afhandling [Clinical practice variation and clinical accounts in a sociological new institutional perspective. Ph.D. thesis]. 2006; DSI rapport 2006.10.

(22) Scott WR, et al. Institutional Change and Healthcare Organizations. From professional Dominance to Managed Care. Chicago: The University of Chicago Press; 1998.

(23) Seemann J. Netværk som forandringsstrategi og strategier i netværk [Networks as a change strategy and strategies in networks]. In: Bentzen EZ et al., editor. Når styringsambitioner møder praksis. Den svære omstilling af syge- og sundhedsvæsenet i Danmark og Sverige [When management ambitions meet practice. The difficult reorganisation of the sick and health care system in Denmark and Sweden]. Copenhagen: Handelshøjskolens Forlag; 1999.

(24) Seemann J, Antoft R. Shared Care – samspil og konflikt mellem kommune, praksislæge og sygehus [Shared Care – interaction and conflicts between local authorities, general practitioners and hospitals]. Research report 3. Copenhagen: Forskningscenter for Ledelse og Organisation i Sygehusvæsenet; 2002.

(25) Alter C, Hage J. Organizations Working Together. Newbury Park, USA: Sage Publications; 1996.

(26) Nielsen JC, Ry M. Anderledes tanker om Leavitt – en klassiker i ny belysning [Different thoughts about Leavitt – a classic in a new light]. Copenhagen: Nyt fra Samfundsvidenskaberne; 2002.

(27) Borum F, Jacobsgaard T, Larsen B. Sygehuse – opgaver, struktur, medarbejdere og teknologi [Hospitals – tasks, structure, employees and technology]. Copenhagen: DIOS; 1981.

(28) Schultz M. Kultur i organisationer – funktion eller symbol [Culture in organisations – function or symbol]. Copenhagen: Handelshøjskolens Forlag; 1990.

(29) Schein EH. Organizational Culture and Leadership – a Dynamic View. San Francisco: Jossey-Bass; 1994.

9 The economy

By Rikke Juul Poulsen, Dorte Gyrd-Hansen and Peter Bo Poulsen

This chapter provides guidance on how a sound economic evaluation can be conducted. Following an introduction to various kinds of economic analyses, guidelines are provided concerning issues, considerations, concepts and methods that are important when assessing the economic element in HTA.

Useful advice and suggeations

- By way of introduction, conduct a systematic review of the literature
- Outline alternatives with a description of expected consumption of resources and anticipated effects. Be alert to what perspective is used in the assessment, and indicate this explicitly
- Collect data on resource consumption, unit costs, probabilities and health gains either via the literature or by primary data collection or a combination of these
- Perform cost calculations (resource consumption is multiplied by unit costs)
- Calculate any health gains (for example, in the form of QALYs or survival)
- Discount costs and consequences, where necessary
- Calculate the incremental cost-effectiveness ratio
- Always perform sensitivity analyses to assess the robustness of the result
- Discuss results and methods in relation to other studies with the focus on weaknesses and strengths, scope for general application, etc.
- Report thoroughly and in a detailed fashion.

9.1 Introduction

On the one hand, there is demand for health services, and thus desires and preferences for the use of various health technologies. Conversely, however, there are also certain limitations in terms of resource restrictions on time, personnel and money, which mean that the range of health services does not always meet demand. Very rapid technological development in the health care sector also means that there is a gap between what is technically possible and what is economically possible. Newhouse (1) has shown that the greatest contribution to growth in health expenditure comes from the use of technology. These gaps make the prioritisation of efforts in the form of choices between different health technologies both relevant and inevitable. On a traditional market, demand will be determined by the price at which an article is offered. However, the market for health services does not function that simply, which is why prioritisation becomes slightly more complicated.

Economic analyses may help determine how resources find the best possible use in the health care sector. The basis for the economic reasoning and economic analysis is provided by the "opportunity cost concept", according to which *the costs of a health technology consist of the gains from other health technologies that have been foregone by committing the resources to the first health technology* (2). However, there may also be utility losses elsewhere in society if the health budget is expanded.

The necessary choice between alternatives (prioritisation) and the recognition that these choices have resource-related consequences is of central importance. Questions that must be answered are: what must be produced in the health care sector?, how should it be produced?, and how should products be distributed among the citizens of society?

In an HTA, the aim of the economic element together with the other elements is to provide information with a view towards improving the basis for decisions in the health care sector through choices between different health technologies, both new and existing. More specifically, the general role of the economic analysis in health technology assessments is to provide information on necessary resource consumption through the use of health technologies and undertake a comparison with the health gains achieved thereby – to assess *value for money* through the use of a given health technology in preference to another. This chapter therefore examines current methods for the performance of economic analyses in connection with an HTA. Where deemed necessary, it is endeavoured as far as possible to refer to sources of further information. It may also be appropriate to gain assistance on the analysis from a professional economist with a background in research or administration.

9.2 Types of economic analyses

Health economic analyses address issues concerning society's priorities, where the objective is to achieve the greatest health gain per monetary unit (e.g. € or $) invested. There are various kinds of health economic analyses, including cost-benefit analysis (CBA), cost-utility analysis (CUA), cost-effectiveness analysis (CEA) and cost minimisation analysis (CMA). Business-economic analyses address how given technologies can be produced at the lowest possible price to achieve a given aim (3). Budget- economic analyses examine who (e.g. hospital ward, municipality, patient) bears the financial burden and gain in connection with a given technology. In addition, the *cost of illness (COI)* concept and type of analysis is encountered frequently, with this being intended to describe the costs of a disease to society, e.g. the smoking problem in Denmark. However, as various alternatives (technologies) are not compared in the COI analysis, because it merely lists the total costs of a disease for society, this cannot be regarded as a full economic analysis (2).

The first aim in the economic element of an HTA is to find out whether the health technology is attractive from a socioeconomic perspective. In terms of business or budget economics, savings may well prove to arise from a given technology, whereas in socioeconomic terms no gain may be achieved, or the situation might even be exacerbated. Thinking in terms of pure budget economics or business economics may therefore lead to suboptimisation of priorities. Socioeconomic analysis is therefore the focus of the economic element in an HTA, and for this reason the rest of this chapter also focuses on this.

9.2.1 Health economic analysis

The aim of the health economic analysis is to clarify the relationship between the costs and consequences of a (new) health technology compared with one or more relevant alternatives currently used in screening, diagnosis, treatment, rehabilitation or prevention. This will yield information on whether the technology is cost-effective based on an overall societal appraisal, cf. Section 9.9.

Unlike certain clinical study designs, there are no fixed standards for how a health economic analysis should be performed, and what requirements it must meet in terms of methods. Elements of the method are also under discussion or under development. A number of European countries have introduced or are in the process of introducing guidelines for economic analyses for medicinal products (4). In Denmark, Danish guidelines for socioeconomic analyses of medicinal products were drawn up in 1998 under the auspices of the *Danish Ministry of Health and Prevention* and the *Danish*

Medicines Agency (5). Where it appears relevant, reference is made to these guidelines. In some countries, specifically Canada, the guidelines are also used in drawing up economic analyses in connection with HTA.

There are four kinds of health economic analysis which may be relevant to consider in connection with HTAs. Identification of the various types of costs associated with the use of a health technology, and their subsequent measurement and valuation in monetary terms, is in principle the same for these four types (2). On the other hand, the methods differ in the way in which the consequences (the health gains) are assessed, and what conclusions can be drawn on the basis of the analyses in connection with decision-making.

Cost minimisation analysis (CMA)
In the simplest type of health economic analysis – cost minimisation analysis – it is assumed that the consequences (the health gain) arising from the use of the health technologies compared are the same. In this type of analysis, it is sufficient to assess the costs. CMA is a special case of cost-effectiveness analysis, in which the health gains from the technologies compared are identical.

Cost-effectiveness analysis (CEA)
In cost-effectiveness analysis, both the costs and consequences arising from use of the health technologies compared are identified, measured and valuated. In this type of analysis, the consequences are assessed in natural units, e.g. years of life gained. Cost-effectiveness analysis provides a basis for arriving at a conclusion as to which of the technologies compared is most cost-effective in achieving a given aim and on what scale (2). It is this type of health economic analysis that is usually employed in HTAs nationally and internationally, cf. Draborg et al. (6) and Larsen et al. (7).

Cost-utility analysis (CUA)
Cost-utility analysis differs from cost-effectiveness analysis in that the consequences are measured and valuated in the form of quality-adjusted life years (QALYs). Over and above a gain in years of life (mortality), the quality of the years of life gained may also be important, not least in the case of chronic diseases. In cost-utility analysis, the years of life gained are therefore quality-adjusted with health-related quality of life. This kind of analysis makes it possible to compare outcomes of interventions across different activities in the health care sector. For example, CUA will make it possible to compare the cost-effectiveness of hip arthroplasties with the cost-effectiveness of the prevention of cardiovascular disease as the same outcome measure (QALY) can be used meaningfully. CUA is regarded as a special case of CEA (8), with the measure here being quality-adjusted years of life.

Cost-benefit analysis (CBA)
Lastly, as the broadest type of analysis, the consequences in the cost-benefit analysis are measured and valued in monetary terms by, for example, enquiring about willingness to pay for a given treatment, with willingness to pay being taken as an expression for the value of the treatment. The benefit of this analysis is that both costs and consequences are assessed in monetary units, and any net gain can therefore be calculated directly. Furthermore, cost-benefit analysis makes it possible to get an overall view as to whether the technology is economically desirable, i.e. whether the gains outweigh the costs. CBA differs from CEA and CUA in that this form of analysis can include a broad range of consequences.

The four types of socioeconomic analysis are summarised in Table 9.1.

Table 9.1. Choice of type of economic analysis

Type of economic analysis	When should the individual type of analysis be chosen?
Cost minimization analysis	1. When the technologies compared are equally effective – then it is only necessary to collect data about costs
⇓	
Cost-effectiveness analysis	1. When activities with the same purpose and measure of effectiveness are compared 2. When the effectiveness of the technologies compared is different, i.e. the difference in costs must be weighed against the difference in effectiveness
⇓	
Cost-utility analysis	1. When health-related quality of life is an important outcome 2. When activities across the health care sector are compared
⇓	
Cost-benefit analysis	1. When non-health effects are also important, e.g. the treatment process itself, the utility of information, etc. 2. When only one technology is assessed (net benefit) 3. When lives are to be valued in monetary units (e.g. € or $) 4.When activities across society are to be compared

9.2.2 Business-economic analysis

In a *business-economic analysis*, it can be useful to provide information for the individual hospital ward, hospital, local authority area or general practice concerning any investment needs and operating costs in connection with the purchase of a new technology. If an HTA is conducted in a hospital ward, it will often be relevant to assess the business-economic consequences as these frameworks are central to the ward's efforts, and the budget must be observed when taking decisions. Such an analysis cannot, however, provide information on *value for money*, whether at local or global level.

A business-economic analysis encompasses an assessment of expenditure and income in connection with the establishment and use of a technology in the individual ward, hospital or local authority area. The analysis can be subdivided into three phases:

- Purchase and establishment of the technology (the investment need)
- Operation and use of the technology
- Derived costs and savings as a result of the establishment and use of the technology.

This information is of course important for the individual ward or hospital faced with a decision about the introduction of new health technology as it provides an indication as to what resources are needed at start-up and during the lifetime of the technology in order to be able to use it.

9.2.3 Budget-economic analysis

Beyond initially taking a decision on whether a health technology is optimal in socioeconomic terms, it is often appropriate in an HTA also to identify what "cash box" accrues to the spending burden and possible gains from use of the technology. Is it the state's, the region's or the municipality's budget that is affected, and, if so, should expenditure be redistributed between the funds affected to ensure introduction of the technology, e.g. an increase in the block grant from the state? This can be investigated by drawing up a *budget-economic analysis*, as an addition to the socioeconomic analysis.

The budget-economic analysis seeks to identify how various funds (budgets), for example the region's and the municipality's, are affected if a new health technology is introduced. Consequences for the individual funds will often differ, and savings for one fund may result in expenditure for another fund. For example, it is conceivable that some of any saving for the region from switching to same-day surgery or accelerated rehabilitation to a greater extent is a consequence of extra expenditure being deployed in the municipalities' increased home care efforts for patients who are being sent home. This phenomenon may lead to budget-based thinking. It is therefore important that the consequences for each relevant budget are considered. In budget-economic analyses, it is therefore relevant to use concepts such as expenditure and income instead of costs and utility. Expenditure may, in addition to costs paid for buildings, equipment, manpower, etc., encompass pure monetary transfers in the form of daily allowances and pensions. In the case of a disease, this may be conceived as being very important for the individual budget. A socioeconomic analysis does not take account of pure monetary transfers because they do not lead to an extra draw on resources, but merely monetary transfers between individuals in society. In Denmark, there are a few examples of health technology assessments which explicitly include budget-economic considerations (9-11).

9.3 Resources, costs, expenditure (some basic concepts)

It was suggested in the previous section that there are differences between expenditures and costs. This is explained in greater detail here.

A number of resource inputs, e.g. manpower, equipment, materials, buildings, are required for an activity to be capable of being performed in the health care sector. A "cost" should be understood to mean a draw on resources in which the basic resources are time, people and equipment.

Where resources are used to provide a treatment with one type of health technology for one patient, the selfsame resources are not available for other patients or for other uses in society (12). To be able to assess the gain from the introduction of a new health technology, it must be examined what must be given up at the same time. This cost is expressed in terms of the opportunity cost (cf. Section 9.5.4), which represents the value of these resources in the best alternative use.

A cost is not always the same as an expense. Expenses are related to a payment from a budget, but are not necessarily an expression of a draw on resources. For example, the purchase of an item of equipment is an expense, whereas a cost is initiated only when the equipment is used and thus worn down and/or the value is reduced due to ageing. Patients' transport costs or costs on medicine in connection with a specific treatment are costs, but these are not expenses for a health budget.

Another example of expenditure is provided by the rates which form the basis for, among other things, the hospitals' settlement with the paying party. A hospital ward's bed day rate is expressed as an average that is typically calculated on the basis of the ward's annual expenditure and the total number of bed days (13). An overall average rate cannot, however, reflect the real draw on resources from various activities and types of disease in a hospital ward, which is why it can rarely be regarded as a cost. Nor does an average bed day charge take account of the fact that the costs typically have a different impact during an admission, where the last days are usually the least expensive (14). Conclusions concerning cost savings from the introduction of new technolo-

gies or organisational arrangements as a result of bed days saved (the last ones), for example in the case of a changeover to same-day surgery, are therefore usually overestimated if based purely on average bed day rates rather than a real assessment of the costs.

Transfers, which should be understood to mean the redistribution of money between groups in society, are not a real cost for society, either (15). Only a re-distribution is involved, for example via a tax payment, but a draw on resources is not initiated, and thus there is no opportunity cost. Typical examples of transfers are sick pay, pensions, VAT[13], etc. An argument can nevertheless be made to include the cost of administration of the transfers, but these are nevertheless often insignificant (2). Conversely, it may be relevant in the budget-economic analysis to include transfers to decide what "budgets" win or lose from any change in, for example, sick pay. The payment of, for example, pension or sick pay is an expense for a budget, but is not a social cost.

The draw on resources in connection with an activity in the health care sector concerns both consumption of *health resources* (e.g. manpower, medicine, equipment), *non-health resources* (e.g. draw on the social sector, the patient's transport to the place of treatment), *informal carer's time* (e.g. family and friends' (unpaid) time spent looking after the patient), *the patient's own time spent* in connection with the activity, both as *lost production* and as a result of illness and death (2,15).

The perspective for the economic analysis is crucial in determining what resources and thus costs should be identified and assessed. This is examined in greater detail in the next section.

9.4 Perspectives

In the health care sector, there are a number of decision-making levels for prioritising health technologies, ranging from a general societal level to the individual region as a hospital owner, and through to the individual clinical ward in a hospital. HTAs are drawn up with a view to decision-making at both clinical and more general political administrative levels.

The broadest and most extensive perspective is the societal perspective, where all relevant costs and consequences of the health technologies considered must be identified, measured and valuated, regardless of whom they accrue to (2). Here, it is just as important to include costs for the patient as costs for the hospital. However, economic analysis are often seen to be conducted for narrower perspectives, e.g. the health care sector, the hospital or the patient, which is important for the scale of the costs to be assessed (see Section 9.5.1, Table 9.2). The analyses may also be performed from the perspective of different budgets or decision-makers, e.g. the state or the Danish National Health Insurance Service, in the form of a budget-economic analysis, as discussed earlier (cf. Section 9.2.3)

It is generally recommended that the economic analysis is based on the broadest perspective possible, and that an analysis with a budget-economic perspective is not efficient, see for example Brouwer et al. (16). If an economic analysis is to be used for societal prioritisation, it must of course have a societal perspective, as the prioritisation otherwise risks becoming suboptimal. An important point here, which is also mentioned by Brouwer et al. (16), is that it should be borne in mind that budgets in the health care system, e.g. in the primary sector and the secondary sector, are merely a set

13 If VAT is applied to all goods in society, the price including VAT will reflect the value of resources in alternative use. VAT will thus have a systematic distorting effect on price, which means that VAT should be included in the analysis (59).

distribution of the resources for treating patients. A technology may be considered cost-effective from narrower perspectives without being so from a societal perspective. For example, it is conceivable that accelerated treatment regimes will save certain costs for the hospitals if the patients are discharged more quickly. However, this may mean that the care is instead "passed on to" relatives or care homes because the patient may not be as resourceful as the person in question would be if he had been treated under the traditional regime. The opposite may also apply, namely that the use of a health technology means higher costs for the hospital, possibly in the short term, than the use of a similar technology, but that these are more than outweighed by cost savings elsewhere. For example, it can be imagined that if the hospitals offer preventive training to pregnant women (if there is evidence of a health benefit) to avoid pregnancy-related pelvic pain and incontinence later in life, this would initially mean increased costs for the hospital. However, it can be imagined that these are outweighed by the costs avoided through fewer and shorter sick reports later in the pregnancy and the avoidance of treatment of serious pregnancy-related pelvic pain and incontinence later in life.

Danish and Canadian guidelines also recommend that analyses should be performed with a societal perspective (5,17) to avoid such situations. If one wants to perform an economic analysis with a narrower perspective, *there must be good arguments for this.* These might be, for example, that the inclusion of other costs would merely confirm the result achieved with a narrower perspective.

HTAs are performed frequently in hospitals, and, as part of this, so too are economic analyses of the introduction of new technologies in specific wards. These analyses often seem to have to be conducted quickly and with a relatively limited budget. In addition, it is crucial for the hospital ward to show the budgetary implications of these measures, cf. Section 9.2.2. If it is not possible in such situations to perform the economic analysis from a societal perspective with a socioeconomic analysis, the possible consequences should at least be discussed in a societal perspective. The same of course applies in other contexts, where it is not possible to conduct a socioeconomic analysis.

Regardless of which perspective is chosen for the specific economic analysis, it must be clear what costs and consequences are included, and these must be in line with the chosen perspective, partly to ensure the comparability of various analyses.

9.5 Costs

Traditionally, the costs in a socioeconomic analysis are assessed in three stages. In the first stage, consumption of resources involved in the use of the alternative technologies is identified. In the second stage, this consumption of resources is measured in physical units, and in the third stage the consumption of resources is valuated, i.e. unit costs are determined for the consumption of resources. This process is described in more detail in the following sections.

9.5.1 Identification of resource consumption

The first step in assessing costs consists of identifying the relevant resource consumption involved in using the health technologies compared in accordance with the perspective for the analysis. Ideally, this is only resource consumption that is expected to vary between the technologies compared as well as between the patients (marginal analysis) that needs to be collected.

In an economic analysis with a societal perspective, all draws on resources must be assessed if considered relevant and important for the technologies examined. Fewer draws on resources may be identified in analyses with narrower perspectives. For example, with a hospital perspective alone, there will only be a focus on resources in the hospital system. It must be decided what relevant cost data must be collected. Methods that can help with this are reviews of earlier studies in this area, the performance of pilot studies, modelling and expert opinions (18). It may be valuable here to construct a decision tree showing the possible courses of the disease and of the therapeutic options, namely the health technologies compared and, as part of this, also gain an overview of resource consumption associated with the technologies, epidemiological knowledge and possible complications, rehabilitation, etc. (16).

Table 9.2 shows the various types of resource consumption and costs in relation to three chosen perspectives, where the societal perspective is the broadest perspective, which includes *all* relevant costs.

Table 9.2. Types of resource consumption and costs in an economic analysis

Perspective			Type of costs	Resource consumption
Society	Health care sector	Hospital	Direct costs: - in hospital	Health personnel, medicine, utensils, tests, capital equipment (plant & buildings), in-patient stay(hotel), outpatient visits, overheads (food, lighting, heat, etc.), (research & training)
			Direct costs: - in the primary health care sector	Consultation with general practitioner, practising specialist, physiotherapist, etc., prescription medicine (the Danish National Health Insurance Service's share), public surveys
			Direct costs: - in other sectors	Home care & home nursing, social events, including support for medicine (municipal grants), aids
			Direct costs: - for patient & family	User payment (medicine, dentist), transport, time spent on investigation/treatment, (unpaid) time spent by family or friends in caring for patients
			Production loss/gain in society	Changes in patients' temporary absence through sickness, reduced ability to work due to sickness and disability, or lost production in the case of premature death
			Future costs	Future unrelated costs including health costs generated as a result of a patient's lifetime being extended or shortened

Production loss is a cost for society due to morbidity (lost/reduced ability to work in the case of illness and disability) and mortality (lost production in the case of premature death), cf. Table 9.2. It should nevertheless be noted, cf. Luce et al. (15), that the value of reduced income may already be included on the effect side in the assessment of QALYs (quality-adjusted life years), which means that there is a potential risk of double-counting of costs arising from production losses.

The inclusion of future unrelated costs as well as production gains in the years of life that may be achieved with a treatment is a controversial subject (15). If production gains are included, so too should future costs. Analysis in which production gains and consumption are included are usually presented in a sensitivity analysis (cf. Section 9.10).

Intangible costs in the form of anxiety, nervousness and the like, which may for example be caused by participation in a screening programme, are *not* included on the cost side in an economic analysis, but may be included on the effect side in estimating willingness to pay or where appropriate in QALYs (2). Besides the fact that they can be included on the effect side, they do not take resources away from other consumption (opportunity cost), which means that they are really not seen as costs.

9.5.2 Some important cost concepts

In the economic analysis, it is important to understand how the costs should be calculated in relation to the health technologies compared. The difference between the assessment of average costs and marginal costs is that fixed costs, such as buildings and overheads, will be included in the average costs, but not in the marginal costs, cf. Table 9.3. When a programme is extended, however, the costs may increase more than proportionally with the extension, whereas the effects may rise less than proportionally. With the focus on changes in the activity in the economic analysis, there will therefore be an interest in answering the question *what will the costs be as a result of a slightly greater or lesser effect?* A calculation of marginal costs – *the extra cost of one extra unit produced* (see Table 9.3) – will be relevant for decision-making here. Brouwer et al. nevertheless argue for the use of average costs where a comparison of two technologies with different infrastructure needs is involved, or if it is wanted to generalise about costs at a national level (16).

Table 9.3. Various cost concepts

Total costs	All costs relating to the production of a quantity of output q; TC = FC + VC
Fixed costs	Costs incurred by production regardless of its scale (FC), e.g. investments
Variable costs	Costs that vary with the scale of production (VC), e.g. materials
Average costs	The costs per unit produced q; AC = TC/q
Marginal cost	The extra cost associated with producing one extra unit; MC = (TC for q + 1 units) – (TC for q units) = δTC/δq
Incremental cost/ differential cost	Difference in costs between two technologies (difference); $IC_{A-B} = C_B - C_A$

The *time horizon* is also a factor in considerations of the assessment of average or marginal costs in economic analyses. Fixed costs are in the longer term variable costs, as there will be scope for making changes in the factors of production, e.g. closing/opening wards (19). In the longer term, the marginal costs will thus approximate average costs. Conversely, this means that some resources cannot actually be realised in the short term, e.g. bed days saved (14). It is therefore important that the time horizon for the decision-making problem is considered before it is decided what costs must be assessed.

Lastly, incremental costs that say something about the difference in costs between two programmes (the differential cost) can also be assessed, cf. Table 9.3. These are often interpreted as being synonymous with marginal costs, as the extra cost for an extra unit of output, which is not correct. Incremental costs are central to decision-making on the use of one technology rather than another, where dominance does not exist, i.e. where one technology is not both better and cheaper than the alternative for comparison (cf. Section 9.9).

9.5.3 Measurement of resource consumption

Resource consumption data can be collected in several ways. As a rule, a distinction is made between prospective and retrospective collection of patient-specific or deterministic data.

With *prospective* data collection, patient-specific resource consumption is usually measured in connection with a clinical study. The typical units for measuring resource consumption are physical units such as time spent on work performed, admission time, medicine (type and dosage), number of tests and examinations, number of surgeries,

number of visits to one's own general practitioner and their duration, days off work through sickness, etc. The importance of the individual resource input for the specific activity determines the level of detail of the data collected, cf. Section 9.5.1. With *retrospective* data collection, resource consumption is not collected continuously, but rather, as the term indicates, retrospectively. For example, by sending questionnaires to patients concerning, for example, contact with their own general practitioners, absence due to sickness, etc. or via extracts of registers concerning admission time, consumption of medication, etc.

With deterministic data (non-patient-specific data), resource consumption is in practice assumed to be the same for all patients. For example, when standard templates are used for specific procedures in surgeries, it will be reasonable to assume that such standard templates represent average material consumption for the individual patients, and it will appear natural here to use this rather than a count of material consumption from a random sample of patients.

There are a number of methods or sources that can be used to collect and measure resource consumption, as described in Table 9.4. These sources break down, as mentioned above, into sources for the collection of stochastic and deterministic data and into prospective and retrospective data collection methods.

Table 9.4. Sources for the collection and measurement of resource consumption data

Patient-specific (stochastic) data			
Sources	**P/R**	**Description**	**Typical data (examples)**
Case Record Forms (CRF)	P	Forms to be filled in. Supplement concerning economic data for clinical CRFs. Completed continuously by the clinician/monitor in the clinical study. Provides scope for the most detailed collection.	Detailed assessment of all resource consumption data in hospital or on an outpatient basis in a clinical study. For example, number of procedures, time, material consumption, admissions.
Cost diaries (diary)	P	Concerns non-hospital data used during the study period, but may also be used in hospital. Completed continuously by the patient or personnel.	Primary sector (e.g. doctors' visits), patient's own expenditure, travel expenses and travel time, absence from work. Also any hospital data.
Questionnaires (where applicable, interview)	R	Completed by the patient or personnel for a given course or parts of it. Where applicable, interview.	Primary sector, the patient's own expenditure, travel expenses and time spent, absence from work.
Registers and data systems	R	1) National Patient Registry and administrative systems, 2) Health Insurance Service Registry, 3) Sick Pay Registry, 4) Pharmaceutical Database.	1) Time of confinement to bed, diagnosis and operation codes, 2) Primary sector data, 3) Payment of sick pay, 4) Medicine consumption.
Patient records	R	Review of records and kardex systems.	Admissions, procedures, outpatient visits.

Non-patient-specific (deterministic) data			
Sources	**P/R**	**Description**	**Typical data (examples)**
Pilot studies	P/R	On a representative proportion of the study patients or similar patients (time studies, statement of materials).	Work input (time) from personnel groups, medicine and statements of material, time of in-patient stay.
Clinical databases	R	Existing clinical databases within the specific areas of disease investigated.	Length of admission, number of patients treated, complication rates.
Previous studies	R	Resource data from previous published studies.	Number of procedures, tests, unit costs.
Expert opinion	--	Experts' assessment of resource consumption in the individual case. Where applicable, as expert panels.	In principle, all data. But essential to consider validity and reliability of data.

Note: P refers to prospective methods and R to retrospective methods.

A number of the sources in the Table 9.4 are often combined when collecting data for a specific economic analysis as the burden for the patient and personnel must also be considered. However, the benefit of primary data collection methods such as economic Case Record Forms (CRFs) completed by the clinician and cost diaries completed continuously at home by the patient is that they can be incorporated direct as part of a clinical study's data collection and collected at the same time (20). Cost diaries and questionnaires/interviews may be relevant in particular, as additions to CRFs, when measuring the proportion of the patient's resource consumption that concerns the primary sector, e.g. visits to the doctor, and the patient's own consumption of health services, e.g. over-the-counter medicine. Beyond a prospective collection of data, existing data sources in the form of registers and patient record systems can also be used (18). Relevant registers include hospital administrative systems and the Danish National Patient Registry (NPR), which can both provide information in the hospital sector. For

the primary sector, the Health Insurance Service Registry may be an option, while it may be relevant to draw on the Sick Pay Registry if data are needed concerning absence through sickness. Generally, however, it should be understood that no systems or registers are specifically set up to assess resource consumption data, and the level of detail may be deficient. Furthermore, they are not always free and it can take a long time to access register data at national level (NPR, the Health Insurance Service Registry, the Pharmaceutical Database, etc.). The National Institute of Public Health has previously issued a summary of registers that can be used within the health care sector (21).

There are also a number of sources for collecting deterministic and non-patient-specific resource consumption data, such as pilot studies, existing clinical databases, previous studies and/or expert opinions. Here, resource consumption is measured for the *average* patient rather than the *individual* patient. For certain clinical databases, there will nevertheless be an opportunity to obtain patient-specific data.

In the past, it was typical in economic analyses to use deterministic resource consumption data, i.e. data not assessed in a patient-specific manner. However, economic analyses are increasingly being conducted prospectively in connection with ongoing clinical studies, which allow for the assessment of stochastic resource consumption data (22). The advantage of this is that individual data are obtained for each patient's resource consumption for a given treatment, and that statistical analysis of costs and the results of the economic analysis become possible, as is the case in the clinical study. The Danish guidelines recommend the use of prospective designs for the collection of resource consumption data (5). As the aim for an HTA is to be based on the existing literature, it will often be found to be impossible to collect prospective economic data, and deterministic data must therefore be used instead. Here, it is then very important to perform sensitivity analysis (cf. Section 9.10) to test whether the results are robust with respect to changes in cost data.

9.5.4 Valuation of resource consumption

As a cost is given by price multiplied by quantity, the third phase in assessing costs is to valuate prices in the form of unit costs. Ideally, the price of resource consumption must correspond to the opportunity cost (23). This means, for example, that the price and thus the unit cost for scarce resources such as radiologists must be set higher than a contractual hourly wage, as the value of their alternative use is high, if the supply of radiologists is less than demanded. Furthermore, the lack of a normally functioning market for health services means that in many cases direct market prices corresponding to the opportunity cost do not exist, but only rates (e.g. in the case of bed days). As opportunity costs are difficult to measure in practice, however, it is often necessary to use rates. Market prices are sometimes available (as, for example, medicine prices), but these do not necessarily reflect the opportunity costs (if there are for example monopoly situations). Some practical examples of valuation of unit costs are set out below in Table 9.5.

Table 9.5. Examples of unit costs in practice for different resource inputs

Type of ressource	Suggestion for a valuation in practice
Labour	Average rate of pay for the specific personnel group (where appropriate, corrected for length of service)
Medicine	Hospital: cost price. Primary sector: the pharmacy's retail price (comprising both the user payment share and the share of the Danish National Health Insurance Service)
Material	Hospital: purchase prices. Primary sector: the patient's own payment (if any) (and the Danish National Health Insurance Service's share)
Capital equipment (plant, buildings)	Operating costs + depreciation. The depreciation of the equipment per annum is calculated on the basis of the investment price, the depreciation period and the discount rate (see also (2), p. 88-95)
Overhead activity	All hospital expenditure on overheads (cleaning, food, lighting, etc.) is distributed on a "step-down" basis to a department's activity, e.g. overheads per bed day (see also (2), p. 74-81)
In-patient stay (hotel)	Daily price for hotel expenditure in connection with hospitalization. Alternatively, distributed on a "step-down" basis as above
Lost production and time spent by the patient	Age- and sex-adjusted rates of pay (average). Where appropriate, shared between sectors in the case of loss of production. CCOHTA guidelines (17) recommend an average rate of pay in the industry

These unit costs will vary with factors such as geography, type of institution, patient category, etc., and the utmost caution should therefore be exercised in using foreign costs in Danish analyses due to differences in health care systems and labour market conditions. This also means that the economic element of an HTA can never satisfactorily consist of a systematic literature review of economic analyses performed internationally. The review of the literature in relation to economics can primarily be used as a source of inspiration for design and data collection in the specific economic analysis and collection of data on effect (see also Chapter 3 and 4 on literature searches and assessment and Section 9.12).

Once the unit costs have been valuated, each patient's resource consumption can be multiplied by the associated unit costs. The total costs are calculated by summing for all patients, and the average total costs for each alternative can subsequently be computed.

In general terms, the strategies for determining costs can be split into two overall approaches: micro-costing and gross costing, which vary with the level of detail and precision (15,24). *Micro-costing* is a direct assessment (e.g. time studies) of unit costs for each input in the treatment of a particular type of patient. These are methods with a high level of detail and thus a high degree of precision. On the other hand, the methods are demanding in terms of resources and not always amenable to general application as the costs will often be combined in a single location. Conversely, treatment costs under the more aggregated *gross costing* approach are arrived at by applying a national average level for large units of input and output, e.g. Diagnosis-Related Group (DRG) or bed day rates. Here, the level of detail and precision is slightly less; on the other hand, the methods are less demanding in terms of resources and more amenable to general application at a national level.

The level chosen will depend on the need for precision, the need for general application, feasibility, and the costs associated with adopting the various methods (16). The micro-costing approach is often used for costs, and thus resource consumption, that are highly central for the analysis, whereas costs that are less central and where precision means less are determined by the gross costing approach. Both strategies are often used in the same analysis for costing the various forms of resource consumption. For example, in an analysis of minimally invasive hip arthroplasty compared with traditional hip arthroplasty, it will be essential to measure resource consumption in connection with the operation at a highly detailed level as it is primarily here that there will be a difference. On the other hand, a bed day rate may be "good enough" in determining costs in connection with admission as this parameter is not so central to the analysis. In an HTA of low-stimulation IVF compared with standard IVF for the treatment of infertility, the micro-costing approach is adopted in determining the costs relating to the IVF treatment, whereas DRG rates are used for estimating costs associated with childbirth (25). The choice of approach should be determined when the HTA analysis and the economic analysis are designed.

The problem in using DRG and other rates (e.g. for the payment of general practitioners) is that these rarely reflect the true opportunity costs, but nevertheless exist as financial costs in the payment of, for example, hospitals and doctors for their resource input in the treatment of patients (16). It is therefore uncertain that the rates cover the total costs, e.g. the DRG rates do not include depreciation of buildings and equipment, and in some cases policy-determined rates may exist without any basis in actual cost calculations, e.g. the DRG rate for long term in-patients.

DRG rates can be used if, for instance, it is the frequency of a procedure that is crucial in the economic evaluation, e.g. use of MRI rather than X-rays for investigating lumbar discomfort; however, when the actual surgical procedure is being examined, e.g. minimally invasive hip arthroplasty compared with standard hip arthroplasty, a micro-costing approach will be necessary to be sure of recording the resource consumption, which will vary between the procedures (e.g. surgery time and materials).

If a more thorough and extensive description of the cost estimate is wanted in health economic analyses, the reader is referred to, for example Johnston et al. (18), Brouwer et al. (16), Drummond et al. (2), CCOHTA (24) and Alban et al. (5).

9.6 Health gains

A health economic-analysis comprises, in addition to an assessment of the costs of alternative technologies, an assessment of the health effects or consequences achievable with the technologies, cf. Section 9.2.1. A direct consequence of the use of a health technology is that the patient's health is expected to change, which can be measured in the form of an *outcome measure in natural units*, or valuated in *quality-adjusted life years (QALYs)* or *willingness to pay* (2). There may also be other consequences of use of the technology, such as the value of information in a screening programme. This may be incorporated in QALYs or willingness to pay.

9.6.1 Outcome measures in natural units

Cf. Section 9.2.1, the effectiveness of health technologies is assessed in the *cost-effectiveness analysis* in natural units and presented as costs per unit of effect.This is relevant where the technologies being compared have the same aim (and thus the same outcome measure) or where health-related quality of life is not important.

Identification

In selecting outcome measures, a distinction is made between intermediate and final endpoints. *Intermediate endpoints* concern changes in a health status related variable in connection with the use of a health technology (5). Intermediate endpoints may be surrogate measures, e.g. reduction in mmHg blood pressure, mmol/l serum cholesterol, or events (avoided), e.g. number of correctly diagnosed heart attacks. The intermediate endpoints are close to the outcome of clinical studies, which is why they are often relevant for clinical decision-making. Conversely, the *final endpoint* concerns certain survival indicators which reflect the probability or the frequency of survival over a specifically defined interval (5). Examples of final endpoints are years of life gained or lives saved. Final endpoints relate to the final objective for the use of the technology, and not only a clinical output, which is why they have greater relevance for the patient and for overall prioritisation (2). An assessment in terms of final endpoints makes it possible to compare for different types of health technologies so far as the final consequences are comparable. Lastly, effectiveness can be assessed with a health profile if only health status, and not survival, is affected by the technology (cf. Section 5.4). Health status measures cannot, however, be directly included as outcome mesures in the cost-effectiveness analysis[14].

Measurement

A source for data on the effectiveness of health technologies is the medical literature, for example in the form of systematic literature reviews or meta-analyses (cf. Section 4.1.3) or clinical databases (cf. Section 5.3). Effectiveness can, however, also be measured directly if the cost-effectiveness analysis is performed prospectively in connection with a clinical study. The outcome measure may then be one of the clinical study's outcomes. Regardless of whether literature reviews, meta-analysis or primary studies are chosen to generate data on effect, the same stringent criteria apply to the quality of data in the clinical studies (see Section 4.1.4). The design for the clinical studies must be of high quality, randomised and controlled, and have the greatest possible internal validity. At the same time, relevance for decision-making is a further requirement for effectiveness data in the economic analysis (2). Randomised, controlled clinical studies provide data on the effectiveness of technologies in study populations. With the focus on decision-making, however, data on effectiveness in daily practice are desired, and so the external validity and scope for general application of the economic analysis increases. In selecting data on effect, internal and external validity must therefore be weighed up. However, it is often a good idea to choose the best possible clinical design and data on effect and, where appropriate, carry out modelling subsequently so that effectiveness in daily practice is incorporated. If data for intermediate endpoints have been assessed, caution must be exercised in directly extrapolating from this to final endpoints unless this is underpinned by a clear biological or medical rationale. An inadequate study period may also make it impossible directly to collect data on, among other things, years of life gained in clinical studies. Extrapolation with data from survival tables and analyses (survival analysis) and Cox regression analyses (proportional hazard) are possibilities here.

Years of life gained and IHD[15]-free years of life gained are used in Willaing et al. (26) as outcome measures in the cost-effectiveness analysis of dietary guidance in the primary sector, where the risk of dying before and after the intervention is calculated. Years of life gained are also used as an outcome in the HTA report concerning influenza vaccination of elderly (27). Often, however, intermediate endpoints are also used, for example in the report on CT cholography, where the outcome measure was "pathologi-

14 Health status endpoints are multidimensonal profiles in which each dimension is measured ordinally. The converse of this is the health index (see Section 9.6.2), in which the various dimensions are weighted together in a cardinal utility endpoint.

15 IHD=Ischaemic Heart Disease.

cal findings" (28), and in the report on Chlamydia, where "severe complications avoided" was used as the outcome measure (11).

9.6.2 Quality-adjusted life years

Health technologies will often have effects with more dimensions than can be incorporated if outcome measured in natural units is chosen. Cost-utility analysis should be employed if the use of a health technology is therefore expected to lead to changes in health-related quality of life for patients or an extension of life with impaired health. In cost-utility analysis, the effects are measured and valuated in the utility measure *quality-adjusted life years* (QALYs). Quality-adjusted life years cater for the fact that health services in the form of health technologies can influence not only residual life (mortality), but also quality of life during this residual life (morbidity), among those at whom the service is aimed (29). To a much greater extent than outcome assessed in various natural units, the QALY measure is attractive in decision-making, and thus also in an HTA context because it is a measure that can be used on every patient population, disease and intervention, and can be used to conduct comparisons across different areas and technologies in the health care sector (17).

Quality-adjusted life years (QALYs) are calculated by quality-adjusting each year of life gained from an intervention with a QALY weight of between 0 and 1, which reflects the utility of a health condition in the form of health-related quality of life over the time under consideration. One extreme point with a QALY weight of 1 indicates that the patient is in a state of perfect health (healthy), whereas a QALY weight of 0 refers to the fact that the patient is dead. Some conditions are rated as worse than death, i.e. with a negative QALY weight. Between these extreme points, there are many states of health with varying degrees of sickness and disability, which will have a QALY weight of less than 1. For example, the utility measure EQ-5D comprises 243 different states of health.

Measurement

For each health technology compared in the economic analysis, the number of QALYs must be measured both before and after a possible intervention. QALYs gained from treatment can then be assessed, and the most advantageous technology chosen. It could be – *in an imagined example* – that home dialysis leads to a slightly higher health-related quality of life compared with hospital dialysis, and therefore home dialysis has a QALY weight of 0.7 versus 0.6 for hospital dialysis. Conversely, the possible residual lifetime is slightly longer for hospital dialysis as it is more effective than home dialysis, for example 9 years versus 8 years. The number of QALYs for home dialysis is therefore 8 x 0.7 = 5.6 versus 9 x 0.6 = 5.4 for hospital dialysis, which means a gain of 0.2 QALYs for one patient by opting for home dialysis. At the level of society, all QALYs gained will be apparent by aggregating QALYs gained for every single patient. The sum of QALYs gained must ultimately be compared with the difference in costs for the two different approaches to dialysis therapy.

QALYs are generally measured using one of the following multidimensional utility measuring instruments: EQ-5D or 15D, where the QALY weight is derived from a population consisting of a cross-section of the general Danish population. The only thing that must be ensured with this method is that, at various times during the study period (e.g. before and after the intervention), the patients complete the utility measurment instrument concerning their health in relation to the dimensions in the chosen instrument. The instrument's set preference scores (QALY weight) and a score algorithm are then used for the individual dimensions, with the number of QALYs gained from the technology then becoming apparent for the sample in question.

Use of EQ-5D is described on the web page http://www.euroqol.org/, while Brooks et al. (30) sets out guidelines for the analysis and reporting of EQ-5D data. Danish weights for EQ-5D are estimated in Wittrup-Jensen et al. (31) and are also published in Szende et al. (32). Use of the 15D instrument is described in-depth in (33-35), and the Danish weights are estimated in Wittrup-Jensen et al. (36). There is also a web page for the 15D instrument: http://www.15d-instrument.net containing, among other things, the questionnaire, registration forms, etc.

In connection with a study, the instrument that best matches the study's purpose and target group should be chosen; EQ-5D is often criticised for being too crude a measure, as it is difficult to demonstrate a difference in the effect of various therapeutic options. On the other hand, the instrument is simple and quick to complete, unlike for example 15D, which has 3 times as many questions and a number of possible responses under each question.

An example of an HTA report in which quality-adjusted life years are used is Haamann et al. (37), in which QALY results from a previous study have been used.

For a more detailed description of the theory and method behind quality-adjusted life years and their calculation, see for example Drummond et al. (2), Gold et al. (8), Kaplan (38), Pedersen et al. (39) and Torrance (40).

9.6.3 Willingness to pay

In the past, it was frequently observed in cost-benefit analyses that "costs saved" for a treatment were used as a measure of the gain. This is as it should be if the costs saved reflect the dominant gain from a treatment. In many cases, however, the total gain will consist of more than the costs saved. An example of this is a cost-benefit analysis of nutritional support during stays in hospital, where the valuated gains from nutritional support to hospitalised patients consist purely of bed days saved, arising from the patients' expected earlier discharge (41). A (simple) consideration of this kind nevertheless has certain clear limitations as costs saved are a much narrower measure of the gain and do not cater for the patient's experience of the course of events, preferences for regaining his or her health more quickly, etc. In general terms, there is in many cases no link between treatment costs saved and the individual consumer's/patient's valuation of the gain from a programme such as, for example, nutritional support or prevention of road accidents (42).

Valuation of the gain therefore often entails more than the potential costs saved. Instead of costs saved, the particular individual's/patient's valuation of a treatment can be obtained by identifying the maximum that the person in question is willing to pay to receive the treatment, i.e. in the form of willingness to pay. On a market that functions normally, the value of a good is equal to what the consumer is willing to pay and is expressed by the market price. In the health arena, on the other hand, there is no such market, partly because the majority of health services in Denmark are paid for from taxation. If the value (benefit) to people in monetary terms from the use of a health technology is therefore to be identified, hypothetical willingness to pay methods must be used as the value cannot be directly seen from the market.

The methods primarily used in the health care sector are contingent valuation and discrete choice analysis, which are survey methods in which individuals are asked about their willingness to pay for a treatment, in connection with the assessment of gains (consequences) in a cost-benefit analysis. With these methods, people are, based on a

carefully described hypothetical scenario, asked directly about their maximum willingness to pay for the consequences of a technology's use (2). This might, for example, concern willingness to pay for *in-vitro fertilisation* (IVF) and thus ultimately for securing a pregnancy or child with a certain probability. In the cost-benefit analysis, the total costs of a health technology are deducted from the total maximum gains, with the net gain being expressed in monetary units. A positive net gain means that the technology should be chosen as the gains outweigh the costs. If the net gain is negative, on the other hand, the technology should not be introduced. In a willingness-to-pay investigation, and thus in the cost-benefit analysis, there is, unlike with the cost-effectiveness analysis, also the option of valuing consequences other than a change in health from the use of a health technology. The process by which the health gain comes to light also means something for the value of the technology. With IVF, it could for example be imagined that a process entailing intense hormone stimulation of the woman, and consequently side effects and a risk of overstimulation, affects one's rating of IVF and its output. The fact that, as a potential patient, one has the possibility of receiving a treatment in future if one falls ill may also have a value (option value). These consequences, which differ from those directly related to health status, can be incorporated in the willingness-to-pay investigation depending on how and to whom questions are put.

Willingness to pay methods are currently developing very rapidly, and renewed interest has arisen for hypothetical willingness to pay studies within the health care sector, e.g. as a result of the introduction of discrete choice analyses. Willingness to pay methods are nevertheless still under development (and probably always will be). The precision of the estimates is uncertain, and it is, among other things, unclear whether willingness to pay varies with the scale of the item under consideration. Willingness to pay estimates can, however, very well be used to identify preferences within the population for specific health technologies, but caution should be exercised when directly interpreting the specific magnitude of a willingness to pay found in a study. Danish guidelines also recommend that willingness to pay methods should not be used alone, but only as a supplement (5). Up to now, however, the methods have been used in few cases in an HTA context. Particularly in Great Britain, the discrete choice experiment has become widespread and is regarded as a good instrument for product development within the health arena as well as in other sectors. The discrete choice experiment has the advantage (unlike the contingent valuation method, in which only one good/one service is sought) that the relative preferences for the individual characteristics associated with a health service are identified. This is done by presenting respondents with a range of choices between goods/services – and, via these choices, the characteristics of the service are modified systematically. In this context, it can (cf. example above with IVF therapy), for instance, be identified how patients weight processes versus outcomes. If price is included as a characteristic, willingness to pay can also be identified for these various characteristics. The discrete choice method can therefore be regarded as a method which, with a high level of detail, can include the population's and patients' preferences in an HTA. For a more detailed examination of the discrete choice method, the reader is referred to certain Danish applications (43,44).

9.7 Discounting

Costs and consequences that only arise more than one year ahead *are discounted* in the economic analysis. Future costs and health consequences must be discounted in order to reflect the fact that individuals and society generally have positive time preferences as favourable consequences (such as health gains) are wanted early on, whereas unfa-

vourable consequences (such as costs) are wanted to be postponed (17). In practice, costs and consequences need to be discounted if their timing differs, and the value at the present time (the current value) of future costs and consequences needs to be calculated in order to be able to compare health technologies in an economic analysis. For example, the costs of a screening programme arise immediately, whereas years of life gained are obtained later. Discounting must not be confused with inflation. However, if prices from various years are used in the analysis, prices for previous years must be adjusted and converted to current prices so that the opportunity costs for resource consumption are expressed in the same current-value (15).

When discounting, costs and consequences arising in t years are depreciated by being multiplied by the factor $1/(1+r)^t$, where r indicates the chosen discount rate (13). The current value of a cost of DKK 5,000, which arises in 3 years, will, with a discount rate of 5%, be $5{,}000/(1 + 0.05)^3$ = DKK 4,319. The current value of a gain of 250 QALYs made after 5 years will, with a 5% discount rate, correspond to a gain of 196 QALYs in present time ($250/(1 + 0.05)^5$). As the examples show, the choice of discount rate is crucial. There are no recommendations in the Danish guidelines concerning health economic evaluations and the use of a specific discount rate, but typical recommendations in other countries have been rates of 3 – 7% (8). Gold et al. (8) recommend, as a starting point, using a discount rate of 3%, but varying this by 5% to ensure comparability with earlier studies, in which a rate of 5% is often used. A discount rate of 3% may seem reasonable at the present time, when the discount rate is generally low. It is always recommended that the discount rate shouls be varied in the sensitivity analysis to investigate the significance of this on the result.

9.8 Modelling of the economic analysis

In some cases, modelling will need to be used in the economic analysis – whether completely or only partially. There are a number of reasons for this, cf. inter alia Buxton et al. (45). Extrapolation of short-term clinical data for the purpose of predicting these data in the longer term, e.g. survival probabilities, or linkage of intermediate endpoints to final endpoints, can lead to modelling in the economic analysis. The performance of the clinical study in a controlled and randomised design which ensures a high degree of internal validity often conversely means that the study has a low degree of external validity. Here, it can be necessary to model the economic analysis in order to be able to generalise about daily practice or between regions in the country. As mentioned previously, it may also happen to be placebo that the new technology is compared with in the clinical study. Here, it may be necessary to use models in the economic analysis to investigate the cost-effectiveness of the new technology in relation to daily practice. Lastly, there may be insufficient economic and clinical data, particularly early in the development/life cycle of a health technology. The economic analysis can, in such a situation, be modelled entirely on the basis of the best available evidence and the expectations that one may have.

Modelling is used frequently in connection with HTA since it is here attempted to take existing literature as the basis. There is often evidence for the effect of a technology in the form of clinical data, survival data and/or data concerning health-related quality of life, and one will then, where appropriate, content oneself with collecting cost data and comparing these with the effects in a model. This is an approach commonly adopted in, for example, British HTA reports, e.g. (46,47); it is often also seen in Danish HTA reports, including in a report on screening for Chlamydia by means of home testing, in which both an epidemiological and an economic model developed abroad and applied

with Danish data (11), are employed. A report on the introduction of hepatitis B vaccination as part of the children's vaccination programme in Denmark (48) and a report on preimplantation diagnosis (49) have also used this method.

Types of frequently used models are *decision trees* and *Markov models*. In decision trees, a sequence of possible events is presented, with each one being assigned a probability. Every path through the decision tree shows one possible sequence of probability and decision events. The value of each possible chain of events can thus be calculated and each outcome weighted with the probability of it occurring (8). A Markov model comprises a finite number of health stages that a patient can go through over a period of time. The essence of this is that the patient will at a particular time (in each cycle) always be in one of these states of health. Between each cycle, the patient can shift from one state of health to another. The probability of such a shift is given by the transition probability. Markov models are suitable where the disease or treatment is characterised by a repetition of the disease state or the treatment algorithm (2), as is for example seen in dialysis patients, where the patients may receive haemodialysis for several cycles/periods and then switch to, for example, peritoneal dialysis, be given a transplant or, in the end, die.

Regardless of whether modelling is necessary, or the economic analysis can be based directly on the clinical study, it may be a good idea, purely in order to gain a comprehensive view, to draw up a decision tree for the possible patient streams as referred to above.

For an in-depth examination of model studies, see for example Philips et al. (50), which provides an overview of various guidelines for the performance of modelling studies and a review of good practice in these studies. In addition, Briggs et al. (51), Drummond et al. (2), Keeler (52), and Buxton et al. (45) provide a basic introduction to modelling.

9.9 When is a health technology cost-effective?

To be able to determine the cost-effectiveness of the health technologies compared, and thus conclude which of the technologies should be preferred from an economic perspective, the total costs assessed must be compared with the total effects assessed for each of the technologies, with future costs and effects being discounted. The effects may be measured either in natural units or in quality-adjusted life years (QALYs), cf. Section 9.6.

When comparing the costs and effects of two technologies (e.g. a new and an old technology), there are nine possible decision outcomes, as illustrated in Table 9.6

Table 9.6. Cost-effectiveness decision matrix

New technology assessed against old technology	Smaller effect En ‹ Eo	Same effect En = Eo	Greater effect En › Eo
Lower cost Cn ‹ Co	1. No clear decision - no dominance	4. Introduce new technology - new dominates old	7. Introduce new technology - new dominates old
Same cost Cn = Co	2. Keep old technology - old dominates new	5. The technologies are equally good	8. Introduce new technology - new dominates old
Higher cost Cn › Co	3. Keep old technology - old dominates new	6. Keep old technology - old dominates new	9. No clear decision - no dominance

The decision, which can be taken on the basis of the cost-effectiveness and cost-utility analyses, is clearest in two situations. One situation is where the new technology leads to a greater effect (e.g. several years of life gained) and at the same time either costs the same or is less expensive to use than the old technology. If this is the case, one must clearly opt to introduce the new technology to replace the old as a greater effect is achieved for less or the same money. The new technology is cost-effective as the costs per unit of effect (e.g. years of life) are lower for the new technology compared with the old technology ($C_n/E_n < C_o/E_o$). In such a situation, the new technology is said to *dominate* the old. The other situation, where the decision based on the economic analysis is also clear, is where, conversely, the new technology leads to a smaller effect and is more expensive than or costs the same as the old technology. Here, the old technology dominates the new as it is both better and less expensive, and should therefore be retained as the cost-effective technology ($C_n/E_n > C_o/E_o$). The two situations correspond to decision outcomes 4, 7, 8 and 2, 3, 6 respectively in the matrix in Table 9.6.

It is more difficult to arrive at conclusions if the analysis results in situations 1 and 9, as shown in the matrix. In these situations, the new technology is more expensive and better (greater effect) or, conversely, less expensive and worse (smaller effect) compared with the old technology. The two technologies do not dominate one another (lack of dominance) as costs and effects each go their own way. We do not know whether we will use the extra money to achieve the extra gain in effect. A decision on the choice of technology cannot therefore be taken merely by comparing the costs and effects of the two health technologies, which could otherwise be done in the other situations. Instead, it must be considered whether the extra effect gained from the new technology (or conversely the old technology) is worth the extra costs required. Here, the *incremental cost-effectiveness ratio* (ICER) is calculated, which expresses the cost of one extra unit of effect produced with the new technology, e.g. the price of achieving one extra year of life. The formula for ICER is shown below.

$$ICER = \frac{C_{new} - C_{old}}{E_{new} - E_{old}} \leq ?$$

Whether we should accept the new (or old) technology as being cost-effective in a situation where it is more expensive and better will ultimately depend upon the maximum price that the decision-maker is willing to pay for the extra effect (2). That is as far as the conclusion in a cost-effectiveness analysis can go if there is a lack of dominance between the technologies compared.

The example below shows costs and effects for various models for influenza vaccination of the elderly (27), cf. Table 9.7

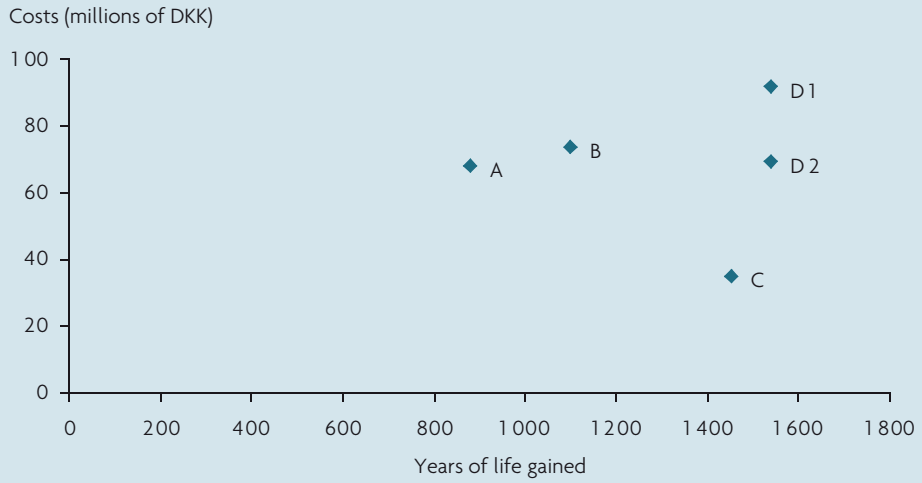
Table 9.7. Costs, effects, cost-effectiveness ratio and incremental cost-effectiveness ratio for various models for influenza vaccination

Organisational model	Years of life gained	Costs (millions of DKK)
A – Unstructured effort	881	68.4
B – Practice vaccination, own payment	1,101	73.6
C – "Copenhagen model", free of charge	1,453	34.7
D1 – Practice vaccination, free of charge	1,541	92.0
D2 – Practice vaccination, free of charge	1,541	69.3

Source: Table 9.6 in (27).

It is not immediately clear which model should be preferred; by plotting the point estimates in a cost-effectiveness plan, however, an intuitive feeling can be gained about the ranking of the various alternatives, cf. Figure 9.1. ICER is given by the gradient of the lines connecting the various points. It is immediately apparent that models A and B can be rejected as they are dominated by the other models (both C and D2 produce more years of life gained at the same or lower costs). Likewise, D1 should also be rejected as the same number of years of life as in D2 is gained, but at higher costs.

Figure 9.1. Graphical representation of costs and effects in the cost-effectiveness plan



Discussion of whether C or D2 is the preferred alternative is again based on economic considerations. C is less expensive, but does not on the other hand yield as many years of life gained as D2. C costs DKK 23,880 per year of life compared with no action (34.7 million/1453 years of life).

The above formula for ICER is used to calculate the incremental cost-effectiveness ratio for alternative D2 relative to alternative C:

$$\frac{69.3 - 34.7}{1{,}541 - 1{,}453} = 0.393 \text{ millions of DKK.}$$

In other words, the extra cost per extra year of life gained from using organisation model D1 rather than model C is DKK 393,000. The question is then whether these extra costs seem worth paying in the light of the extra gains achieved.

If a cost-utility analysis had been performed and the ratio of *costs per QALY* for the technologies compared had been achieved, a comparison could, in the situation of a lack of dominance, have been carried out with previous cost-utility studies, where QALYs were used as an outcome measure. It could thus be assessed whether *the cost per extra QALY gained* with the new (or old) technology was within a reasonable range compared with other technologies and areas. As previously mentioned, however, there are no generally applicable limits concerning what can be considered a reasonable QALY price, although proposals on this have in the past been put forward by, among others, Laupacis et al. (53).

9.10 Handling of uncertainty in economic analyses

Results and conclusions from economic analysis will to varying degrees be subject to some uncertainty about specific values for parameters, assumptions and links. One reason for this is that economic analyses are frequently based on data in the form of deterministic point estimates without distribution and statistical variance. However, as uncertainty about central parameters is important for how the result of an economic analysis can be used in a decision-making process, the uncertainty in the analysis must be handled systematically and quantified. Table 9.8 shows six kinds of uncertainty in an economic analysis.

Table 9.8. Possible forms of uncertainty in an economic analysis

Uncertainty parameter	1. Data input	Do the point estimates reflect the true values of the parameters? Uncertainty may, among other things, be due to the data collection method, e.g. expert opinion on resource consumption
	2. Sample data	Variability in sample data. Various samples taken from the same population can result in different data for resource consumption and consequences (outcome)
	3. Extrapolation	Uncertainty caused by extrapolation from intermediate endpoints to final endpoints and uncertainty from extrapolation beyond the study's time horizon
	4. Generalisability	Can results from the study population and study location be applied generally to other populations and locations? For example, scope for general application of results to daily practice
Model uncertainty	5. Analytical methods	Disagreement about different methods in economic analyses, where the choice of method leads to uncertainty about results/conclusions. For example, including estimation of production gains
	6. Model structure	Uncertainty about the specific method for combining parameters in a model – links between parameters. May, where appropriate, be tested with setting-up of alternative models

A systematic quantification of the uncertainty consists in conducting sensitivity analyses and/or statistical analyses. This shows the decision-maker how *robust* the conclusion of the economic analysis is. If the result does not change when changes are made to assumptions, parameters, etc., the result is said to be robust and reliable.

Table 9.9. Various forms of sensitivity analysis and statistical handling of uncertainty

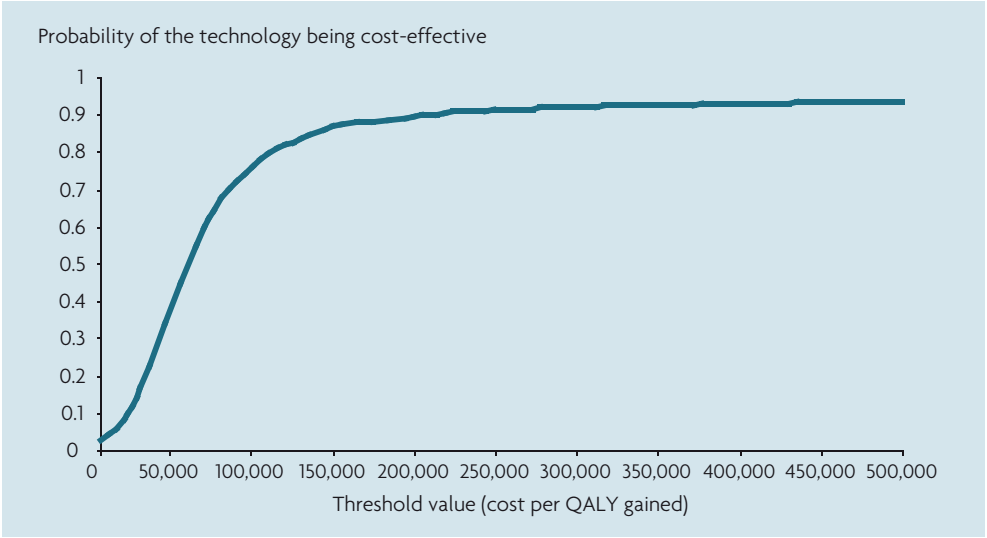
Sensitivity analyses	Simple "one-way"	Every single parameter (e.g. rate of pay) is varied one at a time, and the effect of this on the result is observed. Used most, but (too) simple. A good start	Type 1-5
	Simple "multi-way"	Unlike in the "one-way" approach, two or more parameters are now varied at the same time (scenarios). More realistic, but increasingly difficult the more variation takes place at the same time	Type 1-5
	Extremes	Based on the base-case analysis, two analyses are performed, with the focus on the most optimistic and pessimistic parameters. Shows the range of the result	Type 1,2,3
	Threshold value	Identifies the critical value (threshold) for one or more parameters at which the conclusion of the analysis changes. Only usable for continuous variables	Type 1-4
	Probabilistic	The ranges of variation of the variables are assigned distributions, and a Monte Carlo simulation selects values for all variables. Is simulated many times, so a distribution of the result emerges in which the variance can be estimated	Type 1-2
	Statistical analysis – in the case of sample data	The uncertainty (for variation in the population) is indicated with distributions, variance and confidence intervals for each variable. Possible hypothesis testing	Type 2

Note: Based on Briggs et al. (54).

Sensitivity analyses (see Table 9.9) investigate the sensitivity for the result when assumptions and values change. Sensitivity analyses should *always* follow an economic analysis. When confidence intervals are calculated or hypothesis testing is performed, this typically happens independently for costs and effects. Often, however, it will happen that, for example, the difference in effect between the two technologies is not statistically significant, and the health economic analysis will then be performed as a cost minimisation analysis, as described previously. Here, the problem is that a statistically insignificant difference may be due to insufficient strength in the study to demonstrate a possible statistically significant difference as well as due to there being no difference in effect (55). It is therefore nowadays recommended to a greater extent that confidence intervals be estimated for the combined incremental cost-effectiveness ratio (ICER, see Section 9.9) – either by bootstrapping, when patient-specific data are available, or by Monte Carlo simulation, when data are deterministic (56). With these methods, stochastic analysis is used to generate a distribution of costs and effects for the technologies compared and to calculate confidence intervals for the combined ICER.

This can be illustrated graphically by *cost-effectiveness acceptability curves (CEAC)*, which show the probability of a technology being cost-effective compared with another technology at various threshold values for willingness to pay, i.e. the probability of ICER being below the maximum acceptable ratio (57). Figure 9.2 illustrates a cost-effectiveness acceptability curve. This shows, for example, that if the threshold value is DKK 100,000 per QALY gained, there is a probability of approx. 70% of the technology being regarded as cost-effective. If the threshold value is DKK 200,000 per QALY gained, the probability of the technology being regarded as cost-effective is now 90%.

Figure 9.2. Example of cost-effectiveness acceptability curve (CEAC)



9.11 Reporting

When cost-effect ratios, including incremental cost-effect ratios, are calculated and compared for the health technologies considered, and conclusions are reached about their cost-effectiveness, the results must be incorporated in the HTA report. It is important to be as explicit as possible when reporting economic analyses. Results as well as the design, input data and assumptions must be described so thoroughly that the analysis is transparent to the reader. Assumptions and potentially sensitive data and results must be varied and tested in the sensitivity analysis so that some conclusions can be drawn about how robust the analysis is (Section 9.10). This is due to the fact that an economic analysis is an "all-other-things-being-equal" assessment in which, for example, differences in daily organisation, costs of equipment, etc. may be crucial and often vary from place to place. The economic analysis is thus highly context-dependent and if others are to benefit from and be able to use the results, they must be able to see through this and view the analysis in their own context. Together with this thorough and detailed reporting, the economic analysis and its results must also be written so clearly that the conclusions can be passed on to the relevant decision-makers, cf. the focus of both economic analyses and HTAs on use in decision-making.

The checklist for economic analyses, which is shown in Section 9.12.2, can be used for drawing up and reporting a health economic analysis in connection with HTA.

9.12 Economy-specific aspects of literature reviews

Health economic analyses should always start with a systematic review of the available international literature in the field. To maintain a chronological order in the performance of the economic analysis, this section should therefore be placed at the start of the chapter. However, as a general understanding of health economic analyses is important before such a review of the literature can be conducted, it has been chosen to place this section at the end of the chapter.

In light of the fact that economic analyses are highly context-dependent, it is rarely possible to apply results from foreign studies to Denmark, where the health care system

is often organised and funded differently. In certain cases, however, some of the results might be used; it is conceivable that resource consumption for certain health services could be generally translated from Sweden to Denmark, with Danish unit costs for, say, absence through sickness then merely needing to be calculated. In addition, it is always important to gain a general idea of the international results and, in particular, the chosen methods before embarking on an analysis oneself. The socioeconomic analyses found may provide inspiration for analyses of one's own, and the model may, where appropriate, be applied with Danish data. It is therefore always important to start with a systematic review of the available literature. Such a review of the literature consists of two steps: 1) systematic search and 2) systematic assessment of the literature.

9.12.1 Searches of the literature

The principles underlying searches of the literature have been examined previously in the handbook (cf. Chapter 3), and so only details relevant in connection with searches of economic literature are described here.

In relation to searches for health economic analyses, the main databases will be the *Cochrane Library* including the HTA database and the NHS Economic Evaluation Database as well as Medline and Embase. A broad cross-section of the existing economic analyses in the field is guaranteed by conducting searches in these databases. However, it may be relevant and important to extend the search to include other databases. Here, reference is made to *Etext on Health Technology Assessment (HTA) Information Resources*: (http://www.nlm.nih.gov/nichsr/ehta/ehta.html), which both describes and refers to other relevant databases and options for searching "grey" literature, as well as to Section 3.3.

A number of databases contain MeSH terms for economic analyses. For searches in Medline and the Cochrane Library (Thesaurus), economic analyses (cost-effectiveness, cost-utility and cost-benefit analyses) are indexed under "Costs-and-Cost-Analysis", while in Embase (EMTREE thesaurus) they are indexed under "Economic evaluation". In addition, it may be a good idea to search under free text and, where appropriate, use truncation, e.g. cost* and resource*.

9.12.2 Assessment of the literature

Once the relevant literature has been identified and selected, as described in the foregoing section and in Chapter 4, it will be an advantage systematically to assess the literature in terms of quality, results and scope for general application. Drummond et al. have developed a checklist that can be used to assess the health economic literature. The checklist is presented here in a modified and simplified form, cf. Table 9.10. For the checklist in its entirety, see Drummond et al. (2).

Table 9.10. Checklist for economic analyses

1. Is a well-defined question posed? This will be one or more of the HTA questions
2. Is the perspective for the analysis clearly stated?
3. Are the relevant competing alternatives included and described in the analysis? Have any been omitted?
4. Is the effectiveness of the technologies compared documented? What is the source for this?
5. Are all relevant costs and consequences, corresponding to the perspective, identified?
6. Are the costs and consequences of the technologies measured in appropriate (physical) units?
7. Are costs and consequences valuaed credibly?
8. Are differential timing of costs and consequences handled? Discounting.
9. Are sensitivity analyses performed to test for uncertainty and to test how robust the analysis is?
10. Are the conclusions of the analysis presented as ratios of costs relative to consequences and specifically as incremental cost-effectiveness ratios for non-dominance?
11. Are the conclusions valid and amenable to general application?

Note: inspired by Drummond et al. (2).

When reporting the results, it may be recommended to incorporate the results in a summary table similar to the evidence tables used in systematic reviews of the literature for clinical studies, cf. the example in Table 9.11. The first column specifies the study/author(s) and any reference numbers, the second column briefly describes the aim of the study, and the third column describes the method chosen. The fourth column then describes the number + country + period of time, and the fifth column describes whether a validated method is involved. A description of the results then follows in the sixth column, and the table ends with a description of the limitations that apply to the study, e.g. as a result of the method and context (i.e. internal and external validity). Alternatively, it may of course also be chosen to carry out reporting directly with the checklist's format and headings, but this risks losing the overview gained in an evidence table.

Tabel 9.11. Tabel of evidence – economy

	Subject: (Example: Type 2 diabetes) **Question: (Example concerning economic aspects)**					
Study + author	*Aim*	*Method*	*Number + country + period of time*	*Validated method*	*Findings*	*Limitations*
CDC CDC Diabetes cost-effectiveness group 1998	To estimate the cost-effectiveness of early detection and treatment of type 2 diabetes (single opportunistic screening of individuals aged 25 and over)	Model (semi-Markov Monte Carlo simulation)	Hypothetical cohort of 10,000 individuals USA	Modelling in accordance with current principles of health economics	For all 25+: costs per year of life gained: USD 236,449; costs per quality-adjusted year of life gained: USD 56,649 Cost-effectiveness situation better for younger individuals and African-Americans The bulk of the gain relates to quality of life due to the post-ponement of complications, not to more years of life gained Insensitive to test type	• Data on effect data from DCCT (type 1). • Base-case analysis – no effect on CVD. • Effect via HbA1c • Non-compliance has not been included • Any quality-of-life effects associated with diagnosis and treatment start-up not included.
METASTAR Lee et al. 2000	To estimate the costs or savings of "community screening" of individuals aged 65 and over	Adopts CDC model + assumptions about CVD effect and costs	Wisconsin, USA 12357 offered screening. 826 screened	Assumptions about CVD effect based on UKPDS Assumptions about costs	If a 30% reduction in CVD is assumed and it is assumed that the treatment costs are 30% lower for individuals identified by screening, screening reduces costs	Must be regarded as an illustrative computed example

Reference: The National Board of Health (58).

9.13 Literature for Chapter 9

(1) Newhouse JP. Medical care costs: how much welfare loss? J Econ Perspect 1992 Summer; 6(3):3-21.

(2) Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. 2nd ed. Oxford: Oxford University Press; 1997.

(3) Centre for Evaluation of Medical Methods. Medisinsk metodevurdering. En innføring [Evaluation of medical methods. An introduction]. 2003; SINTEF-rapport.

(4) Drummond M, Dubois D, Garattini L, Horisberger B, Jonsson B, Kristiansen IS, et al. Current trends in the use of pharmacoeconomics and outcomes research in Europe. Value Health 1999 Sep-Oct;2(5):323-332.

(5) Alban A, Keiding H, Søgaard J. Retningslinjer for udarbejdelse af økonomiske analyser af lægemidler. Bilag 1 i Sundhedsministeriet: Udfordringer på lægemiddelområdet. Betænkning afgivet af Sundhedsministeriets Medicinudvalg [Guidelines for the preparation of economic analyses of drugs. Appendix 1 in the Ministry of the Interior and Health: Challenges in the drug field. Report from the drug committee of the Ministry of the Interior and Health]. Copenhagen: Ministry of the Interior and Health; 1998.

(6) Draborg E, Gyrd-Hansen D, Poulsen PB, Horder M. International comparison of the definition and the practical application of health technology assessment. Int J Technol Assess Health Care 2005 Winter;21(1):89-95.

(7) Larsen RJ, Asmussen M, Christensen T, Olsen J, Poulsen PB, Sørensen J. Economic evaluation in international health technology assessments – a study of methodologies. Danish Health Technology Assessment 2003;5(1).

(8) Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press; 1996.

(9) Danish Institute for Health Technology Assessment. Ondt i ryggen: Forekomst, behandling og forebyggelse i et MTV-perspektiv [Back pain: Prevalence, treatment and prevention in a HTA perspective]. Copenhagen:1999;1(1).

(10) National Board of Health. Økonomisk vurdering af vaccination mod mæslinger, fåresyge og røde hunde i Danmark. Redegørelse fra vaccinationsudvalget [Economic assessment of vaccination against measles, mumps and rubella. Report from the vaccination committee]. 1985.

(11) Østergaard L, Andersen B, Møller JK, Olesen F. Screening for klamydia med hjemmetest – en medicinsk teknologivurdering [Screening for chlamydia with home test – a health technology assessment]. 2002; Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects]; 2(4).

(12) Dranove D. Measuring costs. In: Sloan FA, editor. Valuing health care: costs, benefits, and effectiveness of pharmaceuticals and other medical technologies. New York: Cambridge University Press; 1996.

(13) Alban A, Gyldmark M, Pedersen AV, Søgaard J. Sundhedsøkonomiske analyser af lægemidler: en gennemgang af metoder og problemstillinger ved implementering i beslutningsprocesser [Health economic analyses of drugs: a review of methods and problems associated with the implementation in decision-making processes]. Copenhagen: National Board of Health's drugs department; 1995.

(14) Brooks R. The economic framework of day surgery: a plea for appropriate appraisal. Ambulatory Surgery 1998;6:201-206.

(15) Luce BR, Manning WG, Siegel JE, Lipscomb J. Estimating Costs in Cost-Effectiveness Analysis. In: Gold MR, Siegel JE, Russell LB, Weinstein MC, editors. Cost-Effectiveness in Health and MedicineNew York: Oxford University Press; 1996.

(16) Brouwer W, Rutten F, Kopmanschap M. Costing in economic evaluations. In: Drummond M, McGuire A, editors. Economic evaluation in health care. Merging theory with practice. New York: Oxford University Press; 2001.

(17) Canadian Coordinating Office for Health Technology Assessment. Guidelines for economic evaluation of pharmaceuticals. 1997;2nd ed. Ottawa: CCOHTA;1997.

(18) Johnston K, Buxton MJ, Jones DR, Fitzpatrick R. Assessing the costs of healthcare technologies in clinical trials. Health Technol. Assess. 1999;3(6):1-76.

(19) Andersen B, Føns M. Marginalomkostningsbegrebets anvendelse i sundhedsvæsenet – 1. del. Tidsskrift for danske sygehuse [The use of the marginal cost concept in the health care system – part 1. Journal of Danish hospitals]. 1992;6:185-188.

(20) Mauskopf J, Schulman K, Bell L, Glick H. A strategy for collecting pharmacoeconomic data during phase II/III clinical trials. PharmacoEconomics 1996 Mar;9(3):264-277.

(21) Rasmussen S, Madsen M. Registre inden for sundhedsområdet. En oversigt over registre, der kan anvendes i epidemiologisk forskning og sundhedsplanlægning [Registers in the health care area. An overview of registers that may be used in epidemiological research and health care planning]. Copenhagen: DIKE; 2007.

(22) De Graeve D, Nonneman W. Pharmacoeconomic studies. Pitfalls and problems. Int J Technol Assess Health Care 1996 Winter;12(1):22-30.

(23) Boardman AE, Greenberg DH, Vining AR, Weimer DL. Cost-benefit analysis: concepts and practice. New Jersey: Prentice Hall; 1996.

(24) Baladi JF. A guidance document for the cost process. 1996; Version 1.0. Ottawa: Canadian Office for Health Technology Assessment (CCOHTA); 1996.

(25) Ingerslev HJ, Højgaard A, Poulsen PB, Kesmodel U, Dinesen J. Medicinsk teknologivurdering af lavstimulations IVF sammenlignet med standard IVF [Health technology assessment of low stimulation IVF compared with standard IVF]. 2001; Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects] 2001;1(1).

(26) Willaing I, et al. Kostvejledning i almen praksis ved praktiserende læge eller diætist [Dietary counselling in general practice by the general practitioner or a dietician]. Copenhagen: Research Centre for Prevention, Copenhagen County; 2003.

(27) Danish Institute for Health Technology Assessment. Influenzavaccination af ældre [Influenza vaccination of the elderly]. 2000;2(1).

(28) Pedersen BG, Arnesen RB, Poulsen PB, Adamsen S, Hansen OH, Laurberg S. Tyktarmsundersøgelse med CT-kolografi – en medicinsk teknologivurdering. [Colonoscopy with CT colonography – a health technology assessment.] 2005; Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects]; 5(3).

(29) Christiansen T, Clausen J, Kidholm K, Langkilde LK, Pedersen AV, Petersen JH, et al. Tilvalg og fravalg. Om prioritering i sundhedssektoren [Choice and rejection. About prioritisation in the health care sector]. Odense: Odense Universitetsforlag; 1995.

(30) Brooks R, Rabin R, de Charro F, editors. The Measurement and valuation of health status using EQ-5D: A European perspective. Rotterdam, Holland: Kluwer Academic Publishers; 2003.

(31) Wittrup-Jensen KU et al. Estimating Danish EQ-5D tariffs using the time trade-off (TTO) and visual analogue scale (VAS) methods. In Norinder A, Pedersen KM, Roos P (eds.): Proceedings of the 18th plenary meeting of the EuroQol Group; 2002.

(32) Szende A, Oppe M, Devlin N (eds.). EQ-5D valuation sets: inventory, comparative review and user guide. Springer (In press).

(33) Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med 2001 Jul;33(5):328-336.

(34) Sintonen H. The 15D measure of health related quality of life: Reliability, validity and sensitivity of its health state descriptive system. Working paper 41. 1994.

(35) Sintonen H. The 15D measure of health related quality of life: II Feasibility, reliability and validity of its valuation system. Working paper 42. 1995.

(36) Wittrup-Jensen KU, Pedersen KM. Modelling weights for 15D. Paper presented at the 22nd Nordic Health Economists' Study Group Meeting. Odense: 2001; 22 - 25th August.

(37) Haamann P, Larsen M, Juhl HH, Svenning AR. Fotodynamisk behandling af karnydannelse bag øjets nethinde – en medicinsk teknologivurdering [Photodynamic treatment of neovascularisation behind the retina – a health technology assessment]. Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects] 2002; 2(3).

(38) Kaplan RM. Utility assessment for estimating quality-adjusted life years. In: Sloan FS, editor. Valuing health care. Costs, benefits, and effectiveness of pharmaceuticals and other medical technologies. Cambridge: Cambridge University Press; 1995.

(39) Pedersen KM, Wittrup-Jensen K, Brooks R, Gudex C. Værdisætning af sundhed. Teorien om kvalitetsjusterede leveår og en dansk anvendelse [Valuation of health. The theory of quality-adjusted years of life and application in Denmark]. Odense: Syddansk Universitetsforlag; 2002.

(40) Torrance GW. Measurement of health state utilities for economic appraisal. J. Health Econ. 1986 Mar;5(1):1-30.

(41) Offentlig kostforplejning i Danmark [Meals provided by public authorities in Denmark]. 1997; Report no. 1334.

(42) K. Kidholm. Estimation af betalingsvilje for forebyggelse af personskader ved trafikulykker. Ph.D.-afhandling fra det samfundsvidenskabelige fakultet [Assessing the willingness to pay for the prevention of personal injury due to traffic accidents. Ph.D. thesis, social science faculty]. Odense Universitet: Centre for Health Service Research and Social Politics; 1995.

(43) Kjær T, Gyrd-Hansen D, Willaing I. Investigating patients' preferences for cardiac rehabilitation in Denmark. Int J Technol Assess Health Care 2006;22(2):211-218.

(44) Bech M, Kjær T, Lauridsen J, Gyrd-Hansen D. Hvad ønsker studerende af deres fremtidige job? Illustration af et diskret valg eksperiment [What do students want from their future job? Illustration of a discrete choice experiment]. Nationaløkonomisk Tidsskrift 2004;142(1):48-67.

(45) Buxton MJ, Drummond MF, Van Hout BA, Prince RL, Sheldon TA, Szucs T, et al. Modelling in economic evaluation: an unavoidable fact of life. Health Econ 1997 May-Jun;6(3):217-227.

(46) McCormack K, Wake B, Perez J, Fraser C, Cook J, McIntosh E, et al. Laparoscopic surgery for inguinal hernia repair: systematic review of effectiveness and economic evaluation. 2005; Health Technol Assess;9(14).

(47) Mowatt G, Vale L, Perez J, Wyness L, Fraser C, MacLeod A, et al. Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of home versus hospital or satellite unit haemodialysis for people with end-stage renal failure. 2003; Health Technol Assess;7(2).

(48) National Board of Health, Danish Centre for Evaluation and Health Technology Assessment. Indførelse af hepatitis B vaccination som en del af børnevaccinationsprogrammet i Danmark. En medicinsk teknologivurdering [Introduction of hepatitis B vaccination as part of the child vaccination programme in Denmark. A health technology assessment]. 2003;3(1).

(49) Ingerslev HJ, Poulsen PB, Højgaard A, Andersen S, Kølvrå S, Hindkjær J, et al. P ræimplantationsdiagnostik – en medicinsk teknologivurdering. [Preimplantation dagnostics – a health technology assessment]. Medicinsk Teknologivurdering – puljeprojekter [Health Technology Assessment – pool projects] 2002; 2(1).

(50) Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. 2004; Health Technol Assess;8(36).

(51) Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. PharmacoEconomics 1998 Apr;13(4):397-409.

(52) Keeler E. Decision trees and Markov models in cost-effectiveness research. In: Sloan FS, editor. Valuing health care. Costs, benefits, and effectiveness of pharmaceuticals and other medical technologies. Cambridge: Cambridge University Press; 1995.

(53) Laupacis A, Feeny D, Detsky AS, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluations. CMAJ 1992;146(4):473-481.

(54) Briggs A, Sculpher M, Buxton M. Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. Health Econ 1994 Mar-Apr;3(2):95-104.

(55) Briggs AH, O'Brien BJ, Blackhouse G. Thinking outside the box: recent advances in the analysis and presentation of uncertainty in cost-effectiveness studies. Annu.Rev. Public Health 2002;23:377-401.

(56) Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. Health Econ. 2001 Dec;10(8):779-787.

(57) Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves-facts, fallacies and frequently asked questions. Health Econ 2004 May;13(5):405-415.

(58) National Board of Health, Danish Centre for Evaluation and Health Technology Assessment. Type 2-diabetes. Medicinsk teknologivurdering af screening, diagnostik og behandling [Type 2 diabetes. Health technology assessment of screening, diagnostics and treatment]. 2003;5(1).

(59) Bech M, Christiansen T, Gyrd-Hansen D. Handling value added tax (VAT) in economic evaluations: should prices include VAT? Appl Health Econ Health Policy. 2006;5(4):209-213.

10 Synthesis and utilization

The first part of this chapter describes the difficult and important steps in the HTA process in which the subresults achieved must be synthesised to provide a decision-making basis which can answer the questions originally asked and which is suitable as a foundation for specific guidance. A number of factors and criteria that are important to bear in mind or incorporate in the specific process are identified in this chapter. The second part describes how to increase the opportunity for utilization of the results of HTAs.

10.1 The synthesis process in HTA

By Mogens Hørder and Helga Sigmund

Useful advice and suggestions

- The synthesis is different from and more than a summary of the subresults of the analyses
- The synthesis is designed to summarise, weight and assess the subresults with a view to providing one or more summary conclusions and, where appropriate, recommendations
- During the synthesis process, critical importance must be attached to achieving the greatest possible transparency in terms of documentation, the basis for methods, interests and the actual process
- The synthesis must reflect the way in which problems are formulated, present the results, document the results in terms of methods and reveal methodological limitations
- The basis for decisions needs not necessarily be unambiguous, but advantages and disadvantages in the submission of various alternative solutions or scenarios must be described.

10.1.1 General aspects of the synthesis

Once the analysis phase of an HTA has been completed, the results of the subanalyses must be summarised, weighted and assessed. This is referred to as performing a synthesis. The object of the synthesis is to obtain one or more summary conclusions and possible recommendations. It should be stressed in this context that HTAs are not intended to produce a decision, but to assess, integrate and impart knowledge in the form of a decision support which can form the basis for a subsequent decision-making process. The basis for decisions needs not be unambiguous. Often, the advantages and disadvantages of *several* alternative solutions are described, which must be passed on to the relevant decision-making levels.

What is meant by synthesis?

The concept of "synthesis" can be defined in different ways. Three different definitions are cited in Section 4.2.2.2 (1):

1. Synthesis as a combination of parts to form a whole (directly comparable)
2. Synthesis as a dialectic combination of thesis and antithesis (opposed to one another)
3. *Synthesis as a combination of often different conceptual comparisons to form a whole (construction of an interpretation).*

In terms of synthesis in an HTA context, the third definition is clearly the most comprehensive. This means that the parts to be synthesised are *different*. This in turn means that it will be necessary to undertake weightings and interpretations which – in

common with the other methods adopted in HTA – should meet corresponding scientific requirements concerning systems, transparency and stringency.

In practice, it emerges, however, that the synthesis methods adopted in HTA are rarely as scientifically well-founded as the methods of analysis. Usually, the analysis results of an HTA are summarised in an informal, unstructured process, which is not explained in the report. Formal synthesis methods, such as systematic group methods, are used extremely rarely in HTA. The implementation of such group methods is demanding in terms of resources and time, which is difficult to combine with premises such as tight budgets and growing demands for shorter production times for HTAs.

What makes the synthesis difficult

The synthesis phase is clearly the part of an HTA about which the greatest uncertainty exists, despite the fact that it has a central role in an HTA. In purely methodological terms, it has apparently been difficult to get the synthesis included in the systematic work that otherwise characterises the approach in HTA.

One of the reasons may be the special place of the synthesis phase, namely at the interface between the analysis phase and the design of the basis for decisions– i.e. between science and the policy sphere. There may be a lack of knowledge about how HTA results are actually included in the basis for decisions, or what bearing input from an HTA will have on the decisions taken in a given decision-making situation.

Compared to HTA traditions in other countries, where technology and economy often are the only elements covered, the Danish HTA model further includes organisational and patient-related elements. This does not actually make the synthesis process less complex. The broader and more interdisciplinary the approach, the more challenging the synthesis becomes.

10.1.2 Steps in the synthesis process

Formulation of the problem as the point of departure

The synthesis consists of a grouping of subresults known in advance to form a whole. The synthesis process is, however, not (only) a limited step in the last part of an HTA, but takes place throughout the HTA process. It has previously been emphasised that all steps in an HTA must be viewed as interconnected, and this becomes particularly clear during the synthesis phase (2,3).

The synthesis phase links back directly to the problem formulation phase. The following points in the formulation of problems are of particular importance:

- What are the overall policy questions?
- What HTA questions are to be answered?
- What must be investigated?
- What has been excluded?
- What alternatives are to be examined?
- Who is the target group for the results arising from the HTA?
- In what type of decision-making situation is input to be provided?

The synthesis process can only be performed as an integrated part of an overall HTA if these questions have been fully clarified during the problem formulation phase. The

answers to these questions are crucial to how the synthesis is performed as a process and what kind of conclusions and basis for decisions can be provided accordingly.

Information on the following aspects is therefore available as a *point of departure* for the synthesis process: formulation of problems, knowledge of the initiator, target group, expected decision-making situation and the results of the subanalyses conducted. The *end result* sought is for the HTA in its full form to elucidate all relevant conditions and consequences in relation to a given policy/planing problem, and for a suitable basis for decisions to be presented.

The synthesis includes relevant aspects

The complexity of the synthesis process depends to some extent on what type of HTA is involved: is it an HTA which focuses on a single subject, e.g. a single well-defined technology, or a broad HTA which compares a number of alternative interventions or covers an entire area of disease (cf. Section 1.2.4).

The synthesis process includes the results for the relevant consequences and alternatives, related to the given problem. In an HTA in which the synthesis process is based on the question of the application of a technology/intervention, the results of the subanalyses concerning the patient, organisation and economic aspects (and, where applicable, ethics) will be assessed in relation to the primary focus area, namely the intervention itself. It will be possible to include the assessments concerning a possible alternative intervention in a corresponding manner.

Not all HTAs are, however, designed to assess *whether* a given technology should be used. Often, the question is equally *how* it is to be used. Here, it is perhaps not the technology itself, but one of the other main elements, e.g. organisational aspects, that is central to the problem – and will therefore often be what the other aspects should be assessed against.

The *summary* part of the synthesis consists of highlighting *the* results achieved by adopting *strict and relevant methods* for each of the subelements. By attaching critical importance to the methodological basis underpinning the results, *the limits for the external validity of the results* will be identified.

The greatest possible *transparency* should also be sought in the weighting of the elements. It may, for example, be important if some of the subelements are more or less elucidated than others. If this is the case, this should be clearly apparent, and any choices to omit items should be substantiated. In addition, it must always be specified what is documented knowledge (e.g. the level of evidence), and what is not.

Systematic approach and scientifically based methods are essential ingredients of the HTA work. It is therefore an aim in itself, in connection with the synthesis, explicitly to stress any *limitations* that may exist in the results of the HTA. This is, however, an often neglected area. There are a number of examples showing that HTA has fallen into discredit owing to the transfer of results, which the HTA itself has been unable to justify on the basis of methodological limitations.

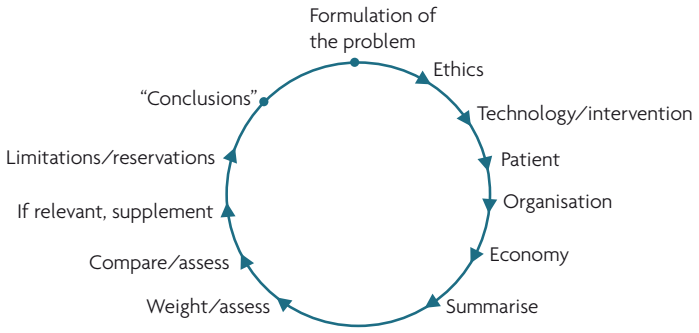
The synthesis process should therefore be performed in connection with constant feedback on both the methods and results of the individual subelements in the analysis, but again based on what is the object of the main problem. This constant feedback can, in the synthesis process, often be combined with a *comparison* with existing litera-

ture on the subject to clarify whether an HTA supports or perhaps extends or distances itself from other (possibly foreign) HTAs or research results from the subareas.

The synthesis process may also lead to the emergence of a need to obtain *supplementary* information. This may typically be data concerning the methodological limitations within the individual subanalysis areas.

As mentioned, it is not always the case that the validity of methods and results is made clear via the synthesis process. On the other hand, there is no tradition for conducting a definite uncertainty analysis in connection with the synthesis in the HTA. The aim should, as part of the synthesis process, at least be a *catalogue* of the elements about which there is uncertainty to be drawn up. A simple way of doing this is to formulate *reservations* within the individual main elements, e.g. concerning economic, organisational and patient-related aspects based on the technology/intervention concerned. The synthesis process is illustrated in Figure 10.1.

Figure 10.1. The synthesis process



Conclusions and possible recommendations

As a basis for the conclusions, the following questions must be clarified during the previous phase of the synthesis:

- What position has been taken (formulation of the problem)?
- What has been investigated/elucidated and with what results (analyses, subresults)?
- What is the methodological basis for the result (scientific basis)?
- Under what conditions do the results exist (limitations/reservations)?

Conclusions must be usable as suitable input for decision-making. They must be able to support the actual policy process and at the same time reveal the premises for it.

"Conclusions" may often be in the nature of *recommendations*. This is typically the case where the weightings and assessments of the synthesis are underpinned by such crucial evidence that there can be no doubt about what should be the solution. Usually, however, HTAs will result in conclusions that are in fact not unambiguous, and which point to several different solutions. The proposal of alternative solutions or scenarios must be accompanied by precise accounts of the pros and cons of the individual solution, and what will be the consequences of choosing one solution over another.

Conclusions and possible recommendations must link back to the initiator and to the decision-making level at which the formulation of the problem is aimed. In other

words, they must be designed to be able to serve as a basis for the decision-making process at clinical, administrative or political level.

In the past, there has been an expectation from the decision-makers that processes of weighing and measuring during the HTA would result in a "one and only" answer list and clear instructions. It has now been recognised that it is not so simple. It is now a question of obtaining information that is as evidence-based and versatile as possible and making the many facets of the basis for decisions as explicit as possible – and thereby promote rationality in the subsequent decision-making process.

10.1.3 The synthesis process in practice

The way in which the synthesis is conducted depends on whether a decision "here and now" in everyday clinical practice is involved or whether it is a major decision that has far-reaching consequences and which incorporates various parts of the decision-making process. The different and sometimes conflicting interests of health professionals, patients, administrators or politicians may be incorporated in this context. Important interested parties are often represented in the project's *reference group* (cf. Section 1.3).

In practice, it is often *the project team* (cf. Section 1.3) that draws up the final basis for decisions. This basis is already built up through the preceding project process, where co-ordination and mutual updating frequently takes place concerning methods and results. The final grouping of the subresults is conducted during the synthesis phase, and a first draft to answer the original questions is formulated. The reference group can be involved in different ways: by obtaining written comments, by meetings with the project team or by holding a consultation exercise with the participation of both the reference group and other people whose comments may be useful for the final work of the project team.

10.2 The utilization of HTA

By Camilla Palmhøj Nielsen

Useful advice and suggestions

- Be at all times aware of the target group for the HTA and analyse the circumstances in which the HTA might potentially be used
- Consider the barriers and potentials for using the HTA
- Decide how its utilization might be facilitated and how the project team can contribute to this
- Plan the prospective utilization into the project from the start and provide ongoing information for the decision-makers.

10.2.1 General aspects of the utilization of HTA

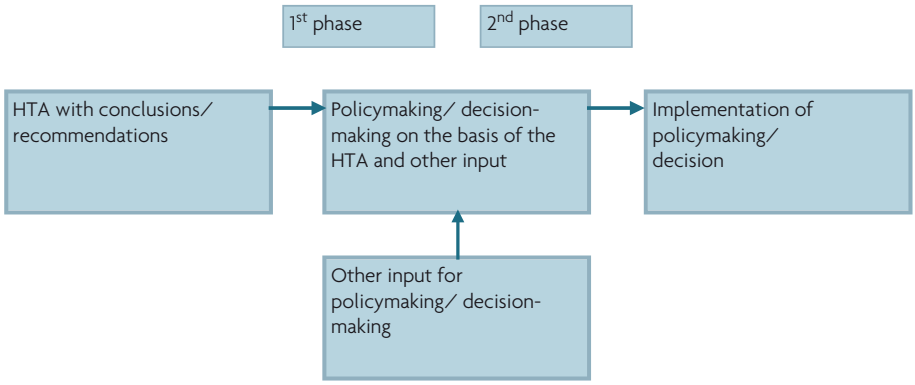
It is important to bear in mind that an HTA is *not* a decision in itself. HTA is input for decision-making. This means that the decision-makers are the primary target group for an HTA. The HTA may go directly to the decision-makers or pass through several administrative stages where it is adapted or supplemented before the decision is made.

There is a distinction between conducting HTAs and making decisions on the basis of HTAs. As indicated in Section 1.1, the production of an HTA is primarily based in a research domain, while its utilization is based in a decision-making domain. The challenge for HTA is to make the connection between these two domains in order to facilitate their utilization. This requires active input from the project team. However, it is

important to emphasise that the responsibility for using an HTA does not lie solely with the project team – it is also the responsibility of the decision-makers, as it requires openness and a willingness on their part to cooperate.

Typically, the utilization of an HTA is in two phases. The *first* phase is centred on ensuring that the decision-makers take the results of the HTA into consideration when making decisions. However, there is an underlying motive in that HTA also contributes to improvements in quality and the efficient use of resources in the Danish health care system. This requires the conclusions/recommendations of the HTA to be part of policy making and to be implemented in practice. *If* the decision-makers reach decisions and subsequently wish to have the conclusions/recommendations of the HTA implemented, this constitutes the *second* phase of the utilization, see figure 10.2.

Figur 10.2. The two phases of utilization of an HTA



10.2.2 Analysis of the conditions of utilization

When an HTA is close to completion, i.e. when the results are known and the publication of the report is imminent, it is time to sum up what has already been done and what is to be done next in order to facilitate the utilization of the HTA and any recommendations it may contain.

The utilization of HTA may be facilitated on several levels:

- At the top political and administrative level, one possibility is to try to link the HTA to existing decision-making processes
- At the institutional level it might be possible to work on ensuring that employees are familiar with the HTA and are thus aware that the HTA can be used in decision-making
- At the HTA project level it is the task of the project team to bear the prospects for utilization in mind during the course of the project and to consider specific possibilities for utilization and implementation as part of the final phase of the HTA.

In order to be able to contribute to the utilization, it is necessary to analyse the contexts, in which the HTA may potentially be used. Different types of HTA projects (see 1.2.4) suit different types of policy processes. It is important to have some understanding of these processes.

Thought must be given to both actors and processes. The extent of changes since the planning phase of the HTA must be considered, as the circumstances in which it is to

be used and the conditions that influence it may change significantly between the start of a project and its completion:

- Does the HTA address the same primary decision-makers as defined in the planning phase, e.g. an initiator (see Sections 1.2.2 and 1.2.5)?
- Which actors can currently contribute to facilitating its utilization?
- In which existing processes can the HTA be utilized (e.g. budget processes)?
- Alternatively, is it necessary to try to create a decision-making process relating to the HTA in question in consultation with the decision-makers, if there is no existing planned decision situation in existence?
- What potentials and barriers to utilization can be identified?

10.2.3 What can be done to facilitate the utilization of HTA?

As described in Section 1.4, it is desirable to establish as direct a link as possible to the decision-makers in the planning phase. If the decision-makers are involved in this early phase, they can help to define the need and formulate the policy issue, making it as certain as possible that the HTA will be useful to them. This can be done by, for example, involving (representatives of) the decision-makers in a reference group, see Section 1.3. It is also essential for the project team to make it clear in the planning phase if the completion will be affected by pressure of time (e.g. in relation to budget negotiations), so that the HTA report is, as far as possible, timed in relation to the need for a decision.

During the course of the project it is important to ensure independence from political interests, so that the research-based information to be communicated in the HTA report can be produced with no interruption. However, in the interest of the later utilization of the HTA, it is desirable to keep the decision-makers informed, without them having direct influence on the professional content of the HTA. This can be done by:

- updating the decision-makers on the progress and planned completion of the HTA, so that they can help to prepare a decision situation that will follow immediately on the completion of the HTA
- informing the decision-makers of the content of the HTA during the course of the project, to ensure that the HTA continues to address the needs of the decision-makers and to prepare its subsequent utilization.

On the completion of the HTA, it is the task of the project team to ensure that communication is targeted so that the report reaches the relevant decision-makers, see Section 11.2. This can be done through direct contact or by other types of communication activities.

Lastly, the project team will have acquired great insight into and knowledge of the field they have analysed in the HTA and will therefore often be particularly well qualified to contribute to the implementation of the decisions made following the HTA. The project team should therefore consider how this might be done. The knowledge acquired can also provide a basis for drawing attention to possible trends by looking at the prospects and any possibilities for evaluation, see Section 1.4.

10.3 Literature for Chapter 10

(1) Merriam-Webster, editor. Webster´s ninth new collegiate dictionary. 9th ed.: G&C Merriam-Webster Inc; 1989.

(2) Øvretveit J. Action evaluation of health programmes and changes. A handbook for a user-focused approach. Oxon, United Kingdom: Radcliffe Medical Press; 2002.

(3) Øvretveit J. Metoder för utvärdering av hälso- och sjukvård och organisationsförändringar: ett användaorrienterat perspektiv [Methods for the evaluation of health service and nursing care and organisational changes: a user-oriented perspective]. Lund: Studenterlitteratur; 2001.

11 Quality assurance and presentation

This chapter concerns the preparation of an HTA report which documents the previous work in all phases, and which can be a tool in the subsequent decision-making process and a later implementation phase. To meet this requirement the report must be quality assured before it is published. The chapter describes approaches and gives instructions for both quality assurance and presentation.

11.1 Peer review by external reviewers

By Stig Ejdrup Andersen and Finn Børlum Kristensen

Useful advice and suggestions

- Peer review is quality assurance as well as support for the author in the final writing phase
- Allow sufficient time for peer review
- Take an active and constructive part in the process.

Prior to an HTA report (from an internal or external project team) being published, at least one expert must assess the manuscript and give suggestions for improvement (peer review). The purpose of a peer review, which can be translated into "critical review by equal", is to aid the authors write a manuscript which is both easy to read and of high professional standard.

11.1.1 Peer review contents

The peer review can be seen as support during the final part of the writing process, in which the manuscript is made ready for publication. However, in order to get peer reviews to improve HTA reports, the authors have to take an active part in the process, decide on proposed changes and revise the report to the necessary extent. It is in the interest of all involved parties that an HTA report is of the highest quality and that the contents can be read and understood by the intended target group.

The individual author or project team is rarely aware of all professional and presentational problems in an HTA report and the editors typically do not have these specialist competencies that are necessary to assess the specific professional problem. Therefore, it is more likely that any errors and omissions can be corrected before publication, if independent experts are given the opportunity to read the text closely. The reviewers are not required to look for a needle in a haystack, but potential improvement can often only be seen by an outsider with special insight or experience within the field.

HTA reports should be balanced and transparent. The text should be logically constructed, short and precise, but at the same time sufficiently detailed for the reader to see through the rationale, understand the methodology as well as acknowledge any methodological problems and interpret their significance for the results. Results should be presented unambiguously, and relevant self-explanatory tables and figures should supplement the text. Methodological limitations should be stated and their significance for the validity of the results discussed. Conclusions and recommendations must be based on results that are not over-interpreted. Finally, heavy, obscure language with unnecessary repetitions should not stand in the reader's way. Consequently, the experts are asked to assess the applied methodology, the validity of the results, conclusions and recommendations as well as the readability and scope of the manuscript (see sample

letter). The assessment should also include a short summary of the manuscript, its strengths (positive feedback) and main weaknesses as well as suggestions for changes that should be made prior to its publication.

Example of letter to reviewers of HTA reports

Dear ……
Thank you for your agreement to assess above draft of an HTA report. The assessment is anonymous.
The National Board of Health wishes to publish readable reports of high professional standard. To aid the authors to prepare the most useful manuscript, please identify strengths as well as weaknesses of the manuscript. Based on HTA questions and research hypotheses, please focus on the suitability of the applied methodology, the validity of the results as well as to what extent the conclusions and recommendations of the report are supported by data. Since HTA reports are frequently read by persons who are not themselves experts within the field, please also comment on the language and scope of the report and assess whether the summary is adequate and representative of the contents and conclusions of the report.
Your assessment, which will consist of a maximum of 3-4 typed A4 sheets, should include:
1. A short summary of the manuscript
2. The strengths of the manuscript (positive feedback)
3. The important weaknesses and omissions of the manuscript
4. Suggestions for changes to be made before the manuscript is published.

If you think there is a conflict of interest connected with your assessment of the manuscript, please inform us as soon as possible.
Your assessment is for the exclusive use by the editors and the authors; thus it is not necessary to write in layman's language or write a layman's summary. The authors will not be informed of your identity.

For the editors, yours sincerely

11.1.2 Peer review process

It normally takes three to five months from the time the manuscript is received until it is ready for publication. Figure 11.1 shows the schematic process of a typical peer review. When the editors first receive the manuscript they assess it. On rare occasions the authors have to modify the work; however, more usually the manuscript is submitted directly to external reviewers for assessment.

Due to the interdisciplinary nature of HTA reports it will most often be necessary to find two or more peer reviewers, for instance organisational experts, health economists, medical specialists or sociologists – at least one of them should preferably also have general HTA expertise. Since most HTA reports are written in Danish, the editors will typically select reviewers from one of the Nordic countries. Persons with conflicts of interest, for instance, the authors' close colleagues or persons from the research environment around the authors, are naturally disqualified from the start. However, some professional environments are so small that it can be difficult to find independent reviewers. Therefore authors of HTA reports are invited to suggest qualified reviewers. The identity of the selected reviewers is however always kept secret from the authors and is only revealed in very special cases – and only when reviewer and editors agree.

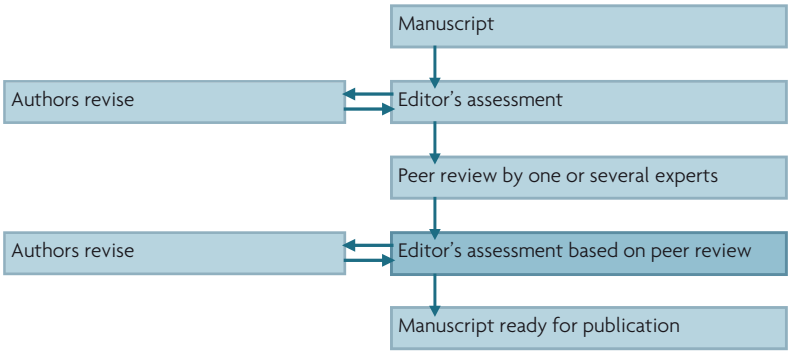
The reviewers, who can be seen as advisers for the editors as well as for the authors, each submit their assessment and suggestions for improvement to the editors. Typically, the reviewers do not know each other's identity, do not communicate with each other and do not need to be in agreement. In situations with significant differences of opinion the editors may ask an additional expert to assess the manuscript.

Based on the assessment of the experts, the editors will decide whether to publish the manuscript. The decision by the editors including the external assessments is submitted to the authors. In the majority of cases the manuscript can be published once the authors have revised the manuscript and responded to the reviewers' critical remarks and suggestions for changes. It may simply be a matter of technical fine-tuning, although not infrequently it will be necessary to make radical changes to the manuscript.

Once the revision is completed the manuscript is submitted to the editors with an accompanying letter stating the changes carried out. The authors can change the manuscript wholly or partly as suggested, but they can also disagree with the editors and the external reviewers on one or several points and thus decline to change the manuscript. In this case their letter should cover the detailed reasons.

The editors reassess the manuscript. Final acceptance is given in writing to the authors, and the manuscript is then handed over to the "HTA publishers", who act as advisers to the authors in connection with the final layout and publication.

Figure 11.1. Peer review process



11.2 Presentation and interaction with the press

By Lisbet Knold and Stig Ejdrup Andersen

Useful advice and suggestions

- A health technology assessment should be communicated actively
- It is necessary to acquire some tools, in terms of linguistics and narrative technique, in order to make an effective presentation to non-professionals
- When presenting a message it is essential to identify a "point" and only to include what is related to this point
- The less relevant the topic is perceived to be by the reader, the more is demanded from the text to motivate the reader
- Make the text vivid and inviting, eschewing heavy words and old-fashioned sentence structures which could make reading difficult.

Presentation and communication are many things and can take different courses. This chapter concerns the presentation of scientific material. The main focus is on the presentation of news, i.e. how to phrase one's message and how to cooperate with the press. The techniques can also be used in connection with other types of presentation. For instance, when one, as a researcher, has to present one's research to laymen or other professionals lacking previous knowledge of the topic in question.

A health technology assessment should be actively communicated. Even the most interesting reports do not in themselves always find their way through to persons who *should* be interested in the results – even if the results live up to serious research standards.

However, researchers typically often spend the least effort on presentation. This is primarily based on three misconceptions:

- That evidence-based results are favoured exclusively due to being of high quality
- That evidence-based results will convince the target groups, exclusively as a result of the high quality
- That when the results are known and accepted, they automatically lead to changed clinical practice.

However, with the dense flow of competing news, it is often necessary to make a special effort for the relevant recipients to become aware of one's research results. Clinicians, politicians and other decision-makers also update their knowledge through the daily press (Ragna Levi 2004)[15], (1).

11.2.1 Which methods can be used?

The conclusions of an HTA project can be published in a number of places, for instance in the series of DACEHTA, in a news mail or a newsletter, on DACEHTA's website (www.dacehta.dk), in the daily or trade press or other media. Unfortunately there is no recipe for success for arousing the surroundings' interest in a project. The news media are essential when one wants to create interest in one's research and contribute to translating the recommendations into practice. If several types of media are used simultaneously this will increase the probability that the news reaches the right ears (2). There are numerous options, for instance:

- Conferences
- Articles in scientific journals
- Articles in professional journals
- Debating points in daily newspapers
- Press releases for electronic media.

Personal contacts and opinion former within the subject area can be valuable participants in the presentation. This could for instance be:

- Members of the project team
- Those in a reference group or the steering committee
- Those from the departments or organisations involved in the project.

11.2.2 How to present scientific material

It is necessary to have an expressed purpose for one's presentation and to know the reality of the recipient, in order to present scientific knowledge efficiently to the target group. Furthermore it is necessary to consider how best to utilize one's knowledge

15 "Focus on presentation"; lecture at the National Board of Health's HTA summer school, June 2004.

about the recipient in the tailoring of a suitable presentation. What should the recipient know and which form is best suited to the need of that person (3)?

One can talk about three different discourses each with its own purpose and thus also each with its own target group and standards on to how to present the message: 1) scientific communication, 2) professional communication, and 3) professional presentation (3).

Scientific communication takes place between professionals and is based on the assumption of equality and symmetry between the one communicating and the one receiving the message. They have a common technical language, share knowledge and ideas and follow the same rules of scientific character. The purpose of the communication is to disseminate new knowledge and awareness within a professional area using scientific reasoning.

Professional communication also takes place between colleagues; however, here the purpose is to solve a professional problem using existing knowledge. It could be, for instance, two physicians discussing a patient's case history. Here, also, there is symmetry and acceptance in the form of common professional assumptions, professional terminology and evidence.

Professional presentation between the professional and the layman – contrary to the two former types – does not take place between equal parties. The communication is based on dissimilarity (asymmetry). Take for instance communication between physician and patient or banking consultant and client (who could be a physician, who would be a layman in this situation). Presentation takes place on a professional basis. But the one communicating has to select contents that are relevant for the recipient and present it in a form that can reach the recipient. If this is to succeed it needs more than merely translating professional terminology into layman's language. In addition, one has to translate and adapt the message into something of use to the recipient and which the recipient can understand based on his own background.

Most researchers are familiar with scientific and professional communication, but have to acquire some linguistic and narrative techniques in order to present efficiently to non-professionals, especially when it comes to presenting complex problems to basically unqualified recipients. It is not possible to uncritically transfer the standards from one discourse to the next.

11.2.3 From report to news text

Narrative models

Traditionally, scientific reports and articles start with background information and an introduction to the topic then followed by detailed method descriptions and finally a conclusion (Figure 11.2). All relevant data are included and statements are documented using source references. This academic narrative model is based on reason-consequence logics taking the recipient towards a reasoning-conclusion.

In news articles and texts for websites the point is presented first. Then follows the background, premises and detailed information about the topic. This construction is also called the journalistic narrative model (or the news triangle) (Figure 11.3). The reader is only presented with data which can serve the main point, documentation and sources are not necessarily stated in the actual article.

The journalistic narrative model can seem more aggressive and postulating, but the model has distinct presentational advantages. Amongst others, the recipient is immediately told what the text is about and even if only the first few lines of the article are read, the most important points are caught (4).

Figure 11.2. Academic narrative model

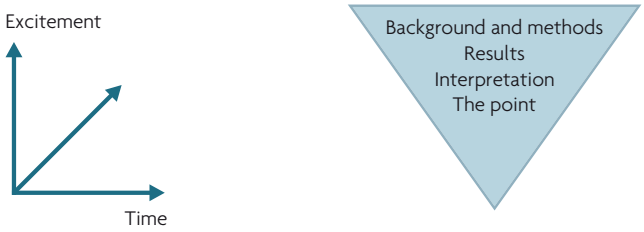
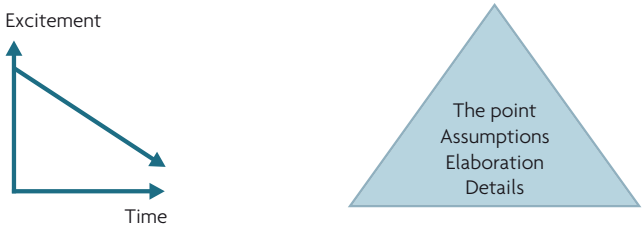


Figure 11.3. Journalistic narrative model (news triangle)



The building blocks of the news text

A news text must have an interesting heading to attract the reader's attention. The heading should *excite, awaken and cover*.

Immediately below the heading is the subheading, which summarises the text in 3-4 lines. In addition to giving a short introduction to the text and elaborating the heading, the subheading should also keep the attention of the readers and make them want to read on. The reader's question "What does this mean for me?" should be answered fairly quickly.

Subheadings divide the text into subsections, show the reader where to find the relevant sections and make it possible to jump to the sections he or she finds of interest. Subheadings are especially important in Internet texts, which the reader often speed-reads (4).

Five basic questions should be considered before beginning to write:

- At whom is the text aimed?
- What is relevant for the recipient to know?
- What is the most important message?
- What should be the tone of the text?
- How should the text be written?

Target group

A successful presentation is based on the universe of the recipient and on what the target group considers relevant. Here one can make use of the experience gained during the project, where one has been in frequent contact with the very groups to which one wishes to present one's conclusions.

HTA projects often have several relevant target groups, for instance:

- Decision-makers in health administrations (region, municipality)
- Politicians (local, regional and national)
- Hospital and department management
- Hospital doctors, general practitioners
- National and international HTA environments
- The general public and patient groups
- The pharmaceutical industry.

Message

The message should feature distinctly and be adapted to the individual target groups, each of which is likely to have completely different prerequisites and interests. A project generates a lot of data and results that can be perceived from many different angles. All professional shades should be available in a good and transparent HTA report. However, in order to present the report forcefully, selection is necessary – "kill your darlings".

Get straight into the message. Identify a point and include only what has relevance for this point. To a great extent, the readers will take for granted that the work has been done properly. Only at the moment they find the sender or the information unreliable will they question where the material comes from and how it has come to light (3).

Often one has to resort to linguistic and technical presentation tricks. The less relevant the readers perceive the topic to be, the more the text has to motivate them. In journalistic jargon, texts are constructed according to the formula *hey – you – see – so*: Capture the reader, make the matter relevant, elaborate on the topic and finally explain the consequences. Researchers may consider having to spice the text with an appetising introduction or a number of colourful cases to illustrate complex contents as violating their professionalism. Although, such text elements seem irrelevant from a professional view point, they can be extremely necessary and relevant for the presentation. Without them, the professional content may not reach the recipient at all.

11.2.4 Language – write clearly

Not all topics are easily presentable, but a differentiation must be made between texts being scientifically or linguistically complex. Why weigh down professionally difficult text with high-flown language and complex technical terms that only a narrow circle of professionals can understand? Instead, make the text vivid and inviting, *without* heavy antiquated words and old-fashioned sentence structures standing in the way of the reader (5).

Look out for other symptoms of linguistic misery:

- A long, confused and information-packed text
- Numerous interposed sentences
- Numerous parentheses

- Front weight (most of the sentence before the verb)
- Passive sentences
- Impersonal language
- Technical terms and loan words.

This is not about writing children's books but about avoiding unnecessary linguistic complexity if possible.

Useful advice to keep the attention of the reader:

- Write vividly and unambiguously
- Write clearly
- Make the text active (use active verbs, not passive and identify a sender of the action)
- Write in short sentences, limit interposed sentences and use full stops
- State the point first (both in the text on a whole and in the individual sentences)
- Consider technical terms
- Be aware of artificial words
- Use common words, not clichés
- Write correctly
- At the end, read the text carefully with the eyes of the recipient.

11.2.5 Press contact

Researchers and journalists – different perspectives

The media's interest in a problem depends on the character of the topic; however, as a project manager one can do quite a lot to generate media interest. For instance, one can give interesting, relevant and professionally documented information. If the message is clear and a report of 100 pages is boiled down to a short introductory text, with at most three relevant points, the chance that the media will take the story is much greater.

Journalists often have a different focus from researchers. Their focus is on actual events, the individual (e.g. the patient or citizen), and possible conflicts. They will want to present the problem in a simple and concrete fashion – most frequently as the pros and cons of an intervention (1).

The researcher, in contrast, often regards the problem as complex, with both the advantages *and* disadvantages of the intervention, the scientific character and the methods applied. The problem is seen from an overall perspective.

Invariably, the journalist has less knowledge than the researcher and will ask questions on behalf of a target group with perhaps even scantier knowledge. It may, therefore, be a good idea to assist the journalist, identifying which stories are contained in the report and elaborating them from the view point of the patient or another relevant individual. But it is also important to identify what one does *not* want to mention, to avoid being taken aback, should the journalist probe.

The researcher cannot instruct the journalist what to write, but he or she can influence and advise. Journalists are often pressed, lack time, are close to a deadline and have limited resources. They, therefore, appreciate receiving factual information (2).

Requirements and prerequisites for successful presentation:

- The presentation must be a process taking the recipient towards a certain target
- The target and means must be closely connected
- The sender must have more knowledge than the recipient (asymmetric relation)
- The presentation must be based on the purpose of the sender (the wish to give the recipient certain knowledge or influence view-points and behaviour)
- The point of departure must be the recipient's universe
- The presentation must be worked out functionally and appropriately
- The sender must respect the recipient (3).

11.3 Literature for Chapter 11

(1) Levi R. Medical Journalism. Exposing Fact, Fiction, Fraud. Lund, Sverige: Studentlitteratur; 2000.

(2) Hansen JOK. I andres brød. Håndbog om informationsjournalistik, virksomhedskommunikation og public relations [In the service of others. Handbook about information journalism, corporate communication and public relations]. Århus: Ajour; 2004.

(3) Jensen LB. Den sproglige dåseåbner – om at formidle faglig viden forståeligt [The "linguistic tin-opener" – about communicating scientific knowledge in a comprehensible manner]. Denmark: Roskilde Universitetsforlag; 2001.

(4) Jensen UJ, Lemée PS, Ravn J, Rosengaard M. Skrivgodt.dk. Sådan skriver du gode tekster til Internettet [Writewell.dk. How to write good texts for the Internet]. Århus: Grandjean Kommunikation/Frydenlund; 2005.

(5) Rask K. Fagsprog – videnssprog [Special purpose language – specialist language]. Copenhagen: Grafisk Litteratur; 2004.

This handbook serves as a practical aid to concrete HTA activities and to advance the way of thinking about HTA. It can additionally be used as an educational tool and forms a basis for the development of methods. It guides the reader through the steps of an HTA, from clarification of questions to implementation of results.

The handbook presents up to date research based methods and approaches to HTA. It covers both the areas of ethics, patient and organization, as well as more established areas such as technology and health economics.

www.dacehta.dk

National Board of Health
Danish Centre for Health Technology Assessment
Islands Brygge 67
DK-2300 Copenhagen S
Denmark
Phone: +45 72 22 74 00

dacehta@sst.dk
www.dacehta.dk