Chapter 1
Health Technology Assessment

Karen M. Facey

1.1 Introduction

This chapter will explore the history of health technology assessment (HTA) and how it has evolved in terms of processes and methods, highlighting elements relevant to patient involvement to lay a foundation for the subsequent chapters of this book. HTA is a policy analysis that seeks to inform decision-makers in national, regional or hospital health services about the use of health technologies. HTAs require systematic processes that critically assess research about the impacts of using the health technology along with context-specific appraisal of the social, economic, legal and ethical implications of the use of the health technology. This is not simply a scientific endeavour. It requires interdisciplinary deliberative discussion and value judgements about the relevance of the evidence for the local health system. HTAs may recommend the use or disinvestment of a health technology and so are subject to political, public and stakeholder scrutiny. As a result there has been pressure to involve those who have a specific interest in the health technology, particularly patients, in the HTA process. However, this is contentious due to concerns about potential bias and representativeness of patient input and the scientific integrity of patient evidence.

K.M. Facey
Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, 9 The Bioquarter, 9 Little France Road, Edinburgh, EH16 4UX, UK
e-mail: k.facey@btinternet.com

K. Facey et al. (eds.), *Patient Involvement in Health Technology Assessment*,
DOI 10.1007/978-981-10-4068-9_1

1.2 Context and History

Health systems, whether funded by taxation, social insurance, personal insurance or private fees, need to organise their services to use available funds efficiently to deliver effective, safe, person-centred care in a timely and equitable manner for the population they serve (Committee on Quality Health Care in America 2001). They have to make choices about who to treat, with what intervention, in what setting and for how long (Newdick 2004). Such questions must be considered not just in the context of the individual patient but in terms of providing the best possible service to all potential users of the health system (Drummond et al. 2006, Chap. 2). Thus resource allocation questions often seek to maximise health gain of the population overall, recognising that there is an opportunity cost to any investment (giving up the possibility of funding an alternative intervention with that money) (Metzler and Smith 2012).

Daniels and Sabin (2008 [1]) stated that resource allocation decisions in healthcare were 'rife with moral disagreements and a fair, deliberative process is necessary to establish legitimacy and fairness of such decisions'. They argued that resource allocation:

1. Processes must be public (fully transparent) about the grounds for decisions.
2. Decisions must rest on reasons that stakeholders can agree are relevant.
3. Decisions should be revisable in light of new evidence and arguments.
4. Should include assurance, through enforcement, that these three conditions are met.

In fact, three decades earlier, the US Senate had noted that 'a reasonable amount of justification should be provided before costly new medical technologies and procedures are put into general use' (Office of Technology Assessment OTA 1976 [vii]). As a result, the OTA created a report providing examples of medical technologies in the fields of diagnostics, implantable devices, vaccines, surgery, medicines and interventional procedures that illustrated the diversity in development, purpose and the use of medical technologies (OTA 1976). It noted that decisions about the use of such new technologies were often made on the basis of evidence about technical feasibility, safety and anticipated need or demand, but that wider consideration of impacts should be assessed, including implications for:

- Patients
- Patients' families
- Society as a whole (environmental impacts, ethics, cultural values)

- Medical care system
- Legal and political systems
- The economy

OTA (1976) stated that to systematically consider these wider impacts of medical technologies, a comprehensive form of policy research was needed to provide decision-makers with policy alternatives. The formal process of 'technology assessment', which had first been used to evaluate other forms of technologies in 1965, was suggested. Technology assessment was described as systematically examining the short- and long-term social consequences (e.g. societal, economic, ethical, legal) of the application or use of technology, considering unintended, indirect or delayed social impacts (OTA 1976).

OTA (1976) described the unique features of technology assessment as being:

- Based on an explicit analytic framework, specified in advance
- Comprehensive in scope, examining impacts on social, ethical, legal and other systems that may not be immediately obvious
- Carried out by a multidisciplinary group
- Able to explicitly identify the groups that would be affected by the technology and evaluate the impacts (and impacts of impacts) of the technology on each party

The report (OTA 1976) outlined a list of questions to be considered for each potential area of impact. Box 1.1 shows the questions about the implications for patients and families of a new heart valve.

Box 1.1: Questions to Assess the Impacts of Medical Technologies on Patients: Heart Valve Example (OTA 1976, reformatted)

What are the implications of the technology for the patient?

What will be the quality of life of the patient who has been treated? Normally active?

Moderately restricted? Physically disabled?

A recipient of an artificial heart could reasonably expect to lead an active, productive, fairly normal life.

What psychological effects can be anticipated? Guilt? (Because of high financial and social costs to family) Anxiety? Feelings of dehumanisation? Dependency? Anxieties and even psychoses might be precipitated in heart recipients who are preoccupied by dependence on an inorganic source of power. Such reactions have been observed in patients receiving dialysis for chronic kidney disease. Furthermore, some of the drugs that might be used as supportive therapy, e.g. steroids, themselves have psychotropic effects.

If nuclear-powered artificial hearts are used, it may be necessary to identify or even monitor movement of recipients in order to protect the nuclear fuel and to recover it after death. Recipients might be required to waive some of the individual freedom most of us take for granted.

Will regimentation result from the use of the technology? Loss of freedom over one's body?

Death from heart disease is sometimes, although not always, swift and painless. Although the benefits of prolonging life with an artificial heart are obvious, the recipient will have to be made aware of the possibility of death from failure of the implant procedure.

Will the use of the technology increase the probability of a lingering and painful death?

Once surgery is complete, the procedure can be reversed only by removing or deactivating the artificial heart, thereby allowing the patient to die.

Will the effects of the new technology be reversible if the patient feels that its benefits are outweighed by its drawbacks? Will the individual be able to choose to die?

What are the implications for the patient's family?

Implantation of an artificial heart will permit survival of the patient, and the benefits to the rest of the family will be numerous. On the other hand, unless the cost of implantation of the heart is covered by some third-party payer, the enormous financial burdens could impoverish the patient's entire family and strain intrafamily relationships.

What will be the costs to the family? How will the new technology affect family structure?

The plutonium contained in a nuclear-powered artificial heart may, however well shielded, emit radiation that could pose some danger to family members who are frequently close to the patient.

Will there be any physical dangers to the immediate family?

Will the device or procedure be psychologically acceptable to the family?

Will active cooperation or assistance of family members be necessary on a continuing basis?

How will the new technology affect individual or family budgets? What purchases will families forego if they have to pay for the new technology?

1.3 Development of HTA

1.3.1 Spread of HTA

Although OTA was criticised as being an 'unnecessary agency' (Banta 2009 [8]) and closed in 1995, it stimulated technology assessment activities in other countries (Banta 2009). In Denmark, in 1982, and Sweden in 1987, national organisations were given responsibility to undertake systematic assessments of all forms of health intervention (including medical technologies, educational programmes, organisation of care) to inform policy and practice (Sigmund and Kristensen 2009; Jonsson 2009). So the ethos and processes of OTA's technology assessment were used under the new name of health technology assessment, with definitions of HTA that were taken directly from OTA's work. These have stood the test of time and have now been adopted by international societies and networks (Box 1.2).

Box 1.2: Definitions

Health technology is the application of scientific knowledge in healthcare and prevention, including technologies such as diagnostics, treatments, medical equipment, pharmaceuticals, rehabilitation, prevention methods, organisational and supportive systems within which healthcare is provided.

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.

(EUnetHTA 2016a)

HTA is a field of scientific research to inform policy and clinical decision-making on the introduction and use of health technologies. Health technologies include pharmaceuticals, devices, diagnostics, procedures and other clinical, public health and organisational interventions.

HTA is a multidisciplinary field that addresses the clinical, economic, organisational, social, legal and ethical impacts of a health technology, considering its specific healthcare context as well as available alternatives. The scope and methods of HTA may be adapted to the needs of a particular health system, but HTA processes and methods should be transparent, systematic and rigorous. In health systems throughout the world, HTA plays an essential role in supporting decision-making.

(Health Technology Assessment International (HTAi) 2016)

The proliferation of HTA in the past two decades is shown by the breadth of membership in the International Network of Agencies for HTA (INAHTA). INAHTA is a society for non-profit HTA bodies, with 51 members in 31 countries in 5 continents (INAHTA 2016). Furthermore, in 2014, the World Health Organization (WHO) issued a declaration recognising that HTA offers rigorous and structured research methodologies and transparent and inclusive processes. It recommended the use of HTA in all its member states to guide policies for rational and efficient use of medicines and devices to inform policies of universal health coverage and support sustainable health systems (World Health Organisation 2014).

1.3.2 The HTA Process

HTA has a scientific basis, involving critical appraisal of evidence available from research. However, as HTA seeks to inform policy about the use or organisation of a health intervention in a national, regional or local context, the process of doing HTA is different in each healthcare system. It takes account of the system's responsibilities, structure, care pathways and policy drivers (Chap. 31).

HTA has been described as:

- Assessment: critical review and scientific summary of the (international) evidence about relevant aspects of the health technology (Garrido et al. 2008)
- Appraisal: wider consideration of the assessment information, taking account of (local) values and other factors (Garrido et al. 2008)

The processes for assessment have been developed over decades and arise from the evidence-based medicine movement. However, HTA goes beyond evidence-based medicine to interpret the evidence in relation to the local healthcare system. For this interpretation, a multi-stakeholder advisory group is often needed. In HTA systems that feed directly into healthcare decisions (such as for reimbursement decisions), this process is called appraisal, but in other systems that are more advisory in nature, this terminology may not be used (Chap. 28).

In the past decade, it has also been recognised that HTA may need to extend its remit beyond traditional assessment/appraisal boundaries to influence the generation of evidence for a health technology over its life cycle of development and use (Facey et al. 2015). HTA bodies can provide helpful advice on clinical studies that are primarily designed for other purposes (such as a regulatory authorisation) or on research specifically commissioned to study particular implications of the health technology (such as comparative effectiveness, economic evaluations or user attitudes). Where there are major uncertainties in the evidence at the time of HTA assessment, further evidence collection may be instigated to collect specific outcomes to confirm the value of a promising health technology in the so-called managed entry agreements (Klemp et al. 2011). HTA bodies can advise in both situations on the evidence that would be of value to HTA.

1.3.3 HTA Methods

HTA is founded on scientific research and seeks to answer clear, structured research questions about the implications (direct and indirect, intended and unintended) of using the health technology. It is often structured using the PICO framework from evidence-based medicine (Sackett et al. 1997):

- **P**opulation (who should be treated)
- **I**ntervention (technical specification of health technologies under study, how they will be given)
- **C**omparator (health technologies currently used in the health service)
- **O**utcome (what outcomes/impacts are important)

Research questions are answered primarily by secondary research (systematic review of published literature with critical assessment of relevant studies) or if no literature can be found, by primary research (undertaking new research).

One of the first detailed HTA handbooks published in English came from the Danish Centre for HTA (DACEHTA) in 2001. It was updated in 2007 (Kristensen and Sigmund 2008) and presented a comprehensive model of HTA based on:

- Clinical effectiveness
- Cost effectiveness organisational issues
- Patient aspects

The handbook covered the planning of HTA, ethical considerations, systematic literature review (for all aspects of the HTA), primary research to understand stakeholders perspectives (qualitative methods, survey methods, analysis of registries and measurement of health status), clinical effectiveness, patient aspects, organisational issues, economic issues, synthesis and quality assurance to formulate a sound basis for decision-making.

In the 1990s and early 2000s, collaborative HTA work was undertaken among HTA bodies in the EUR-ASSESS[1] and ECHTA[2] Projects (Banta et al. 1997, Jonsson et al. 2002). This was followed in 2006, by the European Commission-funded project to develop a European network for HTA (EUnetHTA) and three subsequent Joint Actions[3] of European Union (EU) Member States. The centrepiece of this work from a methodological standpoint has been the HTA Core Model® (EUnetHTA 2016b), which has nine domains:

1. Health problem and current health technologies
2. Description/technical characteristics
3. Safety
4. Clinical effectiveness

[1] Coordination and Development of Health Care Technology Assessment in Europe

[2] European Collaboration on HTA

[3] Joint Actions are initiatives that are co-funded by the European Commission and Member States.

5. Costs/economic evaluation
6. Ethical analysis
7. Organisational aspects
8. Patient and social aspects
9. Legal aspects

The HTA Core Model® documentation is a detailed report of over 400 pages, which describes how each domain should be studied, including assessment elements (research questions) that might be relevant for each domain and methods to study those questions, by secondary or primary research.

Another handbook for HTA by Goodman (2014), based on his HTA 101 course, includes methodology chapters and policy topics that have emerged over the past decade including comparative effectiveness research, managed entry agreements (risk-sharing schemes, patient access schemes), innovation and rapid HTA.

These forms of HTA that study a range of impacts of a health technology are often called 'full HTA' or 'comprehensive HTA'.

Although the focus and methods used for HTA in each country vary, all HTA bodies evaluate the clinical effectiveness of a technology, assessing clinical evidence from international trials in relation to the clinical pathways in their local healthcare system. They are seeking to understand the 'added value' of a health technology compared to their current standard of care. Often, added value is not clear for the entire population, and so a specific sub-group may be identified in whom the added value is higher or who have greater need for a new technology because they have more limited alternatives.

Many HTA bodies also evaluate economic considerations such as cost-effectiveness (value for money) and budget impact (total cost per year of the treatment for all the patients that are expected to receive the treatment). Only a few HTA bodies systematically and explicitly evaluate social, legal or ethical issues or organisational or patient aspects.

One of the major changes to HTA methodology in the 2000s was the move away from comprehensive HTAs to more rapid processes that could inform reimbursement/coverage decisions of medicines. This has meant HTAs occur at the point of market launch when the only evidence available is from the clinical research developed for the regulatory submission, which may not be published (Facey et al. 2015).

To inform reimbursement, HTAs had to be produced much quicker and in larger numbers than comprehensive HTA allowed. These more rapid HTAs also required new processes that were less resource intensive for HTA staff. So there was a move away from HTA researchers undertaking systematic reviews of all published evidence and producing comprehensive reports about all the implications of using a health technology. Instead, submissions of evidence were sought from health technology developers, or rapid literature reviews of other systematic reviews were undertaken. This has resulted in shorter HTA reports targeted at decision-makers (Watt et al. 2008). In the past decade, as new countries have instigated HTA, most have taken on these more rapid processes, and so assessment of the wider implications of using a health technology have been lost (Nielsen et al. 2011).

To inform reimbursement, HTAs had to be produced much quicker and in larger numbers than comprehensive HTA allowed. These more rapid HTAs also required new processes that were less resource intensive for HTA staff. So there was a move away from HTA researchers undertaking systematic reviews of all published evidence and producing comprehensive reports about all the implications of using a health technology. Instead, submissions of evidence were sought from health technology developers, or rapid literature reviews of other systematic reviews were undertaken. This has resulted in shorter HTA reports targeted at decision-makers (Watt et al. 2008). In the past decade, as new countries have instigated HTA, most have taken on these more rapid processes, and so assessment of the wider implications of using a health technology have been lost (Nielsen et al. 2011).

HTAs often find 'uncertainties' in the evidence due to:

- Short-term outcomes studied in controlled clinical trials that may not reflect clinical practice
- Lack of data about the health technology comparator of interest
- Limited evidence about the costs and impacts of the health technology and its comparator over the lifetime of a patient

These are often exacerbated in rapid HTAs, where evidence is only available from limited sources over a short time period.

These uncertainties are often the key areas of discussion by an appraisal or multi-stakeholder advisory committee. Indeed, Hofmann noted that value judgements are needed in economic evaluations, analysis of ethical, legal and social issues and reporting of HTA results and in appraisal and decision-making (Hofmann et al. 2014). However, few HTA bodies are explicit about their scientific and social value judgements (Rawlins 2014, Hofmann et al. 2014).

As (OTA 1976) identified, when there may be differences in values, as broad a group as possible should be involved in preparing the assessment, including adversaries on certain issues. Daniels and Sabin (2008) also indicated that decisions must rest on reasons that stakeholders can agree. Furthermore, as HTAs have been increasingly used to inform reimbursement/coverage decisions that manage patient access to health interventions, public and patient interest in HTA has increased. As a result, various groups of stakeholders and academics have developed principles for HTA (Wilsdon and Serota, 2011) that cover the structure, methods, process and use of HTA. These all include the need to involve stakeholders in HTA.

1.4 Patient Involvement in HTA

HTA processes could be considered as including the five pillars of quality relating to effectiveness, safety, efficiency, timeliness and equity, and so the sixth pillar of quality relating to patient centredness should also be included (Committee on Quality Health Care in America 2001). Moreover, it has now been recognised that patient involvement in HTA can contribute to democratic, technocratic, scientific and instrumental goals (OHTAC Public Engagement Subcommittee 2015).

In this chapter (and for the rest of the book), we use the term ‘patient’ to mean anyone who has direct experience of living with the condition being studied in the HTA or who may be eligible to receive the technology (e.g. specific members of the public who might be invited for vaccination or to undertake a diagnostic intervention). This can include individuals who have had or have the condition, informal caregivers (sometimes called carers) and voluntary groups that advocate for patients, such as patient organisations, self-help groups, user groups and patient associations. This does not include general members of the public or citizens who may use other services in the health system or someone who is a clinical expert.

‘Involvement’ is a term that is used widely but may be understood in different ways in different countries and alternative terms such as engagement, participation and empowerment may be used (Barello et al. 2014). This book presents the concept developed by the HTAi Interest Group for Patient and Citizen Involvement in HTA (the HTAi Interest Group) that patient *involvement* in HTA encompasses two distinct but complementary ways in which HTAs could be strengthened by taking account of patients’ perspectives (adapted from Facey et al. 2010):

- *Research* into patient aspects (patients’ experiences, preferences, perspectives)
- Patient *participation* in the HTA process

Coulter (2004) stressed that as HTA involves value judgments, it should have greater patient and public participation. She stated that a patient-focused HTA would determine the types of questions that patients want to be answered and engage them in determining HTA priorities, designing and conducting assessments and appraisals, receiving and using findings from HTA and debating policy priorities and rationing. In 2010, Gauvin et al. (2010) provided a framework to consider the different levels of patient and public participation that could be used at every stage of HTA. This framework has been developed further in Chap. 5 to identify specific mechanisms of participation that have been used by the HTA bodies who present their work in Part III.

Coulter (2004) also stated that the HTA research process should include a variety of methods to determine the experience, views and preferences of wide groups of patients. The DACEHTA Handbook on HTA (Kristensen and Sigmund 2008) and the EUnetHTA Core Model® (EUnetHTA 2016b) presented methods to obtain robust evidence about patients’ perspectives and experiences, but this is within the context of the full HTA. For the many HTA bodies that focus on the assessment of clinical and cost-effectiveness, and who must do this in a rapid time frame, there are questions about how to develop robust patient-based evidence (Chap. 4). Like all issues in HTA, planning is key and such research should be planned well in advance (Facey et al. 2010) and international, multidisciplinary collaborations encouraged. Part II of this book will present methodologies for qualitative and quantitative research to understand patient aspects, including discussion of these challenges.

In 2014, HTAi undertook an international Delphi process to create consensus on *Values and Quality Standards for Patient Involvement in HTA* (HTAi 2014) as presented in Table 1.1 and Box 1.3. The values clearly relate to either research or participation, but the quality standards may relate more to participation with the assumption that research has its own ethical standards.

Table 1.1 HTAi Values for Patient Involvement in HTA (HTAi 2014)

Value	Descriptor
Relevance	Patients have knowledge, perspectives and experiences that are unique and contribute to essential evidence for HTA.
Fairness	Patients have the same rights to contribute to the HTA process as other stakeholders and have access to processes that enable effective engagement.
Equity	Patient involvement in HTA contributes to equity by seeking to understand the diverse needs of patients with a particular health issue, balanced against the requirements of a health system that seeks to distribute resources fairly among all users.
Legitimacy	Patient involvement facilitates those affected by the HTA recommendations/decision to participate in the HTA, contributing to the transparency, accountability and credibility of the decision-making process.
Capacity building	Patient involvement processes address barriers to involving patients in HTA and build capacity for patients and HTA organizations to work together.

Box 1.3: HTAi Quality Standards for Patient Involvement in HTA (HTAi 2014)

General HTA process

1. HTA organisations have a strategy that outlines the processes and responsibilities for those working in HTA and serving on HTA committees to effectively involve patients.
2. HTA organisations designate appropriate resources to ensure and support effective patient involvement in HTA.
3. HTA participants (including researchers, staff, HTA reviewers and committee members) receive training about appropriate involvement of patients and consideration of patients' perspectives throughout the HTA process.
4. Patients and patient organisations are given the opportunity to participate in training to empower them so that they can best contribute to HTA.
5. Patient involvement processes in HTA are regularly reflected on and reviewed, taking account of the experiences of all those involved, with the intent to continuously improve them.

For individual HTAs

6. Proactive communication strategies are used to effectively reach, inform and enable a wide range of patients to participate fully in each HTA.
7. Clear timelines are established for each HTA with advance notice of deadlines to ensure that appropriate input from a wide range of patients can be obtained.
8. For each HTA, HTA organisations identify a staff member whose role is to support patients to contribute effectively to HTA.
9. In each HTA, patients' perspectives and experiences are documented, and the influence of patient contributions on conclusions and decisions is reported.
10. Feedback is given to patient organisations who have contributed to an HTA, to share what contributions were most helpful and provide suggestions to assist their future involvement.

1.5 Discussion

As Part III of this book shows, HTA bodies vary widely in their roles and functions. Some undertake comprehensive HTAs; others perform rapid HTAs. Some have a remit to do the assessment, others do appraisal, some do both. Some assess individual health technologies in each HTA. Some assess a wide range of health technologies for a condition in one HTA. Some provide scientific advice to health technology developers about their trial design, and some manage registries to collect evidence post HTA to inform a future reassessment.

HTA appraisal committees judge the available evidence within the local social and political context, trying to create fair processes with consistent decisions that can be explained. As Coulter (2004) noted the balancing act of individual needs versus population requirements cannot be left to 'experts' alone. Patients (and citizens) need to understand the choices confronting policymakers and have the chance to be involved in determining priorities and trade-offs, but this must be done in a manner that promotes fair decisions for all users of the health system (Coulter 2004). Indeed, as Menon et al. (2015) stated, patient involvement can help resolve the decision uncertainties that arise in any HTA.

Patient involvement in HTA can help with the difficult value judgments that arise when clinical and economic evidence is limited, or added value is at the cusp of a pre-defined threshold, by explaining the real-world implications for patients. This becomes increasingly important as expedited regulatory pathways (Eichler et al. 2015, Food and Drug Administration 2015), an increased number of products for rare diseases and stratified medicine yield smaller clinical evidence bases. It is also relevant for all forms of health technologies other than medicines, where the evidence base has always been sparser.

HTA has been described as 'a bridge between the world of research and the world of decision-making' (Battista and Hodge 1999 [1464]). I have often modified this image to explain that patient involvement provides the lights on the bridge. It can alter the value judgments made in any HTA by elucidating the unintended and indirect impacts of the health technology, illuminating areas of unmet need, outcomes that matter to patients and informing determination of added value.

1.6 Conclusion

This chapter began with a review of HTA showing that when it was developed 40 years ago, it was intended to assess all the implications of using a health technology, and explicit questions were developed for patients and families. As HTA has evolved and been used to inform reimbursement and coverage decisions, comprehensive assessments are less common, and in many jurisdictions, focus has been placed on clinical effectiveness and cost-effectiveness. Systematic research on patients' perspectives and experiences has often been replaced by processes to help patients participate in HTA. These elements of research into patient aspects and patient participation are complementary, and both are the basis for how HTAi would define patient involvement in HTA. This is important because patient involvement

can identify unique patients' perspectives that can help interpret the clinical evidence base and inform the value judgments that are inherent throughout the HTA process.

Acknowledgements The author would like to acknowledge helpful comments received from Finn Børlum Kristensen, Egon Jonsson, Michelle Mujoomdar and the coeditors on the first draft of this transcript. All views expressed and any errors are entirely the responsibility of the author.

The author is an independent consultant who undertakes paid and unpaid work for HTA bodies and patient organisations and receives expenses to attend meetings. She also undertakes consultancy work for the pharmaceutical industry that is paid and may relate to HTA submissions and patient involvement strategies in medicine development.

References

Banta HD, Werkö L, Cranovsky R, et al. Introduction to the EUR-ASSESS project. Int J Technol Assess Health Care. 1997;13:133–43.

Banta D, Jonsson E. History of HTA: Introduction. International Journal of Technology Assessment in Health Care. Cambridge University Press. 2009;25(S1):1–6.

Barello S, Graffigna G, Vegni E, Bosio AC. The challenges of conceptualizing patient engagement in health care: a lexicographic literature review. J Participat Med. 2014;6:e9.

Battista RN, Hodge MJ. The evolving paradigm of health technology assessment: reflections for the millennium. CMAJ. 1999;160:1464–7.

Committee on Quality Health Care in America. Crossing the quality chasm: a new health system for the 21st century. Washington DC: Institute of Medicine; 2001.

Coulter A. Perspectives on HTA: response from the patient's perspective. Int J Technol Assess Health Care. 2004;20:92–6.

Daniels N, Sabin JE. Accountability for reasonableness: an update. BMJ. 2008;337:a1850. doi:10.1136/bmj.a1850.

Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. 2nd ed. Oxford: Oxford University Press; 2006.

Eichler H-G, Baird LG, Barker R. From adaptive licensing to adaptive pathways: delivering a flexible life-span approach to bring new drugs to patients. Clin Pharm Ther. 2015;97:234–46.

EUnetHTA. Common Questions. http://www.eunethta.eu/about-us/faq#t287n73 (2016a). Accessed 25 Jan 2016.

EUnetHTA. EUnetHTA joint action 2, work package 8. HTA Core model® version 3.0 (pdf). Copenhagen: EUnetHTA; 2016b. http://eunethta.eu/sites/5026.fedimbo.belgium.be/files/HTACoreModel3.0.pdf. Accessed 11 Apr 2016

Facey K, Boivin A, Gracia J, Hansen HP, Lo Scalzo A, Mossman J, et al. Patients' perspectives in HTA: a route to robust evidence and fair deliberation. Int J Technol Assess Health Care. 2010;26:334–40.

Facey K, Henshall C, Sampietro-Colom L, Thomas S. Improving the effectiveness and efficiency of evidence production for health technology assessment. Int J Technol Assess Health Care. 2015;31:201–6.

Food and Drug Administration. Fast track, breakthrough therapy, accelerated approval, priority review. Washington DC: FDA; 2015. http://www.fda.gov/forpatients/approvals/fast/ucm20041766.htm. Accessed 9 May 2015.

Garrido MV, Zentner A, Busse R. Health systems, health policy and health technology assessment. In: Garrido MV, Kristensen FB, Nielsen CP, Busse R, editors. Health technology assessment and health policy-making in Europe. Copenhagen: World Health Organisation on behalf of European Observatory on Health Systems and Policies; 2008. p. 53–78.

Gauvin F-P, Abelson J, Giacomini M, Eyles J, Lavis JN. "it all depends": conceptualizing public involvement in the context of health technology assessment agencies. Soc Sci Med. 2010;70:1518–26.

Goodman CS. HTA 101 – an introduction to health technology assessment. Bethesda MD: National Library of Medicine; 2014. https://www.nlm.nih.gov/nichsr/hta101/HTA_101_FIN. Accessed 5 Apr 2016

Hofmann B, Cleemput I, Bond K, et al. Revealing and acknowledging value judgments in health technology assessment. Int J Technol Assess Health Care. 2014;30:579–86. doi:10.1017/S0266462314000671.

HTAi. HTAi values and quality standards for patient involvement in HTA. (2014.) http://www.htai.org/fileadmin/HTAi_Files/ISG/PatientInvolvement/v2_files/Info/PCISG-Info-PosterValuesandStandards-30-Jun14.pdf. Accessed 31 Oct 2016.

HTAi. What is HTA? http://www.htai.org/htai/what-is-hta.html. (2016.) Accessed 25 Jan 2016.

INAHTA. International network of agencies for HTA. (2016). http://www.inahta.org/. Accessed 4 May 2016.

Jonsson E. History of health technology assessment in Europe. Int J Technol Assess Health Care. 2009;25(Supplement 1):42–52. doi:10.1017/S0266462309090412.

Jonsson E, Banta HD, Henshall C, Sampietro-Colom L. Special section: European collaboration for health technology assessment – developing an assessment network. Executive summary of the ECHTA/ECAHI project. Int J Technol Assess Health Care. 2002;18:213–7. doi:10.1017/S0266462302000235.

Klemp M, Frønsdal KB, Facey K. What principles should govern the use of managed entry agreements? Int J Technol Assess Health Care. 2011;27:77–83.

Kristensen FB, Sigmund HP. Health technology assessment handbook 2007 (2nd edition in English). Copenhagen: National Board of Health; 2008. http://sundhedsstyrelsen.dk/~/media/ECAAC5AA1D6943BEAC96907E03023E22.ashx. Accessed 5 Apr 2016

Menon D, Stafinski T, Dunn A, Short H. Involving patients in reducing decision uncertainties around orphan and ultra-orphan drugs: a rare opportunity? Patient. 2015;8:29–39. doi:10.1007/s40271-014-0106-8.

Metzler DO, Smith PC. Theoretical issues relevant to the economic evaluation of health technologies. In: Pauly MV, TG MG, Barros PP, editors. Handbook of health economic, vol. 2 ; 2012. Amsterdam (Oxford): North Holland (Elsevier)

Newdick C. Who should we treat? Rights, rationing and resources in the NHS. 2nd ed. Oxford: Oxford University Press; 2004.

Nielsen CP, Funch TM, Kristensen FB. Health technology assessment: research trends and future priorities in Europe. J Health Serv Res. 2011;16(Suppl 2):6–15.

Office of Technology Assessment (OTA). Development of medical technology – opportunities for assessment. Washington DC: United States Congress; 1976.

OHTAC Public Engagement Subcommittee. Public engagement for health technology assessment at health quality Ontario – final report from the Ontario health technology advisory committee public engagement subcommittee [internet]. Toronto: Queen's Printer for Ontario; 2015. http://www.hqontario.ca/Portals/0/documents/evidence/special-reports/report-subcommittee-20150407-en.pdf. Accessed 27 Aug 2016

Rawlins MD. Evidence, values, and decision making. Int J Technol Assess Health Care. 2014;30:233–8. doi:10.1017/S02664623140000154.

Sackett DL, Richardson WS, Rosenberg W, Haynes RB. Evidence based medicine – how to practice and teach EBM. New York: Churchill Livingstone; 1997.

Sigmund H, Kristensen FB. Health technology assessment in Denmark: strategy, implementation and developments. Int J Technol Assess Health Care. 2009;25(Supplement 1):94–101. doi:10.1017/S0266462309090485.

Watt A, Cameron A, Sturm L, Lathlean T, Badidge W, Blamey S, et al. Rapid vs full systematic reviews: an inventory of current methods and practice in health technology assessment. Int J Technol Assess Health Care. 2008;24:133–9.

Wilsdon T, Serota A. A comparative analysis of the role and impact of HTA – prepared for EFPIA, PhRMA, medicines Australia and EuropaBio. Charles River associates. Project no. D15891–00. 2011. http://www.efpia.eu/uploads/Modules/Documents/hta-comparison-report-updated-july-26-2011-stc.pdf Accessed 12 Apr 2016.

World Health Organisation. Health intervention and technology assessment in support of universal health coverage. WHO Declaration WHA67.23. Agenda Item 15.7.N24 2014. http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R23-en.pdf?ua=1. Accessed 31 Oct 2016.