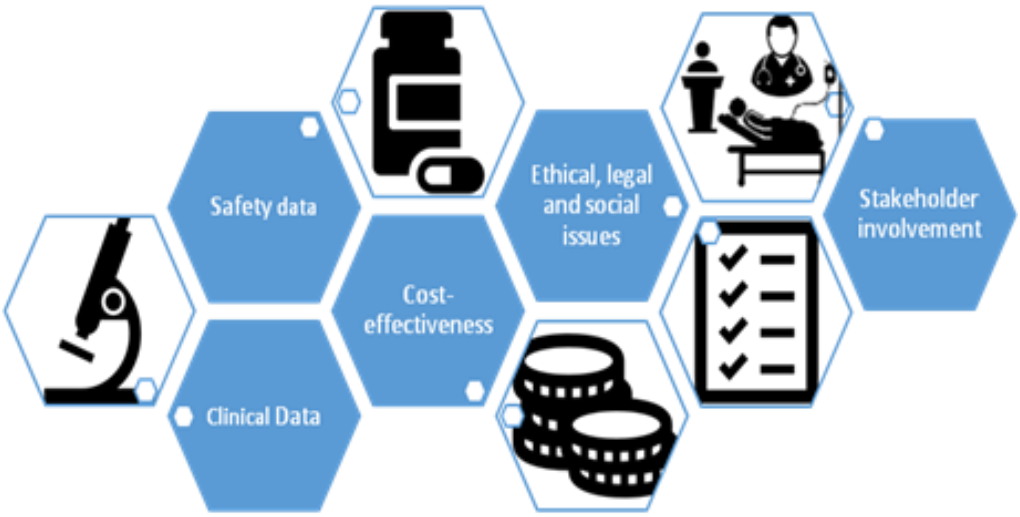
The VALIDATE handbook



VALIDATE

Values in doing assessments of healthcare technologies

The VALIDATE handbook:

An approach on the integration of values in doing assessments of health technologies

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Foreword

We are delighted to present the first handbook addressing how to integrate empirical research (facts) and normative inquiry (values) when assessing health technologies (HTA). This handbook is one of the products of the "VALues In Doing Assessments of healthcare TEchnologies" (VALIDATE) project. The VALIDATE project was initiated to complement how HTA is currently conducted. In current approaches to HTA, evidence is often considered value free (neutral), independent from the perspective of stakeholders. With the VALIDATE approach we show that facts and values are intertwined. This means that HTA should be considered as a type of policy analysis, wherein the assessment of safety, clinical and cost-effectiveness of health technologies, as well as their wider ethical, legal, and social implications is conducted from the view that these aspects are closely interrelated, and wherein stakeholders are involved in a more productive way throughout the process of HTA (i.e., an integrative HTA approach). To reach this objective, an e-learning course has been developed, which will help students to deepen their understanding of the policy and societal context of HTA, the role of stakeholders in HTA, and the interplay between facts and values in identifying the relevant questions and evidence to be addressed in an assessment of health technologies (https://validatehta.eu/e-learning-course/). This handbook is a supporting tool for the e-course since it reflects its theoretical basis as well as presents pragmatic applications through case-studies. Nevertheless, this handbook provides the necessary information and knowledge to guide those who want to embark on an integrative HTA approach, therefore it can be also used as standalone tool.

This handbook is directed to anyone who wants to understand, initiate, or broaden and deepen their knowledge and skills of HTA. Therefore, the targeted audience is broad, including Master/PhD students in HTA, health policy and management, health sciences and biomedical sciences, national/regional/academic HTA scientists, public health professionals, industry, health services researchers and policy makers.

We very much hope that this handbook will serve as a ready-reference among HTA doers and users, contributing to improved evidence-informed deliberative decision-making. Engaging stakeholders actively in deliberations throughout the HTA process enables exchange of views on argumentation and evidence. This will create an opportunity for more cohesive and inclusive societies.

The VALIDATE Consortium

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Part 1. Introduction

Chapter 1. First things first

Abstract

This first chapter of the handbook introduces you to the background and aims of the VALIDATE project and its approach to Health Technology Assessment (HTA). After discussing the general challenges related to the implementation and use of health technology, and the role of HTA in addressing these challenges, the ideas that guide the VALIDATE approach to HTA are introduced. An overview of the handbook is provided, in which these ideas are further developed. This chapter ends with introducing the central case study (Non-Invasive Prenatal Testing) that is revisited in every chapter to help the reader better comprehend and relate on how the VALIDATE approach is implemented in practice.

Key messages of this chapter: the VALIDATE approach states that values and normative analysis are an integral part of HTA and offers an approach for taking this into account.

After reading this chapter, you will be able to understand the central elements of the VALIDATE approach and know in which chapters of this handbook you can find elaborations of these elements.

EU Erasmus+ project VALIDATE

In the EU Erasmus+ strategic partnerships project "***VAL****ues* ***I****n* ***D****oing* ***A****ssessments of healthcare* ***TE****chnologies"* (VALIDATE), Health Technology Assessment (HTA) agencies and academic institutes are collaborating to introduce and train the next generation of HTA experts to a novel, integrative approach to HTA[1]. The objective of the VALIDATE project is to develop an approach to HTA that allows for the integration of empirical analysis and normative inquiry, associated teaching materials and opportunities for internships for HTA students. To achieve this goal, a consortium of seven academic and HTA organizations (Radboudumc, Università Cattolica del Sacro Cuore, Linköping Universitet, Departamento de Salud, University of Amsterdam, Norwegian University of Science and Technology, Hospital Clínic de Barcelona) has developed a consensus statement on what knowledge and skills are required to conduct this novel type of integrative HTA. Based on the consensus statement, an e-learning course and this handbook were developed to educate the next generation of HTA experts in conducting integrative HTA. The handbook can be seen both as an alternative and a supplement to the e-learning course.

[1] For more information about EU Erasmus+ projects: https://ec.europa.eu/programmes/erasmus-plus/opportunities/strategic-partnerships-field-education-training-and-youth_en; more information on the VALIDATE project can be found on: https://www.validatehta.eu.

This handbook will introduce you to the HTA approach developed in the VALIDATE project; we explain, and discuss all the elements of the approach, and provide examples of how the approach could be used. This first chapter will provide an overview of the VALIDATE approach, the contents of the handbook, and the rationale behind VALIDATE. A more in-depth discussion of the philosophy of VALIDATE, that is inspired by pragmatism, can be found in Chapter 7 of this handbook.

Scope of this handbook

Because the VALIDATE approach is primarily aimed at providing a methodology for identifying and addressing normative decisions and issues related to the practice of HTA, with a focus on moral and societal values, the discussion of legal aspects and frameworks is beyond the scope of this handbook. Although legal frameworks set boundaries for the practice of HTA, and it is highly relevant to be aware of them, an HTA practitioner still needs skills to address normative questions (because they are not always answered or are even raised by legal frameworks) and to identify different interpretations of the values that may have been the original impetus for a legal framework.

A task for HTA?

We are living at a time in which our lives are increasingly *technological* lives. What we do, how we communicate, the way in which we experience and interact with the world, is more and more determined by technology. Also, in the domain of health, technology is shaping our way of doing things[2]. We make use of, among others, drugs, devices, vaccines, different ways of organizing healthcare systems, to prevent, diagnose or treat medical conditions and promote health. Although these technologies enable us to improve our health, they also give rise to complex questions concerning the nature of human life, the sustainability and equity of healthcare systems, and their potential impact on our society.

Given these extensive uses of health technology, healthcare systems continuously need to adapt to the challenges that are associated with it. This implies many decisions that need to be made, and to introduce more rationality into decision- and policy-making the area of HTA emerged as an important scientific response to such policy-related endeavours. HTA is a "***multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The***

[2] Although a general definition of 'technology' is hard to give, and there are many discussions on this concept and its nature, we will use the term to refer to "*The application of scientific or other organized knowledge – relating to tools, techniques, products, processes, methods, modes of organisation, or systems – to practical tasks".* And a health technology is: "*Any intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery*". In healthcare, technology encompasses: drugs, diagnostic tests, devices, equipment and supplies, medical and surgical procedures, support systems, and organizational and managerial systems (source: www.htaglossary.net).

purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system" (O'Rourke et al, 2020).

From its very inception, practitioners of HTA[3] have been committed to the *comprehensive* study of the consequences associated with the use of health technologies (i.e., the study of a broad spectrum of consequences, ranging from clinical to economic and social aspects). This grew out of an awareness that health technology can have profound, unintended, and unforeseen consequences, that need to be taken into account when making decisions about the use of such technologies. It was recognized that there are different types of impact that need to be addressed in HTA: safety, clinical effectiveness, cost-effectiveness, and the ethical, legal, and social implications (also known as ELSI) of health technology. Despite this original impetus for HTA to perform this comprehensive study of implications of health technology, its focus has been often narrowed to issues of affordability (Daniels et al, 2016; Lehoux, 2006; ten Have, 2004). Assuming that the budget for healthcare is limited, and that technology is the main cost-driver in healthcare, HTA is often reduced to answering questions like *Is this technology effective? Is it safe? Does it provide 'value for money'?* Although answering these questions may be necessary, it may not cover the broad range of issues and concerns that are raised by health technologies and that need to be addressed by decision-makers. *What is the value of specific innovations? What impact do they have on clinical practice, population health, and social development?* The importance of these questions is recognized, but in the current practice of HTA these questions are often neglected or addressed *separately* as ethical, legal, and social issues (Bellemare et al, 2018; Lehoux et al, 2007).

Although there can be many practical and methodological reasons for this current situation of separate analyses in HTA, one fundamental problem is that the analysis of these different types of impact (e.g., safety, clinical effectiveness, cost-effectiveness, ELSI) are seen as completely different in their epistemic nature (i.e. 'epistemology' is the study of the nature, origin, and scope of knowledge; Refolo, Sacchini, 2016). This distinction between different types of analysis suggests that there are different ways of studying a health technology:

(1) Through *empirical research* (e.g., studying safety, clinical and cost-effectiveness)

(2) Through *normative inquiry* (e.g., studying ethical, legal, and social implications)

Consequently, an assessment of aspects such as safety and cost-effectiveness is seen as *objective* and consisting of the collection of empirically testable ***facts*****,** whereas studies of the wider implications

[3] With 'HTA practitioner' we refer to anyone who may be involved in conducting assessments of health technology. Given the multidisciplinary nature of this exercise, this may involve people from diverse disciplines, ranging from ethics to social sciences to biomedical sciences.

(Ethical, legal and social issues) are seen as *subjective* and solely involving ***value*** judgments (Legault, Suzanne, 2018, Refolo, Sacchini, 2016). This view makes it very hard to see how HTA could legitimately integrate these 'different' types of inquiry, especially when value judgments may be seen as a threat to the legitimacy of HTA itself (Ducey et al, 2017). This also leaves decision-makers uncertain as to how, if at all, to take into account ethical issues.

As a result, health technologies and the practices that are created by them seem to be completely distinct from moral values. It is as if they occur in completely separate, mutually inaccessible, domains, being divided between a 'neutral' domain (e.g., facts about consequences of health technology) and a 'value-laden' domain (e.g., ideas about the (un)desirability of health technology). Consequently, it becomes very difficult to answer questions on the *desirability* of (a particular) using health technology that move beyond presuming that this is captured by assessing their effectiveness and cost-effectiveness. To be able to answer these broader questions on the value of health technology an integrative approach is needed wherein the study of safety, clinical and cost-effectiveness of new healthcare technologies and their wider ethical, legal and social implications are closely integrated. Therefore, a critical analysis of a strict ***fact/value distinction*** in HTA is needed to foster an integrative approach to HTA.

Going back to basics

Instead of assuming a strict dichotomy between empirical and normative aspects of health technology, we propose an approach towards HTA that aims to complement the current practice of HTA and allows it to assess health technologies in a more inclusive fashion (including different consequences and properties of health technology, as well as different stakeholder perspectives). Our goal is to present a framework that supports a more integrative approach to HTA, wherein the study of safety, clinical and cost-effectiveness of new health technologies and their wider ethical, legal, and social implications are closely integrated, and stakeholders are involved in a more productive way throughout the process of HTA. This could help HTA in addressing the type of policy questions that were actually the original impetus for developing (health) technology assessment (Lehoux et al, 2007; Lucivero, 2016; Torgersen, 2019). This means going back to the roots of HTA, defined as a form of policy research (Banta et al, 1993). It should also help HTA to address the needs of a population and developments in the organization of healthcare systems related to including the patients and citizens perspective in decision-making (Abrishami et al, 2017).

Elements of the VALIDATE approach and preview of this handbook

Overview of this handbook

The goal of this handbook is to deepen your understanding of the different elements of the VALIDATE approach. The structure of this handbook is as follows:

Part 1. Introduction

- ***Chapter 1:*** First things first (*Bart Bloemen & Gert Jan van der Wilt*)
- ***Chapter 2:*** The fact/value dichotomy (*Pietro Refolo & Dario Sacchini*)

Part 2. Making it work

- ***Chapter 3:*** The method of reconstructing interpretive frames (*John Grin*)
- ***Chapter 4:*** Scoping (*Wija Oortwijn*)
- ***Chapter 5:*** Approaches in ethics with a touch of meta ethics (*Bjørn Hofmann & Lars Sandman*)
- ***Chapter 6:*** Context matters (*Iñaki Gutiérrez-Ibarluzea & Laura Sampietro-Colom*)

Part 3: The philosophy of VALIDATE

- ***Chapter 7:*** A philosophical summary of the VALIDATE approach (*Bart Bloemen & Gert Jan van der Wilt*)

Part 4: Conclusion

- ***Chapter 8:*** *Summing up VALIDATE (Wija Oortwijn & Gert Jan van der Wilt)*

In the following, an overview of the elements of the VALIDATE approach is provided together with a preview of the different chapters in this handbook. This will help you with getting an idea about what you will learn by reading these chapters.

The VALIDATE approach

The VALIDATE approach starts with revisiting the fact/value dichotomy in HTA. In contrast to the dominant interpretation described above, our starting point is that *each type of impact* of a health technology have *both* an *empirical* and a *normative* (or value) dimension:

- Safety: refers to the sort of outcomes that we wish to avoid *because of our commitment to avoiding harm* (the principle of 'non-maleficence').

- Clinical effectiveness: refers to benefits obtained in clinical practice and are the sort of outcomes that we wish to achieve *because of our commitment to doing good* (the principle of 'beneficence'), e.g., prolong life, alleviate suffering, restore functioning, etc.
- Cost-effectiveness: refers to the sort of outcomes that we wish to achieve *because of our commitment to distributive justice / fairness* (e.g., proportionality between resource commitment and reduction in burden of illness; to ensure equitable access to healthcare).

So, ethical questions concerning the desirability of a health technology are *guiding* the assessment of the impact of a health technology as depicted in Figure 1.

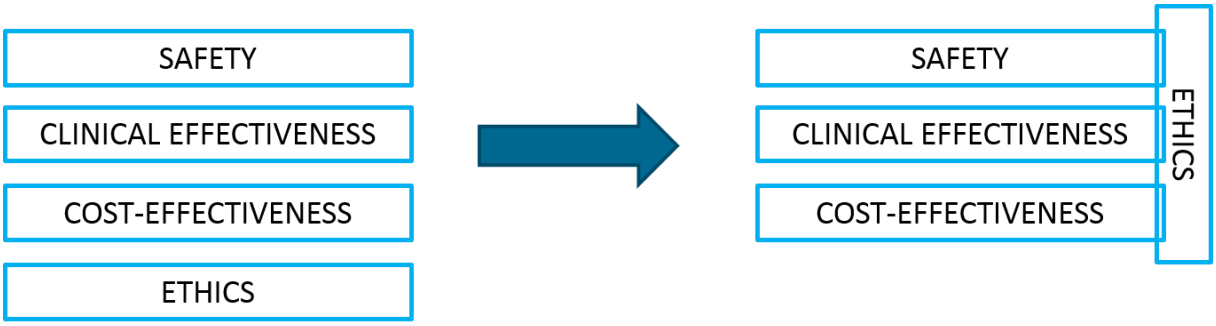


Figure 1. Normativity of assessment aspects

Therefore, ELSI questions concerning health technology are not in a *separate* category with respect to the nature of their analysis, and the role of value judgments. And in every empirical inquiry, the following questions need to be addressed: (i) What sort of things *matter* to us, and for what reason? (ii) What sort of things *may happen* when we would start using this technology? (iii) And, about what sort of things can we obtain *reliable knowledge*? In other words, HTA is not a matter of collecting *THE* facts, but a matter of collecting facts that are considered to be:

- **Relevant:** which consequences are desirable or to be avoided **in view of values** to which we are committed;
- **Plausible:** which consequences can be plausibly associated (on the basis of background theory and/or evidence) with the use of a health technology in a specific context?
- **Amenable to scientific inquiry:** which consequences can be studied by methods of inquiry that are held to produce reliable knowledge and understanding?

☛ **Chapter 2** will provide more information about the history of the fact/value dichotomy, the criticism it received, its role in HTA, and our reconceptualization of the relation between facts and values in HTA.

HTA as a form of policy research

Another important element of the VALIDATE approach is that we view HTA as a form of policy research. Given that HTA aims to provide decision-makers with information on policy alternatives, it should actually be able to address policy-related questions that are raised by health technology. As already discussed, these questions move beyond the affordability of health technologies and demands an integration of empirical and normative analysis. This requires that HTA takes into account the needs of a population and decision-makers, to be able to contribute to an equitable, efficient, and high-quality healthcare system (Abrishami et al, 2017).

To take this policy context into account, HTA should make use of insights from policy sciences. Starting with the realization that there may be different views in society and cultures when it comes to what is regarded as relevant and plausible policy options with respect to the use of health technology, we should learn how to explore and address this pluralism. Understanding these different views is essential when determining which types of information should be produced in an HTA. To explore and understand these views, we propose to make use of the method of ***reconstructing interpretive frames***. This method aims to, by involving and interviewing stakeholders, reconstruct the conceptual schemes that stakeholders use (often implicitly) to make sense of concrete situations and guide their actions. These *interpretive frames* consist of the following elements:

- Judgment of solutions: What is likely to work? Which measures could be helpful in addressing this health problem? Which measures would probably not be helpful, and why not? Is this health technology likely to be effective, appropriate, feasible in this context?
- Problem definitions: What are the key problems of the current situation? Which problems are encountered by patients, their families, healthcare providers or healthcare managers in the care of…?
- Background theory: What are the main causes and mechanisms responsible for the current situation?
- Normative preferences: What is desirable? What is it that we would like to achieve and what is it that we would like to avoid?

These interpretive frames can be considered a type of tacit knowledge: they remain mostly implicit, but can be made explicit. The method for this is called reconstructing interpretive frames. The purpose of making factual and normative assumptions underlying judgments on health interventions and technologies explicit is to enable a critical, constructive scrutiny of those assumptions and to foster learning among stakeholders. Moreover, the output of this reconstruction can be used to understand

the type of policy problem you are dealing with and to make decisions on which type of information should be produced or collected in an assessment.

> ☛ **Chapter 3** will provide more information about the method of reconstructing interpretive frames and insights from policy sciences that are relevant to the practice of HTA.

HTA and the importance of scoping

When the type of policy problem you are dealing with is clear, you have to translate this into research questions. This process of translating policy problems into research questions is called ***scoping.*** To avoid answering the wrong questions, neglecting the concerns and values of decision-makers and stakeholders, it is important that the HTA community addresses more clearly what matters to the relevant healthcare system, as well as the relevant stakeholders, and the reasons why. This should be done before the start of an actual assessment, and based on this the relevant research questions to be addressed should be identified. This could ensure the relevance of the information collected during an assessment, and help policy-makers in explaining their decisions to the populations they serve.

> ☛ **Chapter 4** will provide more information about how to define the objectives and research questions of an HTA by a systematic exploration of relevant aspects of a policy problem and the involvement of stakeholders. It integrates the lessons of Chapters 2 and 3: because the relevance of facts depends on the adopted perspective, and there are different perspectives in society with respect to the desirability of health technology, the objectives of an HTA should be defined by taking into account these perspectives.

HTA and the importance of normative analysis

An important element in defining the objectives and research questions of an HTA is the explication and clarification of what makes a health technology desirable. This helps in identifying relevant outcome measures. For example, the use of cost-effectiveness analysis should be supported by ethical arguments that explain why maximizing efficiency is a relevant goal to be realized by the use of a health technology. The relation between maximizing efficiency and realizing an equitable, efficient, and high-quality healthcare system should be made clear. Such a ***normative analysis*** not only helps in improving

the consistency between decisions that are informed by HTA, it also prevents that HTA focuses upon aspects that are not considered relevant by decision-makers and the population.

Acknowledging a central role for normative analysis in HTA evokes several questions: *how can ethical questions be addressed in HTA? Is there more to ethics than just opinions? Which methods can be used?*

> ☛ **Chapter 5** will discuss the possibility of moral knowledge, different approaches to normative analysis, and introduces an overview of methods for conducting normative analysis in the context of HTA.

HTA and the importance of context

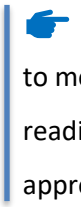
When conducting an HTA, you should also be aware that HTA is context-dependent. Whether the outcomes of an assessment should inform decisions at the national level, regional level, or at the level of a hospital, makes a difference when it comes to its objectives and research questions. In addition, the consequences of health technology are context-sensitive. The effects of health technology are influenced by the needs and demographics of a population, characteristics of a healthcare system, characteristics of the technology itself, the legal framework that guides its implementation, and cultural and social features of the situation in which it is used. These contextual factors all influence the conditions of use of health technology, and should be taken into account to increase validity of the outcomes of an assessment.

> ☛ **Chapter 6** introduces you to several aspects of the context of HTA and shows the importance of context during the assessment process, and discusses the particular perspective of hospital-based HTA.

The philosophy of VALIDATE

To conclude, a central tenet of the VALIDATE approach is that HTA is a practice in which facts and values meet. To be able to address policy-related questions, HTA should not only provide information on the *plausibility* of claims on potential consequences of health technology, it should also assess the *desirability* of these consequences. This requires both an understanding of the technology and its (potential) impact, as well as being able to think about this impact *in light of a set of norms and values*. As stated before, this means that normative analysis is an intrinsic part of HTA.

To propose such a central role for normative analysis in HTA may evoke a critical response. A widely held view – also within the context of HTA – is that there are no ways of rationally resolving disagreements on normative issues. This position is called ***moral scepticism***, which refers to a diverse collection of views that deny or raise doubts about various roles of reason in morality. If we are not able to offer a response to this position, the consideration of ethical issues in HTA is seriously hampered. Therefore, we need to rethink our position towards the nature of ethical issues in HTA.



Chapter 7 will elaborate our view on the nature of ethical issues in HTA, presenting a response to moral scepticism. This response is based on the philosophical tradition of pragmatism. After reading Chapter 7, you will understand the relation between pragmatism and the VALIDATE approach.

The handbook will end with a summarizing chapter, and a **glossary** of specific terms used. For those of you not very familiar with the topics discussed in this handbook it is highly recommended to have a look at the glossary.

Case study: Non-Invasive Prenatal Testing

To help you understand the VALIDATE approach, and relate the different elements to a real-world example, every chapter will return to the case study of Non-Invasive Prenatal Testing (NIPT). It is an example of a health technology that may be used in many different ways and, therefore, raises different ideas about its desirable use. In the following sections, we will shortly introduce this case study by providing background information and highlighting important issues related to assessing NIPT.

Prenatal screening

In many countries, pregnant women are offered different screening tests during pregnancy to identify any complications, diseases, or disorders at an early stage. The primary purpose of screening is to detect early disease or risk factors for disease in large numbers of *apparently healthy individuals*. Therefore, a major difference with diagnostic tests is that screening tests can be offered to individual who have no symptoms or any or any prior reasons for suspecting a higher chance at disease. In the case of prenatal screening tests, this means that they can be offered to any pregnant women irrespective of any prior knowledge on an increased risk of their unborn child having any medical conditions (e.g., based on age or genetic conditions in the family). This differs with available diagnostic

tests that only offered based on a certain form of suspicion that the unborn child will have a specific medical condition.

Besides blood tests that screen for infectious diseases and provide information on blood group, and a structural ultrasound scan that tests for anatomical anomalies, an important category of prenatal screening tests is those that aim to detect foetal chromosomal abnormalities. These tests identify genetic conditions of the unborn child, often focusing upon trisomy 13 (Patau syndrome), 18 (Edwards syndrome), and 21 (Down syndrome). Until recently, the screening strategy for these conditions consisted of offering *combined first-trimester screening* (CFTS) which entails an ultrasound examination and testing blood serum markers that collectively estimates the risk of a trisomy. After a positive test result (increased risk of trisomy), prospective parents where offered the choice to take an invasive prenatal test (e.g., amniocentesis, chorionic villus sampling) to confirm diagnosis or refrain from further testing (Hui et al, 2017).

Non-Invasive Prenatal Testing (NIPT)

In recent years, ***non-invasive prenatal testing*** (NIPT) has rapidly transformed the prenatal screening landscape. Following the discovery of cell-free foetal DNA, NIPT was introduced in clinical practice in 2011 and became increasingly available to pregnant women worldwide (Gadsboll et al, 2020, Hui et al, 2017, van der Meij et al, 2019). NIPT is a prenatal screening procedure that analyses cell-free foetal DNA, which circulates in the mother's blood during pregnancy, in order to obtain information about the foetal genotype. Because only a blood sample of the mother is needed, the procedure does not pose any additional risks of a miscarriage that are associated with the available invasive tests (amniocentesis, chorionic villus sampling). Besides this reduction in risk of procedure-related miscarriage it has other potential advantages. It can be performed relatively early during pregnancy (around the 10^{th} week of pregnancy), it could have a higher reliability than existing tests, and could potentially be used to analyse the entire foetal genome which provides the option of detecting conditions for which no other screening protocol exists.

The integration of NIPT in clinical practice is often being performed in a stepwise manner. For example, in the Netherlands the Dutch NIPT consortium (a multidisciplinary collaborative partnership among different stakeholders involved in public prenatal care) was granted a governmental license to introduce NIPT in the context of an implementation study trial (Trial by Dutch Laboratories for Evaluation of Non-Invasive Prenatal Testing, TRIDENT). In TRIDENT-1, starting in 2014, women with a positive combined test result could choose between NIPT or invasive diagnostic testing. In April 2017, a follow-up study started (TRIDENT-2), in which *all* pregnant women are offered the choice between a combined test *or* NIPT (van der Meij et al, 2019), see also Figure 2. A unique feature of TRIDENT-2 is

that women who elect NIPT can choose a report on chromosomes 21, 18 and 13 either with or without information on the other autosomal chromosomes (i.e., excluding sex chromosomes).

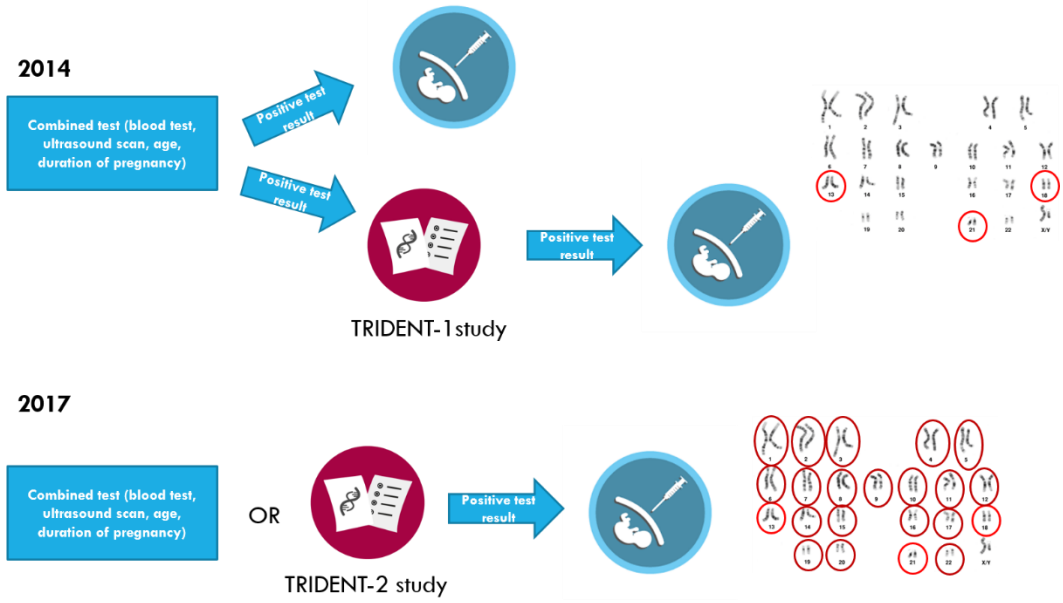


Figure 2. Changing prenatal screening practice in The Netherlands

Potential uses of NIPT

In implementing NIPT, countries make many different decisions with respect to whether it is offered commercially or as part of a national screening program, whether it is offered to all pregnant women or only for women with a particular risk, different ways of reimbursement, and which genetic conditions to screen for (Gadsboll et al, 2020). Especially the aspect of the scope of NIPT (i.e., which genetic conditions are screened) leads to many decisions and debate. Because NIPT could potentially offer genome-wide information, there are many potential models of offering NIPT ranging from screening on specific genetic conditions to proving whole-genome coverage. This stirs debate on whether information on risk factors for late-onset disease, abnormalities related to a mild phenotype, gender, or genetic information on non-clinical conditions should be provided.

Not only the desirable scope of NIPT raises many policy questions, but also its potential use in combination with other health technologies. Because NIPT could potentially offer information on the risk of complications during pregnancy, or conditions of the unborn child that need treatment, it could be used to decide upon, and guide, prenatal treatment (e.g., drugs, surgical procedures, gene therapy). Therefore, although NIPT is often classified as a screening test, it could also be seen as a treatment

strategy. This classification of NIPT may influence the comparators (i.e., comparing it to other prenatal tests or to other ways of treatment) and criteria (i.e., what are the potential benefits?) that are being used to assess its potential value. The relevance of this issue can be seen in the case of the introduction of NIPT in Germany, where the decision of the Federal Joint Committee (Gemeinsamer Bundesausschuss), the supreme decision-making body on determining therapeutic usefulness, cost-effectiveness and medical necessity of a health technology) to define NIPT as a medical procedure was heavily contested (Braun et al, 2018).

The need for an integrative assessment

NIPT is an example of a novel and morally challenging technology that raises ethical questions related to its desirable use and evokes issues relevant to people beyond those who interact with the technology directly. As already mentioned, one important challenge with respect to NIPT is that its desirable scope and purpose can be conceptualized in many, and sometimes contradictory, ways. It can be seen as a technology that only *provides information* on genetic abnormalities, a technology that *helps preventing the birth of children* with genetic abnormalities, or a technology that is able to *enhance reproductive autonomy*. These different views do not only lead to conflicts between stakeholders, but also to contradictory statements/conclusions between different components of an assessment. Economic analyses of NIPT make use of outcome measures such as cost per additional abnormality detected, or cost savings per disabled child not born, that frame NIPT as a technology that becomes more cost-effective when it prevents a sufficient number of births affected by genetic disability. This may suggest a purpose of NIPT that conflicts with the desirable purpose which is suggested by social and ethical analyses (Kibel et al, 2017). This fragmented, and potentially conflicting, assessment of different types of impact of NIPT puts decision-makers in a challenging situation. Therefore, it would be highly relevant to be able to conduct an integrative assessment in which the clinical, economic, social, and ethical aspects of NIPT are comprehensively assessed. In other words, an assessment of NIPT highlights the need for the VALIDATE move in which normative and empirical analysis are integrated.

Value judgments in assessments of NIPT

When conducting an assessment of NIPT, value judgments are inevitable. For example, when assessing the effectiveness of NIPT, questions are raised with respect to which outcomes can be regarded as desirable. This may not be limited to health-related outcomes, and may need the use of normative concepts such as reproductive autonomy (Kessels et al, 2019). And even when standard health-related outcome measures are used, like the Quality-Adjusted Life Years (QALY), normative questions need to

be addressed: '*Whose health benefits should be counted: those of the unborn child of those of the prospective parents? Are QALYs lost when a woman decides, after a positive NIPT test result, to abort a foetus with Down syndrome?'* (Goldhaber-Fiebert et al, 2015).

The VALIDATE approach

The above discussion on NIPT illustrates the central role of normative analysis in HTA. To be able to offer information on potential consequences of NIPT and combine information on different types of consequences in a comprehensive assessment, normative and empirical analysis should be integrated. The VALIDATE approach argues that this integration is best achieved by working out the desirable outcomes that are sought by the use of NIPT. In that way, we can understand and discuss how certain facts can be collected and be relevant in an assessment of NIPT. By making explicit the relation between choices that are made in conducting the assessment and the, collectively determined, desirable ends of NIPT, the assessment becomes more transparent and meaningful (van der Wilt, 2017).

Working out the desirable ends of NIPT, in collaboration with stakeholders, helps in identifying the different views in society (interpretive frames, **Chapter 3**), defining the objectives and research questions of an assessment (scoping, **Chapter 4**), addressing normative questions (**Chapter 5**), while highlighting and taking into account relevant contextual factors (**Chapter 6**). These chapters will return to the case of NIPT to further illustrate these elements of the VALIDATE approach. After discussing the philosophy of VALIDATE (**Chapter 7**), the final chapter (**Chapter 8**) will summarize the VALIDATE approach and return to NIPT.

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Chapter 2. The fact/value dichotomy

Abstract

This chapter is focused on the so-called "fact/value dichotomy". In the current practice of Health Technology Assessment (HTA), value judgments are often considered external to HTA or separate from it and are addressed by experts (in ethics) and decision-makers after the "real" HTA is finished. In other words, facts and values seem to be two completely different "substances" that come from two completely different sources. Is this dichotomy attainable? Is it desirable? This chapter will argue that a strict fact-value distinction is not so easy to maintain, based on insights from Philosophy and HTA practice.

Key messages of this chapter: HTA cannot be considered a matter of collecting *the* facts about a certain health technology, but rather *"a matter of collecting facts that are considered plausibly associated with the use of the technology, relevant, and amenable to accepted methods of scientific inquiry"*.

Having read this chapter you should be able to understand that facts and values are intertwined in HTA, even though the latter may remain implicit or tacit.

Introduction

In Chapter 1, it has been noted that health technologies and the practices that are created by them seem to be completely insulated from moral values. In addition, an assessment of aspects such as safety and cost-effectiveness is often seen as *objective* and consisting of the collection of empirically testable facts, whereas studies of the wider implications (ethical, legal and social issues) are seen as *subjective* and solely involving value judgments. This situation is well-described by Gorski (2017): *"Imagine a large, double-sink such as you might find in the basement of a single-family home somewhere in North America. An impermeable wall separates the two sinks. Each sink is serviced by its own spigot. The righthand spigot emits a red tinctured liquid called "values." The piping from this spigot seems to go down through the floor and into the ground to a deep-water well, labelled "emotion" (or is it "conviction?"). The left-hand spigot emits a blue tinctured liquid called "facts." The plumbing for this spigot seems to go out through the exterior wall to a surface-water source called "observation"*."

This is more or less how some people interpret the relationship between facts (what *is*) and values (what *ought* to be). For them, facts and values are two completely different "substances" that come

from two completely different sources. Facts (e.g., the earth revolves around the sun) are inarguable truths of the external world, given through the observation of nature, and they are objective. They could be ordered into theories and explanations using science's methodological tools (Gorski 2017). On the other hand, values (e.g., to be honest) are personal beliefs that motivate people to act one way or another, cannot be derived from empirical observations, and they are subjective. Unlike facts, they cannot be proven true or false by any sort of scientific method.

This seems to happen also in the current practice of Health Technology Assessment (HTA): facts (e.g., data on safety) are being collected and processed in order to inform regarding possible or likely consequences of using a certain health technology. When the empirical evidence base seems to be sufficiently robust and comprehensive, then the issue about its value (ethical analysis) is raised separately: given these facts, how is it possible to judge the overall value of this health technology?

However, this way of proceeding, apparently so obvious and easy, hides some snare. Indeed, the relationship between facts and value – better known as "fact/value dichotomy" – is one of the most debated topics in Philosophy. It has been addressed in many ways: one debate asks whether it would be possible "to draw" values (moral norms) from the knowledge of nature; another discussion focuses on studying the relationship between descriptive propositions (e.g., the moon is spherical) and normative propositions (e.g., killing is wrong); another one considers whether ethics is an authentic form of knowledge.

In this chapter, two questions will be addressed with respect to this fact/value dichotomy: 1) Is it attainable? and 2) is it desirable? The chapter will argue that a strict fact-value distinction is not so easy to maintain, based on insights from Philosophy and HTA practice. Based on this discussion, an analysis about the consequences of this conclusion for HTA will be performed. The text will be supported by the discussion of two case studies.

The value/fact dichotomy

Origins of the fact/value dichotomy[4]

At the centre of much of the debate around the value/fact dichotomy there is a famous passage from the Scottish philosopher David Hume (1711-1776): *"In every system of morality, which I have hitherto met with, I have always remarked, that the author proceeds for some time in the ordinary ways of reasoning, and establishes the being of a God, or makes observations concerning human affairs; when all of a sudden I am surprised to find, that instead of the usual copulations of propositions, is, and is not, I meet with no proposition that is not connected with an ought, or an ought not. This change is*

[4] Some parts of this text are taken from Refolo et al, 2016.

imperceptible; but is however, of the last consequence. For as this ought, or ought not, expresses some new relation or affirmation, 'tis necessary that it should be observed and explained; and at the same time that a reason should be given, for what seems altogether inconceivable, how this new relation can be a deduction from others, which are entirely different from it. But as authors do not commonly use this precaution, I shall presume to recommend it to the readers; and am persuaded, that this small attention would subvert all the vulgar systems of morality, and let us see, that the distinction of vice and virtue is not founded merely on the relations of objects, nor is perceived by reason" (Hume, 1739).

The passage is also known as "Hume's law," "Hume's guillotine" or as "the is-ought-fallacy," and has been interpreted in several ways. In short, it states that one cannot logically derive an "ought" from an "is", that is, one cannot derive "norms" from "facts" – there is no logical bridge between fact and value.

A similar argument has been defended by the English philosopher George Edward Moore (1873-1958). In his "Principia ethica" (Moore, 1903), he argued against any identification of moral properties with natural properties. In particular, he argued against what he called the "naturalistic fallacy" in ethics, by which he meant any attempt to define the word "good" in terms of natural qualities.

The German sociologist Max Weber (1864-1920) arrived at similar conclusions too (Weber, 1949): he made a strict distinction between "statements of facts" (describing reality) and "statements of value" (relating to an ideal). The former ones were considered objective and the latter subjective. Given this, he argued that Science, as the realm of facts, must be seen as strictly separated from the realm of values, i.e., ethics, aesthetics, and politics.

Despite some differences in terminology, all the aforementioned authors made a clear distinction between facts and values and repudiated any attempt to derive moral values from facts.

The fact/value dichotomy in Philosophy of Science

A version of the fact/value dichotomy was also defended in Philosophy of Science, the academic discipline that deals with questions about what Science is, how it works and the methods through which it produces reliable knowledge.[5] An important movement of the early 1900s, Logical Positivism (also known as Logical Empiricism or Neo-positivism), stated that Science is a formal activity that creates and accumulates knowledge by directly observing, and confronting (i.e., by doing experiments), the natural world. Science tries to discover how the world *really* is by observing it carefully. Hypotheses and theories are generated and tested based on these observations, and only

[5] For more background information about Philosophy of Science, see UC Museum of Paleontology of the University of California at Berkeley, "The philosophy of science", URL = https://undsci.berkelye.edu/article/philosophy

when theories make predictions that can be *verified* – correspond to how the world really is (as known through senses and the use of scientific instruments) – they can be seen as true. This view on Science is known as Logical Positivism because its central claim is that the only source of authentic knowledge is sensory experience or observations, and inferences that can be drawn from these observations by using logical techniques. The term 'Positivism' derives its meaning from the French word *positivism*, which is derived from *positif* meaning: 'imposed on the mind by experience'.

The aim of Logical Positivism was to construct scientific laws and theories to describe and express relationships between observable phenomena. It can be interpreted as a program of radical "re-foundation" of knowledge exclusively based on logics and observations, which should have led to the elaboration of a "unified language" for Science as a whole. Core notions and assumptions of Logical Positivism were:

1) there is a division between the real world, "the given", and its perceptions and expression by humans;

2) the real world, "the given", can be grasped by empirical sciences;

3) the truth, established by empirical sciences, can be expressed in protocol sentences (i.e., statements that describe immediate experience or perception) and observation reports;

4) protocol sentences and observation reports can be understood, described and conceptualized by logical analysis, thereby bridging the division between the world and the words, "the given" and the concept, facts and theory (Burkard, 2018).

The assumption on which the whole philosophical conception of Neo-Positivism was based is the well-known "theory of verification," according to which a proposition is "cognitively meaningful" only if some finite procedure conclusively determines its truth. This signifies that any statement that cannot be verified by an empiricist criterion is meaningless. Metaphysics, ontology, as well as ethics fail this criterion, so they are cognitively meaningless. In this way, Neo-Positivism celebrated a sort of "divorce" of Science from Ethics and facts from values.

Challenging the fact/value dichotomy

However, from the 60s in the 20th century, the fact/value dichotomy as well as the neo-positivistic approach were criticized in many ways and they lost appeal.

In this context, the "philosophical hermeneutics" initiated by Martin Heidegger (1889-1976) and developed by Hans-Georg Gadamer (1900-2002) in his "Truth and Method" (1960) came to play a fundamental role. In essence, Gadamer claimed that understanding is never fixed and final but always

steeped in language, dynamic and fluctuating. “Prejudices” are the very source of our knowledge. Hence, understanding is always personal, human, and subjective. This imply that at work there are always different perspectives or – as they will be called in Chapter 3 – different “interpretative frames”.

This assumption had a significant impact on the methodological presuppositions on which modern Science was built. According to the new viewpoint, there can be no universal standpoint from which “objective knowledge” can be achieved, and all understanding – including scientific understanding – has to be considered as “contextual” and “historical”.

Another important role has been played by the German philosopher Karl-Otto Apel (1922-2017). He pointed out that moral language analysis always requires a criterion to distinguish moral language from any other form of language. This helped to support the thesis that existence of merely descriptive propositions (as scientific propositions) is an illusion, and that it is impossible to separate the normative dimension from a descriptive one. Moreover, Apel argued that the fundamental shortcomings of Positivism spring from a lack of reflection “upon the fact that all cognition of objects presupposes understanding as a means of intersubjective communication” (Apel, 1972). Science is unintelligible as human activity, if one cannot understand the implicit and explicit conventions and notions, or more general, the communication community or language game, which it presupposes. Even tacit conventions about the use of words, not to mention explicit conventions about definitions, theoretical frameworks, or statements of facts in empirical science, imply “an intersubjective consensus about situational meanings and aims of practical life” (Apel, 1972). It follows that objective Science presupposes hermeneutics (or pre-hermeneutics). In this sense, Science is not merely objective, but a “human enterprise”.

Finally, the American philosopher Hilary Putnam (1926-2016) has recently traced the “collapse of the fact/value dichotomy”. According to him, there is a distinction to be made, useful in some contexts, between statements of fact and statements of value, especially of ethical value. Nevertheless, a *strict* dichotomy between fact and value would be indefensible because on the one side normative (e.g., ethical and aesthetic) judgments have always a factual basis, and on the other side scientific judgments encompass normative elements. Consequently, Science cannot be considered as “value-free”, since “Science itself presupposes values which are in the same boat as ethical values with respect to objectivity” (Putnam, 2002).

These and other reflections have considerably reduced the significance of the fact/value dichotomy.

Although the clear distinction between facts and values is nowadays difficult to defend philosophically, it still appears to be strongly present in the common mentality. Only scientific facts are often believed

to be worthy of "serious" consideration, whilst value judgments are frequently considered as subjective, relative, to some extent unreliable, and anyway external to scientific speech.

The value/fact dichotomy in HTA

This seems to happen also in the current practice of HTA: value judgments are often considered external to HTA or separate from it and are addressed by experts (in ethics) and decision-makers after the "real" HTA is finished. This conception of value judgments in HTA is illustrated in Figure 1.

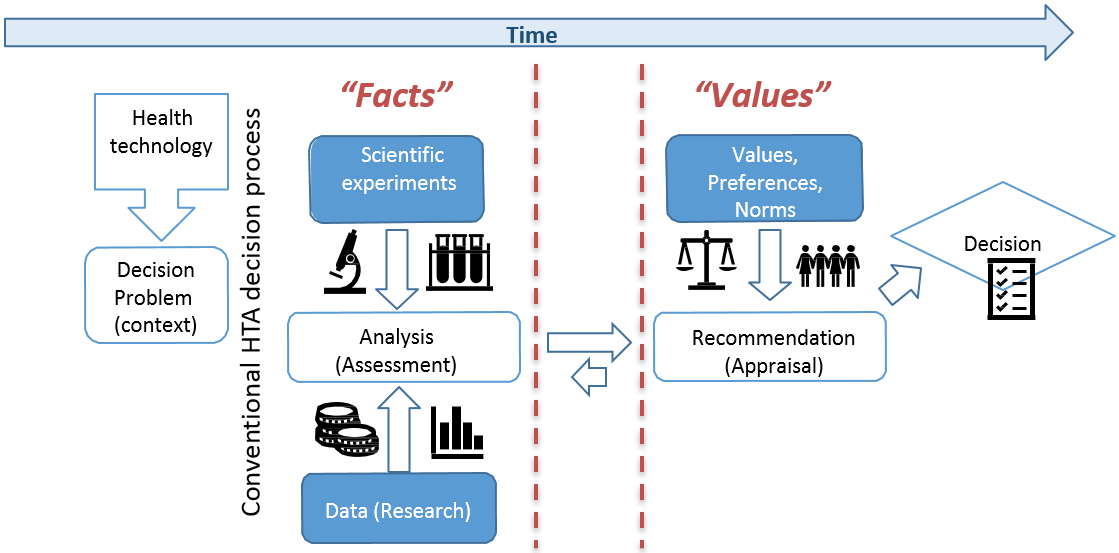


Figure 1. The conventional concept of HTA. Conventional HTA mainly focuses on the collection of quantifiable data, whereas ethical, social, cultural, and legal issues, including values related to the use of health technologies, are addressed independently and at a late stage in the HTA process. In this view, the assessment stage involves the collection of factual information, whereas values only enter the process when interpreting this information and taking into account wider aspects to make a recommendation (the appraisal stage).

An HTA usually starts by presenting a more or less comprehensive description of the sort of consequences that may be expected from the wider adoption of a health technology (van der Wilt, 2016). Under this view, the first step of an HTA process consists in conducting an empirical inquiry of a health technology's safety, clinical effectiveness, and cost-effectiveness. This phase involves the analysis of evidence, which explains the strict correlation between HTA and Evidence-Based Medicine (EBM) (Luce et al, 2010). Subsequently, it is asked whether any ethical issues may be anticipated, given some set of ethical principles, such as beneficence, non-maleficence, autonomy, and justice.

What it has been described here also reflects well the current distinction between *assessment* and *appraisal* in the context of HTA. HTA agencies typically separate the assessment from the appraisal phase in the HTA process. "Assessment" refers to data collection that would be useful to form a basis for decision-making. "Assessment" differs from "appraisal", which generally implies some form of recommendation (normative level) about the implementation/non implementation/disinvestment of

a health technology based on a previous assessment. Such a recommendation can led to several concrete actions: encouraging, discouraging or even prohibiting implementation, reimbursing, funding, disinvesting, etc. Some HTA agencies are restricted to assessments only and do not make recommendations about implementation/not implementation/disinvestment in the healthcare system, while others perform both assessment and appraisal (Sandman et al, 2014).

A challenge with this approach assumes that it is possible to separate facts (empirical inquiry of a technology's safety, clinical effectiveness, and cost-effectiveness) from values (normative dimension). As such, the former are considered objective truth claims (they would tell something about some part of reality), whilst the latter would be subjective, and would come into play only after the facts have been collected.

As outlined above, a clear distinction between facts and values is difficult to maintain in the current panorama of Philosophy. It is, in fact, recognized that value frameworks are already operative at the stage of facts collection. The fact is that many of them remain implicit or tacit may reinforce the illusion of a certain scientific objectivity. Actually, empirical inquiries of a health technology's safety, clinical effectiveness and cost-effectiveness, which are often considered objective, always presuppose normative assumptions, and are value laden. They presuppose a valid hermeneutical prism, i.e., value judgments about which facts have to be considered relevant and which facts do not have to be considered relevant. Without a previous (usually implicit) "intersubjective consensus" (Apel, 1972) about them, no assessment would be possible. In this sense, "effectiveness, safety, cost-effectiveness which many consider assertions are (…) relative evaluations. In each case, the result of the analysis attributes a quality to a health technology using criteria. For each quality attribution there is a choice of criteria, a priority setting and a mode of gathering information to apply the criteria to the technology at stake" (Legault et al, 2018).

An example could help to clarify this point. A very common practice in current HTA is the calculation of the incremental costs that are incurred by adopting a novel health technology and the additional quality-adjusted life years (QALYs) that may be gained, as compared to usual care. These facts derive their relevance from utilitarian theory, stipulating that justice requires that for every gain in QALY a proportional amount of resources should be spent. However, if the consequences of adopting a health technology were assessed from the perspective of a different concept of justice (value judgment), such as egalitarianism, those calculations would be irrelevant, and completely different information would be necessary (van der Wilt, 2016).

Therefore, empirical analysis is always guided by normative assumptions. To be more precise, the relationship between these two dimensions (empirical and normative) is a relation of *plausibility*, *relevance*, and *amenability*.

Plausibility refers to the fact that the only consequences investigated are those of adopting a health technology that are believed to be plausible. For instance, when someone is faced with the task of assessing a drug, there are some things that strike as potentially plausible (e.g., the patient will take the medication) while others as potentially implausible (e.g., the patient will always throw the medication in the garbage). In this sense, plausibility is a function of knowledge and understanding of the technology and the sort of impact it may have. In short, plausibility refers to the question: what sort of effects are likely to occur, in view of knowledge and understanding of the technology, the process in which it intervenes, and its mode of action?

As outlined above, *relevance* is a function of norms and values. The commitment to norms such as the promotion of a certain conception of justice, or the relief of suffering, the avoidance of harm, or respecting autonomy determine the sort of data (outcomes) that become of interest. In short, relevance refers to the question: *what sort of effects are anticipated that are not only likely to occur, but that will also affect our judgment of the technology under scrutiny?*

The two dimensions – what sort of outcomes are plausible given the current knowledge of mechanisms involved, and what sort of outcomes are relevant given the values that are considered as important – are always operative in HTA. Moreover, they work in a concerted way: generally, features that are considered relevant but unlikely to materialize are not pursued. Likewise, features that are considered plausible to occur but of little relevance are not pursued.

Finally, *amenability* refers to the fact that it is possible to investigate those consequences of adopting a health technology that are amenable to some mode of empirical inquiry. For instance, if there is no chance for determining how many patients will not take their medication, an assessment of this aspect will not be possible. In this sense, amenability to scientific inquiry is a function of our methodological and epistemological standards. In short, amenability refers to the question: *is this research feasible?*

Value judgments permeate all levels of HTA. It is beyond the scope of this handbook to show all these interlacements, which are better addressed by specific contributions (Hofmann et al, 2014; 2018). To give some examples, it is possible to mention the relationship between empirical inquiry and normative dimension, as outlined above; or the assessment of ethical, social, legal aspects of a health technology, which are obviously value related; or the HTA itself which is clearly evaluative. Moreover, there are many levels of values at play in the HTA process, for example, in the selection of endpoints

or in selection/presentation of HTA results. There are stakeholder involvement processes with different value perspectives, or other values assessment frameworks that have been developed for HTA, such as multi-criteria decision analysis (MCDA), and so on. A further issue concerns what values are currently taken in account in HTA studies, what is the hierarchy among these values, and what it is the relation among these values.

However, in a more general way, it is possible to say that there are normative aspects *in* and *of* HTA (Van Oudheusden et al, 2019).

In conclusion, it is possible to affirm that facts and values are intertwined in HTA, even though the latter may remain implicit or tacit. In the light of this perspective, HTA cannot be considered a matter of collecting *the* facts about a certain health technology, but rather *"a matter of collecting facts that are considered plausibly associated with the use of the technology, relevant, and amenable to accepted methods of scientific inquiry"* (Reuzel et al, 2000). This should not come as a surprise as HTA is a type of evaluation (Hofmann et al, 2018).

In the next paragraph, the case cochlear implants for prelingually deaf children will be discussed in order to illustrate the relevance of normative assumptions in HTA (van der Wilt et al, 2000). A similar analysis will be performed on the case study of Non-Invasive Prenatal Testing (NIPT) (see **Box 1**).

Case study: Cochlear implants for prelingually deaf children

A cochlear implant is a small, complex electronic device that can help to provide a sense of sound to a person who is profoundly deaf or severely hard-of-hearing. The implant consists of an external portion that sits behind the ear and a second portion that is surgically placed under the skin. An implant does not restore normal hearing but can give a deaf person a useful representation of sounds in the environment and help him/her understand speech.

The cochlear implants emerged in the 1970s. Gradually, the group for whom the technology was deemed potentially appropriate was expanded from late-deafened adults to children, and then to prelingually deafened children, who, by definition, have never acquired spoken language in the natural manner.

A lively debate has developed between proponents of cochlear implants for prelingually deaf children and some deaf activist leaders. The disagreement has become heated with both sides accusing the other of being unethical.

On the one hand, deaf world representatives define the profoundly deaf as a separate culture (minority culture) from the mainstream hearing society. In particular, the term "deaf world" would define "a

grouping of deaf persons, usually profound, who view themselves as a minority culture with its own customs, values, attitudes, knowledge, and language. With the latter characteristics, they claim to have the ability to self-construct as a culture" (Gonsoulin, 2001). The common denominator is deafness, the sign language is their defining language.

In turn, a sign language is a visual language based on body gestures instead of sound to convey meaning. Sign languages are not pantomime, nor are they a visual rendition of the related verbal language: they are full-fledged languages like any other human languages. Wherever communities of deaf people exist, sign languages develop.

Consequently, deaf world representatives strongly reject the concept of deafness as a disability but claim deafness is a culturally defining characteristic. They challenge the performance of cochlear implants in children as a matter of ethical debate. The main concern regards the diminution of a minority culture: "Should cochlear implants work effectively and be widely used, membership in the Deaf World would decrease significantly over time" (Gonsoulin, 2001). An underlying assumption is that preserving minority cultures is a positive value for society as a whole.

On the other hand, proponents of cochlear implants maintain that deafness is a disability, i.e., the failure to achieve an expected level of function. For them, the key (and obvious problem) is that deaf children cannot hear and, therefore, they will be unable to develop spoken language cognition, emotion, etc. Since cochlear implants, when followed by appropriate rehabilitation, restore, albeit imperfectly, hearing to a certain extent, they will also support these other developments (van der Wilt, 2016). An underlying notion is that of normal functioning, and the importance of maintaining or restoring normal functioning, both for individual and for society at large.

When facing the task of evaluating the cochlear implants for prelingually deaf children, the current practice of HTA requires that the assessment of the technology must be conducted along two lines. On the one hand, empirical evidence is collected on the impact of the device on the recipient's hearing capacity, development of spoken language, ability to pursue mainstream education, quality of life, etc. On the other hand, ethical issues are explored, notably the resistance from deaf organizations, claiming that the technology is a threat to deaf culture (van der Wilt, 2016).

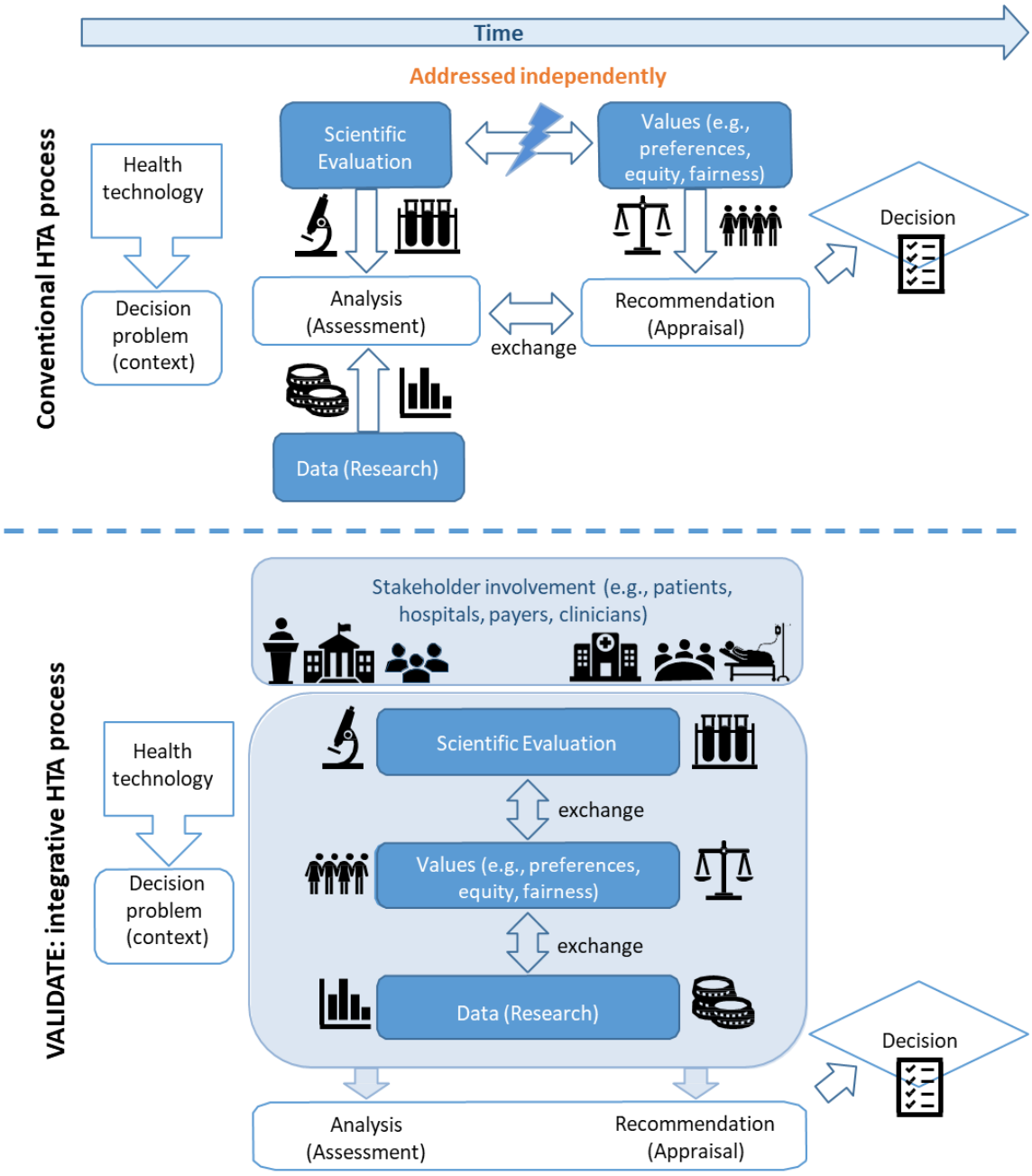
Following VALIDATE's perspective, HTA is more than a collection of facts; facts and values are intertwined in HTA. Therefore, it should not be concluded that there are certain facts about the technology on the one hand (e.g., its impact on a child's proficiency in spoken language) and some ethical issues on the other hand (e.g., the demise of deaf culture). Rather, it is by virtue of normative assumptions that the collected facts can be considered relevant to the evaluation. In fact, deafness

may be framed as a separate culture, or a disability. In the former case, implementing cochlear implants is not a solution, and their assessment will have a certain relevance; in the latter case, implementing cochlear implants is a solution, and their assessment will have another relevance. Under this perspective, any HTA is a specific collection of facts, driven by specific normative assumptions, not a collection of facts that serves as a basis to make up our mind about the comparative value of the technology under investigation (van der Wilt, 2016).

It is significant that – as reported by Lehoux et al (2000) – in 1997 the Dutch Minister of Health decided, very unusually, against the assessment-based advice of the Health Insurance Council that would have provided reimbursement of paediatric implantation on a normal basis. The Dutch Minister's decision was taken after consultation with the deaf community and with the organization of parents of deaf children. Likewise, in 1990 the U.S. Food and Drug Administration (FDA) approved the marketing of the Nucleus 22 channel cochlear prosthesis for surgical implantation in children aged two to seventeen years, while in a subsequent position paper, the National Association of the Deaf (NAD) argued that the FDA had made a number of mistakes, concluding with a recommendation that the FDA *"withdraw marketing approval and revise the procedures employed"* (NAD, 1991).

The example shows how neglecting normative assumptions can lead to a situation in which current practice of HTA proves to be insufficient. The different conclusions of the evaluation are the result of two different value assumptions. Therefore, the so-called "scientific facts" cannot be considered as "objective", and they reflect understanding of the value and meaning of the particular health technology. In other words, normative assumptions always guide the collection of information needed to assess whether a health technology is able to realize certain effects. In the light of this perspective, Figure 1 appears to be different, values permeate all levels of HTA (see Figure 2).

The next questions may be: how to proceed in such case? How to proceed when different normative assumptions are at work? One obvious strategy would be to involve various stakeholders in the HTA process (see Chapter 4).



VALIDATE proposes an integrative HTA approach, where the safety, clinical effectiveness, and cost-effectiveness of health technologies are thoroughly integrated with their wider ethical, legal, cultural, social, environmental, and organisational implications and stakeholders are involved in a more meaningful way during the entire HTA process.

Figure 2. The conventional HTA process vs. the integrative approach of VAILIDATE

Conclusion

The relationship between facts and value – better known as fact/value dichotomy – is one of the most debated topics in modern Philosophy. Even though the clear distinction between facts and values is still present in the common mentality, it is now philosophically indefensible for several reasons.

Therefore, the current practice of HTA, for which value judgments are considered external to HTA or separate from it, should be overcome. It ignores the fact that normative assumptions are operative at all levels of HTA.

In the light of this perspective, HTA is not a matter of collecting *the* facts about a certain health technology, but rather *"a matter of collecting facts that are considered plausibly associated with the use of the technology, relevant, and amenable to accepted methods of scientific inquiry"* (Reuzel et al, 2000).

Box 1. Case study: Non-Invasive Prenatal Testing

One way of conducting the evaluation of Non-Invasive Prenatal Testing (NIPT) consists in performing an empirical inquiry of NIPT's safety, clinical effectiveness, and cost-effectiveness. This phase involves both collection of quantifiable data and analysis of evidence. When the empirical evidence base becomes sufficiently robust and comprehensive, then the issue about its value is addressed separately: given these data, how is it possible to judge the overall value of NIPT? What are the ethical questions arising from the use of the technology? What is its social impact? In this perspective, values are viewed as separate from facts, and only enter the process when data collection is ended.

Is this separation of facts from values attainable? Is this dichotomy desirable? Another way of proceeding is to start by wondering what it is expected by implementing this technology. What is it that one wants to realize, or avoid, by using NIPT? What is its relevance? From this perspective, a group of consequences can be "plausibly" associated with implementation and use of the technology. For example, one might want to prevent the birth of foetuses with chromosomal abnormalities. Neonatal birth defects are a worldwide problem, with many countries having a high incidence rate of these defects. The extensive development of traditional serological prenatal screening has made a significant contribution to reducing the birth of foetuses with chromosomal abnormalities, such as chromosomal aneuploidy. However, even though all high-risk pregnant women who receive traditional serological screening undergo invasive amniocentesis foetal karyotype analysis, there was still a high rate of misdiagnosis in serological screening. NIPT can improve the detection rate of foetal chromosomal abnormalities and prevent the birth of foetuses with abnormalities. Another possibility is that one wants to avoid distress associated with an unexpectedly adverse outcome (for women and their partners). Because invasive tests have a small procedure-related miscarriage risk, many women decline these tests, whilst those accepting testing experience considerable anxiety. Elevated levels of stress and anxiety during pregnancy are associated with potential adverse obstetrical outcomes such as preterm delivery and reduced birth weight and are therefore important to avoid. The fact of having a prenatal test for foetal abnormalities can affect maternal anxiety. A further plausible consequence is

that one wants to facilitate reproductive autonomy. Reproductive autonomy is having the power to decide and control contraceptive use, pregnancy, and childbearing. For example, women with reproductive autonomy can control whether and when to become pregnant, whether and when to use contraception, which method to use, and whether and when to continue a pregnancy. NIPT allows to obtain valuable information on the health of the foetus. For pregnant women or couples, implementation and use of NIPT can offer reproductive autonomy regarding an affected pregnancy, including termination of pregnancy or being able to prepare for the birth of an affected child, relief from anxiety in case of a negative test result and the reduction of invasive follow-up tests. Finally, by using NIPT one might simply want to facilitate informed choice. Informed decisions are those that are founded upon relevant knowledge, and that enable a person to exercise autonomy. NIPT can facilitate a woman's reproductive choice by providing her with accurate information risk-free and early in her pregnancy.

These different views (normative assumptions) do not only lead to conflicts between stakeholders, but also between different components of an assessment. Furthermore, they play a key role in determining which facts are relevant and which facts are not relevant. For example, safety invokes, generically, the value of avoiding harm to people (the well-known moral norm of non-maleficence). What does it mean, exactly, "to avoid harm" to people in the case of NIPT? It should be clear that safety can be conceptualized in different ways, depending on the different normative assumptions (Bloemen et al, 2021). For example, it can be conceptualized in terms of avoidance of procedure-related miscarriages, or in terms of unnecessary worries due to false positive test results. In this sense, the assessment of the impact of a health technology in terms of safety always has a normative dimension. In a similar manner, clinical effectiveness refers to the commitment of doing good (the so-called principle of beneficence). Again, what does it mean to do good in this case? One possibility is to evaluate it in terms of predictive value. However, what constitutes an accurate and reliable test? Clearly, it is not a neutral exercise: acceptable thresholds of different components of test accuracy and reliability (e.g., sensitivity, specificity) invoke value judgments concerning the (un)desirability of certain outcomes, the acceptance of uncertainty, and the severity of conditions being tested for (Bloemen et al, 2021). Finally, similar considerations can be made about cost-effectiveness, whose outcomes can be expressed in different ways. For example, one possibility is to use Euro per quality-adjusted life years (QALYs) gained, another one is to use average cost per trisomy 21 detected for different screening scenarios.

This analysis shows clearly that the assessment of the impact of a health technology in terms of safety, clinical effectiveness, cost-effectiveness, always has a normative dimension.

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Part 2. Making it work

Chapter 3. Interpretive frames, judgement and action

Abstract

One central element of the VALIDATE approach is the recognition that an HTA needs to take into how the variety of actors involved in its object (caregivers, patients, policymakers, researchers, pharma-firms etc.) views on what is relevant, plausible, and valid with respect to the use of health technology. This chapter is focused on what is called in the policy sciences 'interpretive frames', a concept to systematically denote such 'views.'

It starts with a discussion of how interpretive frames help understand that different HTA researchers may adopt different outcome measures, and that these often do not take into account what outcomes are deemed important in clinical practice. Once the nature and role of interpretive frames have been pointed out, the chapter will discuss a method for systematically reconstructing and critically scrutinizing these frames and the way they are chosen. Finally, it will outline the ramifications of the often witnessed disjoint between HTA and clinical practice or policy making, and ways to pre-empt that disjoint. These various notions will be applied to the NIPT case.

Key message of this chapter: Different actors (doctors, policy makers, hospitals, patients, manufacturers et cetera) look into a health issue and associated health technology from different interpretive frames, and hence define problems and judge technologies different. Even within these professions different interpretive frames exist, and some may be underrepresented. Thus, first, reconstructing and scrutinizing interpretive frames may therefore help gain a more critical view on the object of the HTA, e.g., introducing a different comparator. Second, as different actors prevail at the macro-, meso-, and micro-level, an HTA made at one level must take into account interpretive frames from the level that it seeks to inform. Under circumstances, this may have important methodical ramifications, toward forms of participative or deliberative HTA.

After reading this chapter you should

- know the concept of interpretive frame and its rationale
- understand how interpretive frames shape outcome measures, comparators, and other key elements of an HTA

- be able to systematically reconstruct and critically scrutinize interpretive frames and
- understand, on that basis, how to make an HTA optimally useful for clinical practice or policy making.

Introduction

What do HTA researchers do when they assess a health technology, or explore possible interventions to deal with a particular health issue? And why may they think that the resulting HTA will actually contribute to better practice? This chapter will discuss one theoretical notion, interpretive frames, and its implications for these two crucial – not to say: existential - questions for the HTA profession. Before outlining the argument more specifically, an example of a broader HTA project, in which interpretative frames played a key role, is discussed. The project was commissioned by the then Health Care Insurance Board (College voor Zorgverzekeringen (HCIB); now called Zorginstituut Nederland (ZIN))'s HTA department, which is supposed to underpin governmental decisions on insurance package – further called 'the national HTA body'.

It must be stressed that the case (mebeverine for treating patients with irritable bowel syndrome – IBS) comes from a 2003 project that is part of HCIB (later ZIN)'s continuous learning and consequently improving their processes for health benefit package management in the Netherlands (Boer, 2018; Couwenbergh et al, 2013). The national HTA body uses in its assessment the four key criteria employed in coverage decision-making: effectiveness, cost effectiveness, necessity and feasibility (Zorginstituut Nederland, 2013) and which are further operationalized during several years (Zorginstituut Nederland, 2017; Vijgen et al, 2018; Kleinhout-Vliek et al, 2017].

A first lesson from the example was the realization that different actors involved – doctors, policymakers, hospitals, patients, manufacturers, etc.- *and* HTA researchers themselves each have their own perspectives ('interpretive frames' in our terminology) on a particular health technology and its (side-) effects and cost became a key point of departure. Thus, in HTA studies, 'the' problem should not be considered as given at the onset of an HTA study – what the problem 'really' is, is rather one of several questions to be answered.

Second, a key point of departure became the idea that effective health benefit package management was to take into account the interpretive frames of the meso-level (care organizations, insurers and so on) and healthcare professionals in developing package decisions, as it had become clear that these shape actual healthcare practices. While this became even more important due to the Health Care Insurance Act of 2006, which ended governmental involvement in implementation, we also argued that the more principled background is a second notion from the policy sciences: interpretive

frames shape implementation action and therefore must be anticipated in effective policy design. All this led, third, to changes in HTA practices at more attention to 'scoping' (see Chapter 4), more involvement of relevant actors at different moments in the HTA process and more recognition that this process may benefit from iteration loops, rather than following a strictly linear path – typical elements of the VALIDATE approach.

Thus, while this historical case does not to show the current state of affairs of HTA in the Netherlands' ZIN, it is helpful to demonstrate the rationale and nature of some key elements of the VALIDATE approach, especially those related to problem structuring, interpretive frames and effective policy advice. The case focused on mebeverine as a medicinal treatment as part of the treatment repertoire of patients with IBS (Moret-Hartman et al, 2007). In 1995, it had been assessed by the national HTA body in terms of whether it should remain covered, following a parliamentary resolution seeking to better control health expenditures. As a basis for its analyses, the national HTA body had developed four assessment criteria (Table 1). Assessing mebeverine in these terms, the HTA body concluded[6]: a) that the efficacy of the drug had been assessed when mebeverine was initially registered; b) that convincing evidence on the drug's effectiveness was lacking, as meta-analysis showed considerable differences between Randomized Controlled Trials (RCTs); and c) that its therapeutic value is limited. Despite these findings, the national HTA body recommended continuation of coverage since it considered availability of at least one medicinal treatment desirable and, compared with other antispasmodics, mebeverine was considered to have the least side effects.

Table 1. Coverage decision-making criteria. Source: Moret-Hartman et al (2007, Table 2), summarizing Ziekenfondsraad (1995)

Criterion	Description
Efficacy	Its pharmacological action results in a therapeutic effect in clinical research (therapeutic potential)
Effectiveness	Its use in clinical practice results in the aimed goal of the treatment
Therapeutic value	The sum of its relevant characteristics (effectiveness, toxicity, user-friendliness, etc.) qualifying for its position relative to alternative therapeutic interventions
Efficiency (cost-effectiveness)	A medicine is effective and the balance between therapeutic value and costs is favourable in comparison to other treatments

Contrary to this advice, the Minister subsequently decided to discontinue reimbursement. When this decision was taken to court by the industry, the court annulled this decision, arguing that the industry and the Ministry agreed on the inconclusiveness of evidence on the drug's effectiveness

[6] Our translation in Moret-Hartman et al. (2007).

while the reasons to continue its use were much more important than the Ministry's concerns about making the health insurance package more affordable.

Against this background, when the national HTA body took up the issue, it decided not to attempt to resolve the effectiveness question through commissioning a study to conclusive evidence. Rather, it would draft a tender for research exploring whether non-medicinal treatments could be promoted, especially dietary advice. Anticipating that the pharmacy department of the HTA body would not accept a social science study, it decided not to go for that most obvious option. Instead, it commissioned a preliminary study that would elaborate alternatives and assess mebeverine's therapeutic value in comparison to such other interventions, and thus prepare a more comprehensive study. Eventually, a small consortium was selected which would also use the views of patients and general practitioners (GPs) to determine a suitable outcome measure.

The preliminary study reported that while literature showed important differences on the issue of appropriate outcome measures, practice was much less ambiguous. In interviews with GPs, patient satisfaction appeared the common criterion, sometimes accompanied 'decreasing symptoms.' As one researcher put it: *"there are a lot of viewpoints in the literature, but in practice doctors take patient judgement as their guide"* (Moret-Hartman et al, 1995: p. 19). The desired outcomes most mentioned by patients were less abdominal pain and less swollen belly; sometimes, also more frequent defecation was mentioned. On basis of these findings the report proposed a combination of a global assessment of patient judgement, complemented with changes in patient symptoms. In addition, it yielded a proposal for standardized diet: fibres, as they were the only dietary intervention with unambiguously proven effectiveness, and could be encapsulated, securing compliance. Finally, the consortium proposed a main study on the efficacy of mebeverine with both fibres and a placebo as comparators.

The HTA body eventually decided that such a study would make little sense, given that the preliminary study had left two issues unclear: a) the methodological problems behind the ambiguities in previous trials on mebeverine; and b) what would be needed to prevent these problems in subsequent trials. So, ironically, we see, (i) differing views in literature on outcome measures; (ii) a persistent use of efficacy (for admission decision) or effectiveness (to decide on reimbursement) in RCTs; (iii) a deliberate choice by the HTA body, and initially also by the team it grants the preliminary study, to use instead 'therapeutic value' as outcome measure, which (iv) is, in line with clinical practice, operationalized as 'global assessment' but (v) nevertheless eventually replaced by a return to efficacy as the criterion for a follow-on study. So, in a variety of HTA exercises, diverse outcome measures are being used, but never the one that appears commonly used in practice.

Interestingly, after two decades many of the insights that surfaced during this project and our analysis have become common practice. In 2019, the journal of the Dutch Medical Society published a review article for practitioners on state-of-the-art insights on belly complaints (Claessen et al, 2019). Referring to Enck et al. (2016: p. 8) and informed by clinical practice, it recommended as a first step in treatment explanation, reassurance, dietary and lifestyle advice; medicinal intervention may be a second step; when this is not (sufficiently) effective and the treatment relationship works well, behavioural, and psychological therapy may be considered. Citing recent research, they point out that hypnotherapy and cognitive behavioural therapy may be effective in mitigating bodily and quality-of-life symptoms (this has been proven in clinical trials, but it is not clear whether this works for all patients) – they advise to refer motivated patients, who do not respond to treatment steps 1 and 2, to a psychologist. Other developments in international literature are well in line with this. For instance, a review of qualitative research by Håkanson (2014) found that self-care management can be significant, and that it is shaped not also by the patient's physical condition, but also by her or his knowledge about disease/illness-related matters, and her / his sense of agency, i.e., the awareness of the 'owner' of one's volitional actions. In addition, there is ongoing research on the brain gut axis which provides further evidence and insight on this dimension of pathology (see e.g., the review by Quigley, 2018)

These developments, while partly showing progress in research, also reveal the 'wisdom of practice' as it apparently developed, and thus raise a pertinent question: could a different approach to HTA not have helped to make patients benefit much earlier from that wisdom? That question yields additional depth to the above claim that this historical case study may serve to illustrate the rationale underlying the VALIDATE approach, and the emphasis in that approach of problem structuring, reconstructing, and evaluating interpretive frames and formulating effective policy advice.

The case study suggests that asking the following questions will be helpful to explore this:

1. Why is it that different HTA researchers may adopt different outcome measures?
2. Why is it that the outcome measures used by HTA measures do not take into account what outcomes are deemed important in clinical practice?
3. How may we critically assess outcome measures, and the way they are chosen, in HTA and in clinical practice?
4. What may be the implications of the disjoint between HTA and clinical practice regarding outcome measures; and what could be the advantages of overcoming that disjoint?

5. How could clinical practice be more taken into account in HTA?

In the remainder of this chapter, we will answer these questions by introducing the notion of interpretive frames and explain how they inform what Donald Schön (1983) has aptly called reflection-in-action, i.e., judgement that informs action, not by preceding it but rather as interwoven with it, and embedded in the action context. On that basis, we will shed light on questions 1) and 2) above, by discussing how different interpretive frames may prevail in HTA practices, medical literature and clinical practice. We will then explore how to appreciate these differences by asking the question how they may be critically scrutinized. Next, introducing an additional dimension of our case and drawing on some key insights from the policy sciences, we will argue for taking into account judgement in clinical practice in doing HTA and briefly indicate how this may be done.

On action and interpretive frames

When professionals do things, they cannot just be considered to be pre-programmed automata, following if-then instructions. To be sure, under circumstances, they may operate rather instrumentally, constructing artefacts in a goal-following way – what Arendt has called 'work.' Yet, the distinguishing feature of professionals is that they are able to deal with problems that need first be further processed before goals can be assumed – involving 'goal finding' rather than 'goal following.' This modus operandi Arendt has called 'action', a much more creative type of human (not necessarily merely professional) endeavour which essentially is driven by the process of attributing meaning to a situation and to different ways of dealing with it, investigating both from the perspective of one's wider beliefs and normative preferences. Action is driven by 'reason' rather than by 'ratio' (Toulmin, 2009), 'reflection-in-action' rather than 'technical rationality' (Schön, 1983) and 'inquiry' rather than 'analysis' (Dewey, 1938), to mention the language used by just some important authors have from the pragmatist tradition, in which the interwovenness of thinking and action is the central focus, as will be pointed out in Chapter 7. In this pragmatist tradition, action and thinking are understood as essentially intertwined, and embedded in a particular context.

Schön's depiction of these matters, what he calls an 'epistemology of practice', has been grounded in documented observations of professional action. What will be called in Chapter 5 - in the trail of Daniels (1979) - 'the epistemology of ethics', may be seen as a case ('ethical practitioners') in point. Schön conceives of action as a series of 'moves.' Each move is informed by the meaning attributed by the actor to the situation: what is at hand, and how do I appreciate that? That meaning constitutes the way in which the actor defines the problem; (s)he then attempts to move away from it. These moves are part of the actor's continuous reflection-in-action, or inquiry: they result from inquiry, in which the actor iterates between attributing meaning to the situation, considers different solutions

and then decides on a first move, reflecting a tentative view of problem-cum-solution; and the outcomes triggers further inquiry. Each move must be understood as a "conversation with the situation" in which "the situation talks back", and "the practitioner's effort to solve the reframed problem yields new discoveries which call for new reflection-in-action. The process spirals through stages of appreciation, action, and re-appreciation. The unique and uncertain situation comes to be understood through the attempt to change it… Furthermore, the practitioners' moves also produce unintended changes which give the situation new meanings. The situation talks back, the practitioner listens, and as (s)he appreciates what (s)he hears, (s)he reframes the situation once again" (Schön, 1983: p. 131-132) and acts on that. Precisely that constitutes the non-instrumental, creative nature of action, through which it differs from instrumental work or routinized behaviour.

Yet, this does not mean that action varies without limits, or into arbitrary directions. It is guided by the meaning the actor attributes to the situation, expressed in his problem definition. Attributing meaning is shaped by the lenses through which the actor interprets the situation, and although they may occasionally change in processes of 'double loop learning' induced by 'crises and surprises, these lenses are much more stable than the meanings, actions and assessment of solutions they give rise to, and which continuously evolve in day-to-day reflection-in-action. These lenses may be informed by education and are developed and reproduced through practice, where they yield patterns of action in particular kinds of situation.

Elsewhere (Grin et al, 1996a) the notion of 'interpretive frame' has been proposed to denote the ensemble of a stakeholder's judgment of various solutions to a specific problem, problem definition, and the lenses that shape them. Following a scheme proposed by Frank Fischer (1980; 1995: p. 227-240), 2 x 2 layers may be distinguished. Two are specific for the action situation: the problem definition, reflecting the meaning an actor gives to the situation, and the actor's assessment of conceivable solutions (the actor's estimate of their costs, benefits, side effects, and risks). The other two are more generic, forming the lens through which the actor interprets specific situations: the actor's background theories (views and understandings of the processes and causal mechanisms playing a role in situations like the current one, e.g., a doctor' s biomedical and physiological knowledge, or medical-technical insight) and normative preferences (including his sense of identity and preferred relations to others, e.g., his view on his relation to patients and their health condition).

Reconstructing interpretive frames

In order to reconstruct an actor's interpretive frame, one may ask both direct and indirect questions to the either the actor (in an interview) or to written material (through a form of argumentation analysis). *Direct questions*, for the respective layers ask:

- what are costs, benefits, disadvantages, risks, associated with different proposed solutions?
- what is the problem / challenge here, or: what is at hand and how do you appreciate that; or: what are key outcome measures / criteria for success?
- what are key causal factors and mechanisms behind the phenomenon?
- what is the actor's role / mission here, and what is the actor's identity, i.e., how does the actor see her/himself, how does (s)he) wish to relate to others?

Indirect questions are 'why questions.' As Fischer (1995: p. 230-233) has argued, each layer is connected to an adjacent layer by asking 'why' or 'justification' questions. Asking 'why is X a benefit?' or 'why do benefits X and Y outweigh disadvantages M, N?' will yield (part of) the problem definition. Asking why particular outcome measures are important or asking why one is considered more crucial than another will shed light background theories. And identifying the strong and weak points of a specific background theory will mean to explore what types of problem definitions ad associate solutions it will produced, and what relations and identities these help reproduce.

The methodological advantages of asking both direct and indirect question are twofold. First, this will yield more complete reconstructions of an interpretive frame: answers to different questions may complement each other. Second, it may yield more reliable reconstructions: if answers conflict, this is an alerting signal that one needs probe further, to remedy, for instance, a socially desirable or otherwise strategic answer to a direct question; if they are compatible, this is a valuable confirmation.

Understanding differences in viewpoints

We may now shed light on the first two questions above. First, different HTA researchers may adopt different outcome measures because they too differ in background theories and preferences, and operate in different context. In our case study above the national HTA body's researchers, operating in a context where policy relevance is quintessential, defined the problem as the need to reduce the prescription of mebeverine while maintaining it in the package, and thus rejected effectiveness as outcome measures and favoured therapeutic value; that also reflected their background theories which included methodological knowledge and an understanding of placebo effects, as well as the idea that good policy solves the policy problem with measures that can actually be taken, and are based on an understanding of clinical practice. The team that did the preliminary study tendered by the HTA body to deal with that problem, on the other hand, operates in many contexts a year, and needs to maintain its independence and reputation throughout; it defined the problem as the need

to find alternative treatments of which efficacy could be established, looking into the issue first and foremost through the lens of gastrointestinal background theories.

Second, for similar reasons GPs differ from both groups of HTA researchers. GPs define the problem of IBS as one which is primarily rather intangible (no effective medicinal treatment, counselling very time consuming, patients visit frequently) and thus tend to see patient satisfaction regarding the reduction of IBS complaints as the main outcome measure. This reflects their context as well as well as their medical insights (ambiguous aetiology, role of anxiety rather plausible).

Critically scrutinizing interpretive frames

Differences in context and interpretive frames explain why, and how, different actors each define the problem in their own way, pick associate outcome measures and look for solutions that make sense in these terms. But is this not mere relativism? As noted elsewhere (Grin et al, 2004), accepting that different actors in different context may define problem and outcome measures in different ways, this is not necessarily relativism because the recognition that there may be important truth in not just one, but a variety of claims, does not necessarily mean that one cannot tell that some claims are nonsense. One way to tell sense from non-sense will be discussed in Chapter 5: 'coherentism'. in ways outlined in detail in there, essentially means testing whether *"a proposition or belief is true and justified" by checking whether if it is part of a network or set of ethical and other beliefs people hold that are jointly coherent"*.

In this section, a second, related approach, is outlined that may help to avoid relativism (and more fruitfully settle disagreements – (Banta et al, 1993: p. 152)): scrutinize claims on a specific situation and the background theories and preferences underlying them and understand what the potential and limits of each of them. Importantly, as will be stipulated in Chapter 7, this could help HTA experts to play a significant, novel role: facilitate learning among the various stakeholders, generating new understandings and approaches to resolve problems.

As Fischer (1995:, p. 237-239) points out, discussion of notions on these layers involves different kinds of argument. Discussing *claims on the implications of solutions* involves causal arguments, or empirical-analytical reasoning. In such kind of positivist argument, it is possible to falsify claims when they violate facts, and to render them plausible by showing they are supported by facts. In our example, ironically, may be a placebo effect could have been most convincingly demonstrated.

Scrutinizing a claim of *"what the problem really is' or 'what choice of outcome measures is 'correct' "* essentially involves discussing what a situation means: that is, it involves a phenomenological argument (i.e., arguments rooted in our experience of a phenomenon). Now meanings are in the eye

of the beholder, so here we cannot simply falsify meanings. Several things can be done, however, in order to critically scrutinize claims on 'the' problem or outcome measures. Such claims bring together (Hoppe, 2010) problematic conditions, i.e., observable features of the situation that co-constitute 'the' problem, and a problem definition, i.e., the way in which a specific actors sees the situation. So, one thing we may do to scrutinize an actor claim at this level, is to ask what observable problematic conditions support a particular problem definition. While this may not, in the same sense as for empirical-analytical argument, falsify a problem definition, it can help to assess its salience for the situation. The other thing we may do is to compare the problem definition of an actor with the problem definitions or favoured solution of other actors, answering the question 'in whose name may we define the problem in this particular way?'. In our example, the follow-on study proposed in the preliminary study was compatible with the typical interest of medical researchers (what about the efficacy of fibres) but largely neglected what IBS means for patients and GPs.

To judge *background theories*, the key question is how they inform action. That involves hermeneutic-interpretive argument: for one or several situations, one considers what problem definitions and associate solutions would result when interpreting that situation on basis of this background theory. One test thus is to see, as just discussed, whose problem it emphasizes. In our example, this exercise would be salient, as it would point to the fact that the HTA project underemphasized the needs of patients and clinical practice.

Also, a more substantive test is possible, by asking what mechanisms and causal factors are uncovered when looking into the situation from the perspective of this background theory, and which ones are obscured. This, of course, requires a standard. For medical and clinical practices, one such standard has been proposed by van der Wilt (1995), who distinguishes four determinants: healthcare interventions, environmental factors and life circumstances, genetic disposition and lifestyle, and agency of patients. Background theories may now be assessed in terms of the relative weight they attribute to each of these determinants. If one or several such determinants then appear to be (largely) missing in a world of particular practice (e.g., research and development (R&D), or clinical practice), this may point to a blind spot in that world that may need to be remedied. If actors who disagree on the problem definition and favoured solutions, appear to also differ in terms of the place of different determinants in their interpretive frames, this may help to attain useful insight in the precise relations between these actors' viewpoints. They may both be right in particular cases and circumstances, though not in other; or each may provide partial understanding of the disease and potential therapies, so that they and usefully complement each other.

In our example, a Medline search guided by this distinction of four different determinants (Moret-Hartman et al, 2007: p. 321-322) showed, at that time, (i) that research on IBS nearly exclusively focused on gut motility and medicinal intervention into precisely that; (ii) that the limited research done on two alternative hypothesis, food habits and stress, showed that it was quite plausible that these two factors play roles in the pathology underlying IBS and might (at least partly) explain the plurality in trials on medicinal interventions (van Dulmen, 1996); and (iii) that there was also some evidence for influence of visceral hypersensitivity, for a neurotransmitter imbalance, and for infection and inflammation exist. Such insight could be useful in various ways. First, it could provide some preliminary knowledge basis from practice. Second, it could guide the search for alternative solutions. Apparently diet and stress reduction are promising directions, and the fact that drug interventions are consistently about as effective as a placebo suggest that the patient's lifestyle and agency may be of significant importance. Third, findings like those on the potential role of neurotransmitters and inflammation may contribute to better understand the enteric nervous system. Interestingly, and as noted in the introduction, it has recently become clear that the interaction between microbes, intestinal neuroreceptors and the brain may play a role in the pathology of IBS.

Finally, by their nature, one cannot scrutinize *normative preferences* in terms of an external normative standard. Yet, as Fischer has argued - and as Van der Wilt (1995) using cultural theory, Schwarz and colleagues (1990) and Thompson and colleagues (1990) have shown for health practices - normative preferences are dialectically related to different views on the determinants of care: they are mutually coherent. Scrutinizing these standards may thus be done by scrutinizing the ramifications of choices on the latter.

Box 1. Underdeveloped background theories that matter: an example from the NIPT case

When it comes to differences in *empirical* background theories that matter in normative terms, there is an interesting parallel between the IBS and the NIPT case. In the IBS case, we have seen that already a decade ago there were ill-researched indications that alternative treatment might be effective enough to consider them more seriously when assessing mebeverine, such as dietary or psychological interventions. While that was recognized by GPs and other clinical practitioners, the fact that more formal knowledge was underdeveloped inhibited properly talking into account these options in the HTA study undertaken at the national HTA body.

In the NIPT case, already authors like Diana Bianchi (2012) pointed out that, in principle, the field of genomics that was enabling prenatal tests like NIPT, could also yield novel opportunities for foetal therapy. Obviously, the very existence of such opportunities might have a profound impact on the

normative assessment of NIPT and could have given rise to a significantly different design and outcome of an HTA study. However, at the time, there was much less research devoted to the diagnostic use of genomics then to its application to treat, on basis of such diagnosis, fatal disorders through the application of personalized medicine. (Bianchi, 2012: 1047-1049) This is probably one reason why the Dutch Health Council's assessment of NIPT (Chapter 1) briefly paid attention to prenatal therapy but did not include it into its conclusions. A second reason is that in the Netherlands, NIPT had been classified as a screening test, for which assessment criteria have been legally defined in the Population Screening Act; in that context, assessing NIPT in relation to other technologies was not appropriate. Thus, this HTA was shaped not only by different normative viewpoints, but also by blind spots in mainstream medical research and by institutional context (Chapter 6).

Interestingly, and as another similarity to the IBS case, this blind spot got remedied over time. In more recent article, Bianchi and colleagues are pointing at interesting new research findings. For instance, different ways of scanning had shown that deviation from typical foetal development of the brain phenotype starts to occur by the second trimester, allowing time for intervention; and that mouse models suggest that medicinal intervention with e.g., fluoxetine, continued for two years after birth, might yield improved brain growth and hence significantly reduce later cognitive impairment; and there are encouraging indications that this may also be the case in humans (De Wert et al, 2017: 223-224 and Hendriks et al., 2021). These articles claim that other possibilities for prenatal and early-age treatment are on the horizon.

While the actual availability of such treatments would obviously lead to a very different problem definition for an HTA on NIPT, with different comparators, and its outcomes would depend on a range of hitherto hardly explored considerations. For instance, there are still many issues that require *empirical scrutiny* (e.g., the degree to which reduced cognitive impairment also leads to psycho-social benefits and increased wellbeing – Hendriks et al., 2021: 2) and that may raise *normative concerns* (like the proposition that *"people with DS [Down Syndrome] contribute to diversity, and that this is to be regarded as something valuable for society as a whole"*. De Wert et al, 2016: 224).

In passing, the preceding discussion of *how* interpretive frames may be critically scrutinized has also answered another question: how such scrutiny may also contribute to improving scientific insight as well as clinical practice. This draws our attention to the relation between HTA and clinical practice. In the next section we will discuss this issue, building on the above discussion of interpretive frames.

Implications of and solutions for the disjoint between HTA and clinical practice regarding outcome measures

As we have seen, in the IBS the precise definition of the problem differed significantly between HTA researchers in different context, GPs and patients. Furthermore, we have argued that this may be attributed to differences in context and the interpretive frames prevailing in those contexts. Thus, this disjoint is not an exclusive feature of this particular case, but it is plausible that it will occur much more frequently – it has been documented indeed for a wide range of other cases, including the use of cochlear implants (Reuzel; 2001; Reuzel et al, 2007) and different ways of diagnosing and treating Parkinson's disease (van der Wilt, 1995).

There are three basic reasons why this disjoint is of concern. First, following Habermas (1981) a disjoint between the way in which a problem is dealt with in the system world (of e.g., informers of health decision-makers like the national HTA body and HTA researchers advising them) and how it is experienced in the lifeworld (of e.g., patients and the GPs, nurses and other first line practitioners they turn to) is normatively undesirable, because the power differentials between both worlds tend to de-privilege the lifeworld. How can healthcare system fulfil its basic mission at all, if it loses sight on the everyday life of the people it is supposed to serve?

This admittedly rhetorical question has, of course, been recognized in the HTA community – it reflects the rationale underlying the emergence, over the past two decades, of patient involvement in HTA. As Facey (2017; p.12) indicates, it is important to include patients' "experiences, preferences, perspectives" in HTA. Citing Coulter (2004), (s)he argues that this implies a need for greater patient and public participation, so as to ensure that the HTA focus on *"the types of questions that patients want to* be *answered and engage(s) them in determining HTA priorities, designing and conducting assessments and appraisals, receiving and using findings from HTA and debating policy priorities and rationing"*.

Second, as we have seen, HTA research and, especially, medical literature on which it relies, may be limited by particular biases, emphasizing some determinants of a particular health problem more than others. This may affect the assessment of opportunities for more optimal care, explored by health practitioners but hitherto underexplored in literature. In the IBS case, the effectiveness of non-medicinal interventions like diet had hardly been researched, hampering the opportunities to provide evidence-based advice. Similarly, while clinical practitioners are often well aware of the influence of the brain-gut axis, here too lack of research on these issues led to a lack of proper evidence for intervention explored in practice. We have also seen that the understandings and

approaches that had emerged as tacit knowledge in practice, were later confirmed and elaborated in more formal knowledge. Thus, in such cases, HTA researcher may wisely include recommendations to translating these experiences and insights from medical practice into directions of research programming to attain more formal knowledge on different understandings.

There is a dilemma here, however. As experienced HTA researchers are well aware, frequently the reverse issue is the case: pressure from – sometimes rather autonomous – clinical practitioners, hospital managers, industry and other healthcare actors promote options that are not necessarily preferable from the viewpoint of societally optimal care (i.e., care that scores well in terms of the four coverage decision criteria from ZIN (2015): effectiveness, cost-effectiveness, necessity and feasibility). One important issue in such cases, like that of the Da Vinci surgical robot (Oortwijn et al, 2020), are the potential displacement effects: given constrained budgets, expensive novel technologies may draw resources from existing treatments or care provision (Wammes et al, 2020). Responsibly navigating between the two horns of this dilemma is a crucial challenge for scoping (see Chapter 4) as well as for ethical assessment (Chapter 5).

Third, whatever intervention emerges from HTA work as advisable, it must be recognized that such an intervention may be done by a macro-level actor, but will only yield the expected outcomes through the efforts of actors at the meso (e.g., hospitals, manufacturers) and micro levels (e.g., practitioners, patients). Desired outcomes are matter of what Whitaker (1980) has called *co-production* between policy actors and actors involved in policy implementation. Co-production may occur if a policy that helps and incentivizes (Schneider et al, 1990) the latter actors to act in line with policy objectives. It is a key finding from implementation studies (Pressman et al, 1973; Mazmanian et al, 1989; Yanow, 2000) in the policy sciences and literature on the use of knowledge in practice (Weiss, 1980; Dunn, 2008) that co-production is far from self-evident to occur. This can be well understood on basis of the above discussion of differences in context and interpretive frames (Grin et al, 1996a; 1996b). The crucial corollary is, that an intervention proposed in an HTA or a policy may be expected to have actual success if, and only if, patients, GPs and others consider actions expected from them sensible and fitting in their context their context. An action makes sense to these actors if it fits their interpretive frame – more specifically, if offers a solution to a problem that they themselves perceive and that does not violate their background theories and normative preferences (Grin et al, 1996b); evidence form a range of cases provided in van de Graaf et al (1999).

We have called this form of action–oriented agreement between actors differing in context and background theories *congruency.* Congruency is a less strict, more pragmatic form of agreement than the idea of having ‘shared objectives, a ‘shared problem’ or even ‘shared values,’ as it acknowledges

that actors and their context may differ in nature. It is a more interesting form of agreement than 'compromise' (e.g., between different groups of doctors, or between patient interest and policy objectives) as with a compromise all parties loose (how much depending on their power position and strategic and tactical competences), while congruency entails a synthesis of viewpoints, which often goes beyond a trade-off.

In the mebeverine-in-IBS case, we identified as a congruent solution that, absent convincing evidence on specific therapies for identifiable subgroups of patients, physicians might wish to resort to identifying the best treatment for each patient individually. We noted, that, at that time, *"Evidently, this strategy is the current practice of most physicians. It would, however, be advantageous to standardize this process, as standardization can prevent a significant amount of bias"* (Moret-Hartman et al, 2007). As discussed in the introduction, by now the formal knowledge has been developed that allows such standardization.

Box 2. The disjoint between HTA and clinical practice regarding outcome measures in the NIPT case

The three ramifications of the disjoint between the outcome measures used in conventional HTA studies and in clinical practice also express themselves in the NIPT case. First, the discrepancy between typical HTA 'system rationality' and ' lifeworld rationality' expresses itself, for instance, in the use of the average cost per trisomy 21 detected for different screening scenarios as an assessment standard (Bloemen et al., 2021) or to a *"outcome measures such as cost per additional abnormality detected, or cost savings per disabled child not born, that frame NIPT as a technology that becomes more cost-effective when it prevents a sufficient number of births affected by genetic disability"*. (Chapter 1) – standards reminding us of what Richardson (2000) once provokingly called the "Stupidity of the Cost-Benefit Standard". The second ramification, the dilemma between giving too little or too much voice to clinical practice vis-a-vis formal medical knowledge might also express itself in the NIPT case. On the hand, it is clear from Box 1 that formal knowledge on pre-natal treatment of DS that may matter essentially for parents' and society's appreciation of the NIPT test is as yet underdeveloped. The other side of the coin, also mentioned in Box 1, is that, should such treatments be available, there might be a risk that they are imposed by medical professionals or care institutions, despite potentially high costs and notwithstanding potential objections of denying the value of people with DS (cp. the reception of cochlear implants).

These two points together raise the question whether it would be possible to come to a congruent outcome of the HTA, that would be normatively desirable from a societal standpoint (effective, cost-effective and yielding quality of life) *and* would be acceptable to parents: the third issue raised by the disjoint.

For these various reasons, and as illustrated for the NIPT case in Box 2, it is important to ensure that the findings and proposed actions from an HTA study fit problem definitions for patients, doctors, and other key actors in clinical practice. Reaching an overall problem definition that represents such congruency requires proper scoping; doing so while navigating the dilemma sketched above may pose high demands on the art and craft of scoping, as will be discussed in Chapter 4. Iteratively finding solution(s) matching that specific problem definition (may be adapting the problem definition in the process) is a key task for subsequent activities in the HTA processes, in which congruency may be designed through learning between the different actors involved (Grin et al, 1996a; van der Wilt et al, 2015; see also Chapter 7).

As Richardson (1990) has elegantly argued, this cannot be done by simply specifying norms or practice. Fundamentally, the reason is that practitioners are not rule-following beings. Rather, they define their actions in a much more reflective process of exercising judgement, as also portrayed by Schön. Judgement here refers to the Aristotelean notion of *phronèsis*, which has been key to the development of interactive Technology Assessment (Grin et al, 1996a; 1997). *Phronèsis* for Aristotle is to exercise practical wisdom: knowing what needs to be done in concrete situations in order to achieve maximal coherence among our multiple and varied value commitments (Richardson, 1990; Fischer et al, 1993; 2012; Loeber, 2007).

A key feature of *phronèsis* being interpretation through a double hermeneutic (Yanow, 2000) of interpreting both generic principles and the particularities of the situation. Following Arendt's notion of *'Im Stelle jedes Anderen denken'* (think like, and for, all others), it essentially also involves that different viewpoints are being synthesized. Given its hermeneutic nature it may help understand the *formation* of interests, preferences, problem definitions and policy options. Obviously, such understanding is especially useful when analysing socio-technical change, in which preferences may evolve. Under circumstances stakeholders held different views on the technology; through frame reconstruction these could be resolved into different background theories; this occasioned partial revision ('learning'), resulting in agreement on how to proceed. Phronètic approaches to HTA may draw on recent extensions of HTA's methodical repertoire with more pragmatist approaches, such as methods for patient involvement as collaborative partners (De Wit et al, 2017), ethnographic field work (Tjrnhj-Thomsen et al, 2017) and, especially, deliberative methods (Street et al, 2017).

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Chapter 4. Scoping

Abstract

This chapter is focused on the art of crafting health technology assessment (HTA), i.e., scoping, and integrates the lessons of the previous two chapters. Because the relevance of facts depends on the adopted perspective, and there are different perspectives in society with respect to the desirability of health technology, the objectives of each specific HTA should be defined by taking into account these perspectives. Scoping concerns defining the objective and research questions of an HTA by a systematic exploration of relevant aspects from multiple perspectives (e.g., citizens, patients, informal carers, health professionals, decision-makers). There are several ways to do this, but it ought to be conducted in an iterative way, using explicit methods to elicit the values of different stakeholders, taking into account that these values may conflict.

Key messages of this chapter: Scoping is the art of crafting HTA and is central to addressing relevant policy problems via meaningful assessments. Appropriate scoping, using explicit methods, result in findings and proposed actions from HTA that fit the problem representations of relevant stakeholders.

After reading this chapter, you will be able to understand the importance of scoping as well as that scoping needs careful preparing, and the methods used to elicit stakeholder values are dependent on the context.

Addressing relevant policy problems

The type of policy problem addressed in health technology assessment (HTA) has an influence on the type of analytical approach that is appropriate, distinguished by the *scope* (program level or societal level) and *focus* (empirical and/or normative). Translating the policy problem into research questions for each specific HTA is called scoping. More specifically, ***scoping concerns defining the objective and research questions of an HTA by a systematic exploration of relevant aspects from multiple perspectives (e.g., patients, informal carers, health professionals, decision-makers).***

Before describing scoping in more detail, we want to emphasize that - from its original intent - HTA aims to inform decision-making. This means that HTA is context-dependent and as such should reflect policy problems that are considered important to society (see also Chapter 3), taking into account the complexity and dynamics of health systems (see also Chapter 6). However, the extent to

which values at the societal (system) level are taken into account in HTA remains largely unexplored (Lóblová, 2018).

HTA frameworks currently employed by HTA bodies are also not well-suited to take into account the wide range and diversity of stakeholder values (see also Chapter 2). This is leading to insufficient sets of relevant information. The assessment frameworks are typically based on contemporary HTA, using 'substantive' criteria, which are believed to reflect the most important social values. As such, decisions are often based on effectiveness (Wranik et al, 2020) and in some cases economic evaluations, using for example the cost per quality-adjusted life years (QALY) approach. It is known, however, that the QALY approach does not explicitly incorporate considerations of equity (Angelis et al, 2018). Lysdahl and colleagues (2016) also mention that *"the majority of health economics guidance is based upon the assumption that assessment is seeking to support a global decision-maker engaged with maximizing the efficiency of an overall health system…*.", using cost-effectiveness thresholds. This focus may result in suboptimal outcomes at a societal level. Especially in many low and middle-income countries, the use of cost-effectiveness thresholds could lead to flawed decisions on how to allocate scarce resources because decision-makers do not consider maximizing efficiency to be the main or only value or objective of the health system (Bertram et al, 2016; Pichon et al, 2019). This means that the ethical underpinning of cost-effectiveness analyses (e.g., maximizing efficiency) in themselves do not assure adequate ethical or legal reasonableness in coverage decision-making (Abrishami et al, 2017, see also Chapter 2).

It is important that the HTA community addresses more clearly what matters to the relevant health system (societal level), as well as to relevant stakeholders (program level), and the reasons why (Oortwijn et al, 2019). This is clearly reflected in the new definition of HTA (O'Rourke et al, 2020), and which is acknowledged to help HTA users to think beyond cost-containment, safety, and efficacy by addressing larger questions on the impact of health technology on sustainable ethical development (e.g., in the case of COVID) (Mukherjee, 2021). Furthermore, practical guidance has been developed on how to link health system values to the HTA process, using so-called *evidence-informed deliberative processes* (Oortwijn et al, 2021). The guidance states that an HTA body or other relevant organization/committee which has this specific remit, uses relevant criteria for the assessment and subsequent appraisal of health technologies in line with the relevant health system values.

An important issue to consider is, however, that different stakeholders such as patients, the public, providers, payers, industry, and policy makers, may have a wide range of social values and interests that result in different perceptions of which outcomes are considered to be desirable. For example, in decisions on public funding of expensive cancer drugs, patients may argue that the best treatment

should be made available, other patients may argue that their treatment should not be displaced, and taxpayers may reason that it is important to make efficient use of public resources. As such, it might be challenging to find a common problem definition to be addressed in HTA, as explicated by Gerhardus et al (2017) and in Chapter 3 of this handbook. This challenge may pose high demands on the art and craft of scoping and highlights its importance in the HTA process: prior to conducting the assessment it should become clear what the problem is and what the related questions are that the HTA should answer (Gerhardus et al, 2017). So, how to conduct scoping for a meaningful assessment that can be used to inform decision-making?

Scoping the right research question(s)

The explication and clarification of what makes a health technology desirable helps in identifying relevant outcome measures. This then provides important input for HTA, in the sense what evidence and other relevant information needs to be collected to answer the question(s). The available evidence can only be assessed for its relevance and completeness against the background of a specific definition of the policy problem (see Chapter 3). This may differ from health technology to health technology, but also from context to context. In Chapter 1, the case study of **Non-Invasive Prenatal Testing (NIPT)** was introduced, and it was emphasized that its purpose can be conceptualized in many, and sometimes contradictory, ways (see also Bloemen et al, 2021).

In the Netherlands, for example, NIPT was assessed to determine whether it could contribute to improved prenatal screening by providing respective parents with '*meaningful reproductive choices*'. This was defined as making a choice about severe health problems, in an informed way (respecting autonomy of the parents), and being proportional, i.e., respecting the anticipatory autonomy rights of the child (Health Council, 2013). In Germany, NIPT was defined in the HTA as a *medical procedure* (i.e., ability to save healthy foetuses from procedure-related miscarriages), and which was highly contested by different stakeholders in the country (Braun et al, 2018; Bloemen et al, 2021).

As such, consultation of stakeholders may be helpful in producing a variety of ways of how the problem may be conceptualized.

If multiple problem definitions can be brought to light, the HTA team needs to resolve how this is going to affect the overall design of the HTA: which (elements of) of the problem definitions are going to be used to guide the HTA and what research questions will be addressed in an HTA, how they will be addressed, and to point out possible limitations.

To produce HTAs that really address a relevant policy problem, it needs to be discussed and further defined prior to conducting the assessment. This is done through scoping. HTA agencies are often

responsible for scoping, but policymakers (e.g., Ministry of Health), external committees, in consultation with relevant stakeholders and/or experts, can also do this. It appears that HTA agencies are more likely to prepare their own scope if they carry out their own assessment.

Structuring the research question

Most often HTA agencies define the research question(s) – via exploration of relevant assessment aspects - using the so-called PICO or TICO format. The PICO format is a system approaching used to describe which *Patient, population or problem* is targeted, which *Intervention* is evaluated, which *Comparator* is used, and which are the relevant *Outcome* measures. The TICO format describes which *Technology* is being evaluated, for which *Indications* (in terms target disease, population, and intended use), which *Comparator* is used, and which are the relevant *Outcome* measures. The PICO/TICO question may be extended by study design (S). In the context of complex health technologies, a more flexible approach may be required (Wahlster et al, 2016).

The choice of outcome measures relates closely to the criteria that are used in a specific context for decision-making. These decision criteria include, by default, generic criteria such as safety (i.e., avoiding harm), effectiveness (i.e., doing good) and quality of the evidence. In addition, these may also include a number of contextual criteria, i.e., those that are specific to the technology under evaluation.

As stated before, stakeholders may have different views on the desirability of proposed outcomes.

For example, **in the case of NIPT** reproductive autonomy could be a desirable outcome considered from the perspective of pregnant woman in addition to "standard' health related outcomes, such as the QALY (Kessels et al, 2019; Bloemen et al, 2021). Furthermore, we already mentioned in Chapter 1 that outcome measures such as cost per additional abnormality detected, or cost savings per disabled child not born may conflict with the desirable purpose which is suggested by social and ethical analyses (Kibel et al, 2017).

Furthermore, the way in which relevant outcome measures are conceptualized and operationalized is an important task in order to have a common understanding of its desirability.

Bloemen et al (2021) concluded a normative analysis using an HTA report on **introducing NIPT** in the Netherlands. They found that safety was conceptualized in the HTA report as 1) the avoidance of procedure-related miscarriages (due to avoidance of using invasive tests) and 2) avoidance of unnecessary worries concerning the child's health, due to false positive test results. The authors noted that it could be argued that other possible consequences of taking a prenatal test should have

been taken into account when assessing safety in terms of avoiding harm. For example, decisional regret, potential harmful effects on the foetus, societal pressure to take the test, and distress related to difficult decisions that need to be made as a consequence of test results, as well as societal views regarding people born with conditions after screening could have been considered. This example makes is clear that the scope and outcome of the assessment is depending on how a criterion such as safety is conceptualized, whose safety should be considered, and which (negative) impacts are important. Eventually, this may also influence conclusions regarding safety in the HTA report.

The need to involve stakeholders

In order to conduct a systematic exploration of relevant aspects from multiple perspectives, it is advised that HTA doers develop of an initial logic model to depict the health technology that is being assessed, identifying the relevant stakeholders involved and to structure the different outcomes that are found desirable. A logic model is "a graphic description of a system … designed to identify important elements and relationships within that system" (Rehfuess et al, 2018). A logic model can also help to take the variability of participants, context, implementation issues, and their interactions into account (see Chapter 6). The logic model can be used in scoping by iteratively involving stakeholders to identify (associate) outcomes, which may result in adapting the problem definition.[7]

From a survey among members of EUnetHTA is appears that in the scoping phase, industry, patient experts, clinical experts, payers, and providers are frequently involved. It is advised, that when determining the outcomes to be analysed for a specific HTA, to involve patients who are living with the condition in question, in order to ensure that the outcomes are important and relevant from a patient's point of view (e.g., fewer side effects, quality of life issues). Moreover, they may have information on the disease/condition and treatment process/options, which is not accessible to the assessors by evaluating clinical studies.

If the patient is not able to communicate, as a result of the illness or because of being a child, a caregivers' perspective (e.g., **parents in the case of NIPT**) may be useful.

However, still then the question is whose perspective counts and why is it (not) considered in defining relevant outcome measures? Mercer et al (2020) explored experiences and perceptions among patient groups participating in the Canadian Agency for Drugs and Technologies in Health (CADTH)'s pan-Canadian Oncology Drug Review (pCODR) process. In the current appraisal process, the focus is on whether the clinical benefit of a new drug outweighs negative impacts (toxicity and

[7] See for a presentation on how to build a logic model in HTA (on reinforced models of palliative care): https://studylib.net/doc/9680608/presentation-on-building-a-logic-model-of---integrate-hta

associated side effects). However, patient representatives indicated that this was not a meaningful question as what is intolerable to one patient might well be tolerable to another. Thus, from a patient perspective, the more meaningful question "can the HTA process allow for differences between patients?"

In the case of NIPT, the question could be asked whose health benefits should be considered: those of the unborn child of those of the prospective parents? (Goldhaber-Fiebert et al, 2015).

In addition to actively being involved, patient experts can also be asked to review scoping documents or attend (clinical) expert workshops. Clinical experts may be involved by providing data or being consulted on questions such as relevant comparator, clinical value of the product, how the product is used in clinical practice, implication in terms of resource utilization, etc. The role of providers in scoping is to provide data and evidence and they can be involved in stakeholder groups. Providers can review documents and provide general consultation via peer review. Finally, payers could also provide relevant information, data, and evidence in the scoping phase (EUnetHTA, 2017), but there may be other experts depending on the topic under assessment.

Of course, one need to be aware that users/requesters of the HTA may be reluctant to include other perspectives than go beyond the area of direct (policy) interest. However, the involvement of relevant stakeholders to identify, reflect, and learn about the meaning and importance of relevant values and questions, and an evidence-informed evaluation of the identified values (criteria) can contribute to the legitimacy of recommendations and/or decisions, e.g., by improving the quality, consistency and transparency of the HTA process. This has implications for how HTA is conducted.

Stakeholder involvement methods

There are different levels of stakeholder involvement, ranging from communication, consultation to participation, and it can be arranged using qualitative and/or quantitative methods. Communication consists of only informing stakeholders, for example through public meetings, by dissemination to high priority groups using patients' organizations or by using social media. Consultation refers to a structured process for collecting feedback from stakeholders without providing opportunities for meaningful participation (i.e., deliberation). This can be done via several methods, including surveys, interviews, stakeholder meetings and solicited feedback from stakeholders (by invitation), or multimedia analysis (Abelson et al, 2018). Stakeholder participation means that stakeholders are actively engaged in deliberations and can openly exchange views on argumentation and evidence, for example via nominal group techniques, consensus building approaches and expert elicitation

techniques (Peel et al, 2018). In current practice, most HTA bodies apply communication with or consultation of stakeholders in their activities.

Examples of methods for how relevant stakeholders could scope the HTA were explored in the INTEGRATE-HTA project (Wahlster et al, 2016). The INTEGRATE-HTA project aimed to develop concepts and methods for a comprehensive, patient-centred, and integrated assessment of complex health technologies that considers effectiveness and economic, sociocultural, ethical, and legal issues, patient preferences and patient-specific moderators of treatment, as well as context and implementation issues. These concepts and methods were applied in an HTA that examined home based palliative care services with and without an element of caregiver support.

The following methods for scoping were applied depending on the context (Brereton et al, 2017; and Box below):

- *Stakeholder consultation*: Local coordinators in England, Norway and Poland adopted the UK's philosophy for lay stakeholder involvement and all stakeholders were consulted as 'research advisors' to inform researchers' decision-making in the project. Consultations were guided by the National Institute for Health and Care Excellence (NICE) methods for developing public health guidance (NICE, 2020; NICE, 2013) and the INVOLVE[8] briefing notes for involving the public in research. Information was collected and summarized using the EUnetHTA Core Model as an overarching framework for conducting the HTA (see Chapter 5 for more information on the EUnetHTA Core Model).
- *Qualitative research*: A variety of qualitative approaches were used in Germany, Italy, the Netherlands, and Lithuania according to local tradition and researcher preference about stakeholder involvement. These included nominal group technique and categorical coding procedure following grounded theory methodology by Strauss et al (1990); interactive evaluation (see Chapter 5 for more information) and subsequently case reconstruction using constant comparison and thematic analysis.

In the INTEGRATE-HTA project, 132 stakeholders (80 professionals, including health and social care professionals/academics working in palliative care and 52 lay persons, including patients and families undergoing palliative care of 18 years and older) in seven countries (England, Germany, Italy, Lithuania, the Netherlands, Norway and Poland) highlighted similar issues affecting palliative care. This information complemented review level evidence and provided direction when scoping the HTA

[8] A UK national advisory group, set up to support public involvement (i.e. patients, carers and those using health and social services) in National Health Service (NHS), public health and social care research.

(Brereton et al, 2017). The contributions from lay persons primarily provided insights into patients' and carers' experiences of services whereas professionals were able to draw on their experiences of service provision to a wide range of clients and situations. This enabled the researchers to identify both an intervention and comparator model of service provision for the main HTA question. The issues raised were also used to inform sub questions for the assessment of specific aspects (e.g., ethical, socio-cultural aspects). In addition, some of the issues raised by stakeholders (i.e., the need to increase home care provision and for caregiver training/support), resonated with the findings of a review of review level evidence about models of service provision that had been completed at the same time. However, the study populations included no views of ethnic minority groups who are known to have specific palliative care need. As such, care is needed when interpreting the results of this study.

Conclusion

Scoping is a fundamental key element of HTA and the VALIDATE approach. The explication and clarification of what makes a health technology desirable helps in identifying relevant outcome measures. This enables HTA doers and users to discuss how in the assessment certain facts can be collected. By relating the choices that are made in conducting the assessment and the, collectively determined, desirable ends of a health technology, the assessment becomes more meaningful for its intent: informing decision-making (van der Wilt et al, 2017).

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Chapter 5. Ethics, ethics approaches in HTA, and ethics synthesis

Abstract

This chapter is focused on ethics and ethical analysis in HTA and starts with some meta-ethical reflections on how to view ethics from a linguistic, ontological, and epistemological perspective – presenting an alternative to a sceptic or nihilistic view of ethics. Then different methods for doing an ethics analysis in HTA are briefly presented, giving an overview of possible approaches that can be applied depending on the problem at hand. This section is divided into substantive, procedural, mixed, and interactive approaches and use NIPT to illustrate how the different approaches would handle a specific technology. Finally, the chapter ends with presenting how ethics input from existing literature can be synthesized.

Key messages of this chapter: Ethical judgements can have a well-founded basis beyond mere attitudes and feelings. There are a number of approaches for doing ethics in HTA, and the choice of approach is dependent on both key values of the context and the type of decision-problem. In HTA, there are developed models for synthesizing literature on ethics.

After reading this chapter, you will have a brief overview of meta-ethical standpoints. You will also understand there is a selection of ethics approaches to HTA and have a model for synthesizing ethics literature.

Introduction

The chapter starts with an introduction to the language of ethics and how this differs from other types of languages, i.e., what we do when we use ethical language. Here you can learn about what the foundation for the ethics (how we can say that something is moral or not) and whether we can say that we know anything about ethics.

Then we use this basis to investigate how ethical issues can be addressed in HTA. There are many ways to do so, and it is important to know which approach to apply. However, the choice of a particular approach is not value-free; it must be justified by a moral point of view (Patenaude et al, 2017).

Lastly, you can learn about how to synthesize ethics literature. Here also there are several ways to provide an overview over the ethics literature on a specific health technology and to synthesize its insights.

As described in Chapter 2, ethical issues ought to be an integrated part of the assessment of health technology. The extent to which these issues are explicitly identified and discussed may vary and will depend on the decision that is being informed by the health technology assessment (HTA), the expertise available, and the willingness to make ethics an explicit part of the discussion of the appropriateness of the health technology being assessed. At this point it is also important to emphasize that the approaches require a certain degree of competence in ethics in order to avoid a mechanistic use.

I (Meta)Ethics

Is there more to ethics than just opinions?

Often when people are discussing ethics, you might hear someone claim that "Well, there is no such thing as right or wrong, really! It is just a matter of opinion; it is all relative…!" (See also Chapter 2 on the right sink with (red) water from the well of emotions). Generally, people seem to base this idea on the fact that we disagree about ethical or value issues, more than we seem to disagree about issues that we do not consider ethical, what we might view as factual issues.

Within meta-ethics, the branch of philosophy dealing with issues about the ethics language, we find several different theories concerning how ethics should be understood.

The ethics language

When using ethical concepts like good, bad, right, wrong, brave, honest, suffering etc. – we generally seem to be doing something other than just describing how the world is. When saying about a patient, that (s)he is suffering – it is not just establishing a descriptive fact about the world. We also seem to imply that we should act on that information (e.g., to reduce the suffering if possible). Hence, it seems the ethics language is, in many cases, prescriptive. This prescriptive function of the ethics language is at the same time based on descriptive aspects of the situation. In a more technical term, the value term, and its prescriptive function, *supervenes* on more descriptive aspects of the situation. Hence, when we say about a professional, that (s)he is acting wrong, we base this on empirical or descriptive aspects of how the professional behaves, what (s)he says etc. – e.g., hurting people, ignoring their decisions etc. Saying that (s)he is acting wrong is based on specific states of affairs.

In some cases, when using ethics language, we are talking about how the world *should* be, rather than about how it is. Hence, when claiming about a specific technology, that it is unethical due to causing patients harm – we are prescribing that the technology should not be used (regardless of whether it is actually used or not).

In effect, the ethics language does, to some extent, have a different function from other forms of language. It is prescriptive and about how the world should be rather than about how it is. This brings us to the next questions: what are the basic elements of the ethics language, and how can we have knowledge in ethics? The first question is about the ontology of ethics and the latter about the epistemology of ethics.

The ontology of ethics

Now, even if we acknowledge that the ethics language is used with a somewhat different function in distinction to other types of language, it is still an open question what we are referring to when we use concepts like good, bad, right and wrong. Is there something "out there", independent of us and our attitudes, we are referring to? Or are we simply referring to or even expressing our own attitudes towards a specific situation?

While religious traditions will refer to something outside us (God, Allah, etc), some secular traditions assume that ethics terms do not refer to anything outside us, but rather our attitudes in some ways. Hence, to claim about a specific technology that is it good – is to say that "I like this technology". This kind of approach is called *nihilism* in meta-ethics and implies that when we use ethics terms, we are not saying something that has so called "truth value" about the world (but rather what has truth value about ourselves and our own attitudes) (cf. the discussion on scepticism in Chapter 7).

To take a technology, where there is a strong controversy: euthanasia – i.e., actively to inject for example potassium chloride in a patient with the intention that the person should die. Some people find that euthanasia is right, and hence something that should be offered to patients (under certain conditions). Other people find that euthanasia is wrong and should hence not be offered. For a nihilist such a discrepancy would simply imply that different people have different attitudes towards euthanasia (which in turn might depend on a number of different factors like upbringing, culture, religion etc.). In essence, this implies that there is no real contradiction or conflict to resolve – we simply have different attitudes (like some might like coffee and others like tea).

In the meta ethics discussion, perhaps the two most dominating arguments for nihilism is: 1) that there seems to be wide-spread disagreement between people on ethical issues; 2) that it seems difficult to resolve these differences through rational methods. However, it is not obvious that the disagreement

is greater in ethical issues, than in other issues. Other issues are also difficult to resolve without questioning that such issues have "truth value" or exist independent of our own attitudes. To take a current example, even accepting the fact that humans' impact on the climate, the best experts disagree about how much the temperature will rise within, say, 50 years. Moreover, this seems impossible to fully resolve with rational methods. Still, we do think there will be a definite answer to how much the temperature has risen (or rather what the mean temperature is) in the world 50 years from now. So, the opponents of nihilism ask, is there really a principled difference? Why would such disagreement and lack of methods to resolve such disagreement have us conclude there is not truth value to ethical claims, whilst there is truth value to climate claims?

The opponent of nihilism might instead turn to *realism*. A realist claims that concepts like good, bad etc. refers to aspects of the world, existing independent of man and our attitudes. Hence, if we claim that euthanasia is wrong, we do not (only) claim something about ourselves, but about the world "out there". Expressed in other words, the wrongness is a feature of the world and, hence, if someone claims that euthanasia is right, we are using contradictory concepts about the same world, which cannot at the same time both be true. Hence, for a realist, in such a situation we are having a real conflict or contradiction about the issue. So, what are the arguments in favour of the realist view about ethics?

An indirect argument seemingly showing that we are not nihilists, but rather realists, is that we seem to treat ethical disagreements like real conflicts. That is, we try to convince opponents in an ethical debate that they are wrong, by using arguments to support our position, or to undermine our opponents' position. In doing so, we use arguments we assume or hope the opponent will find convincing, i.e., we seem to assume we share a common value foundation of sorts. Hence, in arguing about euthanasia we might use arguments in terms of reducing suffering, respecting autonomy (of patients and professionals), causing harm, etc. Now, this might not necessarily show that we accept realism, we might try to convince only as part of promoting out own attitudes (without thinking we are right in a realistic sense).

An argument following a similar line of thought is that assuming realism to be true is necessary to claim that someone made a mistake or got it wrong about ethics, e.g., in claiming that people in keeping slaves or viewing other ethnic groups as less valuable did wrong - not only according to the standards of our time or of ourselves but from a more objective perspective. In effect, the realist claims that we seem to take ethics too serious to only be about attitudes, and moreover, seem to use similar methods to resolve disagreement as we use in other type of conflicts where we do assume there is an independent answer.

A third line of argument for realism is that there seem to be certain issues where most people agree, e.g., with respect for vicious killing or torture. Hence, at least some issues seem to be handled as ethically absolute.

The epistemology of ethics

Even if we arrive at a realistic view on ethics, can we have knowledge about the values and norms we think exist? Or, to put it in other words, what does it imply to have knowledge in ethics. Traditionally, we define knowledge, as having true and justified beliefs about something. In meta-ethics, we find basically, two different theories about how to have true, justified beliefs in ethics: foundationalism and coherentism.

According to *foundationalism*, we should identify self-evident proposals about values and norms, which we cannot doubt as true and justified. These will then function as a base or foundation, on which we can build (by logical inference) other beliefs. In this way, we will have a set of beliefs in ethics that are true and justified, in resting on a solid foundation.

Two problems arise for this approach. First, can we find such a solid foundation? Second, even if we have such a foundation, can we infer other relevant beliefs from the foundation? Much of the recent discussion has focused on requirements for claiming that something is 'self-evident' advocating different theories concerning this. Still, there is no agreement, and even if we would find such self-evident beliefs, there are still problems in what we can infer from such beliefs. To take an example of an ethical proposition that might seem self-evidently true and justified to people 'We should not inflict (instrumentally) unnecessary suffering to innocent people.' In order to accept such a proposition as self-evident, it needs qualifications about what is instrumentally unnecessary (e.g., suffering that is not required in order to avoid greater suffering etc.), what is suffering, who is innocent etc. Still, assuming such qualifications have been made, and been accepted – what can be inferred from such a proposition? Can we infer that we should (positively) benefit people or that we should respect the autonomy of people, from such a proposition? Not without adding a number of assumptions, that we might not find self-evident – e.g., that suffering also implies absence of benefit, that inflicting suffering has the same ethical status as abstaining from acting so that absence of benefit occurs, that what is unnecessary suffering is up to the person to decide on etc. etc. Hence, critics will argue that for most ethical beliefs we hold, foundationalism does not seem to provide justification.

An alternative route is *coherentism*, arguing that an ethical proposition or belief is true and justified if it is part of a network or set of ethical and other beliefs people hold that are jointly coherent. In this case we do not need to find a solid, self-evident foundation, but rather modify beliefs until they are

coherent. One way to express this coherent set, is to require that the set is in reflective equilibrium. This epistemological approach has also been used as a methodology in ethics, in trying to analyse and modify propositions about ethics in order to make them coherent in relation to other sets of beliefs etc. a person has.

The fundamental problem with coherentism is that two (or more), radically different sets of beliefs (ethical and others) might be internally coherent – hence, implying a certain degree of relativism. Generally, it seems coherentism is more common among moral philosophers and ethicists, at least based on a more pragmatic approach, since coherentism seems more 'useful' when assessing ethical propositions and beliefs. Still, it is a matter of discussion, exactly what should enter into the sets of beliefs to assess for coherence. A common approach is the so called wide reflective equilibrium, which according to Norman Daniels implies: "a method that attempts to produce coherence in ordered triple sets of beliefs held by a particular person, namely: (a) a set of considered moral judgments, (b) a set of moral principles, and (c) a set of relevant (scientific and philosophical) background theories" (Daniels, 1979). In distinction to a narrow reflective equilibrium, we try to find equilibrium, all things considered (e.g., by testing a number of different theories and principles to which fits best, not only try to find coherence between a specific principle and a number of cases). Coherence does not only imply logical coherence but might also imply whether we are psychologically prone to have certain beliefs or not. For example, attitudes might be logically possible but empirically or psychologically uncommon or difficult to hold.

To take an example, we are considering whether to introduce a new technology, with a small probability of curing a dying patient, but with a rather high probability of actually shortening his/her life instead. To find the true and justified standpoint for whether this technology should be used or not, from a coherentist perspective, we should identify relevant principles (e.g., non-maleficence, beneficence, respect for autonomy), and relevant scientific and other facts or theories (e.g., about patient autonomy, the trajectory of the disease the patient is suffering from, the biomedical mechanisms of the technology, data from clinical studies of the technology etc.). Based on these different inputs, we should find a reflective equilibrium. For example, what is a relevant balance between risk of harm and potential benefit will be a tricky issue, but an issue where we will look at other previous decisions in similar situations, to what extent we have allowed patients to strike the balance (without restrictions or not) etc. Since we are not only requiring logical coherence, but a more 'empirical' coherence, there might not only be a single answer to what is the right balance. Moreover, a further challenge is that everything in our set of beliefs etc. can be 'up for grabs', i.e., we might need to reassess how we used to interpret our principles, in the light of new scientific theories or in the light of new technologies etc.

Concluding meta-ethics

The intricate discussions within meta ethics show that there can be more to ethics than just opinion, and many ethicists or philosophers would argue that there is more to ethics than just opinion. This section has aimed to give you a short overview of some theories in meta ethics, trying to answer questions about ethical semantics, ontology, and epistemology. We do not require you to decide which theory you want to side with or find most relevant, just reflect on how these theories might challenge the preconception about ethics you might have. For example, whether you find there is far-reaching relativism when it comes to ethics or if you presume there is a large overlap or consensus in the values and norms adhered to.

Suffice it here to say, that in a given healthcare system, we will need to have a more or less consistent approach to which technologies we should use and in deciding on which technologies to use, we will need to provide arguments to support different alternative options. Hence, from a more pragmatic perspective, we might find a combination of a realist and coherentist approach useful.

II How to make an ethical analysis – different frames and approaches

Even when we have some of the meta-ethical issues settled, it is not clear how we should act in specific situations or how we should evaluate what is good and bad with a specific health technology. Deciding on what is good and bad (values) and right and wrong (norms) is a task of normative ethics. There are a wide range of approaches in normative ethics. Here we will only present some of the main positions that are relevant to HTA. Common to all of them is that they provide perspectives on how to decide what is good/bad and right/wrong. Corresponding to the foundational perspectives in meta-ethics, substantive theories in normative ethics think that there are basic norms, values, or principles that can help us decide on moral issues (on technologies). Corresponding to coherentist perspectives there are procedural approaches in ethics. Let us briefly present each of them.

Substantive approaches in ethics

The main positions in normative ethics are consequentialism and deontology. The first argues that the consequences of an action are what is morally important while the latter argues that we have moral obligations that are decided by other things than consequences.

Utilitarianism: a kind of consequentialism

According to consequentialism we are to act so that the consequences are maximized. Accordingly, we are to implement the technologies with the best consequences. However, what are the best

consequences? There are many answers to that questions, but one common answer provided by utilitarians is that we should maximize the total utility.

In HTA it us urgent to maximize safety, efficacy, effectiveness, and cost-effectiveness. Accordingly, utilitarianism is at the core of HTA's traditional analyses of outcomes. However, as pointed out in Chapter 2, the ethical nature of this integration may not be recognized and ethical aspects may not be explicitly addressed (Hofmann B, 2001; Hofmann, 2005; Hofmann et al, 2014). Integrating equity concerns in cost-effectiveness analysis is one example (Hofmann et al, 2014). Moreover, the goals (consequences) that are assessed may be unclear or diverse. There is a difference if one aims at increasing survival and enhancing human capabilities (van der Wilt et al, 2017).

Hence, it is important to notice that consequentialism is a kind of normative ethics (especially in terms of utilitarianism) which is in many ways integrated in the traditional way of doing HTA.

A utilitarian analysis of NIPT would focus on and compare outcomes of the use of NIPT to alternatives to using NIPT. Outcomes can be health outcomes (reduced mortality and morbidity), values like quality of life, human capabilities, or ability to make informed (reproductive) choice, people's experience of potential discrimination for people with Downs syndrome etc. The decisive question is whether society would have a higher balance of positive consequences over negative consequences with NIPT compared to alternatives?

Deontology

Deontology is a branch of ethics inferring right action from norms based on rationally justified duties. Such basic duties (imperatives) are to treat people equally and as ends in themselves. Although some technologies may have a great maximized utility, we still are reluctant to use them. For example, NIPT can be used (with whole genome sequencing) to screen foetuses in order to select only those foetuses that are predicted to contribute most to a future society. A series of deontological arguments can be made against such use, even though it could maximize utility, e.g., that it does not show the proper respect for human dignity, but also for it, e.g., that it enhances reproductive autonomy.

Deontology can be used in HTA in many ways. It can be used as a "pure deontological analysis" or it can be applied as deontological parts of eclectic approaches. For example, several of the questions in EUnetHTA Core Model's Ethical domain could be viewed as deontological in perspective (assessment elements F0002, F0008, F0009, F0014 in the EUnetHTA Core Model)

Principlism - The four principles approach

Another approach called “principlism” is based on common morality that all rational moral agents are supposed to share. According to principlism we share four basic ethical principles that can be applied to solve moral problems: respect for autonomy, non-maleficence, beneficence and justice. Principlism has been widely used in HTA, for example to assess public access defibrillators (HIQA, 2014).

The four principles have a prima facie nature, which means that the principles must be fulfilled unless it conflicts with an equal or stronger obligation. The principles constitute a basic framework, and they need to be specified and balanced (i.e., the practical activity becomes that of specifying how the principles are to be used in specific situations and balancing the principles with the other competing moral principles).

Principlism has been a popular approach in normative ethics in healthcare because it is simple and feasible. Its simplicity lies in the application of a stable set of ethical themes and concepts. However, this simplicity also constitutes the major limitation of the approach: the risk of leaving out a series of values and perspectives. Furthermore, it has been questioned whether the (in this case four) principles (and only these) are universal.

A principlist approach to NIPT would look at potential benefits to parents (and children), assess to what extent it results in acceptable harm or not, how it supports respect for autonomy and also, how it should be viewed from a fairness or justice perspective. On the latter principle, it could be related the degree of need for NIPT, but also how it would affect resource use in the rest of the healthcare system if used or not used.

Specifying norms

Another critique that has been levelled at principlism is that it oversimplifies how general ethical principles can be brought to bear on concrete cases. According to Henry Richardson, a gap exists between general ethical principles and our ethical judgements of concrete cases (Richardson HS, 1990; Richardson HS, 1997; Richardson HS, 2018). He suggested that in order to bridge this gap, general ethical principles need to be specified. This means adding clauses to the ethical principles such as what, why, when, where, how, by whom, and to whom, something may or may not be done. Richardson also holds that people are usually committed to a host of general ethical principles (e.g., fairness, liberty, sincerity, avoiding harm), and that our judgements and actions in concrete situations are often guided by multiple of such principles. In such cases, it may happen that these principles appear to lead us in

opposing directions. This is where the method of specification comes in. The task, according to Richardson, is to revise (individually or collaboratively) the initial specifications of the general principles involved and to try to advance novel specifications, such that the conflict is resolved. Richardson's model is quite complex, comprising formal rules that should be observed in such a process. Also, he is quite explicit about the assumptions underlying the model: it assumes non-commensurability of ethical principles, it holds that no single ethical principle is absolute, and it endorses a concept of rationality as seeking maximal coherence between our commitments to general ethical principles on the one hand and our daily doings and beings on the other hand. Tom Beauchamp, one of the instigators of principlism, has espoused the method of specifying norms as a compelling extension of principlism (Beauchamp TL, 2007). Richardson has himself elaborated how the method of specifying norms may be relevant in the context of HTA (Richardson HS, 2016). A practical example may be found in (van der Wilt et al, 2018), applying the method to the case of clinical trials of Novel Oral Anti-Coagulants.

Applying the method to NIPT, it would ask which general ethical principles seem to be guiding communal judgements of this technology and its associated practice, and, if they appear to lead us in opposing directions, whether this might be resolved by advancing alternative specifications that would lead to greater coherence.

Procedural approaches

Other approaches in normative ethics are less based on maxims, norms, values, or principles but are procedural. They provide a procedure to find the right answer to whether and how to implement and use a health technology in a good manner. The first approach has already been mentioned.

Wide Reflective Equilibrium (WRE)

Wide Reflective Equilibrium (WRE) is a coherentist model of moral argumentation. As pointed out before, coherentist approaches are opposed to foundational approaches, which assume that there are certain undisputable basic principles from which moral judgments can be derived. In a coherentist approach, no such assumption is made. Instead, the validity of a moral judgment depends on the coherence (or mutual support) among general moral principle, moral judgment, and background theory. The method has become more widely known since it was used and advocated by John Rawls in his Theory of Justice (Rawls, 1971), where it is argued that the concept of justice as fairness is superior to the utilitarian concept of justice. To do so, Rawls argues that justice as fairness coheres

with our considered moral judgments and is independently supported by background theory concerning human behaviour, such as risk-aversiveness and mutual cooperation. The method has been further elaborated by Norman Daniels (see above; Daniels et al, 2016). Examples of assessments of health technology where the method of WRE (e.g., Reuzel et al, 2001; Daniels et al, 2016) has been used include telemedicine-supported home care, genetic engineering, and home environments for adults with significant disability.

Applying this to NIPT, would imply that we look at the principles and judgements made in the system, and one crucial aspect would be to analyze how other fetal diagnostic tools are viewed from an ethical perspective. As coherence is central, accepting other diagnostic tools would provide prima facie reason to also accept NIPT.

Casuistry

Another approach that has been used to address ethical issues in HTA and which has procedural characteristics is casuistry. With deep roots in ancient moral philosophy and modern anti-theoretical bioethics, casuistry uses practical cases with an undisputed solution to solve the moral challenging situation or dilemma in hand. Oriented away from theory or principles and towards the particular, the procedure in casuistry starts by identifying the structure of the case, i.e., by describing the circumstances (who, what, when, where, how, by what means) and the relevant maxims involved, e.g., "the morals of the story." Then it compares the case with similar "paradigmatic" cases. Paradigmatic cases are those where a solution is found which is generally accepted. The comparison of cases should reveal the moral maxims at stake and the subsequent practical implications.

In HTA, Casuistry can be at play informally, e.g., when referring to solved cases such as coverage decisions, but it can also be more formally applied (Reuzel et al, 1999). As with other approaches in applied ethics, Casuistry has its shortcomings, e.g., potential changes in the value base between past precedents and current cases, and it "suffers from the potential limitations of relying on subjective analogic arguments and intuitive judgment about a particular case".

Applying this to NIPT could imply to describe how using or not using NIPT would impact on the pregnant woman and her partner from different perspectives, on the professionals and potentially also the child. A paradigmatic case could be the use of ultrasound for fetal diagnostic purposes. Since fetal diagnostic ultrasound is acceptable, one can use this to argue that so is NIPT. However, there is a problem with this analogy (case) as there may be morally relevant differences between NIPT and ultrasound. NIPT is not applied to assess the date of delivery or get a nice picture to put on the fridge, but mainly to assess any deformations.

Discourse ethics

The central thesis of discourse ethics is that there is a "force of the better argument" driving towards consensus on certain norms and giving universal validity to some presuppositions of a moral discourse. It is based on impartial judgment and on arriving at consensus among those who are affected. While discourse ethics rarely is used in HTA, it inspires consensus-oriented methods in deriving legitimacy of formulating rules for technology use. One example is the interactive, participatory HTA approach (iHTA, see below).

Discourse ethics can be used through an "argumentative discourse" among the HTA experts and other stakeholders, where all (present and future) interests of each potential stakeholder are taken into account. Ethical assessments adopting discourse ethics will be performed in a bottom–up manner. Each stakeholders' perspective would influence "argumentative discourse", informing/(re)defining the overall HTA process. Used this way, discourse ethics would be implemented in a coordinated or interactive manner.

Applied NIPT, discourse ethics might not be suitable to assess the specific technology, but perhaps more as a method to agree on common principles for how to relate to fetal diagnostic methods.

Hence, there are many approaches in normative ethics in general that can be applied to address ethical aspects of health technologies as part of HTA. Moreover, there are also other (mixed or eclectic) approaches that have been developed more specifically to address the normative issues with health technologies. Below we will give a short outline of some of these approaches in order to give you an overview of the field. The space does not allow for in-depth elaborations. For further details you may find the references useful.

Mixed approaches

EUnetHTA Core model

The HTA Core Model 3.0® has been developed in the course of the European network for health technology assessment Joint Action 2 (EUnetHTA JA2). It consists of nine domains, among which is the domain "ethical analysis". The "ethical analysis" domain is divided into six topics; three of them (Beneficence/Non-maleficence; Autonomy; Justice and Equity) are directly related to the Principilist approach to bioethics (see paragraph on Principlism). The other three topics are respect for persons, legislation, and ethical consequences of the HTA. Each topic consists of two to four questions, adding up to nineteen assessment "issues". Authors of HTAs are encouraged to start by gathering information on ethical issues using systematic literature searches, professional guidelines, and the stakeholder

views. In a second phase, it is suggested that users choose from different methods that have been assembled by a working group of the International Network of Agencies for Health Technology Assessment (INAHTA). The choice of the method should depend on factors such as the type of technology, the role and authority of the HTA organization, the time, and resources available and the expertise with ethical analysis available within the organization. For a comprehensive analysis, it is recommended that more than a single method is applied, and experts in ethical analyses are involved, in addition to other scientists and clinicians.

The Socratic (axiological) approach

The Socratic approach is axiological as it tries to uncover and highlight the values, norms and ethical challenges that are relevant for the health intervention, the HTA process, as well as for the decision-making process. The Socratic approach consists of six steps and seven basic morally relevant questions, which are further specified in thirty-three explanatory and guiding questions (Hofmann et al, 2014). The six steps are:

1. Identify the intended purpose of the health technology and reveal the background for the assessment;

2. Identify involved persons, groups, and stakeholders (e.g., patients, relatives, professionals, industry, health policy makers);

3. Identify relevant moral questions (from a list of questions, Table 1) and justify the selection;

4. Perform literature search in accordance with the identified moral questions;

5. Analyse and discuss the moral questions identified (in step 3) on the basis of:

    (a) Existing literature and

    (b) Hearings / statements of involved parties (or their representatives) or qualitative studies (relevant qualitative studies should be included in the literature search);

6. Wrap up and summarize the process.

In relation to NIPT the Socratic approach would add consulting with stakeholder, and here a crucial aspects would be to identify a broad range: disability organizations, parents that have chosen to abort a disabled fetus, parents who have decided to keep a disabled child etc.

The Triangular model

The Triangular model, known as the "personalist model", is rooted in the human person (body-soul unitotality) as reference-value in the reality, according to the Aristotelian-Thomistic view.

For NIPT, the fact that such a diagnostic tool is often associated with abortion (even if it need not be so, since the information might be relevant also for parents who will not consider abortion) – is highly relevant to the principle of defense of human physical life being primary to principles about personal freedom etc.

Consequently, the human person is the aim and the source of the society. This approach includes factual, anthropological and ethical data in a "triangular" normative reflection process. The three steps of ethical process are: 1. Data collection (knowledge level): an in-depth study of all factual data concerning the object of the analysis; 2. Ethical/anthropological analysis (justifying level) according the following principles/operating criteria: a. the defence of human physical life; b. the interconnection between personal freedom and responsibility; c. the therapeutic principle, according to which the human person has to be treated as a totality of body and soul; d. the principles of sociality and subsidiarity, for which public/private bodies are called to help all persons, namely when they are not able to fulfil their needs. The way by which these principles are utilized is similar to Principlism methodology, but with a relevant difference: they are organized in a hierarchic manner; 3. ethical evaluation (assessment) or appraisal (normative) level, that should address and facilitate the practical choices. Triangular model/personalist approach is considered among "local approaches" in the HTA Core Model.

Interactive approaches

We hope that we have not lost the reader with the various approaches for addressing the ethics of health technologies in HTA.

The approaches to ethics in HTA are well described in reports (Hofmann B, 2006; Anderson et al, 2005; Lysdahl et al, 2016) and articles (Hofmann et al, 2015; Assasi et al, 2014; Assasi et al, 2016). It may seem frustrating that there are so many methods (Droste et al, 2010). However, HTA agencies are different, the healthcare systems vary, and the health technologies are diverse. Hence, one method may not fit all purposes. Therefore, it is important to know about the various available approaches for doing ethics in HTA.

With the danger of increasing the confusion of the reader, but with the intention of providing an overview, we now will turn to another source of reflecting on the ethical aspects of health technologies. So far, the approaches have been based on normative ethics, i.e., stemming from ethics and moral philosophy. However, there are also other sources for addressing ethical issues with technology, e.g., from the social sciences. We will below give a teaser of some such approaches. Common to many of these is that they stem from the Science and Technology Studies (STS) where science and technology are understood as in reciprocal and continuous interaction with society. The question is not as much how technology works, but more how to make technology work.

Constructive technology assessment (CTA)

Constructive Technology Assessment (CTA) wants to narrow the gap between innovation and assessment by taking the socio-dynamic processes into account. The core of the approach is an assessed implementation of a technology in society in order to improve the robustness of decisions about technology and to learn about and avoid possible harmful impacts. CTA includes four stages. First, a 'socio-technical' map identifying the most relevant social actors involved. The second stage includes early and controlled experiments, through which unanticipated impacts can be identified. Third, a debate between the various actors involved is organized. Finally, a synthesis report is written aiming at letting societal aspects of innovation become additional design criteria. CTA has been adopted as an approach to technology assessment by public organizations. The CTA approach aims to provide a broad assessment at an early stage of technology development. Discussions between researchers, engineers, manufacturers and future users are used in the development and diffusion of a technology to improve its (potential) effectiveness. In this way, the approach can be seen as a truly integrative method.

When applied to NIPT, the focus would be on the question how this technology might be adapted in such a way, as to conform to a greater degree with prospective users' needs and demands. The technology can be used, for instance, to detect gross fetal abnormalities only (Richardson, 2016; Hofmann et al, 2014; Lysdahl et al, 2016), but also extended to detect still other genetic abnormalities, the clinical significance of many of which is presently obscure.

Social Shaping of Technology

Social Shaping of Technology (SST) involves different stakeholders in a real discourse on the assessment and implementation of a technology. The goal is to reduce bias and improve the validity

and applicability of the HTA (Clausen et al, 2004). The core advantages with this approach are the fruitful analytical perspective on of how technology is implemented in social practice as well as the symmetry between technology and society, not only addressing how technology influences society (as do the technological determinists) or solely attending to how technology is constructed in a social sphere (social construction of technology). One of the challenges is whether the approach is an assessment of a technology or whether it is more part of the construction of it.

Interactive Health Technology Assessment (iHTA)

Interactive Health Technology Assessment (iHTA) is a specific approach to HTA, involving stakeholders throughout the entire assessment process, i.e., people who may experience the consequences of the assessment are involved in defining the research question(s) to be addressed (scoping), in designing the assessment and in the collection and interpretation of the data.

The term 'interactive' refers to an interaction among the various stakeholders: the explicit objective of the HTA is that stakeholders learn from each other. iHTA aims to reconstruct and critically appraise the frames that stakeholders use to interpret the problem and to judge solutions. It does so e.g., by semi-structured interviews with stakeholders. Philosophically, iHTA is an approach to HTA which accepts fallibilism without embracing scepticism, and which puts primacy on practice. As such, iHTA can be considered to be firmly rooted in pragmatism. iHTA has been used to evaluate a wide range of technologies, both within and outside the healthcare domain (Reuzel et al, 2001).

In the case of NIPT, it would ask who would be affected by introducing NIPT into prenatal care, and in what way, and try to involve those parties in the HTA process, collaboratively discovering differences and commonalities in how each of them frames the problem. This, then, is used to define the questions that will be addressed in the HTA. Stakeholders are also involved in discussing the practical implications of the findings for how the technology will be put to use. Overall, a strong emphasis is put on mutual learning among stakeholders and making use of their experiential knowledge (Grin et al, 1996).

Table 1. Overview of the different approaches for ethics in HTA presented in this chapter

Approaches for ethical analysis	
Substantive approaches • Traditional approaches in moral philosophy – Consequentialism • Utilitarianism – Deontology (Duty based ethics) – Principlism – Specifying norms	**Procedural approaches** • Coherence analysis – Wide Reflective Equilibrium • Casuistry • Discourse ethics
Mixed approaches EUnetHTA Core model Socratic (axiological) approach Triangular method (deontology)	
Interactive approaches Constructive Technology Assessment Social Shaping of Technology Interactive, participatory HTA (iHTA)	

How suitable are the various approaches for addressing ethical issues in HTA?

As can be seen, there are a wide variety of approaches available. This poses the question of which method to use. The answer is: it depends. It depends on the issues laid out in Chapter 1. **Table 2** is a summary of the various approaches and how suitable they are for assessing health technologies depending on factual controversies, normative controversies, complexity, and meta-ethical presumptions. Hence, no method is perfect for all purposes and the context is crucial for deciding on the approach.

Table 2. Description and assessment of the various approaches for addressing ethical issues in HTA the table is based on (Lysdahl et al, 2016) and (Hofmann et al, 2015)

Approach	Factual controversy (Plausibility)	Normative controversy (Relevance)	Addressing complexity
Utilitarianism	Not well suited	Well suited	Moderate
Deontology	Moderate	Well	Not well suited
Principlism	Not well suited	Moderate	Not well suited
Specifying norms	Not well suited	Well suited	Moderate
Casuistry	Moderate	Not well suited	Not well suited
Discourse ethics	Not well suited	Moderate	Not well suited
Wide Reflective Equilibrium (WRE)	Not well suited	Well suited	Moderate
EUnetHTA Core Model	Moderate	Moderate	Moderate

Approach	Factual controversy (Plausibility)	Normative controversy (Relevance)	Addressing complexity
The Socratic (axiological) approach	Moderate	Moderate	Moderate
The Triangular model	Moderate	Well suited	Not well suited
Constructive technology assessment (CTA)	Moderate	Well	Not well suited(?)
Social Shaping of Technology	Moderate	Well suited	Not well suited
Interactive Health Technology Assessment (iHTA)	Moderate	Well suited	Not well suited

III Synthesizing ethics input

When we have decided on our meta-ethical perspective (or not) and on the position in normative ethics (or not) or have chosen a specific approach for addressing ethical issues with the health technology, most often we need to gather and synthesize ethical input (e.g., from literature). Again, there are many ways to do this. For the gathering of ethics input from the literature, see for example (Droste et al, 2010; McDougall R, 2015).

If you want to assess or make a good critical interpretive review McDougall has suggested the following six features:

1. Answers a specific research question, which may have been refined and determined during the literature review process, and
2. Analyses the literature as a whole as well as analysing individual findings and arguments within that literature, and
3. Does not utilize rigid quality assessment criteria, but comments within the review itself on quality issues, and
4. Generates theory and puts forward an argument about the literature, and
5. Captures all the key ideas in the existing literature that are relevant to the research question, and
6. Records and reports the search strategy (McDougall R, 2015).

What you synthesize is also of great importance. There are methods for synthesizing reasons (Strech et al, 2012) and arguments (McCullough et al, 2004; McCullough et al, 2007). An overview of the various methods for synthesis of the ethics literature is available (Mertz et al, 2016) and in 2021 the

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for ETHICS will be published.

Conclusion

In this chapter we have introduced the language of ethics and how this differs from other types of languages, i.e., what we do when we use ethical language. Here we have discussed the foundation for the ethics (how we can say that something is moral or not). Here we identified two views, i.e., nihilism and realism. Then we asked whether we can have knowledge about ethical issues, and we investigated foundationalism and coherentism.

Thereafter we use this basis to investigate how ethical issues can be addressed in HTA. There we used various approaches from normative ethics but also from the social sciences. We illustrated that are many approaches and tried to provide some means for assessing them.

Lastly, we provided some references for synthesize ethics input, such as from the ethics literature. The overarching goal of this chapter has been to give you an overview of the field and make you ready to assess and start applying specific methods for doing ethics in HTA.

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Chapter 6. Context matters

Abstract

This chapter shows the importance to consider health system context during the health technology assessment process, including the particular perspective of hospital-based HTA (HB-HTA), and how it may influence in final coverage decision. Context differences rely on type of priorities, epidemiological paradigm, financial capacity, trained professionals, capacitated managers, or empowered patients, and are also influenced by levels of healthcare (meta: global policies; macro: system; meso: hospital, other settings; micro: clinician/patient/caregiver). Moreover, there are geographical and socioeconomic differences among countries on the access to infrastructures of transportation and mobility that define that, certain solutions that could be the right ones at the moment of decision for one setting could not be applied in another setting. Furthermore, there are other aspects that should be considered when discussing the inclusion, use or exclusion of a technology in the benefit package or services to be provided within a healthcare system, such as sociocultural heritage, religion, or socioeconomic distribution of the population to be targeted. All of them influence the overall value and the values from decision-makers, which should be considered in both cases when assessing a technology and in deciding for their coverage in a health system.

Key messages of this chapter: Acknowledging context, where decisions on payment for a technology should be made, is a key factor for a successful assessment. Different health system contexts can have different characteristics, values and informational requirements that should be considered when framing and performing the assessment.

After reading this chapter you will be able to identify what are the differential elements/ factors of a context to consider when planning, scoping, and performing an assessment.

What does context mean?

Professionals differ from system to system (e.g., number, knowledge, skills); patients are diverse (e.g., age, ethnicity, sex, comorbidities, social support, caregivers); societies differ on their cultural heritage, values, religion, approach to health and wealth; health systems differ on their structure, technologies and infrastructure available, funding schemes, decision-making processes, epidemiological paradigm, priorities and priority-setting methods, among others; nations differ on their gross domestic product, the type of political system, the socioeconomic status of their inhabitants, the geographical and

geopolitical characteristics of the country (e.g., centralised or decentralised, federal or regional) and the distribution of budget used for the health and social systems. All those and some other factors can be considered context (see Figure 1). To which extent those aspects influence the need, and the value of health technologies is something that will be discussed in the following paragraphs.

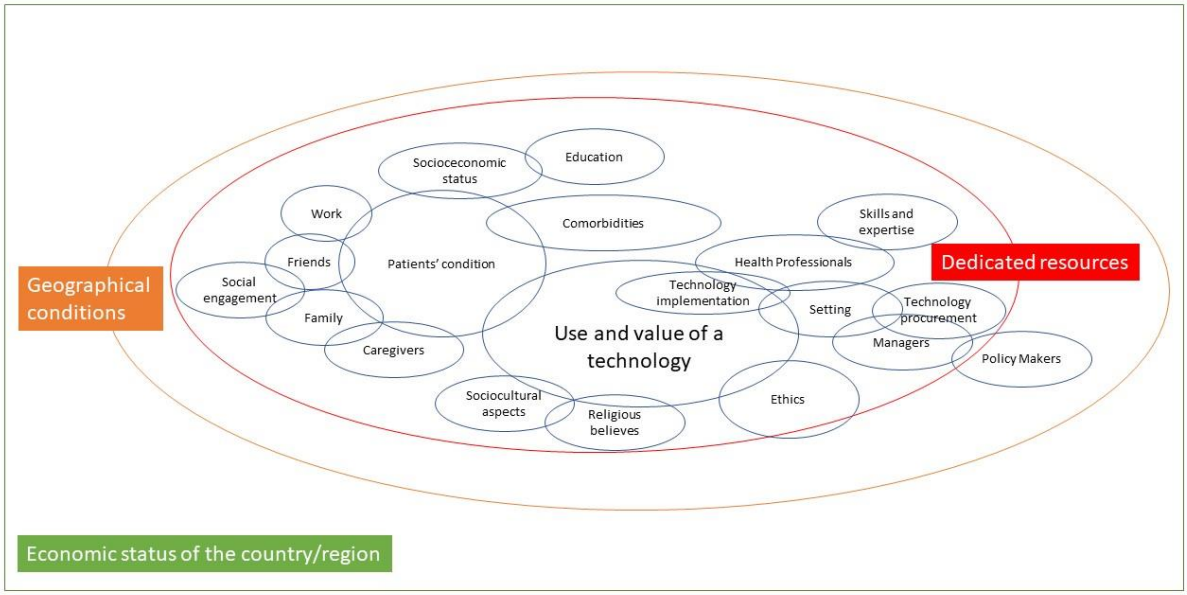

Figure 1. Context related factors that influence the use and value of a technology

So, what do we mean when we talk about context? If we consider the definition by Cambridge dictionary of English language, context refers to "***the situation within which something exists or happens, and that can help explain it***" (Cambridge Dictionary, 2021). The Integrate-HTA project considered the following aspects those to be considered when talking about context and the implementation of a technology: setting, geographical characteristics, epidemiological characteristics, socioeconomic, sociocultural, political, legal, and ethical (Pfadenhauer et al, 2016).

Context and its specificities

HTA was initially born to answer decision-makers questions related to the appropriateness to cover/reimburse innovative and new technologies at macro level, e.g., by health authorities at a country level or by insurance companies in charge of a big amount of population (Banta et al, 1997). In an international meeting and workshop held in Europe someone from the audience asked whether small countries must have HTA units, or they should rely on evaluations or assessments coming from bigger organizations and/or countries; others were questioning if hospitals in a country should rely on the assessments done by the National/Regional agency due to their different characteristics and cultures, as well as if any hospital should have its own health technology assessment approach. This

question that seems to be easy to solve if someone carefully read the definition of HTA promoted by HTAi and INAHTA (O'Rourke et al, 2020), it is of full actuality in the "context" of Europe and within the world.

During the last 15 years, HTA has been devolved to meso level, e.g., hospitals/county councils (Sampietro-Colom et al, 2016). One of the questions that frequently is raised is why this devolution is happening and why hospital/local organizations do not use the results provided by HTA agencies/units. The answer to this question is, again, because of context matters. The questions to answer at national/regional or local/hospital are the same: What clinical and healthcare benefit is the new technology bringing? How do these benefits compare with the current clinical practice? Do the costs incurred by these technologies worth the benefits obtained? What would be the impact in the organization of healthcare? Considering that economic health resources are finite, what investments am I losing if I bet for this technology? While the questions are the same, the approach taken to answer these questions at national/regional versus local/hospital differs. When trying to answer the mentioned questions, it is necessary to follow and to consider what makes HTA different from other health services research disciplines. And the difference is that HTA contextualizes the analysis considering the characteristics where the decision is going to be taken. Therefore, depending on the context where the decision is going to be made, the type and source of the information used for the analysis will differ.

Is the context so deterministic as to provoke differences when informing decisions about health and health technologies? If so, which is the "least common multiple" or minimum context to which we should refer in order to establish HTA activities? The latest is an intriguing question, considering that any difference that justify the need to include new or diverse evidence to that available by other means or that modifies any of the parameters of the PICO question determines a new contextual element that should be taken into consideration, because that would influence the analysis of the facts (see Chapter 5)

The minimum context should be the one that provides the whole information (facts) required to closest determine the value of a technology within given circumstances and framework, nevertheless the relevance given to those facts could differ. Thus, the HTA doer should consider all the conditions around the technology and its use that could affect the final value within a particular context and anticipate them within a realistic framework and required timeframe for decision (Buxton, 1987). Actually, context-based HTA analysis should not be far from what has been called Value Based Healthcare movement, which is determining or at least, approaching to what the final value could be in real life. Reducing the uncertainties or anticipating issues or problems within a determined context

should be considered part of the HTA remit, which is, informing decisions laying all the cards on the table or as many cards as possible.

Macro-, Meso- and Micro-levels of decisions

When discussing context, someone needs to bear in mind the levels of decision and how that relates to which value(s) could be considered in each of those. Those decisions that occur at a continent wide, national or regional level are so-called macro-level decisions, although those at the global level are so-called meta decisions (e.g., where the budget should be allocated to: industry, education, health or when global organizations propose a vaccination policy to countries). Decisions at a healthcare facility level are considered meso-level decisions and finally, those that are targeting the individual healthcare professional level when discussing around the management of a single patient or a subgroup of patients are named micro-level decisions.

Typically, **Macro-level decisions** relate to reimbursement or inclusion/exclusion from benefit package and overall organization and structure of services. In some occasions, they are focused on introducing public health interventions (e.g., vaccination campaigns, population based screening programs, drinking water treatments).

When considering Nations/Regions, the first contextual aspect could be related to the different priorities countries could have, or the different needs countries/hospitals may have stemming from the epidemiological or social point of view, even in a homogeneous space such as Europe or inside the same Nation/Region. The second aspect concerns the characteristics of the healthcare systems, that is their organisational features (financial schemes, procurers, providers and their interactions), their health professionals (including culture, level of skills), the patients and their circumstances (most patients do not have a single pathology and the use of a technology could affect the evolution of the others) and the society and its values, in which they are embedded. The third aspect focuses on the characteristics of the technology, and how it relates to other technologies used for the same indication (not all countries or providers have access to the same technology/ies for a patient or group of patients with similar characteristics), its mechanism of action, the expertise requires, the need to use other technologies, such as diagnostics, prognostic tools, data analytics or algorithms. Finally, other factors to be taken into account are the legal frameworks, the cultural and social features and the increasing concerns around the environmental consequences of producing, transporting, using, recycling or waste landfill of health technologies, among others (Polisena et al, 2018).

Furthermore, apart from those inherent features fully related to the context, there are other factors that also influence, and they are not directly linked to the context, but the choices that those making

decisions put forward. For example, the selection of the value framework by which a technology will be judged. Interestingly, a paper of the Global Policy Forum of HTAi (Oortwijn et al, 2017) pointed out that there is not a single value assessment framework for drugs, medical devices, public health interventions or other type of health technologies in a given country. Differences typically occur when assessing oncology drugs, health technologies to be used to manage rare diseases or when assessing complex interventions. This shows that the value judgements when determining the value among technologies differ among countries and within countries. An example of this is described in Kleijnen et al, 2016. They show that decisions around the reimbursement of a single oncology drug differ among selected European countries, even though they use the same clinical effectiveness evidence to support the decision. In **Box 1,** the case of Non-Invasive Prenatal Testing (NIPT) is presented.

Meso-level decisions, i.e., those taken at healthcare provider (hospital) level, usually take into consideration macro decisions, but more frequently take into account their own specific contextual characteristics. On many occasions, meso-level decisions could influence the success of macro- and micro-level decisions, because they determine the resources, the organization of care and the access to diagnostic tests, treatments and rehabilitation programs.

Several contextual items impact the approach when assessing technologies at National/Regional and local/hospital level, which include: geographical scope, assessment priorities, type of information needed, timing of the assessment, level and type of stakeholder involvement, and deliberative processes.

The information that HTA National/Regional agencies/units provide through their assessments are usually of a very high quality and very comprehensive. Nevertheless, it is not enough, neither appropriate to decide if a specific health technology should be introduced in a hospital. The documents performed by the National/Regional agencies/units usually look at the geographical scope of the health authority asking for the assessment, i.e., country, region, where different types of hospitals co-exist. These documents cannot be used to properly assess if a specific hospital needs a new PET scanner, if it has to introduce a surgical robot, or if it has to invest in a hybrid operating theatre. These decisions, for a specific setting (i.e., hospital) should consider the idiosyncrasy of the hospital, including the available technologies, the capacity and capability and experience of their professionals, their learning curves, the characteristics of the patients and the characteristics and competition of the different healthcare areas in the hospital. Documents aimed to support a decision-making process at macro-level regarding a specific technology are perceived by hospital professionals as far away of their daily clinical practice, and, therefore, usually have little (or none) impact in the final decision taken at the hospital level (McGregor, 2006).

Priorities in the type of technologies to be assessed also differ at National/Regional level versus local/hospital level. At National/Regional level, technologies prioritized for the assessment are those that will be of interest of all (or most) healthcare centres at the country/Regional level. For example, the Spanish HTA Network of HTA Agencies assesses those technologies nominated and prioritized by the Council of Ministries of Health of the Regions (*Consejo Interterritorial*), and technologies to be assessed should be of interest to the majority of Regions (Varela et al, 2018). However, technologies to be assessed by hospitals should be those of interest to the hospital, which not always are the same to the ones prioritized at National/Regional level. Moreover, technologies prioritized among hospitals of the same Region may not be the same, because technology demands from professionals differ depending on the type and characteristics of the hospitals (e.g., university hospital, reference hospital, monographic hospital). Usually, high cost technologies, or those with a potential high impact on the health system, are prioritized by National/Regional HTA agencies/units. Nevertheless, the technologies prioritized by a hospital could be not so expensive, but could represent an investment effort for a department of a hospital or for the hospital itself. One study carried out in Denmark showed that 70% of the demanded and assessed technologies by hospitals had not been assessed by the national HTA agency (Kidholm et al, 2009).

As mentioned above, the information included in an HTA document for a hospital decision-maker, should be the information that the decision-maker find relevant for taking the decision. Therefore, the assessment should take into account the contextual characteristics of the hospital when taking decisions related to innovative and new technologies, such as investment, disinvestment and inappropriate use (see later on domains and context). Moreover, if doers of an HTA want that its recommendations will be considered when hospital decision-makers evaluate the introduction of a new technology, then, they have to perceive the results from the HTA as appropriate and relevant. For that reason, the HTA process undertaken should not only be rigorous, it should also be transparent and examine all the information that contributes to carry out a contextualized analysis for the hospital. For this, it is highly important to involve the health professionals who ask for the new technology during all the HTA process. Recommendations from HTA documents performed without the participation of health professionals who will use the technology are perceived as theoretical or far away from real clinical practice and not acceptable (McGregor, 2006).

Another contextual item to consider in decisions at hospital level is timing. The assessment information always should be provided in time to allow decision-makers to take the decision; this timing is usually shorter at hospital level than at national/regional level. Traditionally, the documents produced by National/Regional HTA agencies/units are very comprehensive and robust, requiring a lot of time (sometimes one year) if they want to follow the quality standards required internationally in HTA

documents (EUnetHTA, 2020) (to mention that established HTA agencies also have some HTA products that are shorter and produced quicker). At the hospital level, decisions on technologies are made constantly and it is therefore necessary to have the information available as soon as possible. For that reason, HTA methodological instruments that conjugate rigor with timing requirements, are used at the hospital level. The mini-HTA is one of the most used methods (AdHopHTA mini-HTA template; Sampietro-Colom et al, 2015).

Finally, the deliberative process to make the final recommendation also differs at hospital level from National/Regional HTA agencies/units. National/regional HTA agencies/units use deliberative processes (e.g., appraisal) that usually involve different stakeholders. Among these stakeholders, health professionals not directly involved in the demand of the technology and patient representatives are included in the appraisal committees (as well as representatives from industry in some HTA agencies) (Bond et al, 2020). In the hospital the recommendations are made with the results from the HB-HTA document and by the assessment team that, as mentioned above, also includes the health professional that was asking for the technology (though this may vary across hospitals). In hospitals, the patient is generally not represented when discussing the results of the HB-HTA to make a final recommendation.

HB-HTA answers questions related with the appropriateness, feasibility, sustainability, economic viability and opportunity-costs of introducing a specific technology in a specific hospital. In that sense, the difference between an HTA performed at national/regional level and an HTA performed at the hospital, is similar to the difference between the efficacy and the effectiveness. In other words, the results obtained from a technology in "ideal" conditions of clinical practice (efficacy) versus the results obtained when the technology is used in every-day clinical practice (Sampietro-Colom et al, 2016)

Summarizing, HB-HTA is performed when HTA is carried out to inform a decision regarding a new technology at the hospital level. It is considering the hospital priorities on technologies to be assessed, the timing to give the answer to decision-makers, the type of information and data that these hospital decision-makers contemplate as relevant for them, and involving the health professionals who are asking for the introduction of the new technology in the hospital from the start (Sampietro-Colom et al, 2016). See **Box 2** for the case of Photodynamic Therapy (PDT) for the treatment of basocellular carcinoma (CBC) as an example.

Finally, **micro-level decisions** concern the care pathway of a single patient or a subgroup of patients. Micro-level decisions define what will ultimately occur with the individual patient, a treatment can be reimbursed by a defined system, or provided by a hospital. but if prescription is not made by the professional and administered to the patient or the patient denies the treatment or the proposed

management scheme, the technology won't be used on those that could have an indication. This means that it is not only a matter of facts and how they could be collected to make decisions, but how information is transmitted and in which context and the perception or perceptions that the different decision-makers could have at the different levels of decision-making. Health professionals with a different profile, knowledge or experience can act differently, patients of different age, socioeconomic status or suffering from different conditions (acute vs chronic, single morbidity vs multimorbidity) could also have diverse perspectives and values concerning their pathology and thus, may influence the uptake of the technology. As it has been described in previous chapters of the VALIDATE handbook, values cannot be separately analysed when collecting facts, and also differ from context to context, including the relevance that is given to the different facts.

Internal versus external validity and how that relate to context

HTA provides the pieces of evidence and information required to explain how a health technology or a group of technologies will work in a specific context. As stated above, the information provided relates with clinical, organizational, and economic aspects; and depending on the level of decision-making, the PICO question, as well as ethical, social and legal aspects. Regarding the clinical impact of a technology (or group of technologies), HTA informs, for example, how much the technology will modify the final health outcomes in a patient, group of patients or system. It is clear that this relates to two epidemiological concepts, that is: "internal validity" and "external validity". Internal validity is "*the extent to which a piece of evidence supports a claim about cause and effect, within the context of a particular study*" and the level of trust, we could have around this evidence. "External validity" relates to how applicable the findings are to the real world or other contexts (e.g., different hospitals/healthcare centres with different organization of care, professionals with different skills and cultures; or different healthcare systems with, e.g., varied financing schemes).

It should be considered that the same technology could be used under different circumstances, within different management schemes or standards, diverse patients, by different health professionals or caregivers and in different places/settings. Therefore, when framing the PICO question (see Chapter 4), to which extent that use refers to different patients (P), within diverse healthcare systems (I), different standards of care (C) or considering different outcomes or different ways of measuring the same outcomes (O), requires context-based information, evidence or analysis. At present, the intended and unintended consequences of implementing a health technology or group of technologies have been simplified in several HTA domains (see Figure 2). In view of that, most HTA analysis consider domains such as: safety, effectiveness, economic aspects, patients and social aspects, ethical, legal, and organizational aspects. The HTA collaboration within Europe, EUnetHTA (EUnetHTA,2021),

considered that certain assessment results could be shared across jurisdictions, such as safety, (relative) effectiveness, health problem, current use of the technology and the description of the technology and its characteristics. However, this is not fully true, considering that aspects such as safety or effectiveness could have different results depending on the characteristics of the patients, or the systems in which those patients will receive healthcare. The former is exemplified by the differences in epidemiological characteristics across populations for specific type of diseases. For example, it is well known that the population from Southern Europe has better cardiovascular profiles than the population from Northern Europe. This has been shown to impact the cost-effectiveness of a technology aimed to decrease high blood pressure in patients that were non respondent to drug therapy. While the cost-effectiveness analysis was positive for patients from Northern Europe (Borisenko et al, 2014) it was not when applying the same methodology to Southern European population data (Soto et al, 2016). The differences in the cost-effectiveness analysis (CEA) results were not just a matter of costs, it was mainly due to effectiveness results based on different epidemiological population profiles. It is obvious that including different population profiles and performing subgroup analysis (according to ethnic and geographical distributions) could help, as differences can occur not only due to the genetic profile of the patients, but also from their lifestyle and environmental exposure; these could influence the final outcomes. Furthermore, it seems to be desirable to implement policies and methods that support and enhance the analysis of real-world data in different contexts with the main purpose of analysing the value in real world conditions (values in this case are included per se).

Another aspect that may impact the differences between internal and external validity is the relevance/importance that patients, caregivers, or systems could give to outcomes chosen in one place that may differ from another place. That said, value judgements on relevant outcomes cannot be separated from values in each given context. For example, just considering facts, a new drug that could treat patients with diabetes showed in ideal conditions (randomized controlled trial) an improvement in the data of efficacy on hyperglycaemic episodes. Nevertheless, the analysis of subgroups showed that not all the patients react in the same way and there were subpopulations that obtain better results than others. Depending on the characteristics of the patients in a certain context (P), the outcomes that are produced in real world conditions (O) and the standard of care in that specific healthcare system (I), an HTA analysis could advise against the reimbursement of the drug, despite the data supporting a possible improvement in efficacy. That relates to facts, but what about the selection of hyperglycaemic episodes as primary outcome of interest without considering other factors, other outcomes and discussing their relative relevance with patients and caregivers. Perhaps, when discussing with them, the outcome of choice could differ and if so, the relevance of the differences in making decisions.

The principle of caution when considering context

Contextualization can lead to a problem of inequity and justice due to providing access to a specific technology in a given region and meanwhile, considering the lack of provision of the same technology in the neighbouring region for a patient with the same characteristics. Thus, someone who aims to untangle the issue of value measurement and context should balance which the consequences of considering the context to its maximum expression could be and how to better inform and diminish the conflicts that some decisions could infer. An approach to the context and the analysis of complex interventions is the Context and Implementation of Complex Interventions (CICI) framework as guidance for the assessment of context when assessing complex interventions. The CICI guidance introduces an overarching framework of the interacting dimensions of context (including setting) and implementation. This framework comprises eight domains of context (i.e., setting, geographical, epidemiological, socio-cultural, socio-economic, ethical, legal and political) and four domains of implementation (i.e., provider, organization and structure, funding and policy) including definitions and descriptions of each of these domains (Pfadenhauer et al, 2016). This approach, although valid, continues being mechanistic in some way and obviates the necessary preliminary discussion on which the values according to the context are. Moreover, the new definition of HTA is currently including domains referred to context that are lacking in the CICI approach, such as concepts of life cycle and environmental aspects (O'Rourke et al, 2020).

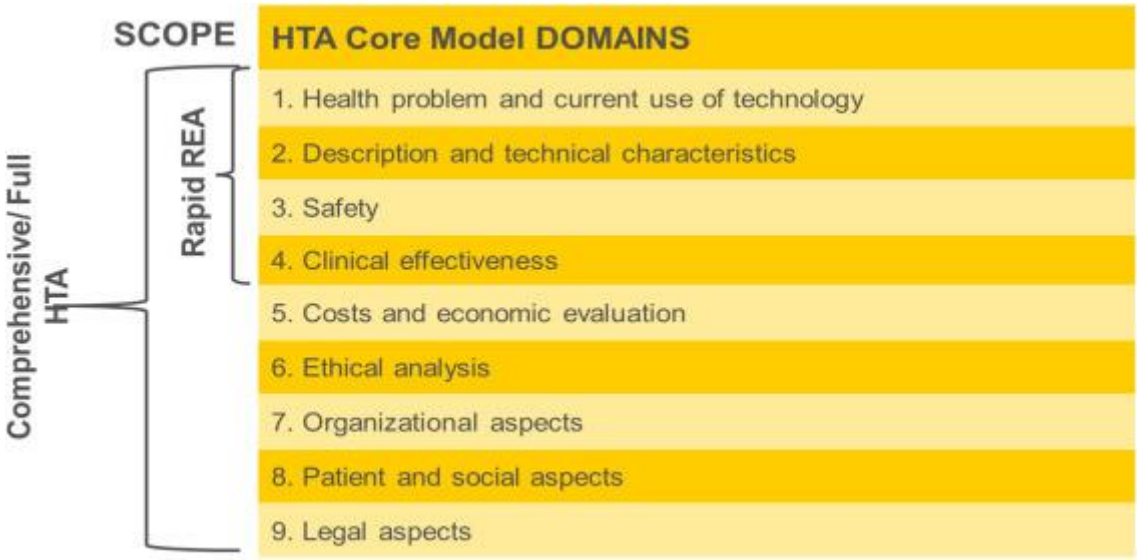

Figure 2. HTA Core Model Domains. Available from: https://eunethta.eu/hta-core-model/

Domains, its information requirements, and context

Among those domains within the EUnetHTA Core Model, we have already declared that, there are some, that are specifically proposed to be related to the context in which the technology will be applied. Moreover, there are technologies that are affected by some domains more than others, so there is also a technology/domain dependency. For example, learning curves, related skills, need of sufficient number of patients and need of other resources are part of the analysis that relate to medical devices or population-based interventions more than to drugs, in which the definition of the indication and the correct prescription are more crucial than those organizational aspects already mentioned. Moreover, the relevance/importance of domains to consider in an assessment as well as the type of information required by decision-maker to make an informed decision is different at macro- and meso-level.

As mentioned above, the content and results of an HTA addressed to a specific hospital, should take into account the contextual characteristics of that hospital, if the aim is that clinicians and hospital managers use that information when taking any decision related to innovative and new technologies, such as investment, disinvestment and inappropriate use. The results from European Project AdHopHTA (Adopting Hospital Based Health Technology Assessment in EU) showed that the type of information expected in an HTA document differ among decision-makers at the macro-level (i.e., health authorities that have to decide about coverage/reimbursement of technologies) and hospital decision-makers (Sampietro-Colom et al, 2015). Regarding effectiveness measures, while most National/Regional HTA agencies make their recommendations using QALYs; hospital decision-makers prefer information that help them to better manage both patients and the hospital itself (e.g., number of patients diagnosed correctly with a new diagnostic test, avoided readmissions at hospital, avoided infections). The sources of the information on effectiveness also somehow differ between National/Regional and local/hospital. As much as possible, hospitals like to include in the assessments information from their own patients when assessing the effectiveness of a specific technology (Soto et al, 2016). Likewise, the hospital decision-makers need that the costs from their hospital be computed in the cost analysis and avoid the use of average (or the most frequent) costs among hospitals (as usually done by National/Regional HTAs' documents). Another contextual item, that it is scarcely included in the National/Regional HTAs documents (Kidholm et al, 2015), and that is considered as an information highly relevant by hospital decision-makers, is the impact of the new health technology in the organization of care (e.g., how is the current healthcare organization going to be changed if the new technology is introduced?). As it is well known, the organization of healthcare differs among hospitals and, therefore, the introduction of a new technology may impact differently depending on the hospital. Finally, the AdHopHTA project also found that the general directors and heads of

departments at hospitals want information on how much the introduction of the new technology can align, support or answer the hospital's overall strategy (Kidholm et al, 2015); this item is not included in the National/Regional HTA documents. Figure **3** show the differences between items and variables of HTA documents at National/Regional and at a hospital level.

Domain	HTA Core model EUnetHTA	HB-HTA Core model AdHopHTA
D1: Health problem and current use	✓ relevant	✓✓✓ most important
D2: Description and technical characteristics	✓ relevant	✓ relevant
D3: Clinical effectiveness	✓ relevant	✓✓✓ most important
D4: Safety aspects	✓ relevant	✓✓✓ most important
D5: Costs and economic evaluation	✓ relevant	✓ relevant
D5.1 Societal point of view		
D5.2 Hospital point of view		✓✓✓ most important
D6: Ethical aspects	✓ relevant	✓ relevant
D7: Organizational aspects	✓ relevant	✓✓✓ most important
D8: Social aspects	✓ relevant	✓ relevant
D9: Legal aspects	✓ relevant	✓ relevant
D10: Political and strategic aspects		✓ relevant
D10.1 Political aspects		
D10.2 Strategic aspects		✓✓✓ most important

Figure 3. Differences in the information asked by National/Regional and hospital decision-makers

All this relates once again to facts, but facts are affected by values and perspectives (see Figure 4).

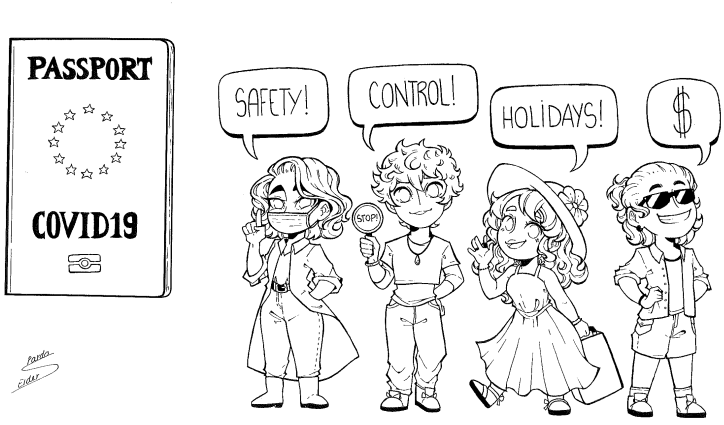

Figure 4. Perspectives around the same facts (Drawing: Eider Pardo; Concept and script: Iñaki Gutiérrez-Ibarluzea)

Let us give some examples in which context-based analysis of some of the domains will result in the recommendation of inclusion, exclusion or modification of a technology or group of technologies.

- A national healthcare system is aiming to improve the outcomes of a population-based screening program by including a technology that allows auto-sampling in those subpopulations that show a low ratio of participation and a high rate of prevalence of the disease in late stages. The analysis of the available technologies shows that the reliability of the technology, in terms of sensitivity and specificity is alike to that of standard sampling. Nevertheless, the analysis of experiences in similar contexts reveals that the level of increase in the ratio of participation is scarce and thus the return of investment is no less than doubtful.
- In a regional healthcare system, there is a need to consider a new medical device, proposed by health professionals for the treatment of a mental illness that is refractory to other existing treatments and requires the permanent implantation of an electrode behind the skull of the patient, and a replacement of the battery every two years. The analysis of safety and efficacy and the costs of the technology including cost-effectiveness are in favour of the technology and its use. The health professionals (neurosurgeons) have the needed skills to perform the procedure that are required and have pressured the medical directors to be a referral centre. However, in a qualitative analysis of the acceptability of the technology by patients of the region, they mentioned that they did not want to afford the risks of the surgical procedure and the battery replacement. Finally, the technology is rejected.
- In a hospital, health professionals have the skills to perform a new surgical procedure and have required the managers to include it in the service package of the hospital. The managers asked for an HTA, an analysis of the number of patients to treat per year, and a comparison against the standards defined in the literature to ensure safety and quality of care is provided. This analysis determined that the number of patients to treat are far below those described in standards, thus the technology is not included.

Finally, apart from the classical domains described, there are other domains that are gaining insight among those performing HTA. Recently, environmental analysis is being included in the new HTA definition among those domains to consider when providing evidence about health technologies (Polisena et al, 2018; O'Rourke et al, 2020). Those newly included domains apart from comprising new facts for the assessment include values that could influence the final decision. It is worth noting, the objectives of the millennium (United Nations, 2021) include good health and well-being, responsible consumption and production and climate action, among others. The consideration of those goals by countries could influence decisions around procurement, reimbursement, or inclusion/exclusion of health technologies in the healthcare systems.

The life cycle of health technologies and context

The new HTA definition (O'Rourke et al, 2020) also included another important change which is the life cycle concept, i.e., the assessment from its early development (Tummers et al, 2020) to reassessment when well established into a health system. Classically, HTA informed decisions have been related to inclusion of technologies in benefit packages, reimbursement schemes and procurement processes. Nevertheless, increasingly HTA has been used to inform decisions around health technologies related variability in practice and decisions on disinvestment of health technologies (Ibargoyen-Roteta et al, 2010; Gutiérrez-Ibarluzea et al, 2017). The value of a technology should be considered **within a context**, **in comparison to** other technologies in use for the same indication and **within a time frame** in which facts are obtained. New pieces of information provide new evidence around the technology in practice when applied to patients, the launch of new technologies can modify the line of treatment in which the technology can be included, and new data can support the disuse of a technology. The value and the values are not immutable, and they are affected by new data, by societal/cultural changes or by the entrance of new technologies. HTA doers and decision-makers should be aware of that and promote reassessments of existing technologies that help reconsidering the management of single or subgroups of patients or modify decisions (Soril et al, 2018).

The legislative context

Finally, the characteristics of the legislative context may influence the final uptake of the health technology assessed. Health is a universal right that has been mentioned in international agreements which include the Universal Declaration of Human Rights (United Nations, 2021), International Covenant on Economic, Social and Cultural Rights (United Nations, 2021), and the Convention on the Rights of Persons with Disabilities (United Nations, 2021). However, the interpretation of what it means and how it can be applied differs. In fact, there are considerations such as how health is defined, what minimum entitlements it encompasses, and which institutions are responsible for ensuring the right to health. At system level, someone could consider the right to health a societal right, meanwhile there are countries in which the right to health is considered at the individual level. In this sense, when budgets are limited and priorities need to be established, the right to health at the individual level collides with the collective right to health. This concept is crucial to support the legitimacy of the conclusions of HTA analysis and the final recommendations. As said, the principle of justice and fairness is considered when making decisions on the right to health in some countries, on the contrary, there are others that consider the right to health at the individual level which provokes judicialization processes that instead of reducing the inequities in the access to healthcare, increases the disparities and inequities in that access. One of the clearest examples is the case of countries in Latin America

(Yamin, 2019). Easy access to court, combined with individual wills, can promote queue jumping and exacerbate inequities in health systems. The final court ruling that supports the treatment of a patient when it is not granted by the provider or is not included in a system or benefit package impacts on the budget, can create jurisprudence and thus affects a group of patients. This can exacerbate the inequities especially to those that could not have access to other treatments due to budget constraints or that have no access to justice, or do not know (education or social gaps) the mechanism by which they could appeal.

Box 1. Context & macro-level decision-making: NIPT as an example of context-based coverage decision-making

Nowadays, NIPT is heterogeneously covered across different healthcare systems (**Table 1**). The approach to assess (analysis of facts) and to appraise (reaching a decision from the facts) this technology has inherently embedded values, and the mentioned heterogeneity is a result of the differences in values that prevail in different healthcare contexts. In other words, the values considered in both mentioned steps of the HTA process (i.e., assessment and appraisal), will determine the final target population who will have access to the technology as well as who is going to pay for it. As shown in Table 1, and with the same available scientific evidence, countries differ in who have access to NIPT. We can also think the other way around; do the established system, the financing schemes, the providers of services and access to the technology by patients influence the analysis of the facts? Do the same aspects influence the decision based on the same facts? Obviously, yes, in fact, the questions that are asked in different systems, although they could seem to be the same, interestingly differ and so the facts that will be considered and how they will be considered.

The assessment (analysis of facts) procedure is approached differently by countries. For example, while the Health Council of the Netherlands has based its coverage decision mainly on effectiveness criteria and ethical and social issues (safety – i.e., avoidance of invasive prenatal test procedures and procedure-related miscarriages-, reliability of test results, higher potential uptake, routinization, reproductive choices, personalized medicine); the Belgian Health Care Knowledge Center based its recommendations on a cost-effectiveness analysis looking at the average cost per trisomy 21 detected for different scenarios (and not the cost per Quality-Adjusted Life Years (QALY) used frequently by HTA agencies) (Gadsboll et al, 2020).

In the appraisal step, when coverage decisions are made (level of coverage and access to the technology), embedded contextual values also determine its results. While in some countries no access (non-coverage) to NIPT exists, others have implemented NIPT for all pregnant women. Most countries are implementing NIPT in a subset of pregnant women population, those who have intermediate-high

risk for foetal aneuploidies after combined first trimester screening (cFTS), which is the gold-standard diagnostic test for foetal aneuploidies nowadays. Nevertheless, also in this target population, there are differences between health authorities when defining the criteria that include intermediate-high risk pregnant women. For example, in Canada, two provinces have different criteria for covering NIPT with public funds in intermediate-high risk pregnant women. Ontario has a broader number of criteria (with two types of Category and a total of 10 criteria included) (Ontario Health Insurance Plan, 2020), while Vancouver (British Colombia) has defined only two specific indications 1) if a woman has had a prior pregnancy where the baby was diagnosed with Down Syndrome, Trisomy 18, or Trisomy 13; or 2) if a woman has received a "positive screen" based on a different prenatal screening tests (Quad, IPS, SIPS, FTS) (Pacific Center for Reproductive Medicine, 2020). Here, again, the inherent values of different healthcare contexts result in different decisions regarding access to NIPT.

Table 1. Context based NIPT funding: criteria and type of coverage (modified from Gadsboll et al, 2020)

	No national coverage	NIPT as an option if intermediate-high risk at combined FTS	NIPT for all	Partially or fully reimbursed by Medicaid/healthcare system (insurance companies)	Self-paid/out of pocket
Northern Europe					
Sweden, Norway, Finland		X		X	
Iceland		X (if women request)		X	
UK Wales	X	(X in negotiations for 2020) X		 X	X
Latvia	X				X
Estonia		X (in negotiation)			X
Lithuania		X			X
Eastern Europe					
Slovakia, Russia, Czech Republic	X				X
Poland, Romania		X			X
Southern Europe					
Spain Regions	X	X		X	X
Portugal		X (some public clinics)			X
Italy Toscana and Bolzano Region		X		X	X (high use in private clinics)
Greece, Cyprus					X
Slovenia		X		X	

	No national coverage	NIPT as an option if intermediate-high risk at combined FTS	NIPT for all	Partially or fully reimbursed by Medicaid/healthcare system (insurance companies)	Self-paid/out of pocket
		(if invasive testing contraindicated)			
Western Europe					
France		X		X	
Germany		X		X	
Netherlands			X	X	
Belgium			X	X	
Austria	X				X
Canada					
Ontario Vancouver		X X		X	
USA					
Medicaid States (n=6) States (n=9) Insurance companies	X	X	X		X
Australia					X

Box 2. Context & meso-level decision-making (Hospital-based-Health Technology Assessment-HB-HTA): Photodynamic Therapy (PDT) for the treatment of basocellular carcinoma

Hospital-based Health Technology Assessment (HB-HTA) is not defined by the setting where it is being carried out. In other words, because the HTA is performed at the hospital level it is defined by the perspective taken when carrying out the assessment, which is the perspective of the hospital where the decision about the introduction of a new or innovative technology is going to be made. The key question is to wonder about the implications and impact for a specific hospital of introducing a specific technology. To illustrate this concept, take Photodynamic Therapy (PDT) for the treatment of basocellular carcinoma (CBC) as an example (Van der Wilt et al, 2016). An HTA from a National/Regional perspective will assess whether this technology can decrease the burden of the disease, and whether the quality and efficiency of the care provided will improve when this technology is used instead of other available technologies for the same clinical indication. It will also assess which patients, or subgroup of patients, can benefit the most from this technology. For that purpose, a review and synthesis of the scientific evidence will be carried out considering randomized controlled trials, cohort studies, case-control studies, and other study designs. Additionally, costs associated to its acquisition and use of the technology will be explored to include them in a cost-effectiveness analysis to elucidate if it is an efficient option. From the results obtained, recommendations regarding who, when and under what conditions should the PDT be adopted will be made; as well as the needed steps to appropriately endow economically the new technology to be introduced into the health system. Up to here, the HTA has demonstrated the added value of the PDT for CBC patients in average healthcare

centres. But HB-HTA goes further and will look at the potential value that this technology may reach in a specific hospital. First of all, it will be necessary to look at the effectiveness and cost section of the HTA and decide how much can be translated to the situation at the hospital (i.e., are the patients in the document similar to the ones of the hospital?, are the costs similar to the costs of the hospital?, etc.). In other words, firstly it will be necessary to review the transferability of the results to a specific hospital (Chase et al, 2009). Secondly, there will be a need to look for additional information and answer other type of questions such as:

- Is the hospital treating patients with CBC and which departments are involved? (e.g., dermatology, ear-nose-throat department, general surgery etc.)
- The available treatments currently used for CBC patients: are they going to be completely replaced by the PDT? What will be the consequences for the organization of this type of care and for the health professionals? Will operating theatres be released? If this is the case, will operating theatres be used for other alternative surgeries?
- Is it necessary to make investments (to buy the technology, to train/educate professionals, to adapt the space for technology allocation)? Are the investments to be recovered? What is the return on investment? Is there any reimbursement by payers? And how much will the reimbursement be?
- Is there any other centre around that is already offering this treatment? Is this service aligned with the overall strategy of the hospital?
- Will a qualified nurse be able to offer the PDT, under supervision of a dermatologist? Is that going to be legally accepted? Is there any risk or penalization associated to this situation?
- Who is the manufacturer of the equipment? Are there several manufacturers? Can we carry out a price negotiation for buying the equipment or training the professionals?
- Should/can the equipment be integrated in the information system of the hospital?
- Is the treatment offering opportunities for newer research or for training of residents?
- Is there any probability that the incidence of CBC will increase in the near future? Is there any other pathology that can be also treated with the PDT?
- Is there any other technology in development that will make PDT obsolete in a couple of years? is the PDT a treatment only to be used by university hospitals? Or is there any chance that in few years this treatment will be also offered at primary care level?

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Part 3. The philosophy of VALIDATE

Chapter 7. A philosophical summary of the VALIDATE approach

Abstract

Because the VALIDATE approach is based upon the premise that normative analysis is, and should be, an integral part of HTA, it should be able to offer a response to moral scepticism. Although a strict fact/value dichotomy is criticized (Chapter 1 and Chapter 2), and there are different methods to do normative analysis (Chapter 5), there is still an explanation needed on how the VALIDATE approach is a legitimate, and reliable, way of answering policy relevant questions on health technology. This chapter will defend the legitimacy of the VALIDATE approach by elaborating its view on the nature of ethical issues in HTA, presenting a response to moral scepticism. This response is based on the philosophical tradition of ***pragmatism***. It will offer a critical examination of the position of moral scepticism and show how it can be overcome by applying elements of pragmatism to the practice of health technology assessment (HTA). This will also make clear that the philosophy of the VALIDATE approach is inspired by, but not synonymous to, pragmatism. Especially the relation between pragmatism and the concept of interpretive frames (introduced in Chapter 3) will become clear.

Key message of this chapter: the philosophy of VALIDATE, partly based on the tradition of pragmatism, is that normative issues can be addressed in a rational way.

After reading this chapter, you should be able to understand that the VALIDATE approach can best be conceived as a framework for evaluating health technology that is inspired by, but not synonymous to, pragmatist philosophy.

Introduction

As already discussed in Chapter 1, a central tenet of the VALIDATE approach is that it regards HTA as a practice in which facts and values meet. There are two main reasons for this view: (i) a strict dichotomy between facts and values is unattainable and undesirable (Chapter 2); (ii) to answer policy relevant questions HTA should not only provide information on the *plausibility* of potential consequences of health technology, but also on the *desirability* of these consequences (Chapter 1). Answering questions on desirability requires being able to think about the impact of a health technology in light of a set of norms and values. Consequently, HTA needs to integrate empirical inquiry (collecting 'facts') with normative analysis ('values'). This enables HTA to explicitly take into account the needs of a population

and decision-makers, by exploring different conceptual schemes that stakeholders use in making sense of a concrete situation (Chapter 3 and Chapter 4). In addition, it increases awareness of the context-dependency of HTA (Chapter 6).

To propose such a central role for normative analysis in HTA may invoke a critical response. A widely held view – also within the context of HTA – is that there is no way of rationally resolving normative questions. Therefore, trying to address these questions may be seen as a threat to the (scientific) legitimacy of HTA. This relates to a general discussion on the possibility of moral knowledge, which is also debated between ethicists (Chapter 5). Although there are methods for analysing and structuring ethical arguments, there remains a worry about the status of the outcomes of such analysis and the experts involved in conducting them. These worries about the subjective nature of normative analysis are rooted in a general position of ***moral scepticism***, which denies that there can be any form of moral knowledge or expertise.

The challenge of ethical issues in HTA: moral scepticism

Although the HTA community seems to be committed to addressing the wider ethical, legal and social implications (ELSI) associated with the use of health technologies, alongside their safety, clinical effectiveness and cost-effectiveness, they are not always included in HTA reports that are drafted to inform healthcare authorities. There are many reasons given for why ELSI issues are neglected or studied in isolation from other aspects of health technology, ranging from methodological to practical reasons (Bellemare et al, 2018). Although practical and methodological obstacles are important to address, one fundamental challenge relates to how the HTA community pictures the natures of ethical issues. Ethical and societal concerns related to health technologies are often considered non-scientific, expressing controversial opinions that cannot be evaluated or supported with *facts* generated by scientific research. HTA agencies would then emphasize the importance of their reports being based on scientific *facts*, avoiding entering into possibly interminable 'oh, yes it is, oh, no it isn't' debates. This is a complex, but crucially important issue. For if the HTA community were to hold on to this distinction between ('objective') facts and ('subjective') opinions, it is not quite clear how it can take into account the wider ethical, legal and social issues associated with the use of health technologies (Legault et al, 2018).

To make some headway in this complex issue, let's take a look at the debate on applied behavioural analysis (ABA; i.e., an intervention program, based on insights from behavioural science, aimed at enhancing, reducing and maintaining certain behaviours) for children with autism. The debate centres around the policy question whether ABA should be recommended (or used, offered, funded) as a treatment for children with autism. This question raises controversies for two reasons: (i) there is

disagreement on the question whether ABA is an *effective* treatment in children with autism, and (ii) there is disagreement on the *desirability* of this treatment: what is it that we want to achieve by using ABA in children with autism? Should the aim be to help the child to recover from autism (assuming that such is possible), or should it focus on other aims (e.g., helping children with autism to cope with all sorts of social situations)? An example of the debate on its desirability can be seen in a statement made by a mother of two children with autism[9]:

> 'It is *possible* to change behaviour using ABA, there is no question of this - though not as effectively as some would have you believe. *But this is beside the point. We ought to be considering whether we should change the behaviour - which is often harmless and often useful*.' (Davison, 2018; emphasis added)

The first part of this statement may be considered largely empirical: 'It is *possible* to…'. The second part of the statement seems to be different, though, and more normative in nature: 'We *ought* to….'. Here, the author challenges the view that changing the behaviour of children with autism is what we should be aiming at. The aim of the treatment, normalization, is challenged. It is challenged, partly because it is considered harmful. But also, because being autistic is considered as a condition that is not all wrong:

> 'If I had the option of not being autistic, I would not take it – nor would I take it for my children. That does not mean life is easy for me, it means I like myself and my children the way we are.' (Davison, 2018).

But if it is indeed a matter of disagreement on a normative issue, it is not immediately obvious how this disagreement can be resolved. Indeed, it is even not obvious that it is settling what is called for, nor is it clear what we mean by it or how it should be achieved. A widely held view – also within the context of HTA – seems to be that there are no ways of rationally resolving such type of disagreements.[10] This position is called ***moral scepticism*****,** which refers to a diverse collection of views that deny or raise doubts about various roles of reason in morality (Sinnott-Armstrong, 2006)[11]. This might explain why ethical concerns, such as those that have been expressed in relation to ABA for children with autism, fail to reach HTA reports that are meant to inform policy makers on the full spectrum of implications of such technologies. This could seriously hamper the consideration of ethical

[9] Davison, 2018, https://autisticuk.org/does-aba-harm-autistic-people/

[10] This observation was made by David Banta and Bryan Luce as early as in their 1993 book, Health Care Technology and its Assessment (p. 152).

[11] Associated with this position of moral scepticism is the fear that an ethicist is imposing his (idiosyncratic, subjective, personal) values on others. It denies the possibility of moral expertise, to avoid this danger of value imposition. There is, of course, a strong relation between denying a role for reason in morality and the possibility of moral expertise. In Chapter 5 of this handbook we try to address this danger of value imposition by discussing methods for ethical analysis that can be used to evaluate moral arguments in a transparent way. For a discussion on the role of expertise in conducting ethical analysis in HTA, see also: Refolo P, Bond K, Bloemen B, Autti-Ramo I, Hofmann B, Mischke C, et al. Core competencies for ethics experts in health technology assessment. Int J Technol Assess Health Care. 2020;36(6):534-9.

issues (or value issues more generally) in HTA. As a result, health technologies and the practices that are engendered by them seem to be completely separated from moral values. They occur, as it were, in completely separate, mutually inaccessible domains. This means that we need to redefine the mission of HTA (which invariably claims to include assessment of the wider ethical, social and legal implications associated with the use of health technologies), or we should reconsider our position towards the nature of ethical issues.

Rethinking the nature of ethical issues in HTA

Different responses to moral scepticism

If it turns out that there is normative disagreement on the desirability of a health technology, as in the case of ABA for children with autism, HTA agencies have several options:

1. Adopting a strategy that can be referred to as the '*disclaimer strategy*'. This consists of proceeding with the HTA as originally planned but pointing out that the relevance of its outcomes is contingent on a particular interpretation of the policy problem, which does not seem to be shared by all stakeholders. The strategy might include the reporting of the scoping exercise (see Chapter 4), pointing out in what respect the interpretations differ, and how that might affect the choices (and outcomes) of the HTA. Although adopting such a strategy would not result in a different HTA, it at least testifies of an awareness of the contingency of its outcomes, and commissioning organizations that need to make decisions on the basis of the HTA can take this into account.
2. A second strategy might be called the '*justificatory strategy*'. It differs from the disclaimer strategy in that it involves a critical appraisal of the results of the scoping exercise by the HTA team. Critical appraisal, here, would not so much refer to a critical appraisal of the evidence of safety and clinical and cost-effectiveness, but to a critical appraisal of background theories and normative preferences (see Chapter 3), requiring different methods of appraisal. On the basis of the results of such an analysis, an HTA agency, preferably in conjunction with the commissioning organization, could decide which interpretations are considered sufficiently plausible and reasonable to inform the choices regarding the HTA. This would help to make those choices explicit and justify them towards a wider audience.
3. The third and last option is the strategy of '*HTA as learning*' (Grin et al, 1996). Here, the agency will conduct a critical analysis of the interpretive frame of stakeholders (similar to the second strategy). In case of multiple, mutually incompatible frames, it would feed back the results of the analysis to the various stakeholders in an attempt to achieve a certain degree of learning among them. The learning would not necessarily be directed to find out who (or

what) is right and who (or what) is wrong. Rather, participants may come to realize the complex nature of the problem, and how factual issues and value issues are intertwined and jointly appear to define what is considered relevant to the assessment. Also, they may come to accept the indeterminacy of certain issues, and be willing to suspend, at least provisionally, their judgement and accept the relevance of the issues to be addressed in the HTA (its terms of reference). This approach has been described by Guba and Lincoln (Guba et al, 1989) and applied in the context of HTA to the use of cochlear implants in deaf children (Reuzel, 2002). Clearly, because of the involvement of stakeholders, this strategy may be more effective in terms of resolving long-standing controversies, but is likely to be more time-consuming too. It stands to reason that HTA agencies and commissioning organizations jointly decide which of these approaches seems most appropriate and feasible in concrete cases, given limitations in time, capacity, and resources.

The VALIDATE approach adopts the latter option ('HTA as learning'), which also challenges the position of moral scepticism. Our main concern is whether we can somehow re-conceptualize the relationship between facts, values and technologies, in such a way that the sorts of concerns that have been expressed regarding the use of ABA in children with autism can be incorporated in HTA in a more productive and satisfying way.

The status and meaning of 'ethical issues': the case of Extra-Corporeal Membrane Oxygenation (ECMO)

The VALIDATE approach differs from mainstream HTA in its conceptualization of 'ethical issues'. In current HTA, ethical issues are considered alongside issues such as safety, clinical effectiveness, and cost-effectiveness. Such classification runs the risk of obscuring both the moral significance of the safety, clinical and cost-effectiveness claims and the empirical content of ethical issues associated with the use of health technology. To explain this further, consider the example of Extra-Corporeal Membrane Oxygenation (ECMO, or heart-lung machine, see Figure 1**)** in new born children with conditions such as meconium aspiration or diaphragmatic hernia (Crow et al, 2009). Outcomes that have been reported in the literature include complications that result from intracranial haemorrhage, improved survival, and cost-effectiveness of ECMO when compared to optimal conventional support. Ethical issues that have been reported to be associated with the use of ECMO in new born children include the compromise of parental autonomy and the dilemmas associated with the discontinuation of ECMO support in case the new born child fails to thrive (Kirsch et al, 2018, Williams et al, 2016). This distinction seems to suggest that there are, on the one hand, outcomes that can be objectively

established (safety and clinical and cost-effectiveness), and, on the other hand, outcomes for which this does not hold (ethical issues).

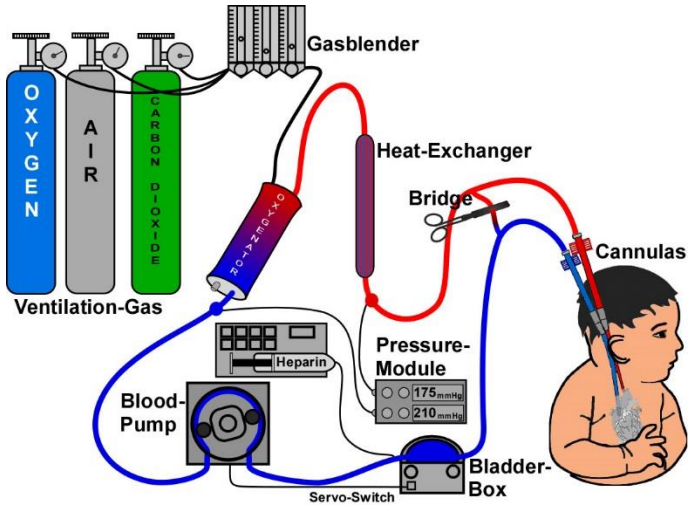

Figure 1. Schematic illustration of Extra-Corporeal Membrane Oxygenation (ECMO). Source: Jürgen Schaub. de:User:Mr.Flintstone [CC BY-SA 2.0 DE. Available from: https://creativecommons.org/licenses/by-sa/2.0/de/deed.en]

The current practice in HTA of distinguishing ethical issues from other issues in this way is, however, dubious. For it tends to obscure the fact that *both* categories of outcomes are morally relevant *and* rooted in an empirical reality of a specific practice (Hofmann et al, 2018). For instance, the issue of complications derives its relevance from a commitment to avoid inflicting harm. Likewise, improved survival derives from a commitment to doing good, and cost-effectiveness from a commitment to distributive justice. At the same time, the issues of parental autonomy and discontinuing ECMO support are based on a particular, real-life practice of care of newborn children with life-threatening conditions.

Box 1. The status and meaning of 'ethical issues': the case of Non-Invasive Prenatal Testing (NIPT)

This mainstream, and problematic, way of conceptualizing ethical issues in HTA can also be seen in assessments of non-invasive prenatal testing (NIPT). Ethical issues concerning NIPT (e.g., which conditions should be tested? When should it be offered? Is it a medical procedure?) are often addressed in separate analyses from studies that assess the safety and validity of NIPT (Kibel et al, 2017). This ignores that an answer to the central normative question related to NIPT, what is its desirable purpose, is already implied by any analysis of its validity and cost-effectiveness. To be able to assess the reliability of NIPT you need to decide on which genetic conditions it should offer information. And any cost-effectiveness analysis of NIPT needs to define its potential benefits and costs, which raises normative questions concerning whose benefits should be taken into account (e.g., the QALYs of the unborn child or the parents) and which time horizon should be considered (e.g.,

should only impacts up to the detection of affected pregnancies be taken into account, or also long-term implications such as reduction in the use of healthcare resources by children born with trisomy 21). This shows that both ethical and clinical analyses of NIPT are rooted in normative commitments. In addition, assessing claims on potential consequences of NIPT, like that it enhances reproductive autonomy, requires both value-laden decisions on how to define certain outcomes and empirical inquiry to understand their particular meaning and realization in the context of NIPT (Bloemen et al, 2021).

The status and meaning of 'ethical issues': the VALIDATE approach

By introducing the *interpretive frame* as a central concept in evaluation (Chapter 3), the VALIDATE approach abandons the current distinction between objective (factual) and subjective (normative) issues. Here, relevant aspects of a particular practice (for instance, the care of newborn children with life-threatening conditions) emerge from a commitment to and working knowledge of certain moral principles (e.g., of not causing harm, of respecting autonomy, of observing justice), in conjunction with a certain knowledge about this practice and its outcomes. Hence, we do not wish to suggest that facts and values cannot be distinguished from each other. We can make a distinction. But the point is that in HTA, *facts and values act in conjunction*, enabling us to acknowledge which aspects of a situation, event or action seem to be relevant and need to be taken into account when we wish to assess how and why they are meaningful to us. In the following section of this chapter we will elaborate this further by exploring the relation between the VALIDATE approach and the philosophical tradition of *pragmatism*.

Pragmatism and the VALIDATE approach

Interpretive frames

As stated above, our main concern is how we can re-conceptualize the relationship between facts and values, in such a what that the sorts of concerns that heave been expressed regarding the use of ABA in children with autism can be incorporated in HTA in a more productive and satisfying way. For this, we turn to the work by Frank Fischer. Fischer developed a model where judgments of specific solutions (e.g., is ABA an appropriate sort of treatment for children with autism?) are closely linked to how a problem is defined (e.g., what ae the problems that are caused by autism?), and where both, judgments of solutions and problem definitions, are informed by background theories (e.g., what sort of long term impact can be expected from teaching people to behave differently form how they are?) and normative preferences (e.g., is it generally acceptable to try to normalize people?). As stated before (Chapter 3), this set of judgment of solution, problem definition, background theory and

normative preferences is referred to as an *interpretive frame*. This can be considered a type of tacit knowledge: it remains mostly implicit, but it can be made explicit. The method for this is called reconstructing interpretive frames (Chapter 3). A key feature of this method is that it does recognize that facts and values can be *analytically distinguished* (e.g., a distinction is made between background theory and normative preferences), but at the same time it emphasizes that they *act in conjunction*, determining what is being perceived as problematic (problem definition) and what is considered both a feasible and appropriate way of resolving the problem (judgment of solution). By reconstructing the interpretive frames of multiple stakeholders, differences in judgments of specific solutions (such as ABA in the treatment of autism) can be related to differences in problem definition, background theories and normative preferences. The purpose of making the factual and normative assumptions underlying judgments on technologies explicit is to enable a critical, constructive scrutiny of those assumptions. HTA experts can play a novel and significant role here. Its major aim is to facilitate learning among the various stakeholders, generating new conceptualizations, perspectives, and approaches to resolve problems.

Interpretive frames and pragmatism

So, the interpretive frame is one of the key elements of the VALIDATE approach. In Figure 2, the four elements of the interpretive frame are presented once more. Problem definitions are in the top left quadrant, judgments of solutions are in the top right quadrant, and background theories and normative preferences are in the lower left and right quadrant, respectively.

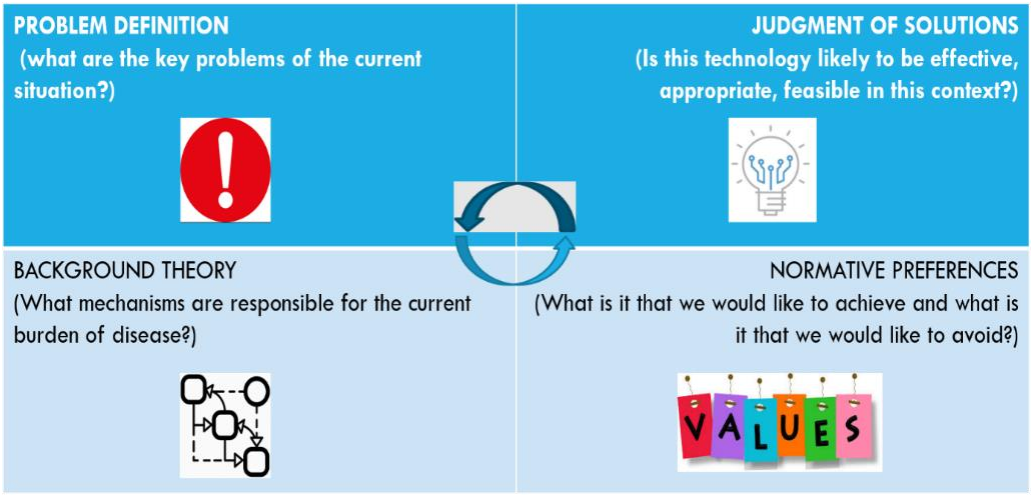

Figure 2. Interpretive frames

This arrangement enables us to think of the interpretive frame as being constituted of two axes, and we can ask: what do these two axes represent? What do problem definition and background theory have in common that distinguishes them from judgments of solutions and normative preferences (the

horizontal axis)? Similarly, we can ask what problem definition and judgment of solutions have in common that distinguishes them from background theory and normative preferences (vertical axis)? To answer these questions, we would suggest the following characterization of the two axes: the horizontal axis represents an axis which runs from primarily descriptive (to the left) to primarily prescriptive (or normative) (to the right). The vertical axis represents an axis which runs from more general (or theoretical, or abstract) (the lower half) to more specific (or practical, or concrete) (the upper half). This can also be held to mean that the upper half is primarily related to practice, to acting, while the lower half is primarily related to reflection, to thinking (see Figure 3).

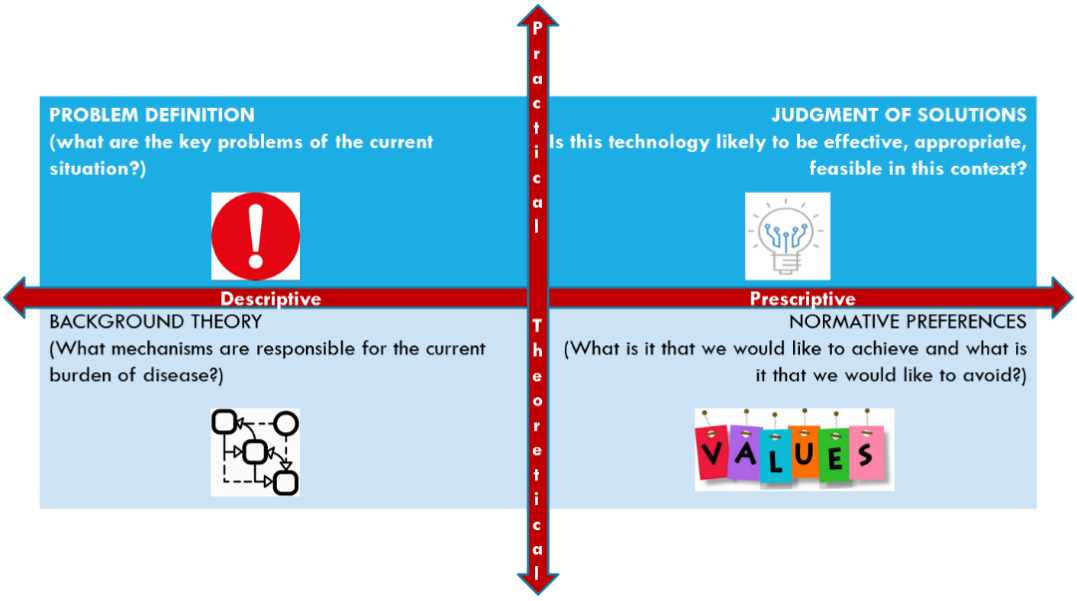

Figure 3. Interpretive frames with proposed axes

Apart from the question how the two axes might best be characterized, with this arrangement of the elements of interpretive frames we can also ask: how do the two poles on each axis relate to each other? Our answer to that question would be that *they mutually constitute one another*. In other words: they need, determine, and presuppose one another. For the vertical axis this means that we would not be able to think in the way we do, if we were not able to act in the way we do, and vice versa. The nature of our actions would be quite different if we were not able to think in the way we can; similarly, the nature of our thinking would be different if we were not able to act in the way we can. This idea of the close *entanglement of thinking and doing* is inspired by ***pragmatism***.

Pragmatism is a tradition in philosophy which originates from the work of a number of American philosophers in the second half of the nineteenth and first half of the twentieth century.[12] One of the common themes in their thinking was the idea that one of the main ways (if not *the* way) in which we

[12] For more information on pragmatism, see also: Catherine Legg and Christopher Hookway 2019, https://plato.stanford.edu/archives/spr2019/entries/pragmatism

acquire knowledge is through acting. The theories and concepts that we have are tools that enable us to act in a certain way. For example, that "bear" refers to a furry creature with teeth is not an inherent or essential property of this term or *the* description of this particular creature, but people found this syllable useful for pointing out dangerous creatures and helping us to survive. So, if we wish to know whether some statement is true, we need to imagine what course of action would be most reasonable if we assume that the statement is, in fact, true. Also, we would need to establish what would follow, or what we would expect to happen, when we were to act along those lines. If our expectation is, in fact, borne out, we may be relatively confident that the statement is true.[13] Acting, then, makes knowledge possible. However, pragmatists would be quick to point out that complete certainty is unavailable; our knowledge is always incomplete, provisional, and subject to refutation (a position that is usually referred to as fallibilism). However, this does not relieve us from the obligation to always be truth-directed, or take an interest in seeking the truth, even though we know that it is an unattainable goal.[14] At the same time, a commitment to fallibilism should make us receptive for alternative interpretations of particular situations or events, provided that there is a shared commitment to think through and test the practical consequences of competing interpretations. This, in fact, holds for both domains, the descriptive and the normative domain: acting under the direction of background theories and normative preferences should reveal whether our general notions are likely to be correct. While, in the view expressed here, action makes knowledge possible, the reverse also holds: a particular way of acting (rationally) is enabled by us having particular knowledge. This is a distinctive feature of pragmatism: is describes an iterative process between thinking and doing.

A similar relation holds between the two poles on the horizontal axis, which runs from primarily descriptive to primarily prescriptive. Our knowledge and experience of how the world is (description) and our knowledge and experience of how the world might be and might be a better place (prescription), constitute one another. Our capacity of being aware of the world existing *in a specific way* is dependent on our capacity of being aware of the fact that the world *could, in some ways, also be otherwise*. Moreover, we have the capacity for not being neutral, or indifferent, toward those different possible worlds.[15] In other words: we would experience our life world in a completely

[13] Although we do consider this focus on the close entanglement between knowledge and practice a strength of pragmatism, we should also be attentive of its limitations. Firstly, it means that pragmatists are unlikely to be particularly interested in knowledge that does not seem to have obvious practical implications. After all, in the pragmatist view, there is no way of ascertaining whether such propositions are likely to be true (or false). This might impose an undue restriction on the sorts of knowledge that seem to be worthwhile to pursue. Also, we have to bear in mind that the issues that the founders of pragmatism had in mind when reflecting on the nature of knowledge and its association with practice, are rather different from the issues that are nowadays on the agenda. A case in point would be the current debate on global climate change. The complexity of many current issues may defy the thinking through of what sort of actions would be most reasonable, if we assume that our account of them is correct; similarly, complexity may defy a straightforward interpretation of what is being observed in such cases. Finally, some issues may require a long time of follow up in order to discover the full range of implications. By pointing to these limitations, we do not wish to suggest that the pragmatist account of knowledge is no longer of use to the present context; rather, these issues need to be addressed in order to see whether and how the classical pragmatist account is still relevant for the complex issues that we are typically facing in the 21st century (see, for instance, Sanderson I. Intelligent policy making for a complex world: pragmatism, evidence and learning. Political studies. 2009;57(4):699-719.

[14] Pragmatism has been characterized as accepting fallibilism, without embracing skepticism; Bacon M. Pragmatism: an introduction. Cambridge: Polity Press; 2012.

[15] See, for instance Sayer A. Why things matter to people: Social science, values and ethical life. New York: Cambridge University Press; 2011.

different way if we were not, at the same time, able to imagine that our life world could, at least in some respects, also be different, and that humans can, at least to some extent, affect their life world (that is: it is not, or not entirely, necessarily the way it is). What would drive humans to explore their life world in order to find out how things work, if there is not, at the same time an idea (even emergent) that such knowledge might be used in order to change this life world (for the better)? And, vice versa, how can notions of how the life world may be changed develop in the absence of knowledge on how the life world is, how it works? Thus, facts (the descriptive) and values (the prescriptive) can be meaningfully distinguished; at the same time, however, these two realms mutually constitute one another. Acknowledging this close entanglement of facts and values is also a distinctive feature of pragmatism.

Conclusion

Having read this chapter, you should be able to understand that the VALIDATE approach can best be conceived as a framework for evaluating health technology that is inspired by, but not synonymous to, pragmatist philosophy. It acknowledges the importance of empirical analysis in this context but denies that HTA is merely a matter of collecting *the* facts about the consequences of health technology. Rather, it holds that HTA is a matter of collecting facts that are considered *relevant*, *plausible*, and *amenable to generally accepted methods of inquiry* (Grin, 2000). This reformulation reveals the normative nature of HTA. For relevance is determined by our commitment to, and interpretation of, values. Plausibility is determined by our understanding of reality (or ontological commitments). And amenability to methods of inquiry is determined by our methodological commitments: what types of inquiry (i.e., research, analysis) do we consider to likely yield valid and reliable knowledge of the world? Reconstructing these frames provides a way of putting HTA and its results in a wider framework and a means for better understanding and constructively exploring the interdependence between these different types of normativity and empirical inquiry. It recommends exploring the contents of interpretive frames as an integral part of HTA. To be sure, this need not always reveal deeply divergent views on the nature of the problem, on the type of solutions that are considered appropriate and the sort of standards by which these should be judged. But it can, in all cases, provide a more satisfying way of justifying the choices that are, inevitably, made in HTA. As such, it can help to bolster the accountability of the processes used by governments to decide technology may (not) be used (e.g., decisions on the introduction, use, reimbursement or disinvestment) to improve the living conditions of its citizens.

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Part 4. Conclusion

Chapter 8. Summing up VALIDATE

Abstract

In the preceding chapters of the handbook, key elements of the VALIDATE approach to health technology assessment (HTA) have been elaborated. In this concluding chapter, we will bring these elements together in an overarching framework. In the VALIDATE approach HTA is proposed as it was originally intended: as a type of policy analysis, wherein the study of safety, clinical and cost-effectiveness of (new) health technologies and their wider ethical, legal, and social implications are closely integrated and stakeholders are involved in a more productive way throughout the process of HTA. In addition, we will highlight what skills and knowledge are needed to use the VALIDATE approach in practice.

Key message of the chapter is that by subsuming HTA in a wider process of practical reasoning about the proper use of health technologies, the VALIDATE approach holds the promise of further enhancing the policy relevance of HTA.

After reading this chapter, you should be able to explain what the VALIDATE approach to HTA is, and what skills and knowledge HTA-doers need for conducting HTA in this vein.

Stakeholder views, empirical research, and normative inquiry

In this handbook we present and discuss the VALIDATE approach (see Figure 1) that is focused on how to integrate empirical research (facts) and normative inquiry (values) when assessing health technologies (HTA). To exemplify this, we used non-invasive prenatal testing (NIPT) as a case study. NIPT is a prenatal screening procedure that analyses cell-free foetal DNA, which circulates in the mother's blood during pregnancy, in order to obtain information about the foetal genotype (see Chapter 1 for an introduction of the case study).

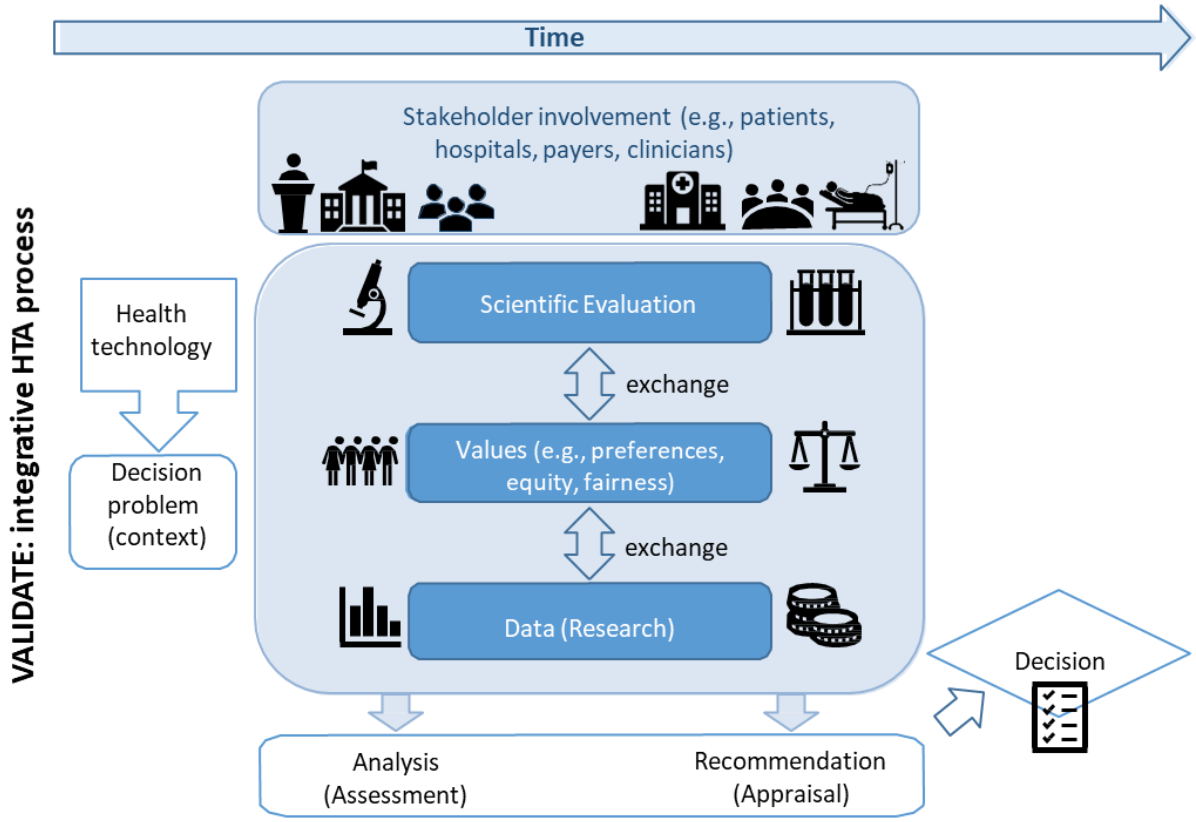

Figure 1. The integrative approach of VAILIDATE

In this chapter, we summarize the key elements of the VALIDATE approach to HTA that have been elaborated in the preceding chapters. We specifically ask what generic lessons may be learned from NIPT as a particular case for HTA: Should the sort of views, held by or expressed on behalf of some of the relevant stakeholders involved (e.g., parents, unborn child), be taken seriously? Why, or why not? (or perhaps rather: when, and when not?) What does it mean, exactly, to take stakeholders' views seriously in this context (of introducing/using NIPT)? And, finally, what is it, exactly, that we hope to learn from stakeholders, and how should we conduct and organize an HTA in order to make this happen?

To address these questions, we propose that a key objective of HTA, consistent with its recent definition (O'Rourke et al, 2020), is to help communities (local, regional, national or supra-national) to develop a shared view of how specific health problems can best be resolved in their specific context, and what role health technologies can fulfil in such endeavour. An inquiry to this end will, of course, include considerations of benefits and (opportunity) costs that are associated with the use of health technologies, but may extend to other considerations as well.

Specifically, ascertaining a proper role for health technologies in resolving particular health problems can substantially benefit from an understanding of the major contributory causes of the health problem, of the physical and cultural context, of potential options for resolution, and of the experiences that have been obtained with these options. Since HTA is an evaluative exercise, the inquiry is guided by, on the one hand, considerations of what is possible, and, on the other hand, considerations of what is desirable and acceptable. As such, the inquiry can be characterized as an instance of practical reasoning: figuring out what needs to be done in a concrete situation, given a commitment to a range of general, normative (e.g., ethical) principles (Fischer, 2007). Such an inquiry is, we would suggest, inherently ambiguous. By this, we mean to say that there is no procedure that, when followed correctly, can unambiguously reveal the right way to act or proceed. This ambiguity results from at least two different sources. Firstly, it results from the necessarily provisional and incomplete nature of the knowledge that is needed in order to decide how to act. A second source of ambiguity results from properties of general ethical principles (see Chapter 5). Following Richardson (1990; 1997), we hold that such principles can best be considered as incommensurable. It means that there is not a single metric (such as utility) to which the various ethical principles can be reduced (see also Chapter 5).

Taking this more integrative perspective on HTA, what we would hope to hear from stakeholders, then, are particularly their views of how specific health problems may best be resolved, and what role they see for health technologies. Not, to be sure, as some form of sacred truth. But primarily as a specific perspective, a perspective that should make us think, or rather: re-think, and urge us to explore the reasons underlying those views, as well as the reasons underlying our own views. Such a perspective is also likely to point to essential aspects of the context (social and physical) that need to be taken into account (see Chapter 6).

As explained in Chapter 3, the method of reconstructing interpretive frames can be usefully applied to reveal how such judgments are related to assumptions about the nature of the problem (background theory) and about the sort of things that ought to be pursued or avoided (ethical commitments). As further explained in that chapter, making such connections explicit renders them amenable to critical and constructive scrutiny. The inquiry should, then, help those who are involved to identify and acknowledge ambiguities, uncertainties and apparent conflicts, and that may occasion them to re-think their views and suspend their judgement. In this sense, the VALIDATE approach may be considered as an approach to HTA that urges the various stakeholders to avail themselves of the opportunities for mutual learning, offered by the inquiry (Grin et al, 1996; Grin et al, 2007; Richardson, 2016).

Making it work in practice

In addition to the knowledge and skills (procedural ad attitudinal) that are currently taught in HTA curricula across the globe (Mueller et al, 2020), the HTA-doer would be well advised to develop the skill of identifying the relations between health technology and its associated primary studies on the one hand, and the underlying assumptions on the other hand. This means that the task of the HTA doer is not only to identify those who may be considered stakeholders and solicit their claims and concerns (Guba et al, 1989) regarding the health technology, but also to assess whether these claims and concerns can serve as a basis for public decision-making and action. It is for this reason that the method of reconstructing interpretive frames plays such a key role in the VALIDATE approach (see Chapter 3). It can help to elicit judgments from stakeholders regarding various approaches to resolve a specific health problem, and to relate those judgments to problem definitions, background theory and ethical commitments. By conducting a critical examination of their content (e.g., evidential support, coherence with knowledge and ethical commitments for which broad support in the relevant community may be presumed), HTA doers can indicate to decision and policy makers whether and why (i.e., on what grounds) they can serve as a legitimate basis for public policy making (the flip side being that it might be hard to justify *not* to take them into account in public decision-making).

A sequence of activities for HTA doers that can be derived from this, is, then:

- Identify stakeholders: given the nature of the health technology and the nature of the health problem that are the focus of the HTA, who can be designated as stakeholders (i.e., those affected by a decision and who are able to bring a specific perspective on the issue to the table)?
- Elicit views (judgments) from stakeholders regarding the subject of the HTA.
- Identify underlying assumptions: what assumptions appear to underlie those views? Ensure to address assumptions regarding what is considered to be the case, that is, how things are, work, and are related to each other, as well as assumptions regarding what is considered desirable and what is best avoided.
- Conduct a critical analysis: can the views that were elicited and their underlying assumptions jointly (that is, as a whole) stand up to scrutiny?
- Provisionally define and negotiate the terms of reference of the HTA: given the outcome of the analysis so far, what would be the key questions to be addressed in the HTA, and how might they best be explored? To ensure a sense of ownership and shared responsibility, this step should preferably be conducted in close collaboration with stakeholders and with the HTA commissioning organization. The latter will usually set constraints on the process on the basis of

available time and resources and on the basis of its (sometimes self-professed) remit. Occasionally, defining the terms of reference of an HTA may require a delicate trade-off between feasibility and policy relevance.

Jointly, we would consider these steps the core of an HTA scoping exercise (see Chapter 4). Clearly, stakeholders have a serious role to play in the process, and the method of reconstructing interpretive frames broadly defines the nature of the input that is sought from them. When, how, and how extensively stakeholders are involved in the HTA process may vary from case to case. Saturation can serve as a useful criterion to assess comprehensiveness of the effort (see, for instance, Saunders et al, 2018).

When adopting the VALIDATE approach to HTA, it stands to reason that HTA doers declare, as part of their reporting, who were designated and actually involved as stakeholders, in what way they were involved, and what claims and concerns were solicited in the process. They would also clarify what assumptions they identified as underlying those claims and concerns, how they assessed the validity of those assumptions, and the key findings of their assessment. In other words, they report the outcomes of the scoping exercise, and indicate what selections were made of topics that were included in the HTA.

Broadening the options for decision-makers

If specific ways of using a health technology were found to be based on assumptions that are sufficiently supported by evidence, coherent with current knowledge and consistent with general ethical principles that may be presumed to obtain, this would enable decision-makers to decide whether they are actually *willing* to act upon those findings and assumptions. They can indicate how the health technology is to be used in their jurisdiction, indicate which general ethical principles are thus expressed, and how potential conflicts between general principles were dealt with. Provided that the process of stakeholder involvement and subsequent analysis has worked well, the resulting decision may also be expected to be sufficiently reflective of viewpoints that are held in the relevant community. On the basis of the results of the HTA, decision-makers could also decide to identify any gaps, uncertainties, inconsistencies or conflicts in currently available evidence or interpretations thereof and suggest ways of addressing those in future studies. In a similar vein, they can indicate if any measures will be taken to monitor whether the proposed use of the health technology works out the way it is expected to do.

Broadening the outcome of HTA in this way would, in our view, further enhance the relevance of HTA to policy- and decision-making. Clearly, however, HTA doers need to discuss with commissioning organizations whether they would endorse adoption of a VALIDATE approach to HTA. If anything, it will require a more iterative process, discussing at various stages findings and ways to proceed, given available time and resources. It stands to reason that the HTA team and commissioning organization jointly decide on which of these issues are, in fact, included in the HTA.

A comparison with current practices of HTA

So how does the VALIDATE approach differ from currently prevailing practices of HTA? Current approaches run the risk of being of limited use in squarely facing ethical dilemmas that are posed by technological developments and attaching practical consequences to this. By collaborating with stakeholders in developing a range of policy options and critically analysing those options for empirical support and congruence with general ethical principles, the VALIDATE approach holds the promise of offering a wider range of options for decision-makers. Here, ethical issues, as assumptions regarding what is desirable, are on a par with assumptions regarding what is the case, jointly and in mutual interaction providing guidance to the inquiry (see Chapter 2; Fischer 2007; Lindauer 2020; van der Wilt, 2005).

One should note that there may be conflicts between the perspectives of different stakeholders, generating controversies with respect to goals, outcomes, and evidence used in HTA. While the VALIDATE approach may help (re)solving or reconciliating these, there may be basic conflicts that cannot be addressed. However, the VALIDATE approach provides an open, transparent, and accountable approach that specifies this. It makes the value issues and judgments as well as stakeholders' perspectives more explicit than contemporary HTA.

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Glossary

The definitions provided here are mainly derived from the international HTA glossary, official collaboration between International Network of Agencies for Health Technology Assessment (INAHTA), Health Technology Assessment international (HTAi) and other partner organizations: http://htaglossary.net/HomePage; and key literature referred to in the Handbook.

Axiology	The philosophy or theory of values. A branch of ethics
Background theory	The set of (interrelated) normative and empirical propositions that shape observations and interpretations of an actor; constitutes one layer in an actor's interpretive frames
Coherentism	The belief that an ethical proposition or belief is true and justified if it is part of a network or set of ethical beliefs people hold that are jointly coherent
Congruency	A pragmatic, action-oriented and contextual form of agreement about an issue. We speak of congruency if a problem definition and matching solution have been found that have a sensible meaning each of the actors involved in the issue, to such an action that joint action is conceivable. As different actors may have different interpretive frames these meanings may differ; quintessential is that they yield action that contribute the joint effort
Context	The conditions and circumstances in which an intervention is applied. For example, the setting (in hospital, at home, in an air ambulance), the time (working day, holiday, night-time), the type of practice, (primary, secondary or tertiary care, private practice, insurance practice, charity). However, may also include geographical characteristics, epidemiological characteristics, socioeconomic, sociocultural, political, legal and ethical considerations
Coproduction	Process in which policy objectives are realized between policy makers and actors involved in policy implementation (a policy's target group). It is usually enabled and promoted by policy instruments that help and incentivize the latter actors to act in line with policy objectives
Epistemology	The philosophy of knowledge and how we gain knowledge
Euthanasia	Actively to inject for example potassium chloride in a patient with the intention that the person should die
Evidence-informed deliberative processes (EDPs)	A practical, stepwise approach for HTA bodies to enhance legitimate benefit package design, based on deliberation between stakeholders to identify, reflect and learn about the meaning and importance of values, informed by evidence on these values
Fact	Something that is true, something that can be verified according to an established standard of evaluation

Foundationalism	The belief that there are some values and norms that are self-evident, which we cannot doubt as true and justified, and which we can build upon
Health determinants	Combination of factors that affect the health of individuals and communities. These factors include the social and economic environment, the physical environment, and the person's individual characteristics and behaviours
Health technology	An intervention developed to prevent, diagnose, or treat medical conditions; promote health; provide rehabilitation; or organise healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program, or system
Health technology assessment (HTA)	A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient and high-quality health system
Hospital-based decisions	A specificity of meso-level decisions. This refers to decisions at the managerial level within a specific hospital. The information and facts collected for those decisions are "in" and "for" hospitals. Hospital based decisions consider the level of complexity of the hospital, the structure, the financial capacity (budget), the skills of the professionals, the characteristics of the patients that could be admitted and the society within the hospital is embedded
Interpretive frame	Perspective on a particular issue in a particular context) comprising two layers that are specific to that issue (the problem definition and solution assessment; and two layers with the more generic beliefs that form the lens through which the issue-in-context is perceived: background theories and normative preferences
Judgement	The action-oriented, contextual process of finding for a particular issue a problem definition and solutions that match it. This process essentially iterates between considering the problem and defining associate solutions which the actor sees as feasible and acceptable
Macro-level decisions	It concerns decisions on allocation and utilization of resources in a region, organization, hospital, etc. This level uses instruments that allow policymakers to establish priorities when allocating funds for different healthcare programs or single interventions
Meso-level decisions	It pertains to the clinical decisions that can be used for the treatment of specific conditions or for groups of patients with similar diseases. Optimal treatment policy for groups of patients with similar clinical characteristics. This level uses instruments that allow clinicians to select treatments that have been shown to provide the best overall outcome for groups of patients affected by the same disease
Meta-level decisions	At this level, politicians and managers make decisions regarding the healthcare of large populations balancing the financial and humanitarian aspects of service delivery. For example, in countries where healthcare is public, politicians need to decide what percentage of the total revenue

	will be delivered for health-care among all the other competing needs, e.g., education, defence, infrastructures, research etc.
Micro-level decisions	It concerns decisions on allocation and utilization of resources in a region, organization, hospital, etc. This level uses instruments that allow policymakers to establish priorities when allocating funds for different health-care programs or single interventions
Multi-criteria decision analysis (MCDA)	An umbrella term to describe a collection of formal approaches which seek to take explicit account of multiple criteria in helping individuals or groups exploring decisions that matter
Naturalistic fallacy	The supposed fallacy of inferring evaluative conclusions from purely factual premises
Nihilism	The belief that all values are baseless and that nothing can be known
Non-Invasive Prenatal Testing (NIPT)	A procedure for gaining information about a foetal genotype by examining samples of foetal DNA obtained from the mother's blood
Normative preferences	Fundamental ontological views, forming one layer in an actor's interpretive frames; for a medical professional these may include the determinants of health and disease seen as central, and the own identity viz-a-viz patients, policy makers and others
Ontology	The philosophy of existence, i.e., of being (of things)
Phronesis	Type of wisdom or intelligence relevant to practical action, implying both good judgement and excellence of character and habits
Principlism	A mid-level theory in normative ethics that believes that we share four basic ethical principles that can be applied to solve moral problems: respect for autonomy, non-maleficence, beneficence, and justice
Problem definition	The way in which a specific actor gives meaning to the situation / make sense of an issue as a discrepancy between the state the actor observes or anticipate, and what the actor considers desired (future) state
Problematic conditions	Observable features of the situation that co-constitute an issue)
Quality-adjusted life year (QALY)	A unit of outcome of an intervention where changes to years of life subsequent to this intervention are adjusted according to the quality of life during those years
Realism	The belief that phenomena (such as things) in the world exist independent of human beings experiencing them
Scoping	Defining the objective and research questions of an HTA by a systematic exploration of relevant aspects from multiple perspectives (e.g., patients, informal carers, health professionals, decision-makers)
Solution assessment	How an actor sees and weighs (side-) effects and costs of specific solutions; constitutes one layer in an actor's interpretive frames

Stakeholder	An individual with an interest in the outcome of the HTA process final decision
Stakeholder involvement	An iterative process of actively soliciting the knowledge, experience, judgment and values of individuals selected to represent a broad range of direct interest in a particular issue, for the dual purposes of: creating a shared understanding, making relevant, transparent, and effective decisions
Value	The regard, merit, importance or worth given to something. It is the basis for showing a preference i.e., making a choice