

5 Health Technology Assessment

Camilla Palmhøj Nielsen¹, Tina Maria Funch¹ and Finn Børlum Kristensen²

¹Danish Centre for Health Technology Assessment, National Board of Health, Denmark

²EUnetHTA Secretariat, National Board of Health, Denmark

Contents

5.1	Introduction	99
5.1.1	Health technology assessment (HTA)	99
5.1.2	HTA and Health Services Research	99
5.1.3	Objective	100
5.2	Methods	100
5.2.1	Literature review	100
5.2.2	Carousel rounds	102
5.2.3	Online survey	102
5.3	Results	102
5.3.1	Overview of the literature	102
5.3.2	Literature review - existing research and research agenda	106
5.3.2.1	The content of analysis in HTA	107
5.3.2.2	HTA products	118
5.3.2.3	Life cycle perspectives of health technologies	122
5.3.2.4	Challenges to HTA methodology	123
5.3.2.5	Development of HTA capacity and HTA programmes	125
5.3.2.6	Policy-HTA links	128
5.3.3	Online survey – research agenda	132
5.4	A research agenda for the future	133
	References	137

Acknowledgements

We are grateful for all ideas provided by participants to a workshop session dedicated to HTA during the working conference 'HSR in Europe', and to the experts who facilitated and reported on these discussions: Susanne Vilhelmsdotter Allander (SBU, Sweden), Karen Macpherson (NHS Quality Improvement, Scotland), Irina Cleemput (KCE, Belgium), Mette Kjølby (HTA-HSR/DHTA, Denmark), Philip Radlberger (LBI-HTA, Austria) and Eva Turk (National Institute of Public Health, Slovenia).

5.1 Introduction

5.1.1 Health technology assessment (HTA)

The development of health services in Europe is strongly influenced by new technologies that can potentially improve population health through more effective care. However, not every technological innovation results in health gains. Many technologies have not produced the expected benefits or have even proved to be harmful. Further, technologies that prove to be effective create a challenge, since applying them may require additional money and other resources or require redistributing existing resources. Innovative technologies also challenge the existing organisational framework of health services by introducing e.g. individualised drugs or new opportunities for treating people in their homes supported by information and communication technologies. These trends emphasise the necessity of ensuring that health technologies are evaluated properly – both to analyse the consequences of using specific technologies and to become aware of the prerequisites of applying the technologies and the required adaptation of organisational structures, work processes and culture. HTA has been created to ensure that health technologies are thoroughly assessed and to provide direct input for decision-making on introducing technologies into health services (Velasco Garrido et al., 2008).

The International Network of Agencies for Health Technology Assessment defines *health-care technology* as: ‘...prevention and rehabilitation, vaccines, pharmaceuticals and devices, medical and surgical procedures, and the systems within which health is protected and maintained’. *Technology assessment* in health care is defined as: ‘...a multidisciplinary field of policy analysis. It studies the medical, social, ethical and economic implications of development, diffusion, and use of health technology’ (www.inahta.org). The EUnetHTA Project has added the following explanatory clarification that emphasizes the process and aims of an assessment: ‘Health technology assessment (HTA) is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused, and seek to achieve best value. Despite its policy goals, HTA must always be firmly rooted in research and the scientific method’ (www.eunetha.net). The practice of HTA within this definition varies considerably across national settings. It informs policy- and decision-making in specific political, economic, and institutional contexts. In order to be useful, HTA has to be designed with processes and outputs that fit the relevant context.

5.1.2 HTA and Health Services Research

HTA is a field that connects clinical research with health services research (HSR) in order to provide a broad based input to policy-making, and to the development of an evidence-based health care practice. According to the theoretical background of HTA, it is not in itself research, but is building on both existing clinical research and on HSR. However, it is now frequently seen that HTA includes primary data collection, and analysis within the fields of clinical research, and/or HSR to answer policy questions satisfactorily, and HTA can therefore be seen as policy oriented research.

The working definition of HSR used in this report is:

HSR is the multidisciplinary field of scientific investigation that studies how social factors, financial systems, organisational structures and processes, health technologies and personal behaviours affect access to health care, the quality and cost of health care and, ultimately, the health and wellbeing of citizens (Lohr and Steinwachs, 2002).

In the field of HSR, HTA is obviously related to analysis of health technologies, but with strong links to the full field of HSR in order to analyse different prerequisites for, and consequences of, the use of health technologies.

5.1.3 Objective

This chapter provides an overview of health services research (HSR) in relation to HTA in Europe. Based on a review of published research, we identified the trends in health services research in relation to HTA so far. In addition, we provide input to a future research agenda by describing the research called for in the existing literature. Besides, this chapter discusses new directions for HTA based on the demands for future research.

In order to give an overview over existing research and an input to a future research agenda, we focus on development of: 1) the content of analysis in HTA (e.g. analysis of economy, organisation, ethics, legal aspects and social aspects), 2) the 'HTA products' developed to adequately meet the needs of policy-makers (e.g. early warning/horizon scanning, rapid assessment, mini-HTA, core HTA), 3) life-cycle perspectives in relation to assessment of technologies, 4) themes/topics which challenges existing HTA methodology, and where HTA should be developed to be able to address the themes more comprehensively in future (e.g. public health interventions, and information and communication technologies, 5) development of HTA capacity and of HTA programmes; and 6) links between policy and HTA. To give input to a future research agenda, we discuss the need for development in relation to theoretical approaches and research methodologies in relation to HTA. Basically the themes concerns two different contributions:

- HSR as part of HTA methods to analyse the consequences of the use of technologies, e.g. health services research concerning the economic, ethical, legal, organisational, and social consequences of the use of technologies
- HSR to develop the HTA methodology as a tool to provide input to policy-making, e.g. development of HTA methodology to assess public health interventions or development of new HTA products to avoid duplication of assessments across Europe.

The chapter is not per se an evaluation of all the HTA studies in Europe, but looks at them from a meta level, in order to get an overview over trends in research and in future research priorities within HSR in relation to HTA.

5.2 Methods

This section describes the methods we applied in this literature review, presenting existing research and input for a future research agenda.

5.2.1 Literature review

In this section, the methods used in the literature review concerning HSR in relation to HTA are summarised, including search strategies, and inclusion/exclusion criteria used for the selection of relevant literature.

Initially we piloted different search strategies to find the strategy with the largest sensitivity and specificity. In general it was difficult to define a strategy which captured relevant articles without losing too many. Based on these pilot literature searches, we decided to search exclusively in PubMed. This decision was made since the search seemed to catch a large majority of the relevant

literature. However, the consequence of this strategy is that we have not specifically searched in specialised databases for articles concerning the 'HTA disciplines' e.g. health economy, organisation, and ethics, and we therefore risk losing the specialised research within each discipline. To compensate for this, we decided that the only Mesh term used for the literature search was 'technology assessment'. This ensured a high sensitivity, but a low specificity of the search, and therefore allowed us to find the large majority of relevant articles included in the rather broad search. The search was conducted on the 19th February 2009, and was limited to include articles dating back ten years. The Literature search included 3360 references. These references were scanned at title/abstract level by two researchers, and were in this process reduced to 555 articles. The next step was to review each article and to decide whether to include or exclude the article according to our selection criteria (see below). This process reduced the number of relevant articles to 188 articles. The systematic literature search was supplemented with reports/books from the EUnetHTA Project, and articles from a recent volume of International Journal of Technology Assessment in Health Care (vol.25, 2009, SUPPL. 2) which contain articles summarising the findings from the EUnetHTA Project. These reports and articles were selected because they are examples of the most recent research within HTA including HSR and because they specifically address the need for development within HTA including need for research. Altogether, 22 reports/books/articles were included. The included literature from the EUnetHTA project is listed in appendix 4A. A table with a summary of results of the literature review is available in appendix 4B, and a more detailed overview over included literature is available in appendix 6.

In total, the literature review was based on 210 references. 189 references reported specific studies, and were relevant to provide an overview of the current research activity in Europe. 21 references were debating articles only. 100 references pointed to areas for further research.

Criteria to select the relevant articles were the following:

Inclusion:

Articles containing HSR in relation to HTA, or debating future needs for HSR in relation to HTA. All languages included.

Exclusion:

Articles which did not include HSR in relation to HTA (e.g. clinical research, health impact assessment, assessment of specific technologies, priority-setting within health care not specifically concerning HTA).

Articles from outside Europe were excluded from this systematic review, but some were still used to show the state-of-the art, to put the European HSR into perspective, and to give input to the section on future research agenda. Additionally, articles from outside Europe were included if they addressed HTA in a European setting. Within HTA, the European and non-European research is closely related, and it is useful to take the non-European research into account when providing input to a future research agenda.

The articles and the EUnetHTA literature were analysed and distributed into relevant categories reflecting the following themes:

- The content of analysis in HTA
 - Economic evaluation
 - Assessing the wider impacts of health technologies

- Best practice in undertaking HTA
- HTA products (all described as additions to the ‘classic’ HTA report)
 - Horizon scanning/early warning
 - Rapid assessment
 - Mini-HTA
 - Core HTA
 - Adaptation toolkit
- Life cycle perspectives of technologies
- Challenges to HTA methodology
- Development of HTA capacity and HTA programmes
 - HTA capacity
 - HTA programmes
 - Priority setting within HTA programmes
- Links between policy and HTA.

5.2.2 Carousel rounds

The carousel rounds of the HTA parallel session at the HSR Europe working conference focused on the following three topics: (1) Assessing the wider impacts of health technologies (e.g. organisational aspects), (2) improving the links between HTA and policy, and (3) assessing technologies which challenge the common HTA methodology. These discussions have provided an input for the future research agenda concerning HTA. For further description of the carousel rounds see chapter 2.

5.2.3 Online survey

Also, an online stakeholder survey was carried out to assess what experts across Europe think about HSR priorities in their country, and in Europe as a whole. In total, 34 European stakeholders (24 researchers, and 7 decision makers) shared views concerning HTA. The results of the surveys relevant to HTA in relation to HSR are reported in this chapter. For further description of the surveys see chapter 2.

5.3 Results

5.3.1 Overview of the literature

This part of the chapter provides a descriptive, graphical overview of the literature included in the literature review in relation to selected variables (only the 189 articles which reports existing research are included, among these are also reports, book, and articles from the EUnetHTA project). The variables chosen for classifying the articles included in this review were: 1) the country of the institution of the first author, 2) the number of nationalities involved in the research, 3) the type of institution(s) involved in the research, 4) the topics of the research, 5) the journal where the research was published, and 6) the distribution of articles in the decade 2000-2009. Overall, this overview intends to provide a visual overview of characteristics of the body of research undertaken in relation to HTA.

Figure 5.1 provides an overview of which countries are active in publishing research in relation to HTA, and it is a clear tendency that British researchers are very active within HSR/HTA. Also, it is shown that a large number of European countries are involved in this field. The Canadian, US, and Australian articles are included, because there are European co-authors or because they include

studies of HTA in Europe.

Figure 5.2 shows to what extent the research is based on collaboration between researchers from different countries. Even if most research is based in one country, it is still clear that collaboration between researchers from different countries is established. This is partly due to a long tradition of (EU-supported) projects among HTA institutions in Europe.

Figure 5.3 provides an overview of the scientific environment in which the research was undertaken. Mixed scientific environment was identified in 81 of 188 cases. Even if the universities are most active, it is remarkable that research in relation to HTA is characterised by involvement of other actors – primarily HTA institutions. However, also private consultancies and industry has published relevant research.

Figure 5.4 provides an overview of the research topics identified in the analysis of the literature. The figure shows that especially research in health economics and in the links to policy have been conducted during the last ten years. However, a broad field of topics has been covered.

Figure 5.5 provides an overview of the publishers of HSR in relation to HTA. Not surprisingly, the International Journal of Technology Assessment in Health Care is the most used journal for publication of HSR in relation to HTA, but also other journals or programmes are represented in the list of publishers.

Figure 5.6 provides an overview of the number of articles published, and the year of publication of HSR in relation to HTA. The number of identified articles varies between 11 and 29 per year.

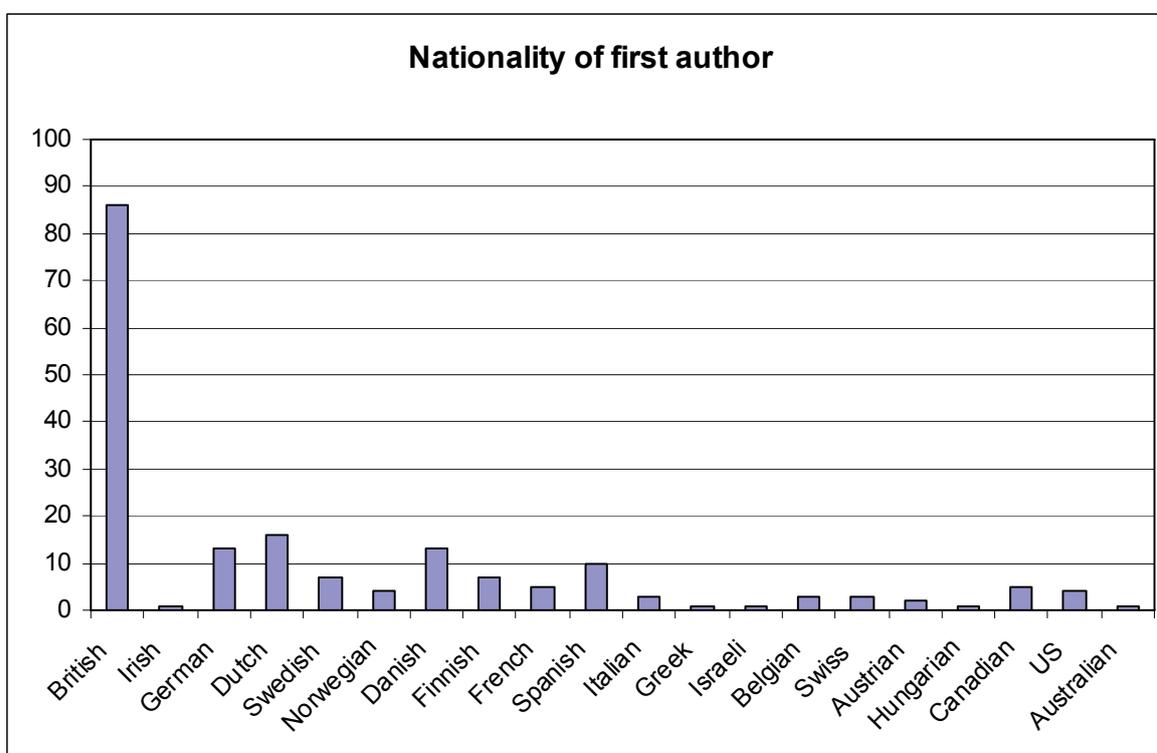


Figure 5.1 Nationality of first author of all studies on HSR in relation to HTA

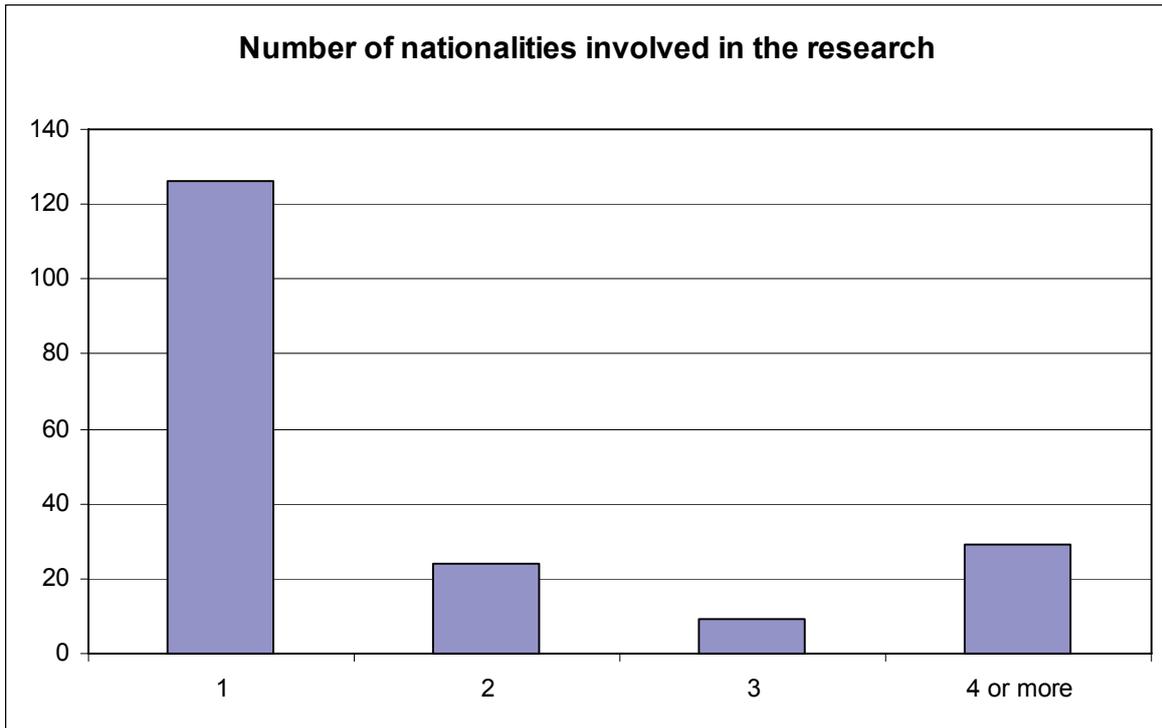


Figure 5.2 Number of nationalities involved in HSR in relation to HTA

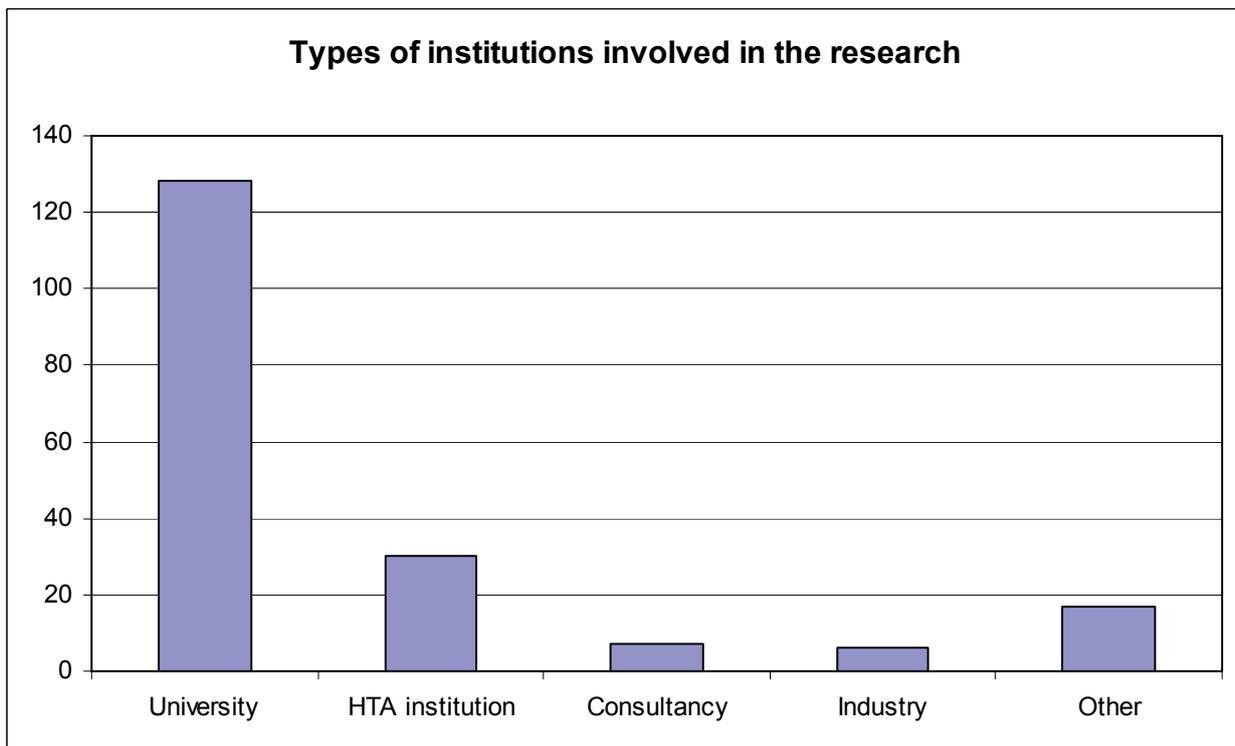


Figure 5.3 Types of institutions involved in HSR in relation to HTA

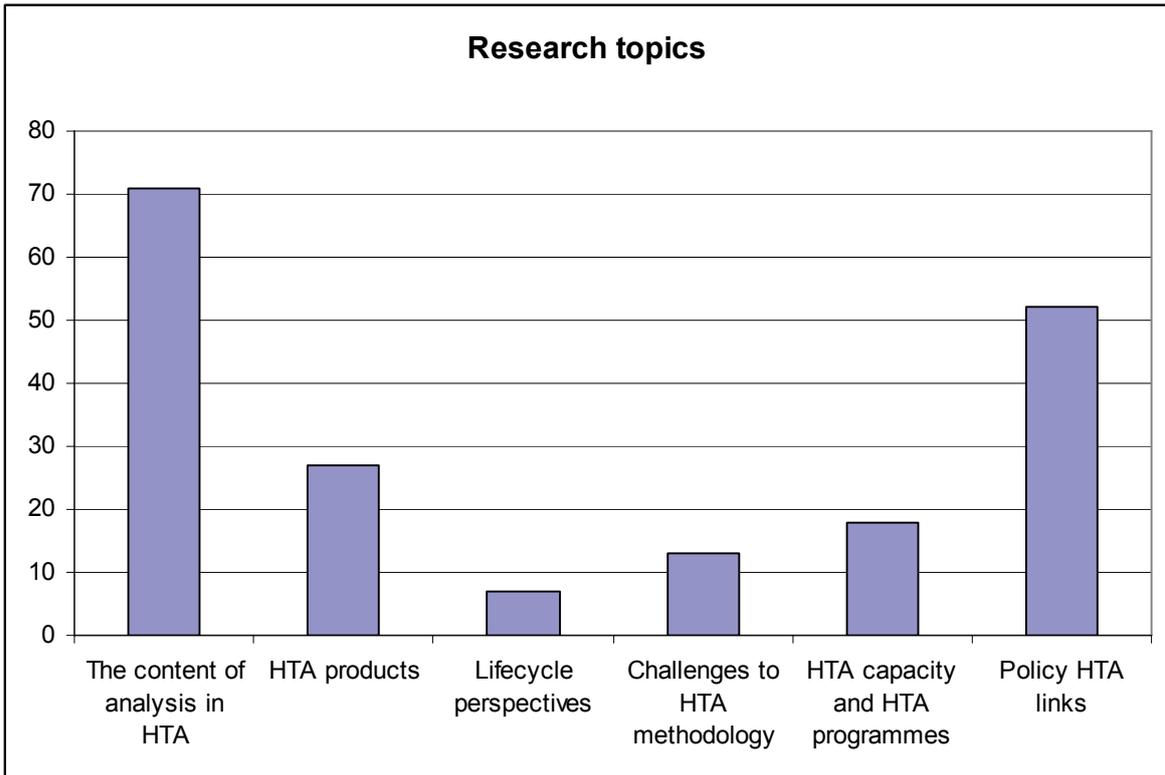


Figure 5.4 Overview of research topics in HSR in relation to HTA

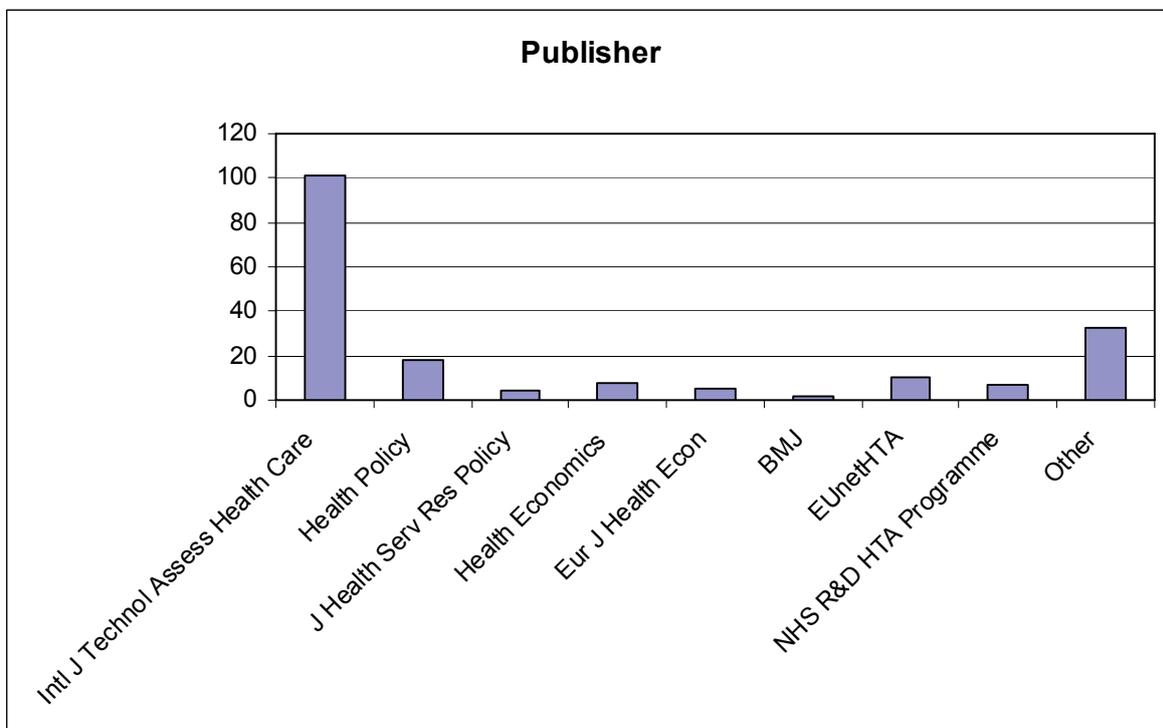


Figure 5.5 Overview of publishers of HSR in relation to HTA

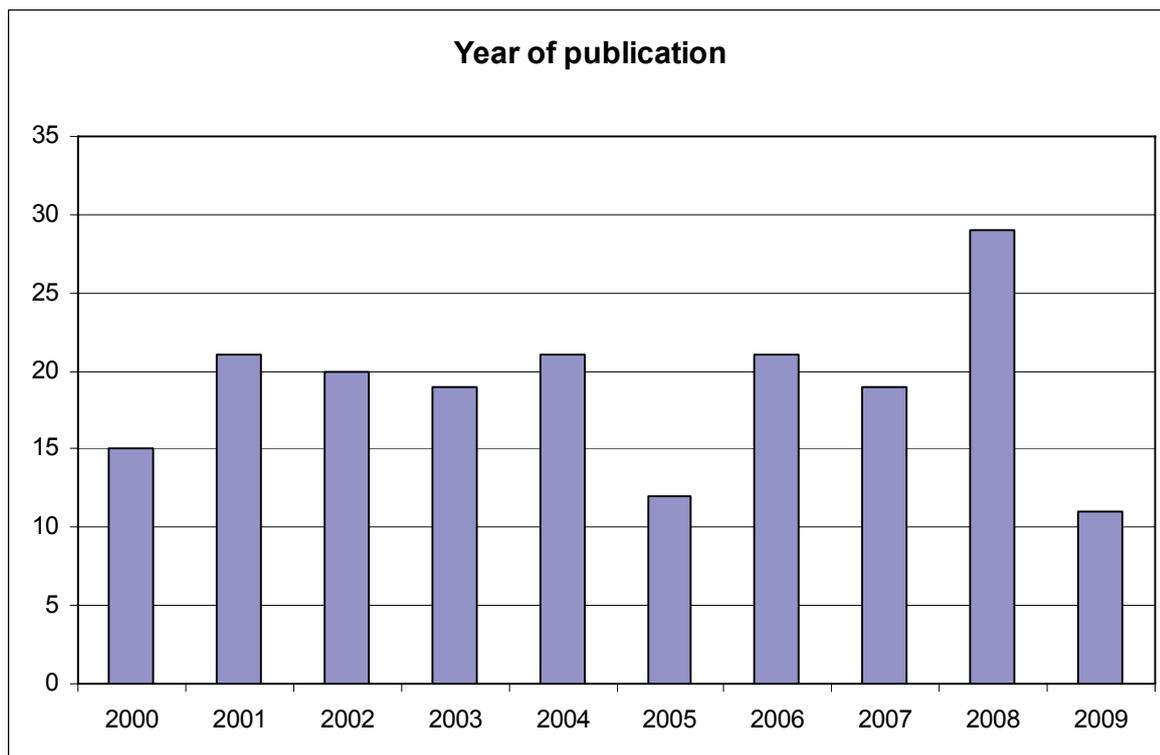


Figure 5.6 Number of studies per year on HSR in relation to HTA

5.3.2 Literature review - existing research and research agenda

This part of the report has the purpose of presenting the content of the existing research and the demands for future identified in the literature. As earlier indicated, the research is categorized into different topics of relevance to HSR in the area of HTA. The figure below shows the percentage of references addressing each topic.

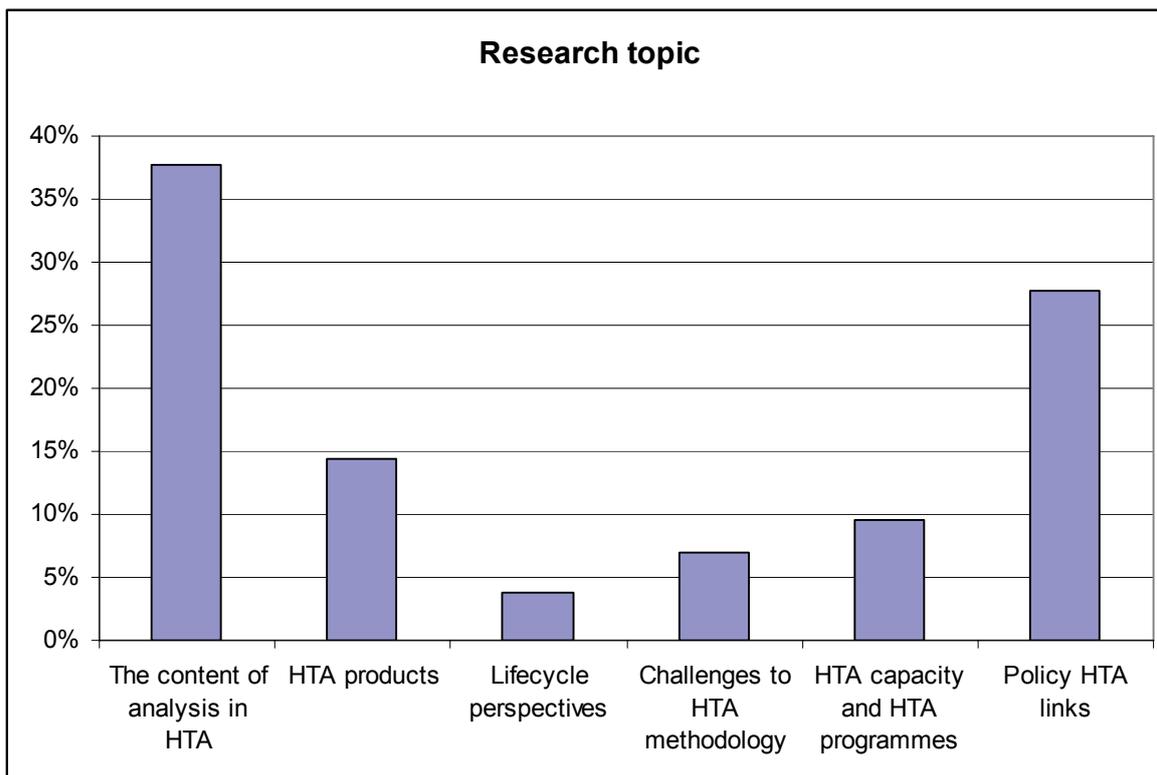


Figure 5.7 Percentage of references on each topic of HSR in relation to HTA

5.3.2.1 The content of analysis in HTA

This part includes research within the ‘HTA disciplines’, and articles concerning best practice in undertaking HTA.

A. Economic evaluation

Economic evaluation is the comparison of two or more alternatives courses of action in terms of both their costs and consequences. Economists usually distinguish several types of economic evaluation, differing in how consequences are measured:

- Cost minimisation analysis (CMA)
- Cost benefit analysis (CBA)
- Cost effectiveness analysis (CEA)
- Cost utility analysis (CUA) (Drummond et al., 2005)

Economic evaluation is a well established research discipline with a broad spectrum of different methods available. This literature review revealed that a lot of research is being done in the area of health economics in relation to HTA, as this was the area in which the greatest body of literature was identified. In total 52 articles reported specific studies, and were relevant to provide an overview of the current European research activity in this area. Additionally, several articles were debating articles that pointed to areas of future research. The research articles dealt with several themes in relation to economic evaluation, e.g. guidelines, cost-effectiveness analysis, the effects of learning curves, estimation of effect and utility, the use of economic evaluation, and influence on decision making.

Five studies concerned cost-effectiveness analysis (CEA), or different aspects of such analysis (Fenwick et al., 2001; Adam et al., 2003; IJzerman et al., 2003; Kristiansen et al., 2003; Fenwick et al., 2006). Two studies illustrated how to construct and interpret a cost-effectiveness acceptability curve (CEAC), and considered the relationship with decision making, concluding that CEACs are useful, as they provide a measure of the decision uncertainty surrounding the choice, and encouraged to a greater use of CEACs (Fenwick et al., 2001; Fenwick et al., 2006). Adam et al. (2003) explored the sources of variations in CEAs, and the possibility of reducing these variations. They found variations in methods due to variations in guidelines, lack of methodological guidance in guidelines, and lack of compliance with these guidelines, and thus raised questions about the validity of results, and pointed out, that this issue makes it difficult to compare the results of different studies. Also, Kristiansen et al. (2003) compared CEAs to other analytical methods, and concluded that variation in results stems from variable factors. Finally, IJzerman et al. (2003) found that pre assessment was useful step in designing a CEA, as it helps meeting the needs of decision makers at local levels.

Four studies concerned the assessment of effects. Two studies concerned the assessment of utility. One study compared the assessment of QALYs based on the SF-6D and the HUI3 utility scoring systems, and found them to differ markedly, and concluded that the challenge is to develop an understanding as to why these classification based utility instruments differ (O'Brien et al., 2003). Another study reviewed the methods applied by the English National Institute for Health and Clinical Excellence (NICE) to obtain utility weights, and concluded that greater transparency and consistency is needed due to methodological variations. Also, one should be careful to compare the results of different CUAs (Stein et al., 2005).

One study concerned assessments of willingness to pay, a method for estimating the perceived benefits in monetary terms, and compared the bidding game format with the open-ended and payment scale format. Again, the estimates vary considerably depending on the formats applied (Frew et al., 2004). Finally Ratcliffe and Longworth (2002) investigated the structural reliability of discrete choice experiments, a stated preference technique for establishing patient and public preferences, by comparing the results of two types of questionnaires with varying levels of some of the attributes included in the questionnaire. The questionnaires were distributed to two samples of women who had just given birth, in order to determine preferences for alternative modes of management and delivery of care to women in labour. Attributes included e.g. continuity of contact with the same medical staff, and location of delivery. They found that the women placed greater importance upon specific attributes as the number of levels for these attributes increased, indicating that the greater level of categories, the higher preference scores will be obtained from such questionnaires.

21 studies concerned different aspects of economic modelling. Five of these articles reported studies on Bayesian modelling (Spiegelhalter et al., 2000; Claxton et al., 2001; O'Hagan and Stevens, 2002; Griffin et al., 2006a; Vallejo-Torres et al., 2008). The studies aimed to demonstrate the usefulness or the benefits of applying this approach, or reviewed the application of this method. Two studies showed that the Bayesian approach incorporates more data than other models, and is thus suited for informing decisions at all stages of a technologies lifecycle (Griffin et al., 2006a; Vallejo-Torres et al., 2008). However, two other studies concluded by pointing to areas of further development of the approach, e.g. how to incorporate expert knowledge (Spiegelhalter et al., 2000; O'Hagan and Stevens, 2002).

Nine articles dealing with economic modelling compared different modelling approaches, or guidelines and/or presented guidance for economic modelling (Hjelmgren et al., 2001; Soto, 2002; Grieve et al., 2003; Karnon, 2003; Barton et al., 2004; Philips et al., 2004; Brennan et al., 2006; Philips et al., 2006). The studies that compared guidelines showed that some harmonization of methodological requirements and recommendations exists (Hjelmgren et al., 2001), however, other studies concluded that some disagreement, especially regarding how to incorporate data into models, and how to assess uncertainty, exists (Philips et al., 2004; Philips et al., 2006). Finally, one article presented a systematic process for choosing methods of economic modelling, developed by the authors, and concluded that application of this process would increase transparency of economic evaluations, which is helpful for decision makers (Grieve et al., 2003). Also in relation to guidelines, von der Schulenburg et al. (2007) reviewed international standards in relation to a legislative framework in Germany, and concluded by providing recommendation of a detailed assessment-process specific for the German way in implementing cost-benefit ratios within regulatory decision making in Germany.

Three articles dealt with the importance of considering decision uncertainty, pointing to the fact that this is an important part of economic modelling. Two articles dealt with probabilistic sensitivity analysis, and concluded that analysts should consider the dual requirement of both estimating expected net benefit, and characterizing decision uncertainty (Claxton et al., 2005; Griffin et al., 2006b). One study developed an alternative approach to dealing with uncertainty based on 'option pricing techniques', that takes the fact that costs might vary over time, making investments dependent on time, into account (Palmer and Smith, 2000).

Other aspects dealt with in relation to economic modelling were the quality of the evidence the models are based upon (Cooper et al., 2005), discrete event simulation (Rodriguez Barrios et al., 2008), Markov models (Rodriguez Barrios, 2004), and the dynamic modelling approach (Boas et al., 2001). Generally this literature review shows that several modelling techniques exist, and that there is quite disagreement between the authors about the most appropriate method to apply, how to apply it, and the benefits of the models.

Two studies addressed the importance of the systematic search for data as part of an economic evaluation. Drummond et al. (2008a) assessed the extent to which the systematic review of the clinical literature informs the economic evaluation in NICE technology assessment reports (TARs), and concluded that much of the relevant data for estimating QALYs are not contained in systematic reviews, and that the chosen method for summarizing the clinical data may inhibit the assessment of economic benefit. Problems would be reduced if data requirements are discussed at an early stage. Also, Hanratty et al. (2007) concluded that a structured search for the highest quality information on clinical effectiveness is essential to improve the quality of economic methods.

Three studies concerned methods of how to estimate learning effects, that is the consequences of increasing effectiveness over time (Ramsay et al., 2000; Ramsay et al., 2001; Ramsay et al., 2002), and concluded that learning curves are rarely considered formally in HTA. Also, these studies found methods for estimation of learning effects in other statistical fields, demonstrating the value of considering other fields when addressing methodological issues in HTA.

Two studies explored ways of identifying economic evaluations for reviews (Nixon et al., 2004; Alton et al., 2006) and found, that a search in NHS Economic Evaluation Database, by means of the Cochrane Library, or the Centre for Reviews and Dissemination, along with a supplementary search

in PubMed, is generally an appropriate, cost-effective strategy (Alton et al., 2006). However, they found time lags between the publication of economic evaluations, and the appearance of abstracts relating to them in the database (Nixon et al., 2004). Also in relation to reviews, one article provided a criteria list for assessment of the quality of economic evaluations in order to make future reviews more transparent, informative, and comparable. The criteria list was developed by the Consensus on Health Economic Criteria (SHEC) project using a Delphi panel consisting of 23 international experts (Evers et al., 2005).

Two studies compared evaluations submitted to NICE by manufacturers and other assessment groups (e.g. university based)(Miners et al., 2005; Chauhan et al., 2007), and found that results from economic evaluations addressing the same question diverge, and that the estimated incremental cost effectiveness ratios submitted by manufacturers were on average significantly lower than those submitted by other assessment groups. Additionally, two more studies concerned NICE, the methodological challenges encountered in producing an independent economic evaluation, the exact factors considered in NICE assessments, and their relative importance and trade offs (Dakin et al., 2006; Griffin et al., 2008). Finally, one article investigated the consequences of type of sponsorship statistically, but did not demonstrate such a relationship. However, they concluded that it is necessary to improve the quality of studies sponsored by industry (Hartmann et al., 2003).

Seven studies concerned the use of economic evaluations, and the influence on decision making. One study examined decision makers' views on different reporting formats, concluding that decision makers require both an initial screen of study content plus more detail should they find the study relevant or interesting (Thurston et al., 2008). Four studies concerned the use of economic evaluations in the UK decision making, concluding that the evaluations should be more charged, and the constraints of the local decision making environment should be reflected. Also, the accountability in policy decisions necessitated that the information, upon which decisions are based, were accessible (Bryan et al., 2007; Williams and Bryan, 2007; Williams et al., 2007; Williams et al., 2008). Another study examined the influence of economic evaluations on decision making in relation to the EUROMET survey, and found several barriers, e.g. transfer of results, and practical relevance (Hoffmann and Graf von der Schulenburg, 2000). Finally, Cookson and Hutton (2003) summarized the concerns at a European level in relation to reimbursement decisions regarding pharmaceuticals and medical devices, and concluded that there is considerable scope for improvements of decision making without damaging incentives to innovate, e.g. the national purchasers themselves could become more transparent and accountable. Additionally, one Italian article provided an overview of the relationship between health care costs and HTA, and an overview of the use of HTA between 1980 to 2006 in nephrology in Italy (Lettieri and Masella, 2007).

In addition EUnetHTA has contributed to analysis of how to provide core elements of an economic analysis which can be used to adapt to different settings (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008).

In summary, this literature review showed, that economic modelling, guidelines, cost-effectiveness analysis, the effects of learning curves, estimation of effect and utility, the use of economic evaluation, influence on decision making, and the use of economic analysis in different settings were some of the themes that make up the majority of the current research activity dealing with economic evaluation in relation to HTA. However, in spite of the great amount of research, there is still disagreement concerning the methods to apply when conducting an economic evaluation as

part of an HTA. Hence, even though the economic aspect might have well established methodologies available, there is still lack of clarity about recommendations and best practice concerning economic evaluation in relation to HTA.

The studies primarily applied quantitative methods, or reviewed quantitative methodology. Those studies, that concerned the use of economic evaluations, and the influence on decision making, were the only studies that applied qualitative methods, or a combination of qualitative and quantitative methods. The studies were predominantly conducted in university environments. Also, the research activity was most prevalent in the United Kingdom.

Research agenda

In relation to economic evaluation in HTA, 27 articles pointed to areas of future research.

First of all, several authors pointed to the fact that there is no current agreement of several measurements in economic evaluations, e.g. how benefit should be measured, how health related quality of life should be described and valued, how QALYs should be aggregated, and if QALY is an appropriate measure (Stein et al., 2005; von der Schulenburg et al., 2007; Brazier, 2008). Also, when preferences are measured, it should be explored what factors influence these choices, and if these measures are reproducible (Ratcliffe and Longworth, 2002). Also, in relation to future estimates, how both future costs and future resources should be estimated is still disagreed upon. In relation to level of analysis, it is questioned whether national unit or local unit costs should be used when producing national guidance (Miners, 2008). In relation to modelling, questions such as how the model structure is decided upon, what methods are appropriate to identify evidence, how to integrate data it into the models, how to incorporate expert knowledge, and how modelling is best performed and reported are posed (O'Hagan and Stevens, 2002; Philips et al., 2006; Cooper et al., 2007; Spiegelhalter et al., 2000). Three articles addressed learning curves, which is curves describing the increased skill levels after introduction of a technology. It should be explored what influence learning curve effects have on economic evaluations, how they should be estimated, and how they should be incorporated into economic evaluations (Ramsay et al., 2000; Ramsay et al., 2001). One study found that there were a number of more sophisticated statistical methods that could be used to model the learning curve effect during HTA. Now, the relative performance of these methods requires assessment before general recommendations can be made (Ramsay et al., 2002).

In general, there is still a disagreement concerning the most appropriate perspective to apply in economic evaluations (Stein et al., 2005; von der Schulenburg et al., 2007). It should be explored which alternative structures, processes, and mechanisms in the health care systems organisation that are best suited for technology coverage decisions (Williams et al., 2008). Also, Hoffmann and von der Schulenburg (2000) questions if the health care system provides an optimal framework for use of economic evaluation studies in making decision about the provision of health care services.

Finally, it is debated how decision uncertainty is to be properly addressed in economic evaluations (Philips et al., 2004; Claxton et al., 2005). All of these concerns, related to the design of economic evaluations, emphasize the fact that even though several methods are available in economic evaluation, there is still disagreement concerning best practice.

Taking the decision makers' views into account, Williams et al. (2008) pointed to the fact that further assessment of the feasibility and value of a formal process of clarification of the objectives, which

we seek from investments in healthcare, is needed. Also, it should be explored which designs of economic evaluations, are best suited to take into account the needs of the decision makers both in terms of evidence requirements and the way complex evaluations are presented (Hoffmann and von der Schulenburg, 2000; Bryan et al., 2007; Williams et al., 2008). Also in relation to decision makers, further studies of the use and utility of economic evaluation in the decision making process is needed (Stein et al., 2005; Kulp and Greiner, 2006). Also, further research into how to ensure transparency, and the consequences of lack of transparency, is needed (Hoffmann and von der Schulenburg, 2000; Claxton et al., 2005; Cooper et al., 2005). Finally Cookson and Hutton (2003) inquire research into how national purchasers can become more transparent in the way they use evidence.

In relation to international standards and guidelines, Jönsson (2008) questions the entire purpose of using such standards in economic guidelines, and von der Sculenburg et al. (2007) questions if it is even possible to set international standards for economic evaluation . One point is that international standards needs to be continuously developed (Jönsson, 2006). Also in relation to methodological guidelines for economic evaluation, Adam et al. (2003) requests more detailed guidance in the guidelines to ensure that their recommendations are appropriately followed, as this would reduce the variability between studies.

Other topics discussed in the literature concerning economic evaluation were the case of rare diseases (Griffin et al., 2008), orphan drugs (McCabe et al., 2007), availability of data relevant for economic evaluation (Jönsson, 2007), and the consequences of time lags between product launch and routine use (O'Hagan and Stevens, 2002).

B. Assessing the wider impacts of health technologies

The wider impacts of HTA include assessment of the ethical, legal, organisational, and social aspects of health technologies. In total, nine articles reporting studies concerning the wider impacts of HTA were identified in the literature search. Four of these articles pointed to areas of further research. Additionally, EUnetHTA included the wider aspects of HTA in the Core model, and the Adaption toolkit.

Ethics

The ethical domain of HTA deals with prevalent morals, values and behavioural models of the society relevant for the technology. It has been argued that ethics should be part of HTA since its inception in the beginning of the 1970'ies. A variety of methods to integrate ethics in HTA exists. Both qualitative methods taken from existing research disciplines, and methods developed specifically for the integration of ethics in HTA have been applied. Also, working groups within both INAHTA and HTAi have tried to come to some agreement of which methods are most appropriate to approach the ethical issues, and most recently EUnetHTA developed methodology to address the ethical domain as part of the Core model. However, still only few HTAs address these issues in depth.

Eight of the nine articles identified were relevant for the ethical domain, which implies that the ethical domain is the one most studied among the wider impacts in relation to HTA.

Four articles were methodological articles that provided and addressed specific methods of how to include the ethical issues in HTA (Møldrup, 2002; Hofmann, 2005; Autti-Rämö and Mäkelä, 2007; Saarni et al., 2008). The model presented by Saarni et al. (2008) was developed within the

EUnetHTA Project. The authors argued, that the model is easy and flexible to use in different organisational settings, and concluded, that integrating the ethical considerations into HTA can improve the relevance of HTA in both developed and developing countries. Autti-Rämö and Mäkelä (2007) explained the eclectic approach developed by the Finnish HTA office, and concluded, that the ethical domain is an important part of an HTA, as it helps decision makers realize the consequences of implementing a new healthcare technology in many aspects. Hofmann (2005) presented an approach for integrating moral issues, and argued that the approach both had a broad theoretical foundation, and had shown to be useful in practice. Also, he pointed to the fact that the inclusion of this domain in HTA is of great value to policy makers. Finally, Møldrup (2002) proposed an 'Internet Citizens jury' as a method to explore, among other domains, the ethical implications of pharmacogenomics from a citizen's perspective, and recommended incorporation into the common methodology of HTA.

Three articles analysed and discussed why ethics should be part of HTA, and the reasons for the lack of its inclusion (Lehoux and Blume, 2000; ten Have, 2004; Hofmann, 2008). Hofmann (2008) analysed ten arguments for making ethics part of HTA, in order to explain why it has taken so long to include ethics, and why there is no standard methodology, even though it has been argued that ethics should be part of HTA since its inception. The author concluded that health care is a moral endeavour, and the vast potential of technology poses complex moral challenges. Thus, a thorough HTA would include reflection on these moral aspects. A reason why the lack on inclusion of ethics in HTA might be, that it is still not clear what is meant by "integrating ethics", and that the goal of its integration is not made explicit. Ten Have (2004) also analysed why ethics still play a minor role in HTA, and concluded that ethics in HTA should go beyond issues of application in clinical practice, and focus also on the definition of problems, the demarcation of technical and nontechnical issues, and the morally problematic implications of technologies. Lehoux (2000) compared the professed objectives of HTA with typical practice, and explored the possible explanations for the discrepancies involved, and concluded that the ability of HTA to more fully address important issues from a public policy point of view would increase if the socio-political nature of health care technologies were made more explicit.

Finally, van der Wilt (2000) explored the ethics of technologies where broad consensus regarding valued and disvalued outcomes were lacking, and concluded, that if HTA aims to enhance the accountability of the decision making process, regarding funding and use of health technology, it is a major challenge for HTA to deal adequately with existing value pluralism.

All of the studies either applied or discussed qualitative methodology. The research was mainly undertaken at universities.

In EUnetHTA, ethics were included in the Core model (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008).

Several articles addressed ethics, and discussed the opportunities and challenges in relation to specific technologies that are considered controversial or ethically complex (e.g. genetic screening).

Legal aspects

The legal aspects of HTA address legislation and regulatory questions concerning the technology under assessment. For an issue to be considered a legal one, one must be able to point out the legal source (stipulation, convention, or agreement) that makes the issue legally relevant. Also, this

is what separates the legal domain from domains concerning ethics, social issues and safety.

No articles explicitly focusing on the legal aspects in relation to HTA were identified in the literature review. Only Møldrup, C. (2002) addressed the role of legal aspects in relation to genetic screening as part of the Internet citizens' jury. EUnetHTA included legal aspects in the Core model (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008).

Organisational aspects

The organisational aspects in HTA focus on the delivery modes of the assessed technologies. These include aspects of e.g. the management, financing and controlling issues, and can thus contribute to assessments by clarifying challenges and barriers in implementing health technologies.

Only one article identified in the literature search addressed the organisational aspects of HTA (Fulop et al., 2003). The authors aimed to make a case for a greater emphasis in research on how health services are managed, organised and delivered, and discussed the theoretical differences between and within disciplines, and discussed their implications for research methods (Fulop et al., 2003). They concluded, that the challenge for researchers from various disciplines is to see how far they can work together to carry out research in this important field. The challenge for this research is that the findings are valued and used by health service professionals, managers, and users.

In addition, organisational issues are incorporated into the EUnetHTA core model (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008), and the adaptation tool kit (Rosten et al., 2009; Turner et al., 2009a; Turner et al., 2009b; NCCHTA, 2007; Chase et al., 2008).

Social aspects

The literature revealed a great deal of mixing of different concepts such as social aspects, and patient perspective under this heading. According to EUnetHTA, the social domain of HTA takes the patient as a point of departure in the analysis of the manifold social implications of a health technology. The analysis should reveal the resources needed when using a technology, and the consequences of its use in the life of the patients.

No articles focusing explicitly on the assessment of social aspects were identified in the literature review. Again, only Møldrup, C. (2002) addressed the role of social aspects in relation to genetic screening as part of the Internet citizens' jury that aims at exploring both ethical, social, and legal implications.

EUnetHTA included social aspects as part of the core model, and introduced a broader range of literature on this topic, which has not been included in this review (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008).

Research agenda

Four articles pointed to areas of further research within the area of assessing the wider impacts of health technologies.

In relation to ethics, it should be explored what role it should play in HTA (e.g. as a separate domain

or incorporated to all domains). Also, it should be explored if it is possible to agree on any common standards and develop methodological guidelines for the inclusion of the ethical aspects (Hofmann, 2008). In relation to the EUnetHTA core model, it should be explored whether it represents and promotes a “western”, individualistic perspective that fits only certain types of health care organisations, and whether the methods and issues of ethics is transferable between countries and cultures (Saarni et al., 2008). In relation to assessment of ethical, legal and social implications, Møldrup, C. (2002), based on the experiences of HTA in Denmark, proposed the application of an internet citizen’s jury, consisting of a randomly selected and demographically representative panel of citizens that fill out an online questionnaire, and recommended the incorporation of the method into HTA methodology.

In relation to organisational aspects, the stakeholders involved in the day to day organisation of health care need to be involved, if organisation research is to have an impact on policy and practice. Also, a wide range of disciplines and methods need to be considered (e.g. sociology, organisational studies, policy analysis, economics and history). The major obstacle is that researchers from the various disciplines that can contribute to assessment of organisational aspects operate in different paradigms both within and between theoretical approaches. So, it should be explored, how multi-disciplinary research can be encouraged. Also, researchers themselves need to take responsibility for thinking outside their own paradigms (Fulop et al., 2003). Additionally, one article underlined the future need for inclusion of organisational analysis in HTA due to demand from policymakers (Battista and Hodge, 1999).

In general, very few articles dealing with assessing the wider impacts of health technologies were identified in this literature review. This shows that there is a lack of research into the methodology of these domains in relation to HTA in general and there still is a need for methodological development. However, the lack of identified research in this literature review might be due to search strategy that only included a search for literature in the database PubMed.

C. Best practice in undertaking HTA

Best practice in undertaking HTA is both related to methodology of HTA, and the reporting of HTA. In total, 11 articles identified in the literature search reported studies on the best practice of HTA. This included studies on harmonization, transparency, inclusion of qualitative data in HTA, and international comparisons of HTA practice. Of these 11 articles, seven articles pointed to areas of further research.

Four studies focused on harmonization and best practice of HTA. Velasco Garrido et al. (2002) developed and disseminated best practice in undertaking and reporting HTA as part of the ECHTA/ECAHI project. They concluded by identifying needs for methodological developments, e.g. methodology for assessing the wider impacts of technologies. Additionally, Drummond et al. (2008b) discussed and proposed a set of fifteen key principles that can be used in assessing existing, or establishing new HTA activities, focusing on HTA activities that were linked to, or included a particular resource allocation decision. They concluded that there were no single way to conduct HTAs that would meet the needs of all decision makers, stakeholders, and societies. However, application of the proposed principles could potentially improve the process as the quality and credibility of HTA would be enhanced. Perleth et al. (2001a) attempted to define ‘best practice’, and proposed a framework for the classification of information on maintaining or improving effectiveness and efficiency in health care systems. They concluded that none of the activities to organize research findings, disciplines, methods, and tools provided an all embracing concept to

maximise value to health, and that each activity had to be supplemented with others. The choice of combination of methods depended on the nature of the problem, the perspective of the decision, and the availability of evidence. Finally, Hutton et al. (2008) reviewed advantages and disadvantages of standardization of evidence requirements for HTA, taking into account the views of multiple stakeholders. They drew on experiences from recent initiatives intended to promote the harmonization of HTA, and experience from related fields. They concluded, that there was considerable uncertainty among stakeholders regarding the benefits of harmonization of HTA, and that a more desirable target might be to be able to justify differences in decisions by reference to evidence, values, and priority, and that transparency is essential.

In addition the EUnetHTA products – mainly the core model – can be seen as a further implementation of the conclusions from the ECHTA/ECAHI project, and contributed to developing a more standardized form for reporting HTA (FinOHTA, 2008; Lampe et al., 2009; Pasternack et al., 2009; Lampe and Pasternack, 2008; Lampe and Mäkelä, 2008).

Two studies focused on the inclusion of qualitative data and methodology in HTA. Leys (2003a) focused on how qualitative research findings could be useful as an additional source of information, or as ‘evidence’, in HTA. He concluded, that qualitative findings could obtain a greater status as ‘evidence’ by improving the knowledge of the nature of qualitative research, if researchers themselves respected methodological prerequisites, and if researchers clarified their theoretical perspectives, research aims, and use of research methods. Additionally, Leys (2003b) illustrated why social scientists and qualitative researchers should contribute more to the HTA debate, and why health care professionals and policy makers could learn from experiences and debates in social sciences, and concluded that the data-driven scientific culture in HTA needed to be broadened by approaches and methods giving insight in data that cannot be quantified easily, such as the wider impacts of technologies.

Three articles reported international comparisons of HTA practice. One article described the time-trends in health technology assessment from 1989 to 2002, and thereby gave an overview of the content of HTA reports, focusing on type of technology, type of assessors, and applied methods. The authors concluded that there were increases in the number of published HTA reports during the time period, but no major developments in the methodology. Also, applied methodology depended on the type of assessors (e.g. outsourcing to external partners) (Draborg and Gyrd-Hansen, 2005). A further article gave an international comparison of the definition and practical application of HTA, and found that generally the HTAs focused on the clinical aspect of health technologies, leaving economic, patient-related, and organisational aspect less analysed (Draborg et al., 2005). Finally, Draborg and Andersen (2006) performed an analysis of the factors that influenced assessment methods in HTA, and found no major developments in the assessment methods between 1989 and 2002.

The studies were mainly undertaken in university settings, and analysed literature, except the international comparisons that applied primary data analysis.

Transparency

As part of the discussion on best practice, a lot of attention has been given to transparency issues – both in relation to use of methods, and to reporting of HTA. An example of this is the INAHTA checklist which promotes different requirements for creating increased transparency in the reporting of HTA (Hailey, 2003).

As the implementation of HTA in EU member states increased, this led to a series of EU funded projects from 1993-2002, including EUR-ASSESS, and the ECHTA/ECAHI. The recommendations of these projects are currently being implemented through the EUnetHTA Project, and include a core model of HTA reports, and an adaption toolkit to expand proper sharing and production of information – including promoting transparency.

Furthermore, two articles identified in the literature search reported studies dealing with issues of transparency. However, several articles dealing with best practice in general had concluding remarks on the importance of transparency, and several articles were debating articles focusing on this subject.

Porzolt et al. (2005) compared two HTA reports on the same topic in order to address issues of transparency, and variations in HTA methods. The authors concluded, that efforts to guarantee transparency in the original studies, and in the HTA reports themselves, needed to be taken, as such lack of transparency may affect policy decisions. Schlander (2008) explored the robustness of NICE assessment methods when addressing a complex clinical problem, and used the evaluation of Attention Deficit/Hyperactivity Disorder (ADHD) treatment strategies as an example of such. He concluded, that NICE assessment of ADHD treatment strategies were incomplete, and likely prone to bias, which may cause implications for the generalizability.

Another article reviewed and discussed the issues associated with standardisation, taking into account the perspectives of multiple stakeholders (Hutton et al., 2008), while two articles debated issues of transparency in NICE technology assessments in the case of drug evaluations (Maynard, 2007; Poole et al., 2007).

Three reports debated and critiqued the lack of transparency in HTA reports in general, and opted for more focus on transparency issues (Sorenson et al., 2007; Sorenson et al., 2008; Kanavos et al., 2009)¹.

Research agenda

9 articles pointed to areas of research in relation to best practice in undertaking and reporting HTA.

In relation to harmonization, the possibility of benefit from harmonization of HTA evidence requirements with those of related decision making processes is worthy of further exploration. In relation to the economic domain, there are potential benefits of more standardization. However, as the wider impacts of HTA are generally under researched, these issues must be considered before the value of harmonization can be considered (Hutton et al., 2008). Also, in relation to the wider impacts Leys' articles addressed how qualitative research findings could be useful as an additional source of information or as 'evidence' in HTA. However, it should be explored how qualitative research could obtain a greater status as 'evidence', and what criteria that should be set for judging the qualitative research, and overall, how qualitative research can be improved, and become more trustworthy (Leys, 2003a; Leys, 2003b). Finally, in relation to best practice, resources should be devoted to increase quality and quantity of both primary and secondary research as well as the establishment of networks to synthesise, disseminate, implement, and monitor 'best practice' (Perleth et al., 2001a).

¹ This work related to the three reports was done with financial support from Pfizer Inc.

In relation to an international comparison of the characteristics of HTA reports that found several variations in how HTA is performed, a future topic for research could be to analyse whether these characteristics affect the influence HTA has on decision making (Draborg et al., 2005).

In relation to transparency, two debating articles concerned the NICE procedure. A current practice, when external assessment groups perform assessments, is that NICE provides the results of an assessment in a read-only version. A general view is that the procedure lacks transparency which is unacceptable to stakeholders (Maynard, 2007; Poole et al., 2007). According to Poole et al. (2007) the cost effectiveness models could be produced by consensus under the joint direction of NICE and industry, reducing costs, and hasten access to health technologies that all agree are good value for money.

5.3.2.2 HTA products

Besides 'classic' HTA reports, where the elements of HTA typically are thoroughly analysed, a variety of different types of HTAs have emerged, typically from the work of HTA agencies. A lot of literature addressed HTA production in general. However, a more limited literature addressed specific 'HTA products' which have been developed to meet the needs of users of HTA.

Studies addressing mini HTA, rapid assessments, and horizon scanning/early warning were identified in the literature. Additionally, Core HTA and an adaptation toolkit for 'translation' of foreign HTA reports has been developed as part of the EUnetHTA Project. These HTA products will be addressed in the following.

A. Horizon scanning/early warning

Health technologies in an early stage of its life cycle sometimes spread rapidly in a health care system despite lack of convincing evidence. Also, new technologies exist, that may be underused, resulting in lack of benefit for patients.

Horizon scanning/early warning is a method evolved from the work of HTA agencies. The International Information Network on New and Emerging Health Technologies (EuroScan) is an international collaboration established in 1999. EuroScan defines the focus of horizon scanning as those technologies that are not yet adopted by the healthcare system, and those that are in the phase of adoption. The purpose of horizon scanning is to provide input to decision making that is timely and relevant.

The members of EuroScan have agreed on a common terminology, classification, and understanding of their activities. Their activities consist of five main components which are the identification and filtering of technologies, prioritization, early assessment, dissemination, and monitoring the assessed technologies.

Nine articles concerning different aspects of horizon scanning were identified. One article provided an overview of processes and practices of horizon scanning, and concluded that EuroScan has played an important role in the harmonization process so that effective collaboration, reduction of duplication, and further development of procedures have become possible. Because of the common understanding, there is a certain stability and integration across the functions of horizon scanning (Wild and Langer, 2008). Another article reported from a workshop that reviewed the achievements and progress of EuroScan, reaffirming the benefits of collaboration (Simpson et al., 2008). Four articles evaluated different aspects of what constitutes proper horizon scanning and/or how horizon scanning could be improved. This includes the use of selection criteria, the sources to search in the

process of identifying technologies, and the effectiveness and accuracy of horizon scanning. (Douw et al., 2003; Simpson et al., 2004; Douw and Vondeling, 2006; Murphy et al., 2007). Douw and Vondeling (2006) found a lack of consistency and transparency in the processes where technologies are selected for assessment, and Douw et al. (2003) found variations between the approaches to the use of the internet as a source of evidence. Finally, Simpson et al. (2004) concluded that the HSS itself has an influence on the impact of a health care technology as helping to control adoption and diffusion is their main purpose. Also, the use of imperfect gold standards may bias results. Two articles explored aspects of adaptation of established programmes to Danish horizon scanning, as part of the establishment of horizon scanning activities in Denmark, and found that a health care perspective should be applied, technologies should be prioritized on the basis of marginal benefits, marginal costs, budget impact, impact on access to care, and additional criteria with an impact on health policy, such as the educational needs, and organisational changes associated with the new technology. A decision to introduce horizon scanning was made based on these findings (Douw et al., 2004; Douw et al., 2006). Finally, one article explored the intra-scientific citation (bibliometric impact) of the Swedish early warning reports (SBU Alerts), and the science base of these reports, and found that publications, used as sources in a SBU Alert, also were highly cited within the scientific community, which increases the appropriateness of using bibliometric indicators in evaluations of clinical research, and suggests that decision makers through SBU Alert are getting scientifically sound advice (Lundberg et al., 2008).

In relation to horizon scanning, EUnetHTA produced a newsletter on new and emerging health technologies for European policy makers in collaboration with EuroScan (Simpson and Wild, 2008). The process was reported in an article, which described the process of producing this newsletter. In conclusion, the dissemination of an EU-wide newsletter would be feasible, but time-consuming. Although a newsletter appeared to fulfil a need for information on emerging and new health technologies, it was not considered the right tool to avoid duplication of effort in the present international constellation of horizon scanning for new health technologies (Wild et al., 2009).

B. Rapid assessment

Rapid assessment is another tool to produce input to decision making in a timely fashion. The rapid assessments are typically carried out by HTA agencies within a timeframe of six months or less. A number of programmes exist. However, they vary in scope and methods. At this point, no common definition and methodology of rapid assessment exists, and the quality of the assessments varies.

The literature review identified only three European articles concerning rapid assessments. One German article compared different rapid assessment programmes with respect to scope, methods, and time to complete assessments, and introduced and discussed a model for processing rapid assessment in the German context. In conclusion, no common definition of “rapid assessment” existed (Perleth et al., 2001b).

Two British articles compared two different types of rapid assessments. However, they were not specifically labelled as such. One study described a method for the rapid appraisal of new interventional procedures that classified requests for funding within 48 hours using a BUPA algorithm, and compared its results with those derived from a slower, more thorough method. They found the outputs derived from the different methods to be similar (Warren, 2007). The other British study compared and contrasted NICE single technology reports, with no comparator, to full HTA reports, and concluded that there remained uncertainty concerning the extent to which single technology assessments adequately address the specific decision problem (Kaltenthaler et al.,

2008).

C. Mini HTA

Mini HTA is a tool mainly used in hospital settings when making decisions about the uptake of new technologies. It typically consists of a form containing a number of questions corresponding to the domains of a thorough HTA. This tool aims at providing input to decision making within few weeks adjusted to the local settings.

Only two articles concerning mini HTA were identified in the literature search. Both studies were Danish studies undertaken by Danish University Hospitals. Both studies evaluated the use of mini HTA, and the attitudes of decision makers towards the tool. The studies revealed that different versions of the tool, and with varying quality, are commonly used in hospital settings in Denmark. However, despite the varying quality of assessments the mini-HTA still had a positive influence on the administration of costs, transparency in decision making, quality of the decision making process, rational prioritization, and increased dialogue between the management level and employees (Ehlers et al., 2006; Folkersen and Pedersen, 2006).

D. Core HTA

Core HTA has been introduced by EUnetHTA and bBuilt on recommendations from previous European HTA projects, EUnetHTA introduced Core HTA as a specific structure for undertaking and reporting HTA. Core HTAs are intended to serve as a basis for local HTA reports. Core HTAs do not contain recommendations on technology use. The main aim was to avoid duplication of HTA reports in Europe since there are many examples of reports on technologies produced synchronically across Europe – and also across the rest of the world.

The core model was reported in five different publications. One model for medical and surgical procedures (Lampe and Mäkelä, 2008), and one for diagnostic technologies Lampe and Pasternack, 2008) was developed. A handbook introducing the model was published (FinOHTA, 2008), and two articles presented the idea behind the core model (Lampe et al., 2009), and the testing of the model during the development phase (Pasternack et al., 2009). These articles concluded, that the HTA Core Model enables effective international production and sharing of HTA results in a structured format, and that the HTA Core Model can be developed into a platform that enables and encourages true HTA collaboration in terms of distribution of work and maximum utilization of a common pool of structured HTA information for national HTA reports. The face validity of the Model was confirmed during the project (Lampe et al., 2009; Pasternack et al., 2009).

An article reporting the work of ECHTA working group 3 was also identified in the literature search. They aimed to identify possible joint assessments, and to coordinate findings and existing resources within the community to support joint assessment. One of the conclusions were, that the informal network among HTA agencies, that had already been collaborating for several years, offered - already in 2002 - an invaluable opportunity for future collaboration at the European level. However, at that time difficulty of project management and inadequate funding were the two most important barriers (Estrada et al., 2002).

E. Adaptation toolkit

EUnetHTA also developed an adaptation toolkit. This product was a further development of an already existing activity among the HTA agencies, which used foreign HTA reports, and 'translated' them into the relevant setting. The aim was to avoid as much duplication of work as possible by

reusing e.g. the systematic review from the foreign report. EUnetHTA worked to structure the activity by publishing a glossary of HTA adaption terms (Rosten et al., 2009; NCCHTA, 2007). Also, the adaptation toolkit itself Chase et al, 2008), and three additional articles, described the development of the toolkit and the glossary (Rosten et al., 2009; Turner et al., 2009a; Turner et al., 2009b).

Research agenda

In relation to HTA products, 13 articles pointed to areas of future research.

In relation to horizon scanning, Simpson et al. (2008) reported the discussions at a EuroScan workshop. Some of the questions that were discussed were if EuroScan should continue to focus on both identification and early assessment, if subgroups focusing on methodological topics and development should be created, if closer collaboration was possible, and the possible benefits of creating a common horizon scanning centre. Even though EuroScan has played an important role in harmonizing horizon scanning activities, and in the establishment of an international network, activities still differ, e.g. in terms of size, resources, and operational level, which results in differences in methodology applied. Especially regarding the priority setting process, which should be made more transparent, e.g. in relation to the sources used (Douw et al., 2003; Douw et al., 2006; Wild and Langer, 2008). Also, the outcomes of horizon scanning activities should be investigated in order to evaluate the accuracy (Simpson et al., 2004). The recent cooperation between EuroScan and EUnetHTA aimed at further development of information sharing. However, even though the aim of wider dissemination of information on new and emerging technologies still remains, the methods for doing this in a way that satisfies intended audiences still need further development. Two options were posed. One would be to investigate the various interests through a consensus method, and the other to pursue EuroScan's earlier idea of developing a core set of early awareness information in a database (Wild et al., 2009).

In relation to rapid assessment, Perleth et al. (2001b) inquired exploration into how the full HTA could be made shorter in order to produce input to decision making in a timely fashion. Today, there is no common definition of this type of HTA product, and the quality and detail vary. Both quality and process should be considered (Kaltenthaler et al., 2008).

The mini-HTA is also a product that varies greatly in quality. The process of evaluation varies, and mini-HTAs are rarely subject to peer review. Further studies exploring the quality of the mini-HTA are needed (Ehlers et al., 2006).

In relation to the ECHTA/ECHAI project, it was concluded that information on the factors, that make joint projects fail, is of key importance when planning future joint assessments, but further collaboration at a European level is recommended (Estrada et al., 2002). The developers of the EUnetHTA Core model stated, that further testing and refining of the model is needed to ensure optimal usefulness and user-friendliness. Also, even though the model is useful, clear scoping and good coordination in timing and distribution of work would help improve applicability, and avoid duplication of work (Lampe et al., 2009; Pasternack et al., 2009).

Finally, the adaption toolkit, also developed by EUnetHTA, is the first of its kind, and future work is required to address quality assurance of the tool (Turner et al., 2009a).

5.3.2.3 Life cycle perspectives of health technologies

Many existing healthcare interventions diffused before the establishment of the current assessment and evaluation procedures. Assessment of ineffective or inappropriately applied practices is growing as a priority for international health policy, both for improved quality of care, and for sustainability of resource allocation.

The literature review identified four articles related to life cycle perspectives. One article introduced a method of constructive medical technology assessment that aim to change the development and diffusion of a medical device to improve its later clinical effectiveness, illustrated by the case of heart assist devices, and concluded that the method is reliable (Hummel et al., 2000a). One article concerned coverage with evidence development (CED) as a specific approach to cover promising new technologies for which the evidence remains uncertain. The aim of the article was to carry forward the debate on the use of CED as well as highlight areas that warrant further research. They concluded that CED might provide a better way forward than current procedures in securing most benefit from existing and emerging health technologies. However, the involvement of patients on CED should be further investigated (Hutton et al., 2007). One article was specifically related to drugs, focusing on how the different paradigms of pharmaceutical regulators and healthcare authorities creates uncertainty for pharmaceutical companies planning their research and development investment, as licensing is no longer a guarantee of market access (McCabe et al., 2008). Finally, one article reviewed the work of NICE in the area of cancer treatments, and how the recommendations have an impact on treatment uptake of new cancer treatments (Summerhayes and Catchpole, 2006).

In addition, EUnetHTA also focused on the life cycle perspective in relation to assessment of technologies, but so far concentrated on the earlier stages of the life cycle by focusing on evidence generation on promising health technologies. A web based toolkit for evidence generation was developed (Quentin et al., 2008). Two articles reported the results (Carbonneil et al., 2009; Quentin et al., 2009). However, the core model encouraged that new technologies should always be compared to existing technologies, and the model can also be used to assess possible obsolete technologies.

Research agenda

Five articles pointed to and debated areas of future research in relation to coverage with evidence development (CED) and disinvestment.

In relation to NICE and CED, it is a general concern how to set the limits of how much uncertainty there should be before a recommendation is issued, that a technology only is to be used in the context of research. It is also a concern whether the focus should be solely on the quality of the evidence, or if the potential budgetary impacts and clinical importance also should be considered. Such decisions should be made transparent (Chalkidou et al., 2007). Also in relation to CED, the involvement of patients in the decision making should be further investigated (Hutton et al., 2007).

In relation to a NICE disinvestment programme, some of the debated issues were the priority setting process, the data availability, and the organisation of such a programme (Pearson and Littlejohns, 2007). Maynard et al. (2004) stated that NHS needs better information from NICE on the equity implications of both new and existing technologies. Walker et al. (2007) stated, as an area to develop research, that disinvestment programmes to help local decision makers is a key step in improving the allocation of NHS resources and removing geographical inequalities.

5.3.2.4 Challenges to HTA methodology

Even though HTA methodology is not one single well-defined entity a degree of common understanding of basic characteristics has been develop over the years. However, the literature review revealed that a number of different themes/topic challenges HTA methodology and require development of the methodology.

In the review 20 articles addressed the different challenges. Two articles address challenges in relation to assessment of public health interventions, and assessment of health promotion/disease prevention, and describes difficulties in relation to lack of evidence and to focus on the broad perspective of optimisation of health rather than on individual clinical care (Dauben et al., 2002; Holland, 2004).

Three articles describe challenges in relation to assessment of information and communication technologies, in particular telemedicine. Myhre (2000) describes the lack of HTA reports concerning telemedicine and the need for assessments of cost-effectiveness in this area. Two articles comment that HTA has set the standards for acceptable facts related to assessment of new technologies and emphasises that literature on evaluation of telemedicine has been developed apart from the HTA environments. Therefore there are normative differences between HTA and evaluation of telemedicine, and there is a need to accept that assessment of telemedicine needs different models than conventional health technologies (Williams et al., 2003). Finally, May et al. (2003) describe two case studies of HTA of telemedicine and points out the normative difficulties related to application of HTA in a field where the technology differ from traditional technologies within healthcare.

Two articles depict issues related to assessment of organisational interventions. The first article points out that the 'classic' HTA report has to need to develop due to customer needs and mentions assessment of organisational impact of technology use as one area, which needs development (Milne et al., 2003). The second article supports this statement and emphasises the demand for assessment of how health services are organised and delivered (Battista, 2006).

Equity issues are raised in two articles which discuss the lack of focus on impact of technology use on health inequities of access and outcome, and the lack of focus on this issue in the HTA methodology (Milne et al., 2003; Williams and Cookson, 2006).

The need for development of methodologies to ensure a stronger social embedding of HTA practices are studied in one article. Webster argues that HTA needs to become more open to alternative sources of information and expertise in order to ensure embedding of HTA practices in wider society. The article points out that this exercise would strengthen policy-making, but also the science and methodology of HTA itself, because HTA would become more reliable and socially resilient (Webster, 2004).

Two articles discuss the need to improve methodology to be able to assess fast evolving technologies or technologies in development. Two studies present the methodology of 'constructive technology assessment' - an approach which take the dynamics of technology development into account - as a complementary approach to traditional HTA (Hummel et al., 2000b; Douma et al., 2007).

Seven different articles document challenges in relation to specific types of technologies or situations. Drummond et al. (2007) illustrate challenges in relation to orphan drugs, where the market is small and the drugs often expensive. Typically the drugs cannot prove to be cost-effective under the standard methods of HTA, and therefore adequacy of standard HTA methods is

discussed. Similar issues are raised in relation to expensive cancer drugs which have proven to be effective, but not cost-effective (Waugh, 2006). Two articles concern assessment of medical devices. One article emphasises a number of methodological considerations, e.g. timing of assessment, and selection of patient population, and states that HTA can be useful if it takes the specifics of the technology into consideration, if the process is appropriate and fair, and if the HTA is done under full participation of industry (Siebert et al., 2002)². The other article examines EU and member state regulation of medical devices including HTA growing role as a tool for market approval (Altenstetter, 2003). Malone and Maceneaney (2000) examine the need for a simplified model for assessment and a phased evaluation of interventional radiology to overcome the lack of RCT's in early stages of technologies. Photodynamic therapy is discussed as a case of a technology which is introduced in NHS prior to full evaluation. The role of NICE in the process is examined, and the article shows challenges for HTA in relation to playing a part in decision-making related to technologies that are introduced in daily practices within healthcare without thorough assessment (Foot et al., 2004). The last article describes the current state of evaluation of health interventions in EU (including HTA) in 2003 and describes different methodological challenges, e.g. the need to expand the methodology to include assessment of the wider impacts of technology use, and the need to consider broader dimensions such as comparative effectiveness (McDaid et al., 2003).

Finally one article briefly examines the need to focus on impact on patients related to technology use (Milne et al., 2003).

Research agenda

The areas that are included in description of the future research agenda is closely linked to the existing research since many of the articles examined above aim to identify and discuss challenges rather than to come up with concrete solutions. However, seven articles more specifically point to and debate areas of future research in relation to challenges to the HTA methodology.

In the area of public health interventions, it is recommended that HTA agencies need to pay more attention to disease prevention and health promotion in their assessment activities, and to consider strategies addressed to broader communities such as community prevention and action related to health promotion. Also assessment methods in this area need to be broadened to include side effects, cost-effectiveness, and ethical and social implications. More HTAs need to be done (Dauben et al., 2002). Methods should include assessment of health status rather than only clinical services (Holland, 2004).

In relation to equity more research is needed into methods for managing equity-efficiency trade offs, in particular in relation to wider public health interventions (Williams and Cookson, 2006).

Concerning assessment of medical devices it is emphasised that development needs to take place in relation to harmonisation of requirements for the information to be submitted and the procedures applied in HTA in Europe (Siebert et al., 2002)¹. Concerning assessment of e.g. orphan drugs more research is required into the methods of assessing the societal value of health technologies (Drummond et al., 2007)

Two articles take a broader look at HTA and give an overall assessment of needs for research in relation to HTA methodology. One article states that many challenges await the further development

² Authors of this article are experts from medical device industry. The article is based on debates with an HTA expert group.

of HTA. In relation to HTA methodology two areas are emphasised – adaptation of HTA to an evolving analysis object, e.g. fast evolving technologies and information and communication technologies, and assessment of how health services are organised and delivered (Battista, 2006). The other article underlines the need for research concerning ways of measuring and summarising evidence about patient impact, organisational impact and the impact of equity of new technologies (Milne et al., 2003).

5.3.2.5 Development of HTA capacity and HTA programmes

An always important issue for the HTA community is to build capacity, and develop existing programmes, to ensure sustainability of HTA in Europe. Related themes are 1) how to ensure that an HTA programme prioritises assessment of the right technologies to ensure as much benefit of HTA as possible, and 2) how to improve the links between policy and HTA to improve the impact of HTA.

A. HTA capacity

Internationally there is a growth in HTA activities. However, despite this growth, many European countries have none or only limited HTA capacity, especially low and middle income countries.

There are several obstacles to the introduction of HTA. In many countries, there is a general lack of awareness of HTA, and the manpower to conduct assessments is insufficient. Hence, an important aspect of capacity building is the establishment of educational programmes to promote training and knowledge in HTA. Moreover, data availability in many countries is low and the quality and validity of morbidity and mortality data is questionable. For these reasons, HTA-developing countries are usually dependent on studies carried out in other countries. However, while some data might be transferable to some extent, such as clinical data, other data, such as resource utilization, costs, cost-effectiveness data, prices, ability, and willingness to pay, vary from country to country.

These issues are particularly relevant due to the recent uptake of several new member countries in the European Union. The literature review revealed, that some efforts, European and international, are undertaken in areas of capacity building. Furthermore, one of the main goals of the EUnetHTA Collaboration is to increase transparency and transferability of HTAs.

The literature review revealed that European initiatives of capacity building are undertaken in the case of Romania (Corabian et al., 2005) and Estonia (Gibis et al., 2001). In Romania, an initiative group was mentored by representatives from a Canadian HTA agency, assisting in the promotion of HTA. However, they found that success in implementing a programme depend on essential factors such as local political, economical, and educational support for the initiative (Corabian et al., 2005). In Estonia a SWOT analysis was performed to identify the strengths, weaknesses, opportunities, and threats to introducing a HTA programme. Also, in this case, they found that the future shaping of HTA depends on the local environment, and that further assessment is necessary in the future (Gibis et al., 2001).

EUnetHTA published a handbook on capacity building to support the development of HTA in Europe. The handbook aims to provide practical guidance on how to establish HTA in countries with limited capacity (Moharra, 2008b). Also, in this work, it was concluded, that setting up organisational structures and establishing effective HTA programmes that guide key policy decisions is a challenging task, and that there are no standard models or pathways (Moharra et al., 2009).

As a part of the ECHTA/ECHAI project, Working Group 5 provided an overview of current HTA education and training programmes in Europe, revealing that education programmes are limited in the EU12 countries. Additionally, the working group developed a curriculum of a European Master of science in HTA (Antes et al., 2002). Likewise, the Ulysses Program, a training programme developed in corporation between Canadian, Spanish, and Italian HTA agencies, aimed at evaluators who will produce HTA and decision makers who will use HTA. They concluded that because there is a growing need for human resources with special training in HTA, further efforts need to be devoted to strengthening the international research capacity in HTA (Lehoux et al., 2005).

B. HTA programmes

The description and analysis of different organisational aspects of HTA programmes also seem to be of increasing interest. The particular organisational features of the body producing HTA reports may influence the diffusion of knowledge, and the effect of those activities on policy making.

The literature search revealed two European articles concerned with the performance and description of HTA programmes. One article focused on the differences and similarities of HTA agencies, and found that governmental agencies had a profound impact on the prescriptiveness of their assessment (Martelli et al., 2007). The other article discussed the challenges facing HTA in Europe, and found that the primary concerns of European health care policy makers were expenditure control or cost containment, efficiency, and equity (Cookson and Maynard, 2000).

Also, EUnetHTA published a survey on characteristics of existing HTA organisations to provide information on how to develop vigorous HTA organisations in Europe. The survey revealed that HTA organisations had not changed significantly in the past ten years. Also, common aspects and barriers were experienced by HTA agencies regardless of their geographical setting and years of experience. Finally, networking among HTA organisations play an important role in development and sharing of HTA activities (Moharra et al., 2008a).

As part of the ECHTA/ECHAI project, a system for routine exchange of information concerning ongoing or planned evaluation, and their findings, priority setting, and emerging technologies, was developed (Hagenfeldt et al., 2002). Additionally, EUnetHTA explored the state of development in relation to information sharing, finding that most HTA agencies had professionals dedicated to information management (Kubesch et al., 2008), and further developed a programme for effective international and external communication of an international network (Neikter et al., 2009).

C. Priority setting

The resources for HTA within existing HTA programmes fall short of that needed to evaluate all health care technologies. For resources to be used cost effectively, priorities are set by the HTA agencies concerning which technologies to assess. Several methods exist to make this prioritization, and some are more transparent and systematic than others. Different HTA agencies apply different methods for priority setting.

In total seven articles concerning different aspects of priority setting were identified in the literature search dealing with both the evaluation of applied methods, and development of new methods.

Two articles evaluated the methodology of two priority setting approaches in UK, and the Netherlands respectively (Oortwijn et al., 2002; Shepherd et al., 2007). Shepherd et al. (2007)

evaluated a speciality mapping approach that was based on the principles of a systematic review, and included a stakeholder model. They found that specialty mapping could make a positive contribution to the policy agenda, with several research and policy gaps being fed into existing prioritization channels. However, adequate time, resources, and capacity are required, particularly in engaging stakeholders and developing a care pathway. Oortwijn et al. (2002) illustrated the application of theoretical principles to priority in The Netherlands to an alternative process. The procedure consisted of three steps, choosing, rating, and weighing criteria, and they found that the procedure could be further developed.

One article described and evaluated the relative importance of the different sources used for priority setting by the NHS HTA programme. They found that the largest source for setting priorities was widespread consultation that also had a low success rate. The second largest source was systematic reviews that had the best success rate (Chase et al., 2000). Another study developed an economic prioritization model for ex ante evaluation of HTA to assist those involved in the selection and prioritization of HTA topics, using decision analytic techniques, also applied to the NHS HTA programme. The main conclusion was that ex ante assessments of the value for money were feasible. However, substantial work was required to ensure that valid reliable, consistent, methods were used, to ensure efficient use of valuable research time (Davies et al., 2000). Additionally, two of the references were reports from the NHS HTA programme. One report demonstrated the benefits of applying decision theory and value of information analysis (DA-VOI) to inform a prioritization process of the NHS HTA programme. They showed that the method could be applied even within short timelines (Claxton et al., 2004). The other report developed a method (PATHS) for economic evaluation at the stage of research prioritization, and concluded that the model had a useful part to play in the research prioritising process alongside existing criteria (Townsend et al., 2003). Finally, one article reported the work of the ECHTA/ECHAI project that developed a system for routine sharing of information in HTA, partly to assist HTA programmes in the process of setting priorities. However, they found that because of the various contexts in which HTAs were undertaken, no single procedure could be recommended (Hagenfeldt et al., 2002).

Research agenda

17 articles pointed to future areas of research in relation to the development of HTA capacity and HTA programmes.

Debating the challenges that face HTA in Europe, Cookson and Maynard (2000) outlined two policy challenges that are particularly pressing. First there is the need to broaden the focus of HTA beyond clinical technologies and toward the wider “technologies” for organisation and delivery of care, and second there is the need to start evaluating the implications of health technologies for equity and inequality as national governments realign policy toward equity goals.

In relation to capacity building, further research is needed in the area of transferability of assessments to provide immediate help to decision makers. Often crude economic models are not available in countries with limited resources, and in many cases the cost effectiveness might actually be lower in these countries affecting the transferability of results. Furthermore, the requirements for reimbursement should be more simple and realistic, as well as more straightforward and strict, as these are major obstacles for decision makers (Gibis et al., 2001; Gulacsi et al., 2004; Gulacsi, 2007). In relation to HTA programmes Martelli et al. (2007) claimed that further assessment of the impact of HTA on policies and technology diffusion is an interesting issue. Also, strong HTA networks do exist, but there is still a need to strengthen the link to policy,

especially taking into account the countries with limited resources and experience in HTA. These issues should become a shared responsibility between HTA producers and the various types of users. A recommendation from the ECHTA/ECHAI project was on Clearinghouse activities, providing functions related to the exchange of information on ongoing HTA projects, HTA results, and functions related to priority setting for HTA, claiming that added value can be achieved by comparative research among countries, and by bringing together a wide variety of different national methodological approaches (Hagenfeldt et al., 2002). The EUnetHTA Project state, that better coordination and communication among HTA programmes is needed. Collaboration is especially important for countries without institutionalized HTA programmes, and particular support for introducing formal HTA should be dedicated to Eastern and Central Europe to address the growing interest in HTA. Furthermore, collaboration could help overcome resistance to barriers such as training staff (Moharra et al., 2008b; Moharra et al., 2009). In relation to the development of education and training programmes in HTA, the overall research capacity should be increased in this area. Also, in developing such programmes, attention should be paid to the collaborative processes both between research disciplines, HTA institutions, and EU countries (Antes et al., 2002; Lehoux et al., 2005; Moharra et al., 2009).

In relation to information units in HTA programmes, further research should be undertaken to generate more detailed information on the organisation on which the information unit is situated, in order to get a more complete picture of the context and scope of work in HTA information units (Kubesch et al., 2008).

In relation to priority setting, the literature revealed need for further development of the different methods presented. Generally, the methods should be further refined, their constructs validated, the impact of different ways of defining weighing factors, and their impact on the final priorities, should be evaluated, and the methods should be valued across a variety of topic areas (Oortwijn et al., 2002; Townsend et al., 2003; Claxton et al., 2004; Shepherd et al., 2007). Further research is also needed to determine why some sources of information contribute more to the priority setting process than others. Finally, research is needed into the actually established procedures of different HTA programmes (Chase et al., 2000). There is also a need to compare ex ante and immediate ex post assessment of implementation with long term follow up of actual implementation (Townsend et al., 2003). In relation, Davies et al. (2000) claimed that the value of providing decision makers with quantitative estimates of pay back of HTAs needs to be compared with softer qualitative approaches to prioritization of research portfolios for HTA projects.

5.3.2.6 Policy-HTA links

Studies found within this area address two different themes. On part of the literature concern broad issues in relation to policy processes where HTA is involved. The other more specifically concern stakeholder involvement in HTA processes.

A links between policy and HTA

The development of links between policy-making and HTA has been a built-in theme in relation to HTA since the first HTAs were produced in the 1970ties. This was a result of the fact that HTA was 'invented' to give input to policy-making at different levels. Thus, development of and research in the policy loop - 'policy-HTA-policy' - is an important theme since the utilisation of HTA is necessary to justify the use of resources on production of HTA. In short... if policy-makers do not see the benefit of HTA, and find it useful when making decisions, HTA is not viable. Therefore, researchers and HTA institutions has shown a growing interest in developing HTA so that it is useful to policy-

makers, and in documenting the impact of HTA on policy-making.

44 contributions (articles, reports, and one book) were identified which deal with the links between policy and HTA.

A total number of 11 publications addressed the policy-HTA links in a UK setting. In one comprehensive report, the impact of the NHS HTA programme was assessed (Hanney et al., 2007). The overall conclusions were that the programme has had considerable impact on knowledge generation, perceived impact on policy, and to some extent on practice. One article evaluated the impact of a technology appraisal process in the South and West Development and Evaluation Committee by measuring awareness, influence, and quality of reports among clinical and managerial staff, and concluded that the process was perceived to have an impact on policy decisions among the staff. However, impact on practice could not be identified with routine data (Dixon et al., 2003). Another article debated the use of evidence (mainly economic evidence) in the development of local health policies, and based their conclusions on an in-depth study of Health Improvement programmes in England. The questionnaire based study concluded, that the main ways of increasing the use of evidence were to produce more evidence-based national guidance, and to disseminate summaries to local decision makers (Weatherly et al., 2002). In addition to these three publications, a total of eight articles analysed the policy-HTA links specifically in relation to NICE processes. Two articles analysed the implementation and impact of NICE guidance. One looked at impact on GP prescribing and found only little impact unless the guidance coincided with information from other sources (Wathen and Dean, 2004). The other studied the extent and pattern of implementation, using multiple methods, and concluded that implementation of the guidance has been variable. However, guidance was more likely to be implemented when there was strong professional support, a strong, stable evidence base, no increased or unfunded costs in organisations with good systems for tracking guidance implementation, and where the professionals involved was not isolated (Sheldon et al., 2004). Two articles discussed the general procedures of NICE (Buxton, 2001; Paul and Trueman, 2001), while two other articles analysed the use of cost-effectiveness analysis/economic appraisal, and discusses the consequences for the use of NICE appraisals (Towse and Pritchard, 2002; Williams et al., 2007). One examined concerns from patient groups in relation to NICE decision-making processes (Devlin et al., 2003), and finally did one article analyse NICE's use of cost effectiveness as an exemplar of a deliberative process which include both scientific context-free evidence about the general clinical potential of a technology, scientific context-sensitive evidence about particular evidence in realistic scenarios, and colloquial evidence to a context, and to supply the best evidence short of scientific evidence to fill in any relevant gaps (Culyer, 2006)

A series of articles analysed HTA, and its influence on health-care priority setting, based on case studies in England/Wales, France, the Netherlands, and Sweden (Berg et al., 2004; Carlsson, 2004; Orvain et al., 2004; Stevens and Milne, 2004). The overall conclusion on this 2004 overview was that translating HTA into policy is a highly complex business, and that its influence on policy making remains marginal (Oliver et al., 2004).

Two articles investigated the usefulness and impact of HTA in hospital settings in France and Italy, and the French article concluded positively that HTA has had significant impact on the implementation of technologies (Bodeau-Livinec et al., 2006; Lettieri et al., 2008).

Six different articles addressed the questions of impact (Britton and Jonsson, 2002; Oortwijn et al.,

2008), priority setting for adoption of health technologies (Shani et al., 2000), integration of HTA recommendations into organisational and clinical practice (Gagnon et al., 2006), needs of decision makers (Andradas et al., 2008), and lessons learnt from a user perspective in relation to a HTA programme. These studies took place in different European countries.

Furthermore seven articles investigated different themes in relation to the policy-HTA-link (Drummond and Weatherly, 2000; van der Wilt et al., 2004; Hutton et al., 2006; May, 2006; Packer et al., 2006; Moret-Hartman et al., 2007; Hartz and John, 2008).

A series of articles, letters, and replies debated the links between policy and HTA by focusing on why HTA reports building on the same methods and material in relation to PET in oncology led to different conclusions and policy decisions (Højgaard, 2003; Van Tinteren et al., 2003; Kristensen et al., 2004). Further the authors discussed the requirement for documentation in relation to future HTAs of diagnostic methods.

Finally, EUnetHTA published a book containing eight separate chapters analysing the policy-HTA-links in Europe. This included reviews of e.g. the impact of HTA on policy-making, the needs and demands of policy-makers, and an overview of the producers of HTA in Europe (Velasco Garrido et al., 2008).

B Stakeholder involvement in HTA

Five European articles concerned stakeholder involvement in HTA processes. Two articles specifically focused on the involvement of consumers. One article gave an overview of consumer involvement in processes of INAHTA member organisations (Hailey and Nordwall, 2006), while the other described consumer involvement in the NHS HTA programme (Royle and Oliver, 2004). Both articles described current status of involvement, and particularly the second article emphasized the need for explicit, inclusive, and reproducible methods for supporting consumer involvement. The same theme was dealt with in a Canadian article which identified what consumer organisations considered meaningful involvement, what the current practices in Canadian HTA processes were, and developed a model for involvement based on priorities and needs (Pivik et al., 2004). Two articles analysed stakeholder involvement more generally in NICE processes (Culyer, 2005; Milewa, 2008). The articles analysed the processes where NICE was created, and discusses the unique way of involving stakeholders, but also concluded that there is a need for more flexible approaches to stakeholder involvement in order to ensure legitimate and transparent processes. Two Canadian articles also analysed stakeholder involvement – one as a means to improve the impact of HTA (McGregor and Brophy, 2005), and one in involving the values and judgements of stakeholders in policy coverage decisions (Abelson et al., 2007). The final article described the processes developed in the EUnetHTA Project with the purpose of involving stakeholders in the further development of European collaboration in relation to HTA. The article focused on stakeholder involvement in common processes across a large number of HTA institutions, and included European umbrella organisations in the development of a stakeholder policy (Palmhøj Nielsen et al., 2009).

Research agenda

20 articles and 1 book pointed to future areas of research in relation to the links between policy and HTA. 19 of those deal with issues in relation to links between policy and HTA, e.g. impact of HTA on policy decisions, while 2 articles concern stakeholder involvement in HTA.

Concerning the links between policy and HTA four articles just briefly comments on future research needs. Oortwijn et al. (2008) state that there is a need for routinely evaluation of the impact of HTA and at the same time the methodology for this should be further developed. Maynard and McDaid (2003) points out the need for research concerning dissemination and implementation mechanisms in general, and Drummond and Weatherly (2000) state that research is required into several aspects of implementation. Finally Dixon et al. (2003) emphasises that more work is required in relation to looking at the impact of assessment and this research need to address the process of producing and implementing the evidence.

Other articles go into more detail. In 4 articles the impact of HTA is assessed in different settings in United Kingdom, and the articles all emphasises specific research needs. Hanney et al. (2007) state that further research should cover more detailed comprehensive case studies, as well as enhancement of a specific framework to assess the impact of HTA (the payback framework). Also it would be valuable to establish a project that collate health research impact studies in an ongoing matter and analyse them in a consistent fashion. Farmer and Chesson (2001) emphasis that it is important to evaluate the impact of HTA agencies, and this has to be done pragmatically rather than outcome based. Weatherly et al. (2002) point out that more efforts should be placed on understanding how local health policies affect cost-effectiveness and the ways in which local decision makers can better interpret economic study results in their own circumstances. Sheldon et al. (2004) analysed the evidence of implementation of NICE guidance in the early period and state that it would be interesting to see whether the results have changed due to the attention that NICE is giving to implementation. In general more research is demanded to understand the professional and organisational response to evidence based guidance and the relative contribution of various implementation strategies to practice patterns need to be evaluated.

One article analyse impact of HTA recommendations on organisational and clinical practice in Catalonia and concludes more generally that studies of the impact of HTA recommendations are needed to extend the validation of the framework used in the article and to develop an integrated method to assess the HTA adoption into practice (Gagnon et al., 2006). Another article looks at priority setting for the adoption of technologies in Israel and concludes that frequent assessment of previous decisions according to new clinical or economic data is important to have dynamic, efficient and transparent processes (Shani et al., 2000)

An article evaluates the connections between HTA and budgeting at hospital level, and concludes that further research is needed to understand the possible level of integration between HTA processes and budgeting processes (Lettieri et al., 2008).

Three articles concern relations between HTA and Industry (including reimbursement systems). Lothgren and Ratcliffe (2004) describes that HTA agencies are very much focused on assessment of pharmaceuticals and call for research that examines the marginal return of investment on HTA that arise from focusing so much on pharmaceuticals compared with non-pharmaceuticals. Schubert (2002) sees it as an important area to study the problem of demonstrating cost-effectiveness of a product before it is available for use and to introduce conditional reimbursement to allow for collection of real world evidence. This research could contribute to a better collaboration between HTA agencies and industry and improve transparency in assessment processes. Finally Hutton et al. (2006) develop a framework and classifies reimbursement systems in relation to health technologies. In that relation it is necessary to gain more experience with the framework and with finding a formal basis for comparison of reimbursement systems, and their

appropriateness for particular decision contexts.

Four articles and one book either analyses links between policy and HTA at a European level or as comparative studies including several European countries. Banta (2001) looks at the links between HTA and policies in the area of screening and concludes that it is necessary for HTA at European level to systematically develop and share information on assessment of screening to be able to give input to policy-makers in this field. Packer et al. (2006) studies international diffusion of technologies and concludes that producers of HTA need more knowledge concerning the usefulness of tools available to policy makers to control how diffusion of technologies operates. Oliver et al. (2004) investigate HTA's influence on priority setting in four European countries and concludes that HTA is not able to meet expectations from policy makers in relation to incorporating the necessary broad perspectives (e.g social, equity, and ethical considerations), and that HTA methodology therefore has to be developed. The report from the European HTA project, ECHTA/ECHAI, concerning HTA in policy and practice emphasises that there is a need for documentation of impact. Further, research in the organisation of European healthcare systems is needed, particularly with respect to their decision making structures (von Below et al., 2002). Building on these recommendations EUnetHTA published a book concerning HTA and policy-making in Europe including several studies of the theoretical links between policy and HTA: impact of HTA; links between health systems, health policy, and HTA; needs and demands of policy makers etc. All chapters address questions concerning research needs, and the general conclusion is that much more solid, theory based, comparative research is needed in relation to impact of HTA, decision making structures in different countries, the consequences of different ways of organising HTA organisations etc. (Velasco Garrido et al., 2008).

Only two articles focus on research needs in relation to stakeholder involvement. Coulter (2004) emphasises that a systematic attempt to engage the views of citizens is needed and research could contribute to finding ways of balancing interest groups. An article which reports experiences from the EUnetHTA project agrees and states that continued attention should be given to acquiring wide stakeholder representation to ensure balance between different stakeholder groups, and more research is needed to find ways of balancing stakeholder input into HTA processes (Palmhøj Nielsen et al., 2009).

These research issues illustrates a huge need for detailed studies of different aspects of links between policy and HTA and general policy processes in Europe where HTA is used as input. However, the research needs describes above also illustrates that studies of policy and HTA in different setting or in relation to specific technologies often results in research demands described in other parts of this chapter. Different methodological challenges and content of HTA reports are often core questions in relations between HTA producers and policy makers, and therefore the identified research needs are broader than just policy related research questions.

5.3.3 Online survey – research agenda

As part of the HSR-Europe project, an online survey was carried out to assess the HSR priorities of experts across Europe. In total, 34 European stakeholders (including 24 researchers and 7 decision-makers) shared views on HTA. The three areas most frequently given priority were the relationship between HTA and policy- and decision-making (71%), the impact of HTA (62 %) and incorporating consumer and patient aspects in HTA (50 %) (Figure 5.8). These priorities corresponded to the main research priorities of the European researchers. However, the seven European decision-makers in this survey stated that the relationship between HTA and innovation

processes is their main research priority (42%), and the relationship between HTA and policy- and decision-making was among the areas these decision-makers gave lowest priority (14%).

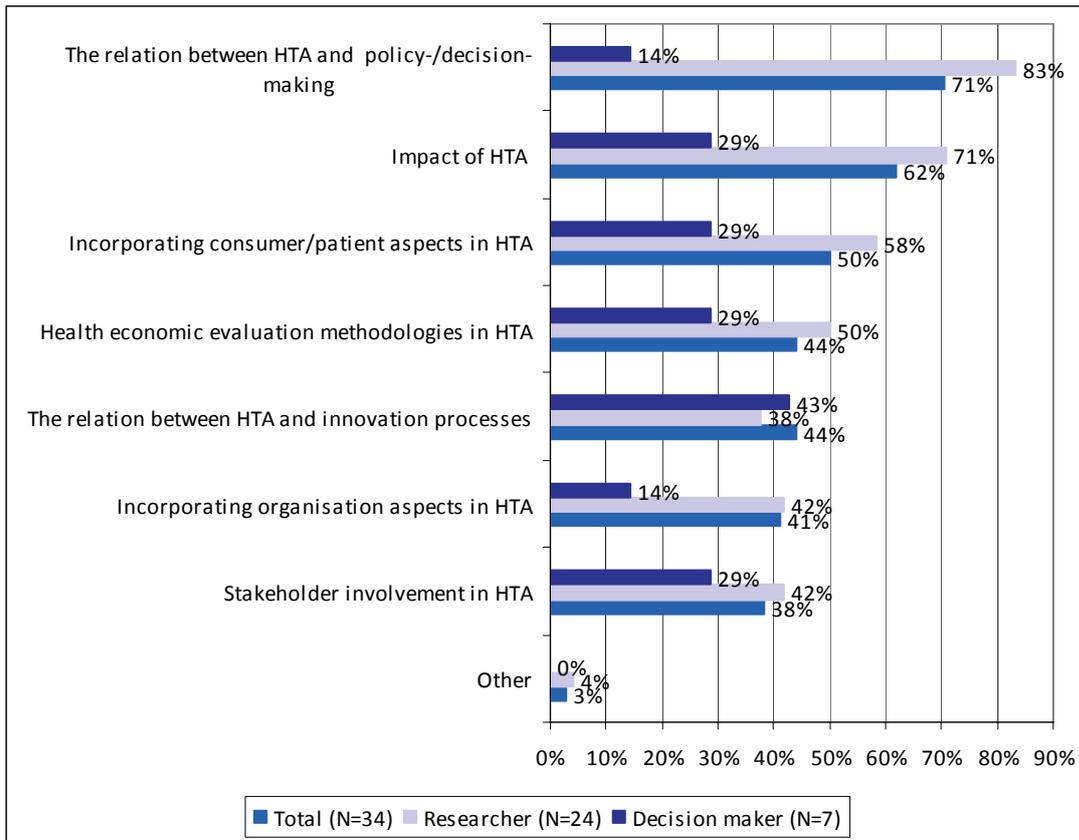


Figure 5.8 Future research agenda for health technology assessment

The research priorities emphasised in this survey correspond very well with the research needs found in the literature review. The articles included in the review addressed several research needs related to the six themes presented above.

5.4 A research agenda for the future

This chapter shows that HSR in relation to HTA can be categorised into six broad themes: (1) the content of analysis in HTA (such as analysis of economy, organisation, ethics, legal aspects and social aspects), (2) the HTA products developed to adequately meet the needs of policy-makers (such as early warning and horizon scanning, rapid assessment, mini-HTA and core HTA), (3) life-cycle perspectives in relation to analysis of technology use, (4) themes and topics that challenge existing HTA methods and for which HTA should be developed to be able to address the themes more comprehensively in the future (such as public health interventions and information and communication technologies), (5) development of HTA capacity and of HTA programmes and (6) links between policy and HTA.

The future research agenda for HSR in relation HTA can be categorised into the same areas and the main areas where more research are demanded are summarised below:

In relation to economic evaluation as part of HTA, the research needs called for in the literature generally reflected the fact that there is no current agreement on the best practices in economic evaluation. For example, it should be further explored how benefits should be measured, how health-related quality of life should be described and valued and how quality-adjusted life-years should be aggregated and whether this is an appropriate measure (Brazier, 2008). Further, the appropriate methods for measuring and valuating preferences, future costs and resources are still disagreed on (Ratcliffe and Longworth, 2002). Several research needs were also addressed in relation to modelling, such as appropriate modelling techniques, how to identify appropriate evidence and how to incorporate expert knowledge (Cooper et al., 2007). In conclusion, despite major research activity on economic evaluation in HTA, there is disagreement on the best practices in undertaking and reporting economic evaluation in HTA. In addition, when new methods are identified, the researchers call for empirical testing and further development of these methods.

The general disagreement on the most appropriate methods to apply in economic evaluation in HTA might reflect an essential issue of HTA: that decision-makers have different needs. Variety in the research questions posed therefore requires different methods. The health technologies that have been assessed are at different stages of the life cycle. The availability of data therefore varies, which might also require different approaches. These issues are reflected in the fact that major issues discussed in the literature are also related to international standards and guidelines. Jönsson questions the entire purpose of using international standards in economic guidelines (Jonsson, 2008), and von der Schulenburg questions whether setting international standards for economic evaluation is even possible (von der Schulenburg et al., 2007). One point is that international standards need to be continually developed as methods develop (Jonsson, 2006). However, the literature generally reflects a call for transparency, which is a major goal for guidelines.

In relation to assessment of the wider effects aspects of HTA, the fact that very few articles deal with these aspects reflects a need for primary research into the organizational, social, legal and ethical effects of using health technologies. HTA methods also need to be developed to ensure that these aspects are included. In relation to ethics, it should be explored whether agreeing on common standards and developing methodological guidelines for including the ethical aspects are possible. However, a major question is whether ethics should be a separate domain of HTA or be incorporated into all domains (Hofmann, 2008). In relation to organisational aspects, numerous disciplines and methods need to be considered in developing HTA methods, such as sociology, organisational studies, policy analysis, economics and history. In the literature review it is concluded that a major obstacle is that researchers from the various disciplines who can contribute to assessing organisational aspects operate in different paradigms both within and between theoretical approaches. It should therefore be explored how multidisciplinary research can be encouraged. Further, researchers themselves need to take responsibility for thinking outside their own paradigms (Fulop et al., 2003). To include qualitative research as a source of evidence, it should be explored how qualitative research could be placed higher in the hierarchy of evidence, what criteria should be set for judging the qualitative research and, overall, how qualitative research can be improved and become more trustworthy (Leys, 2003b). The latter could be viewed as a call for a bridge between the qualitative and quantitative research paradigms, a topic which is both addressed in the literature review and discussed at the carousel rounds on HTA at the working conference. The review calls for including social and legal aspects in HTA, but the literature discusses the needs in these areas

less extensively. In conclusion, there is a general call for primary studies and methods of assessing the wider effects of HTA. Increased effort is needed to bridge the research paradigms contributing to HTA.

In relation to the best practices in undertaking and reporting HTA, the possible benefits from harmonising HTA evidence seem to be the potential benefits of more standardisation. However, as the wider effects of HTA are generally underresearched and often more context-specific, the value of harmonisation must be more carefully considered (Hutton et al., 2008). In relation to best practices, resources should be devoted to increasing the quality and quantity of both primary and secondary research and establishing networks to synthesise, disseminate, implement and monitor best practices (Perleth et al., 2001a).

Several HTA products have been developed to meet the needs of policy-makers: Horizon scanning, rapid assessment, mini-HTA, Core HTA and an adaptation toolkit. The efforts of EuroScan have generally resulted in common agreement on the definitions of horizon scanning. Further effort could be focused on methodological topics and more close collaboration (Simpson et al., 2008). Future effort should be given to the priority-setting process, which should be more transparent in relation to the sources used (Douw and Vondeling, 2006). The recent cooperation between EuroScan and EUnetHTA aimed at further developing information-sharing. However, even though the aim of more broadly disseminating information on new and emerging technologies remains, the methods for doing this that would satisfy the intended audiences still need to be developed further. Two options were posed. One would be to investigate the various interests through a consensus method, and the other would be to pursue EuroScan's earlier idea of developing a core set of early awareness information in a database (Wild et al., 2009). In relation to both rapid assessment and mini-HTA, the literature review revealed that both the quality and the process of the two methods should be explored further (Perleth et al., 2001b; Ehlers et al., 2006).

Further collaboration and sharing of information is continually required at the European level. EUnetHTA represents the major effort so far. The developers of the EUnetHTA core model state that further testing and refining are needed to ensure the optimal usefulness and user-friendliness of the product. In addition, even though the model is useful, clear scoping and good coordination in the timing and distribution of work would help improve the applicability and avoid duplication of work (Lampe et al., 2009; Pasternack et al., 2009). The adaptation toolkit, being the first of its kind, requires future work to address quality assurance (Turner et al., 2009a).

The life-cycle perspectives of technologies are related to both coverage with evidence development and disinvestment (assessing established technologies). The call for further research in this area mainly concerned how to set the limits of how much uncertainty there should be before issuing a recommendation that a technology only be used in research. It is also a concern whether the focus should be solely on the quality of the evidence or whether the potential budgetary effects and clinical importance should be considered (Chalkidou et al., 2007). In relation to disinvestment, some of the major issues that are debated are the priority-setting process, the data availability and the organisation of such a programme (Pearson and Littlejohns, 2007).

Assessing technologies that challenge HTA methods also requires more research in relation to assessing complex technologies, such as public health interventions, organizational interventions and rapidly evolving technologies. First, more experience needs to be gained in relation to broad assessment of these technologies, but HTA methods also need to be developed to include the

experiences obtained.

Further research is also needed on the development of HTA capacity and HTA programmes. In relation to capacity-building, further research is needed on the transferability of assessments to provide immediate help to decision-makers. The literature review shows that crude economic models are often not available in countries with limited resources, and in many cases the cost-effectiveness might actually be lower in these countries, affecting the transferability of results. Further, the requirements for reimbursement should be simpler and more realistic, straightforward and strict, as this is a major obstacle for decision-makers (Gulacsi et al., 2004). Strong HTA networks do exist, but the link to policy still needs to be strengthened, especially considering the countries with limited resources and experience in HTA. These issues should become a shared responsibility between HTA producers and the various types of users (Martelli et al., 2007). An article showed that better coordination and communication are needed among HTA programmes. Collaboration is especially important for countries without institutionalised HTA programmes, and particular support for introducing formal HTA should be dedicated to eastern and central Europe to address the growing interest in HTA. Further, collaboration could help to overcome the resistance to barriers such as staff training. The overall research capacity should be increased in the development of education and training programmes in HTA. In developing such programmes, attention should be paid to the collaborative processes between research disciplines, HTA institutions and EU countries (Moharra et al., 2009).

The literature review shows that research on the links between policy and HTA needs to be strengthened in four different areas. First, using HTA in policy-making needs to be explored in much more detail – preferably in comparative studies to provide more knowledge on the characteristics of policy-making processes in European countries. The impact of HTA on policy and practice also needs to be studied to provide more insight into the conditions for disseminating and using HTA. Good practices for involving stakeholders and an overview of European practices for involving stakeholders need to be obtained to improve the legitimacy of HTA as part of policy-making processes and, finally, knowledge on HTA as a tool for changing the clinical practices of various categories of specialists is requested to gain insight into the practices of behavioural change within various specialities (Velasco Garrido et al., 2008).

A last area in which a need for research is identified concerns comparative and relative effectiveness. This topic was not prominent in the literature review but is a growing activity within HTA, and is a growing interest due to fiscal investment in comparative effectiveness in the United States. The methods of assessing the effectiveness of technologies and the relationship between practices in the United States and Europe generally need to be clarified.

Within all areas there is a need for more knowledge as described above. At the same time a number of newer research areas, which were not distinctly present in the review of existing research, were identified. Examples of demands for future research are: research concerning assessment of the wider effects of using technologies; research concerning coverage with evidence development and disinvestment; research concerning assessment of public health intervention, organisational interventions, and of information and communication technologies; research on the links between policy and HTA; and research on relative effectiveness.

References

- Abelson, J., M. Giacomini, P. Lehoux, and F. P. Gauvin (2007). Bringing 'the public' into health technology assessment and coverage policy decisions: from principles to practice, *Health policy (Amsterdam, Netherlands)*, vol. 82, no. 1, p. 37-50.
- Adam, T., M. A. Koopmanschap, and D. B. Evans (2003). Cost-effectiveness analysis: can we reduce variability in costing methods? *International Journal of Technology Assessment in Health Care*, vol. 19, no. 2, p. 407-420.
- Altenstetter, C. (2003). EU and member state medical devices regulation, *International Journal of Technology Assessment in Health Care*, vol. 19, no. 1, p. 228-248.
- Alton, V., I. Eckerlund, and A. Norlund (2006). Health economic evaluations: how to find them, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 4, p. 512-517.
- Andradas, E., J. A. Blasco, B. Valentin, M. J. Lopez-Pedraza, and F. J. Gracia (2008). Defining products for a new health technology assessment agency in Madrid, Spain: a survey of decision makers, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 1, p. 60-69.
- Antes, G., E. Briones, M. Britton, B. Burnand, G. Engel, P. Gallo, C. G. Pinto, M. I. Siebzeher, B. Jonsson, K. Landa et al. (2002). Education and support networks for assessment of health interventions. Working group 5 report, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 423-446.
- Autti-Rämö, I. and M. Mäkelä (2007). Ethical evaluation in health technology assessment reports: an eclectic approach, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 1, p. 1-8.
- Banta, H. D. (2001). Health policy, health technology assessment, and screening in Europe, *International Journal of Technology Assessment in Health Care*, vol. 17, no. 3, p. 409-417.
- Barton, P., S. Bryan, and S. Robinson (2004). Modelling in the economic evaluation of health care: selecting the appropriate approach, *Journal of health services research & policy*, vol. 9, no. 2, p. 110-118.
- Battista, R. N. and M. J. Hodge (1999). The evolving paradigm of health technology assessment: reflections for the millennium, *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, vol. 160, no. 10, p. 1464-1467.
- Battista, R. N. (2006). Expanding the scientific basis of health technology assessment: a research agenda for the next decade, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 3, p. 275-80; discussion 280-2.
- Berg, M., T. van der Grinten, and N. Klazinga (2004) Technology assessment, priority setting, and appropriate care in Dutch health care, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 35-43.
- Boas, G., H. van der Stel, H. Peters, M. Joore, and L. Anteunis (2001). Dynamic modeling in medical technology assessment. Fitting hearing aids in The Netherlands, *International Journal of Technology Assessment in Health Care*, vol. 17, no. 4, p. 618-625.
- Bodeau-Livinec, F., E. Simon, C. Montagnier-Petrissans, M. E. Joel, and E. Fery-Lemonnier (2006). Impact of CEDIT recommendations: An example of health technology assessment in a hospital network, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 2, p. 161-168.
- Brazier, J. (2008). Valuing health States for use in cost-effectiveness analysis, *PharmacoEconomics*, vol. 26, no. 9, p. 769-779.
- Brennan, A., S. E. Chick, and R. Davies (2006). A taxonomy of model structures for economic evaluation of health technologies, *Health economics*, vol. 15, no. 12, p. 1295-1310.
- Britton, M. and E. Jonsson (2002). Impact of health technology assessments. Some experiences of SBU, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 4, p. 824-831.
- Bryan, S., I. Williams, and S. McIver (2007). Seeing the NICE side of cost-effectiveness analysis: a qualitative investigation of the use of CEA in NICE technology appraisals, *Health economics*, vol. 16, no. 2, p.

179-193.

- Buxton, M. (2001). Implications of the appraisal function of the National Institute for Clinical Excellence (NICE), *Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research*, vol. 4, no. 3, p. 212-216.
- Carbonneil, C., F. Quentin, S. H. Lee-Robin, and European network for Health Technology Assessment (EUnetHTA) (2009). A common policy framework for evidence generation on promising health technologies, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 56-67.
- Carlsson, P. (2004). Health technology assessment and priority setting for health policy in Sweden, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 44-54.
- Chalkidou, K., A. Hoy, and P. Littlejohns, 2007, Making a decision to wait for more evidence: when the National Institute for Health and Clinical Excellence recommends a technology only in the context of research, *Journal of the Royal Society of Medicine*, vol. 100, no. 10, p. 453-460.
- Chase, D., R. Milne, K. Stein, and A. Stevens (2000). What are the relative merits of the sources used to identify potential research priorities for the NHS HTA programme? *International Journal of Technology Assessment in Health Care*, vol. 16, no. 3, p. 743-750.
- Chase D, Milne R, Hicks N et al. (eds.) (2008). EUnetHTA HTA adaptation toolkit. Work Package 5. Southampton: EUnetHTA. http://www.eunethta.net/upload/WP5/EUnetHTA_HTA_Adaptation_Toolkit_October08.pdf. Accessed 24.03.2011.
- Chauhan, D., A. H. Miners, and A. J. Fischer (2007). Exploration of the difference in results of economic submissions to the National Institute of Clinical Excellence by manufacturers and assessment groups, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 1, p. 96-100.
- Claxton, K., P. J. Neumann, S. Araki, and M. C. Weinstein (2001). Bayesian value-of-information analysis. An application to a policy model of Alzheimer's disease, *International Journal of Technology Assessment in Health Care*, vol. 17, no. 1, p. 38-55.
- Claxton, K., L. Ginnelly, M. Sculpher, Z. Philips, and S. Palmer (2004). A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme, *Health technology assessment (Winchester, England)*, vol. 8, no. 31, p. 1-103, iii.
- Claxton, K., M. Sculpher, C. McCabe, A. Briggs, R. Akehurst, M. Buxton, J. Brazier, and T. O'Hagan (2005). Probabilistic sensitivity analysis for NICE technology assessment: not an optional extra, *Health economics*, vol. 14, no. 4, p. 339-347.
- Cookson, R. and A. Maynard (2000). Health technology assessment in Europe. Improving clarity and performance, *International Journal of Technology Assessment in Health Care*, vol. 16, no. 2, p. 639-650.
- Cookson, R. and J. Hutton (2003). Regulating the economic evaluation of pharmaceuticals and medical devices: a European perspective, *Health policy (Amsterdam, Netherlands)*, vol. 63, no. 2, p. 167-178.
- Cooper, N., D. Coyle, K. Abrams, M. Mugford, and A. Sutton (2005). Use of evidence in decision models: an appraisal of health technology assessments in the UK since 1997, *Journal of health services research & policy*, vol. 10, no. 4, p. 245-250.
- Cooper, N. J., A. J. Sutton, A. E. Ades, S. Paisley, D. R. Jones, and Working Group on the Use of Evidence in Economic Decision Models (2007). Use of evidence in economic decision models: practical issues and methodological challenges, *Health economics*, vol. 16, no. 12, p. 1277-1286.
- Corabian, P., D. Hailey, C. Harstall, D. Juzwishin, and C. Moga (2005). Mentoring a developing health technology assessment initiative in Romania: an example for countries with limited experience of assessing health technology, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 4, p. 522-525.
- Coulter, A. (2004). Perspectives on health technology assessment: response from the patient's perspective,

- International Journal of Technology Assessment in Health Care, vol. 20, no. 1, p. 92-96.
- Culyer, A. J. (2005). Involving stakeholders in healthcare decisions--the experience of the National Institute for Health and Clinical Excellence (NICE) in England and Wales, *Healthcare quarterly* (Toronto, Ont.), vol. 8, no. 3, p. 56-60.
- Culyer, A. J., (2006). NICE's use of cost effectiveness as an exemplar of a deliberative process, *Health economics, policy, and law*, vol. 1, no. Pt 3, p. 299-318.
- Dakin, H. A., N. J. Devlin, and I. A. Odeyemi (2006). "Yes", "No" or "Yes, but"? Multinomial modelling of NICE decision-making, *Health policy* (Amsterdam, Netherlands), vol. 77, no. 3, p. 352-367.
- Dauben, H. P., O. H. Forde, M. L. Loud, S. O. Isacsson, F. Paccaud, E. Sanchez, and T. S. Steiger (2002). Health promotion and disease prevention as a complement to community health indicators. Working group 1, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 238-272.
- Davies, L., M. Drummond, and P. Papanikolaou (2000). Prioritizing investments in health technology assessment. Can we assess potential value for money? *International Journal of Technology Assessment in Health Care*, vol. 16, no. 1, p. 73-91.
- Devlin, N., J. Appleby, and D. Parkin (2003). Patients' views of explicit rationing: what are the implications for health service decision-making? *Journal of health services research & policy*, vol. 8, no. 3, p. 183-186.
- Dixon, S., P. Coleman, J. Nicholl, A. Brennan, and S. Touch (2003). Evaluation of the impact of a technology appraisal process in England: the South and West Development and Evaluation Committee, *Journal of health services research & policy*, vol. 8, no. 1, p. 18-24.
- Douma, K. F., K. Karsenberg, M. J. Hummel, J. M. Bueno-de-Mesquita, and W. H. van Harten (2007). Methodology of constructive technology assessment in health care, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 2, p. 162-168.
- Douw, K., H. Vondeling, D. Eskildsen, and S. Simpson (2003). Use of the Internet in scanning the horizon for new and emerging health technologies: a survey of agencies involved in horizon scanning, *Journal of medical Internet research*, vol. 5, no. 1, p. e6.
- Douw, K., H. Vondeling, J. Sorensen, T. Jorgensen, and H. Sigmund (2004). "The future should not take us by surprise": preparation of an early warning system in Denmark, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 3, p. 342-350.
- Douw, K. and H. Vondeling (2006). Selection of new health technologies for assessment aimed at informing decision making: A survey among horizon scanning systems, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 2, p. 177-183.
- Douw, K., H. Vondeling, and W. Oortwijn (2006). Priority setting for horizon scanning of new health technologies in Denmark: views of health care stakeholders and health economists, *Health policy* (Amsterdam, Netherlands), vol. 76, no. 3, p. 334-345.
- Draborg, E. and D. Gyrd-Hansen (2005). Time-trends in health technology assessments: an analysis of developments in composition of international health technology assessments from 1989 to 2002, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 4, p. 492-498.
- Draborg, E., D. Gyrd-Hansen, P. B. Poulsen, and M. Horder (2005). International comparison of the definition and the practical application of health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 1, p. 89-95.
- Draborg, E. and C. K. Andersen (2006). What influences the choice of assessment methods in health technology assessments? Statistical analysis of international health technology assessments from 1989 to 2002, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 1, p. 19-25.
- Drummond, M. and H. Weatherly (2000). Implementing the findings of health technology assessments. If the CAT got out of the bag, can the TAIL wag the dog? *International Journal of Technology Assessment in Health Care*, vol. 16, no. 1, p. 1-12.

- Drummond, M. F., M. J. Sculpher, G. W. Torrance, B. J. O'Brien, and G. L. Stoddart (2005). *Methods for the economic evaluation of health care programmes*, Oxford, Oxford University Press.
- Drummond, M. F., D. A. Wilson, P. Kanavos, P. Ubel, and J. Rovira (2007). Assessing the economic challenges posed by orphan drugs, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 1, p. 36-42.
- Drummond, M. F., C. P. Iglesias, and N. J. Cooper (2008a). Systematic reviews and economic evaluations conducted for the National Institute for Health and Clinical Excellence in the United Kingdom: a game of two halves? *International Journal of Technology Assessment in Health Care*, vol. 24, no. 2, p. 146-150.
- Drummond, M. F., J. S. Schwartz, B. Jonsson, B. R. Luce, P. J. Neumann, U. Siebert, and S. D. Sullivan (2008b). Key principles for the improved conduct of health technology assessments for resource allocation decisions, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 3, p. 244-58; discussion 362-8.
- Ehlers, L., M. Vestergaard, K. Kidholm, B. Bonnevie, P. H. Pedersen, T. Jorgensen, M. F. Jensen, F. B. Kristensen, and M. Kjolby (2006). Doing mini-health technology assessments in hospitals: a new concept of decision support in health care? *International Journal of Technology Assessment in Health Care*, vol. 22, no. 3, p. 295-301.
- Estrada, M. D., K. Asplund, R. Barrington, K. Faisst, J. P. Kahan, I. Kjonniksen, A. Mariotto, R. Milne, A. Ruther, S. Stilven et al. (2002). European joint assessments and coordination of findings and resources. Working group 3 report, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 321-360.
- Evers, S., M. Goossens, H. de Vet, M. van Tulder, and A. Ament (2005). Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 2, p. 240-245.
- Farmer, J. and R. Chesson (2001). Nice lessons to be learned, *International Journal of Technology Assessment in Health Care*, vol. 17, no. 2, p. 222-235.
- Fenwick, E., K. Claxton, and M. Sculpher (2001). Representing uncertainty: the role of cost-effectiveness acceptability curves, *Health economics*, vol. 10, no. 8, p. 779-787.
- Fenwick, E., D. A. Marshall, A. R. Levy, and G. Nichol (2006). Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation, *BMC health services research*, vol. 6, p. 52.
- FinOHTA (2008). HTA core model handbook. Helsinki: EUnetHTA. <https://fio.stakes.fi/htacore/handbook.html>. Accessed 24.03.2011.
- Folkersen, J. and P. H. Pedersen (2006). Attitudes to the use of a decision support method when introducing new medical technology at the University Hospital of Copenhagen, *Ugeskrift for laeger*, vol. 168, no. 21, p. 2069-2074.
- Foot, B., R. Foy, U. Chakravarthy, and R. Wormald (2004). Increasing use of a new health technology during the wait for NICE guidance: findings from the third national tracker survey of photodynamic therapy, *Journal of public health (Oxford, England)*, vol. 26, no. 1, p. 52-55.
- Frew, E. J., J. L. Wolstenholme, and D. K. Whynes (2004). Comparing willingness-to-pay: bidding game format versus open-ended and payment scale formats, *Health policy (Amsterdam, Netherlands)*, vol. 68, no. 3, p. 289-298.
- Fulop, N., P. Allen, A. Clarke, and N. Black (2003). From health technology assessment to research on the organisation and delivery of health services: addressing the balance, *Health policy (Amsterdam, Netherlands)*, vol. 63, no. 2, p. 155-165.
- Gagnon, M. P., E. Sanchez, and J. M. Pons (2006). Integration of health technology assessment recommendations into organizational and clinical practice: A case study in Catalonia, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 2, p. 169-176.

- Gibis, B., J. Artilles, P. Corabian, K. Meiesaar, A. Koppel, P. Jacobs, P. Serrano, and D. Menon (2001). Application of strengths, weaknesses, opportunities and threats analysis in the development of a health technology assessment program, *Health policy (Amsterdam, Netherlands)*, vol. 58, no. 1, p. 27-35.
- Grieve, R., J. Hutton, and C. Green (2003). Selecting methods for the prediction of future events in cost-effectiveness models: a decision-framework and example from the cardiovascular field, *Health policy (Amsterdam, Netherlands)*, vol. 64, no. 3, p. 311-324.
- Griffin, S., L. Bojke, C. Main, and S. Palmer (2006a). Incorporating direct and indirect evidence using bayesian methods: an applied case study in ovarian cancer, *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*, vol. 9, no. 2, p. 123-131.
- Griffin, S., K. Claxton, N. Hawkins, and M. Sculpher (2006b). Probabilistic analysis and computationally expensive models: Necessary and required? *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*, vol. 9, no. 4, p. 244-252.
- Griffin, S. C., H. L. Weatherly, G. A. Richardson, and M. F. Drummond (2008). Methodological issues in undertaking independent cost-effectiveness analysis for NICE: the case of therapies for ADHD, *The European journal of health economics : HEPAC : health economics in prevention and care*, vol. 9, no. 2, p. 137-145.
- Gulacsi, L., I. Boncz, and M. Drummond (2004). Issues for countries considering introducing the "fourth hurdle": the case of Hungary, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 3, p. 337-341.
- Gulacsi, L. (2007). The time for cost-effectiveness in the new European Union member states: the development and role of health economics and technology assessment in the mirror of the Hungarian experience, *The European journal of health economics : HEPAC : health economics in prevention and care*, vol. 8, no. 2, p. 83-88.
- Hagenfeldt, K., J. Asua, S. Bellucci, M. F. Jensen, B. Morland, W. Oortwijn, R. Salmi, A. Stevens, and G. H. ten Velden (2002). Systems for routine information sharing in HTA. Working group 2 report, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 273-320.
- Hailey, D. (2003). Toward transparency in health technology assessment: a checklist for HTA reports, *International Journal of Technology Assessment in Health Care*, vol. 19, no. 1, p. 1-7.
- Hailey, D. and M. Nordwall (2006). Survey on the involvement of consumers in health technology assessment programs, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 4, p. 497-499.
- Hanney, S., M. Buxton, C. Green, D. Coulson, and J. Raftery (2007). An assessment of the impact of the NHS Health Technology Assessment Programme, *Health technology assessment (Winchester, England)*, vol. 11, no. 53, p. iii-iv, ix-xi, 1-180.
- Hanratty, B., D. Craig, J. Nixon, S. Rice, J. Christie, and M. Drummond (2007). Are the best available clinical effectiveness data used in economic evaluations of drug therapies? *Journal of health services research & policy*, vol. 12, no. 3, p. 138-141.
- Hartmann, M., H. Knoth, D. Schulz, S. Knoth, and A. Meier-Hellmann (2003). Industry-sponsored economic studies in critical and intensive care versus studies sponsored by nonprofit organizations, *Journal of intensive care medicine*, vol. 18, no. 5, p. 265-268.
- Hartz, S. and J. John (2008). Contribution of economic evaluation to decision making in early phases of product development: a methodological and empirical review, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 4, p. 465-472.
- Hjelmgren, J., F. Berggren, and F. Andersson (2001). Health economic guidelines--similarities, differences and some implications, *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*, vol. 4, no. 3, p. 225-250.
- Hoffmann, C. and J. M. G. von der Schulenburg (2000). The influence of economic evaluation studies on decision making. A European survey. The EUROMET group, *Health policy (Amsterdam,*

- Netherlands), vol. 52, no. 3, p. 179-192.
- Hofmann, B. (2005). Toward a procedure for integrating moral issues in health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 3, p. 312-318.
- Hofmann, B. (2008). Why ethics should be part of health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 4, p. 423-429.
- Højgaard, L. (2003). Are health technology assessments a reliable tool in the analysis of the clinical value of PET in oncology? Who audits the auditors? *European journal of nuclear medicine and molecular imaging*, vol. 30, no. 5, p. 637-641.
- Holland, W. W. (2004). Health technology assessment and public health: a commentary, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 77-80.
- Hummel, J. M., W. van Rossum, G. J. Verkerke, and G. Rakhorst (2000a). Medical technology assessment: the use of the analytic hierarchy process as a tool for multidisciplinary evaluation of medical devices, *The International journal of artificial organs*, vol. 23, no. 11, p. 782-787.
- Hummel, M. J., W. van Rossum, G. J. Verkerke, and G. Rakhorst (2000b). Assessing medical technologies in development. A new paradigm of medical technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 16, no. 4, p. 1214-1219.
- Hutton, J., C. McGrath, J. M. Frybourg, M. Tremblay, E. Bramley-Harker, and C. Henshall (2006). Framework for describing and classifying decision-making systems using technology assessment to determine the reimbursement of health technologies (fourth hurdle systems), *International Journal of Technology Assessment in Health Care*, vol. 22, no. 1, p. 10-18.
- Hutton, J., P. Trueman, and C. Henshall (2007). Coverage with evidence development: an examination of conceptual and policy issues, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 4, p. 425-432.
- Hutton, J., P. Trueman, and K. Facey (2008). Harmonization of evidence requirements for health technology assessment in reimbursement decision making, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 4, p. 511-517.
- IJzerman, M. J., R. P. Reuzel, and H. L. Severens (2003). Pre-assessment to assess the match between cost-effectiveness results and decision makers' information needs: an illustration using two cases in rehabilitation medicine in The Netherlands, *International Journal of Technology Assessment in Health Care*, vol. 19, no. 1, p. 17-27.
- Jönsson, B. (2006). Time for a common standard for cost-effectiveness in Europe? *The European journal of health economics: HEPAC: health economics in prevention and care*, vol. 7, no. 4, p. 223-224.
- Jönsson, B. (2007). Economic evaluation for pharmaceuticals in Germany, *The European journal of health economics : HEPAC: health economics in prevention and care*, vol. 8 Suppl 1, p. S1-2.
- Jönsson, B. (2008). IQWiG: an opportunity lost? *The European journal of health economics : HEPAC : health economics in prevention and care*, vol. 9, no. 3, p. 205-207.
- Kaltenthaler, E., P. Tappenden, A. Booth, and R. Akehurst (2008). Comparing methods for full versus single technology appraisal: a case study of docetaxel and paclitaxel for early breast cancer, *Health policy (Amsterdam, Netherlands)*, vol. 87, no. 3, p. 389-400.
- Kanavos, P., U. Persson, and M. Drummond (2009). The future of health technology assessment in Europe, , vol. 2, p. 75-128.
- Karnon, J. (2003). Alternative decision modelling techniques for the evaluation of health care technologies: Markov processes versus discrete event simulation, *Health economics*, vol. 12, no. 10, p. 837-848.
- Kristensen, F. B., E. Adams, E. Briones, D. Coburn, K. Facey, N. W. Hansen, J. Hoeksema, and B. Morland (2004). Health technology assessment of PET in oncology: re *Eur J Nucl Med Mol Imaging* 2003; 30:637-641, *European journal of nuclear medicine and molecular imaging*, vol. 31, no. 2, p. 295-7; author reply 297-8; discussion 298.
- Kristiansen, I. S., K. Stavem, K. Linnestad, and K. M. Pedersen (2003). Evaluation of medical methods--can

- we rely on cost-benefit-analysis? Tidsskrift for den Norske lægeforening : tidsskrift for praktisk medicin, ny raekke, vol. 123, no. 5, p. 657-660.
- Kubesch N, Parada A, Moharra M, Estrada MD, Cortés M, Espallargues M, et al. (eds.) (2008). Information management in HTA organisations. EUnetHTA Work Package 8. Barcelona: EUnetHTA, 2008. [http://www.eunetha.eu/upload/WP8/WP8Outcomes/Information%20Management%20in%20HTA%20Organisations-%20Survey%20report-CAHTA-May%202008\(EUnetHTAProject\).pdf](http://www.eunetha.eu/upload/WP8/WP8Outcomes/Information%20Management%20in%20HTA%20Organisations-%20Survey%20report-CAHTA-May%202008(EUnetHTAProject).pdf). Accessed 25.03.2011.
- Kulp, W. and W. Greiner (2006). Health economics and HTA, Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz, vol. 49, no. 3, p. 257-263.
- Lampe, K and I. Pasternack I (eds) (2008). EUnetHTA HTA core model for diagnostic technologies 1.0R Work Package 4. Helsinki: European Network for Health Technology Assessment. <http://www.eunetha.net/upload/WP4/Final%20Deliverables/HTA%20Core%20Model%20for%20Diagnostic%20Technologies%201%200r.pdf>. Accessed 24.03.2011.
- Lampe K, Mäkelä M (eds) (2008). EUnetHTA HTA core model for medical and surgical interventions 1.0R Work Package 4. Helsinki: European Network for Health Technology Assessment. <http://www.eunetha.net/upload/WP4/Final%20Deliverables/HTA%20Core%20Model%20for%20Medical%20and%20Surgical%20Interventions%201%200r.pdf>. Accessed 24.03.2011.
- Lampe, K., M. Mäkelä, M. Velasco Garrido, H. Anttila, I. Autti-Rämö, N. J. Hicks, B. Hofmann, J. Koivisto, R. Kunz, P. Karki et al (2009). The HTA core model: a novel method for producing and reporting health technology assessments, International Journal of Technology Assessment in Health Care, vol. 25 Suppl 2, p. 9-20.
- Lehoux, P. and S. Blume (2000). Technology assessment and the sociopolitics of health technologies, Journal of health politics, policy and law, vol. 25, no. 6, p. 1083-1120.
- Lehoux, P., R. N. Battista, A. Granados, P. Gallo, S. Tailliez, D. Coyle, M. Marchetti, P. Borgia, and G. Ricciardi (2005). International Master's Program in health technology assessment and management: assessment of the first edition (2001--2003), International Journal of Technology Assessment in Health Care, vol. 21, no. 1, p. 104-112.
- Lettieri, E. and C. Masella (2007). Health-care costs and health technology assessment, Giornale italiano di nefrologia : organo ufficiale della Societa italiana di nefrologia, vol. 24 Suppl 40, p. s22-36.
- Lettieri, E., C. Masella, and U. Nocco (2008). Budgeting and health technology assessment: first evidence obtained from proposal forms used to submit the adoption of new technology, International Journal of Technology Assessment in Health Care, vol. 24, no. 4, p. 502-510.
- Leys, M. (2003a). Health care policy: qualitative evidence and health technology assessment, Health policy (Amsterdam, Netherlands), vol. 65, no. 3, p. 217-226.
- Leys, M. (2003b). Health technology assessment: the contribution of qualitative research, International Journal of Technology Assessment in Health Care, vol. 19, no. 2, p. 317-329.
- Lohr, K. N. and D. M. Steinwachs (2002). Health Services research: an evolving definition of the field, Health services research, vol. 37, p. 15-17.
- Lothgren, M. and M. Ratcliffe (2004). Pharmaceutical industry's perspective on health technology assessment, International Journal of Technology Assessment in Health Care, vol. 20, no. 1, p. 97-101.
- Lundberg, J., M. Brommels, J. Skar, and G. Tomson (2008). Measuring the validity of early health technology assessment: bibliometrics as a tool to indicate its scientific basis, International Journal of Technology Assessment in Health Care, vol. 24, no. 1, p. 70-75.
- Malone, D. E. and P. M. Maceneaney (2000). Applying 'technology assessment' and 'evidence based medicine' theory to interventional radiology. Part 1: Suggestions for the phased evaluation of new procedures, Clinical radiology, vol. 55, no. 12, p. 929-937.
- Martelli, F., G. La Torre, E. Di Ghionno, T. Staniscia, M. Neroni, A. Cicchetti, K. Von Bremen, W. Ricciardi, and NI-HTA Collaborative Group (2007). Health technology assessment agencies: an international

- overview of organizational aspects, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 4, p. 414-424.
- May, C., M. Mort, T. Williams, F. Mair, and L. Gask (2003). Health technology assessment in its local contexts: studies of telehealthcare, *Social science & medicine* (1982), vol. 57, no. 4, p. 697-710.
- May, C. (2006). Mobilising modern facts: health technology assessment and the politics of evidence, *Sociology of health & illness*, vol. 28, no. 5, p. 513-532.
- Maynard, A. and D. McDaid (2003). Evaluating health interventions: exploiting the potential, *Health policy* (Amsterdam, Netherlands), vol. 63, no. 2, p. 215-226.
- Maynard, A., K. Bloor, and N. Freemantle (2004). Challenges for the National Institute for Clinical Excellence, *BMJ* (Clinical research ed.), vol. 329, no. 7459, p. 227-229.
- Maynard, A. (2007). Transparency in health technology assessments, *BMJ* (Clinical research ed.), vol. 334, no. 7594, p. 594-595.
- McCabe, C., A. Tsuchiya, K. Claxton, and J. Raftery (2007). Assessing the economic challenges posed by orphan drugs: a comment on Drummond et al, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 3, p. 397-401; author reply 401-4.
- McCabe, C., K. Claxton, and A. O'Hagan (2008). Why licensing authorities need to consider the net value of new drugs in assigning review priorities: addressing the tension between licensing and reimbursement, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 2, p. 140-145.
- McDaid, D., R. Cookson, and ASTEC Group (2003). Evaluating health care interventions in the European Union, *Health policy* (Amsterdam, Netherlands), vol. 63, no. 2, p. 133-139.
- McGregor, M. and J. M. Brophy (2005). End-user involvement in health technology assessment (HTA) development: a way to increase impact, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 2, p. 263-267.
- Milewa, T. (2008). Representation and legitimacy in health policy formulation at a national level: perspectives from a study of health technology eligibility procedures in the United Kingdom, *Health policy* (Amsterdam, Netherlands), vol. 85, no. 3, p. 356-362.
- Milne, R., A. Clegg, and A. Stevens (2003). HTA responses and the classic HTA report, *Journal of public health medicine*, vol. 25, no. 2, p. 102-106.
- Miners, A. (2008). Estimating 'costs' for cost-effectiveness analysis, *PharmacoEconomics*, vol. 26, no. 9, p. 745-751.
- Miners, A. H., M. Garau, D. Fidan, and A. J. Fischer (2005). Comparing estimates of cost effectiveness submitted to the National Institute for Clinical Excellence (NICE) by different organisations: retrospective study, *BMJ* (Clinical research ed.), vol. 330, no. 7482, p. 65.
- Moharra M, Kubesch N, Estrada MD, Parada T, Cortés M, Espallargues M, et al. (eds.) (2008a). EUnetHTA Survey report on HTA organisations. EUnetHTA Work Package 8. Barcelona:EUnetHTA. http://www.eunetha.eu/upload/WP8/WP8Outcomes/HTA%20organisations%20report_final_EUnetHTA_Project.pdf. Accessed 25.03.2011
- Moharra M (edt.) (2008b). EUnetHTA handbook on health technology assessment capacity building. EUnetHTA work package 8. Barcelona: EUnetHTA, http://www.gencat.cat/salut/depsan/units/aatrm/pdf/eunetha_wp8_hb_hta_capacity_building.pdf. Accessed 24.03.2011.
- Moharra, M., M. Espallargues, N. Kubesch, M. D. Estrada, A. Parada, H. Vondeling, A. Lo Scalzo, S. Cristofides, E. Turk, M. Raab et al (2009). Systems to support health technology assessment (HTA) in member states of the European union with limited institutionalization of HTA, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 75-83.
- Møldrup, C. (2002). Medical technology assessment of the ethical, social, and legal implications of pharmacogenomics. A research proposal for an Internet citizen jury, *International Journal of*

- Technology Assessment in Health Care, vol. 18, no. 3, p. 728-732.
- Moret-Hartman, M., G. J. van der Wilt, and J. Grin (2007). Health technology assessment and ill-structured problems: a case study concerning the drug mebeverine, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 3, p. 316-323.
- Murphy, K., C. Packer, A. Stevens, and S. Simpson (2007). Effective early warning systems for new and emerging health technologies: developing an evaluation framework and an assessment of current systems, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 3, p. 324-330.
- Myhre, K. I. (2000). Telemedicine and medical technology assessment, *Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke*, vol. 120, no. 19, p. 2312-2314.
- NCCHTA (NIHR Coordinating Centre for HTA) (2007). Glossary of HTA adaptation terms. Southampton: EUnetHTA.
<http://www.eunetha.net/upload/WP5/Glossary%20of%20HTA%20Adaptation%20Terms%20November%202007.pdf>. Accessed 24.03.2011.
- Neikter, S. A., N. Rehnqvist, M. Rosen, and H. Dahlgren (2009). Toward a new information infrastructure in health technology assessment: communication, design, process, and results, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 92-98.
- Nixon, J., S. Duffy, N. Armstrong, D. Craig, J. Glanville, J. Christie, M. Drummond, and J. Kleijnen (2004). The usefulness of the NHS Economic Evaluation Database to researchers undertaking technology assessment reviews, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 3, p. 249-257.
- O'Brien, B. J., M. Spath, G. Blackhouse, J. L. Severens, P. Dorian, and J. Brazier (2003). A view from the bridge: agreement between the SF-6D utility algorithm and the Health Utilities Index, *Health economics*, vol. 12, no. 11, p. 975-981.
- O'Hagan, A. and J. W. Stevens (2002). Bayesian methods for design and analysis of cost-effectiveness trials in the evaluation of health care technologies, *Statistical methods in medical research*, vol. 11, no. 6, p. 469-490.
- Oliver, A., E. Mossialos, and R. Robinson (2004). Health technology assessment and its influence on health-care priority setting, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 1-10.
- Oortwijn, W. J., H. Vondeling, T. van Barneveld, C. van Vugt, and L. M. Bouter (2002). Priority setting for health technology assessment in The Netherlands: principles and practice, *Health policy (Amsterdam, Netherlands)*, vol. 62, no. 3, p. 227-242.
- Oortwijn, W. J., S. R. Hanney, A. Ligtvoet, S. Hoorens, S. Wooding, J. Grant, M. J. Buxton, and L. M. Bouter (2008). Assessing the impact of health technology assessment in The Netherlands, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 3, p. 259-269.
- Orvain, J., B. Xerri, and Y. Matillon (2004). Overview of health technology assessment in France, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 25-34.
- Packer, C., S. Simpson, A. Stevens, and EuroScan: the European Information Network on New and Changing Health Technologies (2006). International diffusion of new health technologies: a ten-country analysis of six health technologies, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 4, p. 419-428.
- Palmer, S. and P. C. Smith (2000). Incorporating option values into the economic evaluation of health care technologies, *Journal of health economics*, vol. 19, no. 5, p. 755-766.
- Palmhøj Nielsen C, Lauritsen SW, Kristensen FB, Bistrup ML, Cecchetti A, Turk E and European network for Health Technology Assessment (EUnetHTA) (2009). Involving stakeholders and developing a policy for stakeholder involvement in the European network for health technology assessment, *EUnetHTA. Int J Technol Assess Health Care*. 2009 Dec;25 Suppl 2:84-91.
- Pasternack, I., H. Anttila, M. Mäkelä, T. Ikonen, P. Rasanen, K. Lampe, H. van Brabandt, I. Cleemput, C. de

- Laet, M. Marchetti et al. (2009). Testing the HTA core model: experiences from two pilot projects, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 21-27.
- Paul, J. E. and P. Trueman (2001). 'Fourth hurdle reviews', NICE, and database applications, *Pharmacoepidemiology and drug safety*, vol. 10, no. 5, p. 429-438.
- Pearson, S. and P. Littlejohns (2007). Reallocating resources: how should the National Institute for Health and Clinical Excellence guide disinvestment efforts in the National Health Service? *Journal of health services research & policy*, vol. 12, no. 3, p. 160-165.
- Perleth, M., E. Jakubowski, and R. Busse (2001a). What is 'best practice' in health care? State of the art and perspectives in improving the effectiveness and efficiency of the European health care systems, *Health policy (Amsterdam, Netherlands)*, vol. 56, no. 3, p. 235-250.
- Perleth, M., D. Luhmann, B. Gibis, and S. Droste (2001b). Rapid assessments"--quick evaluation of medical technology, *Gesundheitswesen (Bundesverband der Arzte des Offentlichen Gesundheitsdienstes (Germany))*, vol. 63 Suppl 1, p. S79-84.
- Philips, Z., L. Ginnelly, M. Sculpher, K. Claxton, S. Golder, R. Riemsma, N. Woolacoot, and J. Glanville (2004). Review of guidelines for good practice in decision-analytic modelling in health technology assessment, *Health technology assessment (Winchester, England)*, vol. 8, no. 36, p. iii-iv, ix-xi, 1-158.
- Philips, Z., L. Bojke, M. Sculpher, K. Claxton, and S. Golder (2006). Good practice guidelines for decision-analytic modelling in health technology assessment: a review and consolidation of quality assessment, *PharmacoEconomics*, vol. 24, no. 4, p. 355-371.
- Pivik, J., E. Rode, and C. Ward (2004). A consumer involvement model for health technology assessment in Canada, *Health policy (Amsterdam, Netherlands)*, vol. 69, no. 2, p. 253-268.
- Poole, C., S. Agrawal, and C. J. Currie (2007). Let cost effectiveness models be open to scrutiny, *BMJ (Clinical research ed.)*, vol. 335, no. 7623, p. 735.
- Porzsolt, F., H. Kajnar, A. Awa, M. Fassler, and B. Herzberger (2005). Validity of original studies in health technology assessment reports: significance of standardized assessment and reporting, *International Journal of Technology Assessment in Health Care*, vol. 21, no. 3, p. 410-413.
- Quentin F, Carbonneil C, Lee-Robin SH (eds.) (2008). EUnetHTA web-based toolkit to facilitate European collaboration on evidence generation on promising health technologies. 7, strand A. Paris: EUnetHTA. [http://www.eunetha.net/upload/Work%20Package%207/WP7A%20Deliverable%20Dec%202008%20\(adjusted\).pdf](http://www.eunetha.net/upload/Work%20Package%207/WP7A%20Deliverable%20Dec%202008%20(adjusted).pdf). Accessed 24.03.2011.
- Quentin, F., C. Carbonneil, C. Moty-Monnereau, E. Berti, W. Goettsch, S. H. Lee-Robin, and European network for Health Technology Assessment (EUnetHTA) (2009). Web-based toolkit to facilitate European collaboration on evidence generation on promising health technologies, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 68-74.
- Ramsay, C. R., A. M. Grant, S. A. Wallace, P. H. Garthwaite, A. F. Monk, and I. T. Russell (2000). Assessment of the learning curve in health technologies. A systematic review, *International Journal of Technology Assessment in Health Care*, vol. 16, no. 4, p. 1095-1108.
- Ramsay, C. R., A. M. Grant, S. A. Wallace, P. H. Garthwaite, A. F. Monk, and I. T. Russell (2001). Statistical assessment of the learning curves of health technologies, *Health technology assessment (Winchester, England)*, vol. 5, no. 12, p. 1-79.
- Ramsay, C. R., S. A. Wallace, P. H. Garthwaite, A. F. Monk, I. T. Russell, and A. M. Grant (2002). Assessing the learning curve effect in health technologies. Lessons from the non-clinical literature, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 1, p. 1-10.
- Ratcliffe, J. and L. Longworth (2002). Investigating the structural reliability of a discrete choice experiment within health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 1, p. 139-144.
- Rodriguez Barrios, J. M. (2004). The role of models in economic evaluation of healthcare, *Farmacia hospitalaria : organo oficial de expresion cientifica de la Sociedad Espanola de Farmacia Hospitalaria*,

- vol. 28, no. 4, p. 231-242.
- Rodriguez Barrios, J. M., D. Serrano, T. Monleon, and J. Caro (2008). Discrete-event simulation models in the economic evaluation of health technologies and health products, *Gaceta sanitaria / S.E.S.P.A.S*, vol. 22, no. 2, p. 151-161.
- Rosten, C., D. L. Chase, N. J. Hicks, R. Milne, and European network for Health Technology Assessment (EUnetHTA) (2009). Enhancing understanding: the development of a glossary of health technology assessment adaptation terms, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 42-47.
- Royle, J. and S. Oliver (2004). Consumer involvement in the health technology assessment program, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 4, p. 493-497.
- Saarni, S. I., B. Hofmann, K. Lampe, D. Luhmann, M. Mäkelä, M. Velasco Garrido, and I. Autti-Rämö (2008). Ethical analysis to improve decision-making on health technologies, *Bulletin of the World Health Organization*, vol. 86, no. 8, p. 617-623.
- Schlender, M. (2008). Is NICE infallible? A qualitative study of its assessment of treatments for attention-deficit/hyperactivity disorder (ADHD), *Current medical research and opinion*, vol. 24, no. 2, p. 515-535.
- Schubert, F. (2002). Health technology assessment. The pharmaceutical industry perspective, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 184-191.
- Shani, S., M. I. Siebzeiner, O. Luxenburg, and J. Shemer (2000). Setting priorities for the adoption of health technologies on a national level -- the Israeli experience, *Health policy (Amsterdam, Netherlands)*, vol. 54, no. 3, p. 169-185.
- Sheldon, T. A., N. Cullum, D. Dawson, A. Lankshear, K. Lowson, I. Watt, P. West, D. Wright, and J. Wright (2004). What's the evidence that NICE guidance has been implemented? Results from a national evaluation using time series analysis, audit of patients' notes, and interviews, *BMJ (Clinical research ed.)*, vol. 329, no. 7473, p. 999.
- Shepherd, J., J. Briggs, L. Payne, C. Packer, L. Kerridge, and M. Ashton-Key (2007). Setting the future policy agenda for health technology assessment: a specialty mapping approach, *International Journal of Technology Assessment in Health Care*, vol. 23, no. 4, p. 405-413.
- Siebert, M., L. C. Clauss, M. Carlisle, B. Casteels, P. de Jong, M. Kreuzer, S. Sanghera, G. Stokoe, P. Trueman, A. W. Lang et al. (2002). Health technology assessment for medical devices in Europe. What must be considered, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 3, p. 733-740.
- Simpson, S. and C. Wild (eds.) (2008). On the horizon. European newsletter on new and emerging health technologies, EUnetHTA. http://www.eunethta.net/Public/Communication/Newsletter_WP7_2008. Accessed 24.03.2011.
- Simpson, S., C. Hyde, A. Cook, C. Packer, and A. Stevens (2004). Assessing the accuracy of forecasting: applying standard diagnostic assessment tools to a health technology early warning system, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 3, p. 381-384.
- Simpson, S., C. Packer, P. Carlsson, J. M. Sanders, I. G. Ibarluzea, A. F. Fay, and I. Norderhaug (2008). Early identification and assessment of new and emerging health technologies: actions, progress, and the future direction of an international collaboration--EuroScan, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 4, p. 518-525.
- Sorenson, C., P. Kanavos, and M. Drummond (2007). Ensuring Value for Money in Health Care: The role of HTA in the European Union, , p. 45-138.
- Sorenson, C., M. Drummond, and P. Kanavos (2008). Ensuring Value for Money in Health Care The role of health technology assessment in the European Union, .
- Soto, J. (2002). Health economic evaluations using decision analytic modelling. Principles and practices-- utilization of a checklist to their development and appraisal, *International Journal of Technology*

- Assessment in Health Care, vol. 18, no. 1, p. 94-111.
- Spiegelhalter, D. J., J. P. Myles, D. R. Jones, and K. R. Abrams (2000). Bayesian methods in health technology assessment: a review, *Health technology assessment (Winchester, England)*, vol. 4, no. 38, p. 1-130.
- Stein, K., A. Fry, A. Round, R. Milne, and J. Brazier (2005). What value health?: A review of health state values used in early technology assessments for NICE, *Applied health economics and health policy*, vol. 4, no. 4, p. 219-228.
- Stevens, A. and R. Milne (2004). Health technology assessment in England and Wales, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 11-24.
- Summerhayes, M. and P. Catchpole (2006). Has NICE been nice to cancer? *European journal of cancer (Oxford, England : 1990)*, vol. 42, no. 17, p. 2881-2886.
- ten Have, H. (2004). Ethical perspectives on health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 71-76.
- Thurston, S. J., D. Craig, P. Wilson, and M. F. Drummond (2008). Increasing decision-makers' access to economic evaluations: alternative methods of communicating the information, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 2, p. 151-157.
- Townsend, J., M. Buxton, and G. Harper (2003). Prioritisation of health technology assessment. The PATHS model: methods and case studies, *Health technology assessment (Winchester, England)*, vol. 7, no. 20, p. iii, 1-82.
- Towse, A. and C. Pritchard (2002). National Institute for Clinical Excellence (NICE): Is economic appraisal working? *Pharmacoeconomics*, vol. 20 Suppl 3, p. 95-105.
- Turner, S., D. L. Chase, R. Milne, A. Cook, N. J. Hicks, C. Rosten, L. Payne, S. Coles, E. Bell, and European network for Health Technology Assessment (EUnetHTA) (2009a). The adaptation of health technology assessment reports: identification of the need for, and development of, a toolkit to aid the process, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 28-36.
- Turner, S., D. L. Chase, R. Milne, A. Cook, N. J. Hicks, C. Rosten, L. Payne, S. Coles, E. Bell, and European network for Health Technology Assessment (EUnetHTA) (2009b). The health technology assessment adaptation toolkit: description and use, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 37-41.
- Vallejo-Torres, L., L. M. Steuten, M. J. Buxton, A. J. Girling, R. J. Lilford, and T. Young (2008). Integrating health economics modelling in the product development cycle of medical devices: a Bayesian approach, *International Journal of Technology Assessment in Health Care*, vol. 24, no. 4, p. 459-464.
- van der Wilt, G. J., M. Rovers, H. Straatman, S. van der Bij, P. van den Broek, and G. Zielhuis (2004). Policy relevance of Bayesian statistics overestimated? *International Journal of Technology Assessment in Health Care*, vol. 20, no. 4, p. 488-492.
- van Tinteren, H., O. S. Hoekstra, and M. Boers (2003). The need for Health Technology Assessments of PET, *European journal of nuclear medicine and molecular imaging*, vol. 30, no. 10, p. 1438-9; author reply 1439.
- Velasco Garrido, M., M. Perleth, M. Drummond, F. Gurtner, T. Jorgensen, A. Jovell, J. Malone, A. Ruther, and C. Wild (2002). Best practice in undertaking and reporting health technology assessments. Working group 4 report, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 2, p. 361-422.
- Velasco Garrido, M., F. B. Kristensen, C. Palmhøj Nielsen, and R. Busse (2008). Health Technology Assessment and Health Policy-making in Europe: Current status, challenges and potential, United Kingdom, World Health Organization on behalf of the European Observatory on Health Systems and Policies.
- von Below GC, Boer A, Conde-Olasagasti JL, Dillon A, Gibis B, Grilli R, et al. (2002). Health technology assessment in policy and practice. Working group 6 report. *Int J Technol Assess Health Care*.

- Spring;18(2):447-55.
- von der Schulenburg, J., C. Vauth, T. Mittendorf, and W. Greiner (2007). Methods for determining cost-benefit ratios for pharmaceuticals in Germany, *The European journal of health economics : HEPAC : health economics in prevention and care*, vol. 8 Suppl 1, p. S5-31.
- Walker, S., S. Palmer, and M. Sculpher (2007). The role of NICE technology appraisal in NHS rationing, *British medical bulletin*, vol. 81-82, p. 51-64.
- Warren, V. (2007). Health technology appraisal of interventional procedures: comparison of rapid and slow methods, *Journal of health services research & policy*, vol. 12, no. 3, p. 142-146.
- Wathen, B. and T. Dean (2004). An evaluation of the impact of NICE guidance on GP prescribing, *The British journal of general practice : the journal of the Royal College of General Practitioners*, vol. 54, no. 499, p. 103-107.
- Wagh, N. (2006). Health technology assessment in cancer: a personal view from public health, *European journal of cancer (Oxford, England : 1990)*, vol. 42, no. 17, p. 2876-2880.
- Weatherly, H., M. Drummond, and D. Smith (2002). Using evidence in the development of local health policies. Some evidence from the United Kingdom, *International Journal of Technology Assessment in Health Care*, vol. 18, no. 4, p. 771-781.
- Webster, A. (2004). Health technology assessment: a sociological commentary on reflexive innovation, *International Journal of Technology Assessment in Health Care*, vol. 20, no. 1, p. 61-66.
- Wild, C. and T. Langer (2008). Emerging health technologies: informing and supporting health policy early, *Health policy (Amsterdam, Netherlands)*, vol. 87, no. 2, p. 160-171.
- Wild, C., S. Simpson, K. Douw, S. Geiger-Gritsch, S. Mathis, and T. Langer (2009). Information service on new and emerging health technologies: identification and prioritization processes for a European union-wide newsletter, *International Journal of Technology Assessment in Health Care*, vol. 25 Suppl 2, p. 48-55.
- Williams, A. H. and R. A. Cookson (2006). Equity-efficiency trade-offs in health technology assessment, *International Journal of Technology Assessment in Health Care*, vol. 22, no. 1, p. 1-9.
- Williams, I., S. Bryan, and S. Mclver (2007). How should cost-effectiveness analysis be used in health technology coverage decisions? Evidence from the National Institute for Health and Clinical Excellence approach, *Journal of health services research & policy*, vol. 12, no. 2, p. 73-79.
- Williams, I., S. Mclver, D. Moore, and S. Bryan (2008). The use of economic evaluations in NHS decision-making: a review and empirical investigation, *Health technology assessment (Winchester, England)*, vol. 12, no. 7, p. iii, ix-x, 1-175.
- Williams, I. P. and S. Bryan (2007). Cost-effectiveness analysis and formulary decision making in England: findings from research, *Social science & medicine (1982)*, vol. 65, no. 10, p. 2116-2129.
- Williams, T., C. May, F. Mair, M. Mort, and L. Gask (2003). Normative models of health technology assessment and the social production of evidence about telehealth care, *Health policy (Amsterdam, Netherlands)*, vol. 64, no. 1, p. 39-54.

