

2017 Policy Forum

From theory to action:
Developments in value frameworks to inform
the allocation of health care resources

"Not everything that counts can be counted and not everything that can be counted counts."¹

Wija Oortwijn
HTAi Policy Forum Scientific Secretary 2016-2017

¹ William Bruce Cameron (1963) "Informal Sociology: A Casual Introduction to Sociological Thinking"
<http://quoteinvestigator.com/2010/05/26/everything-counts-einstein/>

1. Introduction

Health Technology Assessment (HTA) is the process for assessing the value of health technology. This means that HTA organisations use frameworks to assess the value of health technologies; while additional value parameters (i.e., criteria) might be used (and more implicitly) in making decisions to allocate health care resources. An example of the latter is that there are concerns that political pressures may enhance access to cost-effective health technologies for certain patient groups while other patient populations may lose out within available budgets.² This has led to an increased attention for the development and use of value frameworks to inform decisions regarding allocation of scarce health care resources around the globe.

The overall objective of the Policy Forum meeting 2017 is to explore current experiences with value frameworks used to inform the allocation of health care resources. It will also explore new proposed frameworks, and if and how they are better shaped to the needs of decision-makers.

The purpose of this Background Paper is to present an overview of existing and new/emergent value frameworks that have recently been developed and the key issues at stake. We provide a representation of different value frameworks, not necessarily striving for completeness, in order to inform discussions during the 2017 Policy Forum meeting. The information comes from scientific and grey literature mainly published in the past few years, identified by: the author through a structured search in Google Scholar and of reviewing websites of relevant organisations developing value frameworks, the HTAi Policy Forum Committee, Policy Forum members and the wider HTAi community.

With regard to existing value frameworks, we present how value frameworks are used by HTA agencies (that are a member of the Policy Forum) and if and how they have changed over time. For this purpose we have asked the HTA agency members to fill in/update the Table (2) that was presented in the Background Paper of 2013' Policy Forum.³

Outline

Section 2 of this Paper describes the background to the choice of this topic, including an overview of past Policy Forum discussions. The subsequent Sections (3-5) provide an overview of existing and new value frameworks with regard to:

- coverage/reimbursement decision-making;
- clinical decision-making;
- decision-making to purchase a health technology at provider level.

It is worthwhile to mention that the majority of providers in the US are incurring at least some financial risk for patients and are therefore engaging in value appraisal that is identical to that of the payer.⁴

In Section 6, we present examples of how value frameworks have been used in practice and that illustrate key challenges related to the topic. The case studies have been carefully selected, using the valuable input from Policy Forum Members. Finally, in Section 7 the main issues are summarised to feed into the 2017 Policy Forum meeting.

² Godman, B., Oortwijn, W., De Waure, C., Mosca, I., Puggina, A., Specchia, M.L., Campanell, P. Van der Tuin., J. Links between pharmaceutical R&D models and access to affordable medicines. European Parliament. Directorate General for Internal Policies. Policy Department a: economic and scientific Policy. European Union, PE 587.321 EN. IP/A/ENVI/2015-06, October 2016. Available via: [http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU\(2016\)587321](http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU(2016)587321)

³ 2013 Policy Forum Background Paper. HTA and Value: Assessing value, making value-based decisions and sustaining innovation.

⁴ Information provided by a Policy Forum Member.

2. Background

Nowadays, there is access to some disruptive health technologies (e.g. Hepatitis C drugs), while other health technologies are emerging, and expecting, to quickly access the market (e.g. personalised medicines, in-vitro diagnostics, especially molecular diagnostics, and disruptive medical devices). On the other side decision-makers at different levels in the health care systems are faced with the difficult task to maintain high quality, innovative, and sustainable health care while managing health care budgets, safeguarding equity, access and choice. The tension between rising health care costs and the ability to finance these for everyone in society at sustainable costs is well recognised but getting more intense. The rising health care costs, and the perceived disconnect between the price and value of health technologies is one of the reasons that has led to a proliferation of value frameworks around the globe.⁵

To inform decision-making processes and to underpin final decisions, definitions (or conceptualization) of what is considered as a valuable health technology has to be made. This conceptualization is frequently based on, or complemented by, the development of what it is called "value frameworks", where different criteria are worth taking into account when assessing "value". The way in which value is being assessed is determined by a judgment on the relative importance of a range of criteria that may differ between (political and cultural) contexts (e.g. appraisal committees in different countries). The criteria could be the same across value frameworks and include, for example, burden of disease, effectiveness, cost-effectiveness, and budget impact. The criteria by themselves, however, also include value judgments. For example, in selecting relevant end-points and deciding on comparators when determining effectiveness of a health technology. In addition, the criteria (and related decisions) are often valued differently by stakeholders such as patient representatives, health professionals, policy makers, payers, academic researchers, industry members, carers, citizens, etc. Many of the value judgments are therefore implicit or tacit. Acknowledging and explicitly addressing value judgments may improve the accountability of HTA and related decision-making processes.⁶

The topic of 'value' has been (partly) discussed during HTAi Policy Forums that have been held in the past; i.e.:

- 2013 Policy Forum – "HTA and value: assessing value, making value-based decisions and sustaining innovation"; and
- 2016 Policy Forum – "Changing HTA paradigms" (theme 2 – rethinking value, affordability and access)

Below, we present the key elements from these Policy Forum discussions that are relevant in order to identify learnings and to build upon during 2017 Policy Forum meeting. Better understanding of past developments may make it easier to grasp the elements that led to the developments of new frameworks, as well as those that will drive the future.

2013 Policy Forum discussion

In 2013, the Policy Forum addressed the topic "HTA and value: assessing value, making value-based decisions and sustaining innovation". During the 2013 Policy Meeting various elements were discussed that may be seen as constituting value, and several quantitative and qualitative approaches to determining value used by different countries were considered. In addition, developments by that time in value-based pricing (UK, Germany and Canada), value-based insurance design (USA) as well as the impact of value assessments on innovation processes were also discussed.

2016 Policy Forum discussion

During the 2016 Policy Forum meeting ("Changing HTA Paradigms"), the concept of value was discussed in relation to affordability and access of health technologies. In this context, the use of multi-criteria decision analysis (MCDA), the relation of value to price, and alternative reimbursement models were discussed. In the supporting Background Paper, developments of value-based assessment by HTA agencies in Europe intended to support population health / payer considerations were briefly described,

⁵ Philipson, T.J., Shafrin, J. Are you just a number? How new value frameworks miss the point. Available via: <http://www.forbes.com/sites/tomasphilipson/2016/08/04/are-you-just-a-number-how-new-healthcare-value-frameworks-miss-the-point/#2e0b5924687f>

⁶ Hofmann, B., Cleemput, I., Bond, K., Krones, T., Droste, S., Sacchini, D., Oortwijn, W. Revealing and acknowledging value judgments in HTA. *International Journal of Technology Assessment in Health Care*, 2014 Dec;30(6):579-86. doi: 10.1017/S0266462314000671;

as well as recent attempts in the US that are mainly intended to inform patient-clinician conversations. These latter frameworks include assessing the value of treatment to patients, consumers and health care providers (e.g. by the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN) and Memorial Sloan Kettering Cancer Center (MSKCC)). In addition, the framework of the Institute of Clinical Effectiveness and Review (ICER) to determine value-based prices was described.⁷

2017 Policy Forum meeting

Recently, other relevant new value frameworks have emerged (e.g. Balanced Assessment System (BAS) targeting middle-income countries⁸), as well as developments in methodology for measuring value (Advance-HTA⁹ and INTEGRATE-HTA¹⁰ – projects funded by the Research Framework Programme of the European Commission (FP7) until the end of 2015). Some of the newer value frameworks aim to address the limitations presented by older frameworks, i.e. to properly consider the value of innovative and complex health technologies as well as to focus on patient-centeredness.

As described in the 2013 Background Paper and recently confirmed during a conference on US value frameworks¹¹, there is no uniform definition of value. It depends, for example, on the backgrounds of authors (e.g. economics, medicine, psychology)¹². In the field of HTA, most definitions relate to value for-money/willingness to pay (WTP) or include broader concepts such as the importance or desirability that patients (or society) place on a health state, or the social/psychological aspects of living with an illness or of using a technology, and/or the ethical implications of technology use.¹³ It is, however, known that the way in which value of health technology is viewed, measured and incorporated into the decision-making process is context dependent. It is, therefore, important to understand that recent and current global social, environmental and economic problems (e.g. financial crises, climate change) have raised public awareness and led people to demand stakeholders to become more accountable. Also, healthcare systems around the globe seem to evolve toward more accountability for outcomes and move to value-based reimbursement. Fair allocation decisions are expected to concern all relevant stakeholders. However, the principles and considerations that people think are important or relevant differ.¹⁴ This means that inclusion of different stakeholders' viewpoints influences the concept of value and, therefore, the criteria to include in the value frameworks. Consequently, the nature of value frameworks proposed or adopted by different stakeholders or health systems varies.

Key questions to be addressed in this Background Paper are therefore:

- What are the domains/elements of determining value in these frameworks?;
- What – if any - are the ways to aggregate domains/elements leading to a recommendation or decision (e.g. use of Quality Adjusted Life Years (QALY) for benefits, attachment of different WTP to QALYs depending on severity and condition treated; use of MCDA);
- Why have these new frameworks been introduced?;
- Are they a better fit for purpose to decision-makers' needs and to addressing different stakeholder viewpoints (i.e. are they considered legitimate and fair)?;
- Are they the same or different from earlier work?;
- Are 'older' frameworks that have been updated taking into account emerging needs?;

⁷ 2016 Policy Forum Background Paper. Changing HTA Paradigms. D. Husereau on behalf of the HTAI Policy Forum, 8 January, 2016.

⁸ Danko, D.(2014). Health technology assessment in middle-income countries: recommendations for a balanced assessment system. *Journal of Market Access & Health Policy*, 2: 23181 - <http://dx.doi.org/10.3402/jmahp.v2.23181>

⁹ <http://www.advance-hta.eu/>

¹⁰ <http://www.integrate-hta.eu/>

¹¹ Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016.

¹² Shams, L., Akbari Sari, A., Yazdani, S. (2016). Values in Health Policy – A Concept Analysis. *International Journal of Health Policy and Management*; 5(11), 623–630. doi 10.15171/ijhpm.2016.102

¹³ 2013 Policy Forum Background Paper. HTA and Value: Assessing value, making value-based decisions and sustaining innovation.

¹⁴ Heitman, E. Ethical issues in technology assessment: conceptual categories and procedural considerations. *International Journal of Technology assessment in Health Care* 1998; 14: 544-566

- Does one-size value framework fit all types of health technologies?;
- Can the value frameworks be used for assessing the value of emerging disruptive health technologies?

These questions are addressed in presenting existing and new value frameworks below, according to certain criteria including (whenever feasible):

- Name and initiator/funder of the value framework;
- (Potential) purpose of framework – linking it to the HTA process: Identification of health technologies, prioritisation, assessment, appraisal/decision-making, other;
- Target audience: Policy-makers, Payers, Physicians, Patients;
- Whose values are at stake (from which perspective is the value framework determined: patient, the provider, the payer(s), the public in general, several stakeholders);
- Objectives of the framework;
- Specific health technology (e.g. diagnostics, vaccines, drugs etc.) / condition to be addressed;
- Principles underlying the framework (i.e. why is it introduced);
- Key elements in determining value;
- Aggregation of key elements (if any);
- Evolution of the domains of value included in these frameworks;
- Methodology used for developing the value framework (have multiple stakeholders been involved?);
- Use in practice.

The overall intention is to give meaning to the patterns of change that are unfolding, i.e. shifts in valuing health care which are caused by the combined effect of changing economic, socio-cultural, and technological realities. These insights can help guide the transformation of thinking about the role of industry in developing valuable innovations and HTA required to sustain future health care systems.

3. Value frameworks in coverage/reimbursement decision-making

As stated in the 2013 Policy Forum Background Paper, most health systems base coverage/reimbursement decisions on some kind of formal or informal determination of the value of a health technology. Payers, however, frequently perceive value as a function of benefit minus the cost, WTP for benefit, and how to handle uncertainty.^{15,16}

The aspects considered by decision-makers regarding coverage decisions traditionally include the direct and indirect effects, such as the level of clinical benefit (compared to the current standard) and incremental cost-effectiveness. More recently, indirect, unintended or 'hidden' outcomes (e.g. challenges of patient autonomy, potential benefits and harms for other stakeholders) are increasingly being considered to allow for value based decisions.¹⁷

¹⁵ Paris, V., Belloni, A., July 2013, Value in Pharmaceutical Pricing, OECD Health Working Paper, No 63, OECD Publishing: Paris. DOI:10.1787/5k43jc9v6knx-en

¹⁶ Towse, A., Barnsley, P. (2013). Approaches to identifying, measuring, and aggregating elements of value. *International Journal of Technology Assessment in Health Care*, Oct;29(4):360-4. doi: 10.1017/S0266462313000524; NPC Conference September 2016.

¹⁷ Tanios, N., Wagner, M., Tony, M., Baltussen, R., van Til, J., Rindress, D., Kind P., Goetghebeur, M.M., and the International Task Force on Decision Criteria. (2013). Which criteria are considered in healthcare decisions? Insights from an international survey of policy and clinical decision makers. *International Journal of Technology Assessment in Health Care*, 29(4), 456-465. doi:10.1017/S0266462313000573.

Existing value frameworks - examples

An overview of value frameworks used by HTA organisations in selected jurisdictions was presented in the 2013 Background Paper. In order to see if and how these frameworks have changed over time, taking into account the current needs of the health care system, we asked Policy Forum members to fill in/update the Table that previously presented these details. The results from the organisations that responded are presented in Table 1. below. Please note that:

- Column heading US¹⁸
- + = yes;
- Blue text = information from organisations not included in the 2013 Background Paper (MSAC, BCBSA, KP);
- Red text indicates updates/changes since 2013 as provided by organisations included in the 2013 Background Paper (PBAC, CADTH, TLV, ZIN, NICE). Additional information provided by (some of) these organisations is presented as well.

Table 1. Value frameworks used by Policy Forum Members

	Australia		Canada	Sweden	Netherlands	UK	US ¹⁸	US
	MSAC	PBAC	CADTH	TLV	ZIN	NICE	BCBSA TEC	KP
Types of technologies/ interventions assessed								
• Drugs		+	+	+	+	+	+	+
• Devices	Permanently implantable therapeutic devices indirectly, when they require a new surgical procedure		+	+	+	+	+	+
• Procedures, diagnostics, tests, surgeries	+		+	To some extent	+	+	+	+
• Public health interventions	in theory, but rare in practice		+			+		+
• Systems/services/delivery	in theory, but rare in practice		+		+	+	+	+

¹⁸ All coverage decisions are made independently by the 36 member Blue Cross and Blue Shield Plans. Collectively, the plans provide health care coverage to 106 million beneficiaries, approximately one in three of the US population

	Australia		Canada	Sweden	Netherlands	UK	US ¹⁸	US
Information requirements	Required: comparative clinical benefit and safety, health economic information to establish value for money, budget impacts. Other aspects of value as listed below are also assessed when relevant.	Required: comparative clinical benefit and safety, health economic information to establish value for money, budget impacts. Other aspects of value as listed below are also assessed when relevant.	Clinical benefit; health economic information required to establish value for money. Other evidence on equity, public health, and budget impacts may be submitted.	Clinical benefit; health economic information required to establish value for money. Other evidence on disease burden/severity and equity impacts may be submitted.	Four criteria: Necessity, Effectiveness, Cost-Effectiveness Appropriateness. This includes burden of disease, budget-impact but also social, legal, ethical and organisational aspects.	Clinical benefit; health economic information required to establish value for money. Other evidence on societal preferences, equity impacts, innovative characteristics, and budget impact may be submitted.	Clinical assessment, weighing benefits and harms to assess net health benefit. The process aligns with the SMRA/ASMR, but is dichotomous: there is or is not sufficient evidence of improvement in net health benefit. BCBSA is considering, but have not implemented, stratified judgements of level of net health benefit.	When an analysis is conducted, KP seeks published clinical trials, KP research, compiled health outcome data, and registries, and Permanent expert opinion. The clinical expert opinion from Permanent physicians and other health care professionals is used to guide the problem formulation for the analysis and to understand current clinical practice and operational considerations, including available alternatives.
Assessment of therapeutic value (preferred/required approach)								
• QALY	+	+	+	+	+	+		
• SMR/ASMR							+ (see above)	
• Benefit assessment categorization								
Assessment of economic value (preferred/required approach)								Assessment of the economic value is not required as part of the evidence review of a given technology. Consideration after a positive outcome from an evidence review, when KP is a determining deployment strategy.
• CUA	+, preferred	+, preferred	+	+	+	+		
• CEA	In some cases	In some cases	+	In some cases	In some cases	In some cases		
Assessment of economic value (preferred/required approach)								Assessment of the economic value is not required as part of the evidence review of a given technology.
• CMA	In some cases	In some cases	+	+	In a few cases	Yes (newly Abbreviated TA)		
• CBA				In some cases				

	Australia		Canada	Sweden	Netherlands	UK	US ¹⁸	US
Patient subgroup analysis required or considered	+	+, where applicable	+	+	+	+		Considered if methodologically sound and population is relevant.
Aspects of value assessed								
• Size of therapeutic effect	+	+	+	+	+	+	+	+
• Quality of clinical evidence	+	+	+	+	+		+	+
• Burden/prevalence of disease	+	+	+	+	+			+
• Relevant clinical endpoints	+	+	+	+	+		+	+
• Clinical uncertainty	+	+	+	+	+	+		+, Qualitatively
• Cost-effectiveness (and degree of uncertainty in economic analyses)	+	+	+	+	+	+		Consideration of published, high quality cost studies would be after a positive outcome from an evidence review, when KP is a determining deployment strategy.
• Quality of clinical and economic modelling evidence	+	+	+	+	+			Quality and relevance of clinical modelling would be considered if available. Economic modelling would be considered after the evidence review if KP is a determining deployment strategy.
• Budget impact	+	+	+	In some cases	+			Consideration after a positive outcome from an evidence review, when KP is a determining deployment strategy.
• Severity of disease	+	+	+	+	+		+	+
• Availability of treatment alternatives	+	+	+	+	+	+	+	+
• Public health impact	+	+	+					+
• Innovative characteristics	Focussed on those which improve health	Focussed on those which improve health						Not explicitly, operational impact noted and studied more formally with deployment strategy.

	Australia		Canada	Sweden	Netherlands	UK	US ¹⁸	US
• Legal/ethical/equity considerations	+	+	+	+	+			+
• Patient affordability	+	+			+			Consideration after a positive outcome from an evidence review, when KP is a determining deployment strategy. However, KP would be mindful at the time of the evidence review of a technology that has the potential to provide a safe, high quality outcome that is more affordable than current alternatives. This would be a qualitative consideration.
• Social values/preference	+	+			+	+		Qualitatively
• Other specify								How the patient may benefit
Decision threshold	None fixed.	None fixed.		None fixed. Examples around 500,000 SEK (USD\$74,000)	None fixed, but there are three categories which reference values based on the burden of disease are defined: 0,1 - 0,4 DALY: up to € 20.000 per QALY 0,41 - 0,7 DALY: up to € 50.000 per QALY 0,71 - 1,0 DALY: up to € 80.000 per QALY	Cost per QALY threshold of approx. £20,000 - £30,000	BCBSA does not conduct assessments of economic value. However, a few of member Plans have adopted a value approach to drug benefits, largely using QALYs to assess cost-effectiveness. These Plans use value assessment to tier drugs, with patients paying lower out of pocket portion for drugs deemed high value. There are typically four tiers.	

Additional information provided:

NICE will be implementing an Abbreviated Technology Appraisal process using a cost-comparison value framework. The additional value framework provides a simplified approach for the evaluation of health technologies that provide similar or greater health benefits compared with existing NICE-recommended technologies, at similar or lower costs. The additional value framework was subject to a consultation process. To allow NICE to meet an expected increase in demand for technology appraisal guidance by providing a robust but less resource-intensive process option for technologies where cost-utility analysis is not necessary to evaluate value.

TLV develops its practice continuously and publishes guidelines on how to conduct health economic assessments. The "framework" is a very rough instrument of making a standardized description resulting in an HTA product. When health economy is assessed TLV no longer considers costs in added life years and they are hesitant to include productivity effects, given the risk of age discrimination. TLV has since 2014 introduced tripartite talks between the agency, the county councils and the pharmaceutical companies. This allows for risk sharing and this has in turn put a higher emphasis on uncertainties. In addition, TLV involves stakeholders in discussions on the ongoing development of the agencies' practice.

ZIN mentioned that the cost-effectiveness guideline has been updated since 2013. Also, the guideline for the clinical assessment (Stand van de Wetenschap en Praktijk) has been updated. The main reason for this was adaptation to the most up to date scientific knowledge. Changes to the framework were also based on last standing discussions with the stakeholders; for instance on the role of cost-effectiveness. There has been involvement of different stakeholder groups: decision-makers, clinicians, payers, patients, public as well as politicians – addressing the needs of the health care system.

HTAi 2016 Asia Policy Forum

As input for the HTAi Asia Policy Forum Meeting in November 2016, which was focused on assessing value for expensive medicines, delegates were asked to complete a questionnaire, including questions about current approaches to assessing value. Five out of the seven countries participating (China, Japan, Malaysia, Singapore, and Thailand) mentioned that an explicit value framework is in place, while Taiwan mentioned not to use an explicit value framework. The countries using an explicit value framework all mentioned to use the following criteria: QALYs, cost per QALY, and added clinical benefit and cost. The majority (4/5) also uses therapeutic added value and added clinical benefit as criteria. Qualitative methods (such as deliberation and discussion) are most often used for weighing the decision making criteria. Furthermore, three countries mentioned to use different value elements or value frameworks for drugs and medical devices. An example mentioned was that cost per QALY is used for assessing drugs, while this might not always be feasible for medical devices. Hence, the focus is on added clinical benefits and cost.

EUnetHTA

Since 1993, the European Commission has funded several HTA projects to enhance collaboration between Member States (MS) in the European Union (EU). Since 2006, EUnetHTA¹⁹ has coordinated these activities. EUnetHTA is a "network of government appointed organisations (from EU MS, EU-accession countries, plus EEA and EFTA countries) and a large number of relevant regional agencies and non-for-profit organisations that produce or contribute to HTA in Europe".²⁰ The collaboration has already resulted in among other things methodological guidelines²¹ and tools such as the HTA Core Model® - a methodological framework for shared production and use of HTA information in the field of diagnostic technologies, medical and surgical interventions, drugs and screening technologies. The purpose is "to enable production of high quality HTA information in a structured format to support the production of local (national or regional) HTAs and reuse of existing information".²² This model is considered as the value framework to be used by HTA organisations when assessing technologies within the EU. Current practice, however, shows diverging outcomes even when the same criteria are used (Table 2). Torbica, Drummond, Ferré et al (2015) found that the approach taken is linked to the underlying culture and values of a country, the specific institutional context and the organisation, governance and financing of the health care system.²³ For example, France has recently introduced, in addition to the assessment of added clinical benefit (ASMR), an economic evaluation for drugs and medical devices that may be eligible to a higher price than comparators because they claim to bring added clinical benefit.²⁴

¹⁹ <http://www.eunetha.eu>

²⁰ <http://www.eunetha.eu/about-us/organisation>

²¹ <http://www.eunetha.eu/eunetha-guidelines>

²² <http://www.eunetha.eu/hta-core-model>

²³ Torbica, A., Drummond, M., Ferré, F., Tarricone, R., Fattore, G. Economic evaluation and health technology assessment in Europe and USA. A comparative analysis. Executive Summary. Deliverable 4.1. MedtecHTA. February, 2015. http://www.medtecha.eu/wps/wcm/connect/272245ac-ebec-4709-a7b1-35a8a6c9c8bd/ExecutiveSummary_+MedtecHTA+WP4_D4.1.pdf?MOD=AJPERES

²⁴ Information provided by a Policy Forum Member.

Table 2. Recommendation regarding (selected) oncology drugs having received marketing authorisation (2011-2013) in selected EU countries^{25,26}

Abbreviated indication	Brand name (generic)	HTA recommendation					
		Germany	The Netherlands	France	England/Wales	Scotland	Poland
Breast cancer	<i>Eribulin</i>	Equal benefit	Added benefit	Added benefit	Negative	Negative	Negative
Colorectal cancer	<i>Aflibercept</i>	Added benefit	Not assessed	Equal benefit	Negative	Negative	Positive
Gastric cancer	<i>Tegafur/ Gimeracil/ Oteracil</i>	Not assessed	Lesser benefit	Lesser benefit	Not assessed	Positive	Negative
Melanoma	<i>Ipilimumab</i>	Added benefit	Added benefit	Added benefit	Positive	Negative	Positive
Non-small cell lung cancer	<i>Crizotinib</i>	Equal benefit	Not assessed	Added benefit	Negative	Negative	Negative
Prostate cancer	<i>Abiraterone</i>	Added benefit	Equal benefit	Added benefit	Positive	Negative	Positive
Renal cell carcinoma	<i>Axitinib</i>	Added benefit	Not assessed	Added benefit	Positive	Negative	Positive

The HTA Core Model currently includes nine domains: Health problem and current use of technology, Description and technical characteristics of technology, Safety, Clinical effectiveness, Costs and economic evaluation, Ethical analysis, Organisational aspects, Patient and social aspects, and Legal aspects. The development of the Model has evolved over the years by using public consultation. The current version (3.0) of the HTA Core Model® dates back from December 2015. In comparison with the former version, one of the changes was that the Social Aspects domain has been renamed to Patients and Social Aspects domain, and its content has undergone a major revision.²⁷

²⁵ Based on: Kleijnen, S., Lipska, I., Leonardo Alves, T., Meijboom, K., Elsada, A., Vervölgyi, V., d'Andon, A., Timoney, A., Leufkens, H.G., De Boer, A., Goettsch, W.G. (2016). Relative effectiveness assessments of oncology medicines for pricing and reimbursement decisions in European countries. *Annals of Oncology*, 27 (9): 1768-1775. doi: 10.1093/annonc/mdw233. Epub 2016 Jun 20

²⁶ The same pattern of diverging outcomes across EU countries was presented for diabetes drugs in the Inception Impact Assessment Report "Strengthening of the EU cooperation on HTA" of the European Commission (2016). The report is open for public consultation from 4 October 2016 until 13 January 2017. Available at: http://ec.europa.eu/dgs/health_food-safety/dyna/enews/enews.cfm?a_id=1724

²⁷ <http://eunethta.eu/sites/5026.fedimbo.belgium.be/files/HTACoreModel3.0.pdf>

In 2009, the EUnetHTA Collaboration joined forces with other partners in the European Union and the European Commission to conduct joint assessments and implement the results. This so-called Joint Action has evolved over the years; Joint Action 3 (JA3) started on June 1, 2016 (see Figure 1).

Figure 1. Overview HTA cooperation in the EU (funded by EC)



Source: based on Ecorys, 2013²⁸ EUnetHTA JA2 Final Technical Report, 2016²⁹

In total, EUnetHTA has finalised 20 joint assessments (see Table 3).³⁰ EU cooperation on HTA projects has the potential to increase the quality of HTA while reducing duplication and research efforts for both the HTA body and the health technology developer. An assessment can either be a rapid Relative Effectiveness Assessment (REA) or a full HTA. A REA assesses the incremental therapeutic value of technologies and covers the following domains: health problem and current use of technology, description and technical characteristics, safety and clinical effectiveness. A full HTA takes a broader perspective and includes also the following domains: costs and economic evaluation, ethical analysis, organisational aspects, patient and social aspects, and legal aspects.

In particular, the results of research on relative effectiveness of health technologies could be shared between MS. In 2011, EUnetHTA JA1 published a background review on REA.³¹ In this report it was concluded that most of countries carry out some form of REA to support national reimbursement decisions of drugs, but the scope (comparators and cost considerations) and the methodology used vary across countries.³² Consideration of cost-effectiveness and ethical issues often depend on the health system, reimbursement processes as well as the socio-cultural context and the level of GDP per capita in specific MS.

²⁸ Ecorys. Study providing an economic and governance analysis of the establishment of a permanent secretariat for the European Cooperation on Health Technology Assessment. Rotterdam, 2013. Available at: <http://www.eunetha.eu/news/eunetha-ja2-final-technical-report-approved-be-submitted-european-commission>

²⁹ EUnetHTA JA2 Coordinator. EUnetHTA JA2 Final Technical Report. Executive Summary, May 2016. Available at: <http://www.eunetha.eu/news/eunetha-ja2-final-technical-report-approved-be-submitted-european-commission>

³⁰ <http://www.eunetha.eu/joint-assessments>

³¹ EUnetHTA JA WP5: Relative Effectiveness Assessment (REA) of Pharmaceuticals – Background review July 2011 (version 5B).

³² Goettsch, W. Presentation: "Relative effectiveness assessment of pharmaceuticals (WP5) EUnetHTA JA1": EUnetHTA Conference 8 December 2011, Gdansk, Poland.

Table 3. Overview of finalised joint assessments within EUnetHTA

	Full HTA	Relative Effectiveness Assessment	National adaptation of REA/Full HTA ³³
EUnetHTA Project (2006-2008)	<p>Drugs</p> <ul style="list-style-type: none"> • MSCT Angiography • Drug Eluting Stents (combination drugs/medical device) 		
EUnetHTA JA (2010-2012)	<p>Drugs</p> <ul style="list-style-type: none"> • Pazopanib <p>Other technologies</p> <ul style="list-style-type: none"> • Abdominal Aorta Aneurysm Screening • Prognostic tests for breast cancer recurrence 		<ul style="list-style-type: none"> • Abdominal Aorta Aneurysm Screening (Austria, Croatia, Norway)
EUnetHTA JA2 (2012-2015)	<p>Drugs</p> <ul style="list-style-type: none"> • Use of Intravenous immunoglobulins for Alzheimer's disease including Mild Cognitive Impairment <p>Other technologies</p> <ul style="list-style-type: none"> • Faecal Immunochemical Test versus guaiac-based faecal occult blood test for colorectal cancer screening • Structured telephone support for adult patients with chronic heart failure 	<p>Drugs</p> <ul style="list-style-type: none"> • Canagliflozin for the treatment of type 2 Diabetes Mellitus • Sorafenib for the treatment of progressive, locally advanced or metastatic, differentiated Thyroid Carcinoma, refractory to radioactive Iodine • New drugs for the treatment of Chronic Hepatitis C • Ramucirumab in combination with Paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction Adenocarcinoma • Vorapaxar for the reduction of thrombotic cardiovascular events in patients with a history of myocardial infarction • Zostavax for the prevention of Herpes Zoster and post herpetic Neuralgia <p>Medical devices and other technologies</p> <ul style="list-style-type: none"> • Balloon Eustachian tuboplasty for the treatment of Eustachian tube dysfunction • Biodegradable stents for the treatment of refractory or recurrent benign Oesophageal Stenosis • Duodenal-jejunal bypass sleeve for the treatment of Obesity with or without type 2 Diabetes Mellitus • Endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke • Renal denervation systems for treatment-resistant hypertension • Transcatheter implantable Devices for mitral valve repair in adults with Chronic Mitral Valve Regurgitation 	<ul style="list-style-type: none"> • Faecal Immunochemical Test versus guaiac-based faecal occult blood test for colorectal cancer screening (Austria, Romania, Estonia, Slovenia, Spain, Switzerland) • Canagliflozin for the treatment of type 2 Diabetes Mellitus (Netherlands, Spain, Italy, Luxembourg, Malta, Portugal, Slovakia, Spain, Sweden) • Sorafenib for the treatment of progressive, locally advanced or metastatic, differentiated Thyroid Carcinoma, refractory to radioactive Iodine (Scotland, Belgium, Portugal, Slovakia, Spain) • Ramucirumab in combination with Paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction Adenocarcinoma (Austria, Belgium, Finland, Slovakia) • Zostavax for the prevention of Herpes Zoster and post herpetic Neuralgia (Austria, Belgium, Netherlands, Sweden) • Balloon Eustachian tuboplasty for the treatment of Eustachian tube dysfunction (Austria, Finland, Spain, Slovakia) • Biodegradable stents for the treatment of refractory or recurrent benign Oesophageal Stenosis (Austria, Netherlands, Slovakia, Spain) • Duodenal-jejunal bypass sleeve for the treatment of Obesity with or without type 2 Diabetes Mellitus (Austria, Netherlands, Spain, Slovakia) • Endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke (Austria) • Renal denervation systems for treatment-resistant hypertension (Austria, Italy, Slovakia, Spain, Scotland) • Transcatheter implantable Devices for mitral valve repair in adults with Chronic Mitral Valve Regurgitation (Austria)

³³ This concerns the results in national/regional setting in order to avoid duplication, to promote good practices in HTA processes and to effectively use time and financial resources. See: <http://www.eunetha.eu/national-uptake>

European Parliament

In September 2016, the European Parliament (Committee on the Environment, Public Health and Food Safety – ENVI) presented a draft report on EU-options for improving access to medicines. In the report it is clearly stated that the following criteria need to be taken into account for pricing and reimbursement of drugs: real therapeutic added value of a medicine (compared to the best available alternative), the social impact, the cost benefit, the budget impact and efficiency for the public health system. Furthermore, the European Parliament calls the EC to “harmonise pricing and reimbursement criteria to take into account the level of innovation and the social and economic cost-benefit analysis, and to put in place a European classification on the added value level of medicines”. The options will be worked out in more detail (until 2019).³⁴

Besides EU value frameworks, recent value frameworks in the US, include:

Memorial Sloan Kettering Cancer Center – DrugAbacus

DrugAbacus is a web-based tool to help patients and physicians determine what cancer drugs should cost based on several criteria: efficacy, tolerability, novelty, research and development costs, rarity³⁵, population burden, unmet need, and prognosis.³⁶ Patient experiences are included in determining tolerability and clinical experts scored the novelty of each drug. DrugAbacus also allows users to weigh each criterion in determining the right price for them and thereafter it is compared to the actual price.³⁷ In total, more than 50 cancer drugs that were approved by the US FDA between 2001 and 2015 are included in DrugAbacus.³⁸

Institute for Clinical and Economic Review (ICER)

The value framework from ICER aims to include affordability in the assessment and reimbursement decisions.³⁹ It has been described in the 2016 Background Paper as follows: “The ICER Framework is being used to develop “value-based” prices for 15 to 20 FDA approved drugs over the next two years....which is “the price range within which all patients could be treated with reasonable long-term care value without adding short-term costs to the health care system that would contribute to health care spending growing faster than the overall economy.” At this moment in time, ICER is in a process of soliciting proposals for revision to the value framework, with input from all stakeholders, and with a focus on determining more explicit ways to capture value domains outside of incremental cost-effectiveness. The aim is that the revision process will be finalised by January 2017.⁴⁰

In Section 4, more information on these two value frameworks is presented by comparing them to other US value frameworks used in clinical decision-making.

³⁴ Cabezón Ruiz, S. (rapporteur). Draft Report on EU options for improving access to medicines. (2016/2057(INI)). European Parliament. Committee on the Environment, Public Health and Food Safety, 19.9.2016. Available at: <http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+COMPARL+PE-587.690+01+DOC+PDF+V0//EN&language=EN>

³⁵ Defined as projected incidence of the disease in 2015 as per the American Cancer Society Facts & Figures Report.

³⁶ Defined as severity of the disease that the drug is targeting to treat.

³⁷ <http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+COMPARL+PE-587.690+01+DOC+PDF+V0//EN&language=EN>

³⁸ <http://www.drugabacus.org/>

³⁹ Bach, P.B. (2015). New Math on Drug Cost-Effectiveness. *The New England Journal of Medicine* 373, no. 19 (November 5, 2015): 1797–99, doi:10.1056/NEJMp1512750.

⁴⁰ Policy Forum Member Feedback on the outline of this Background Paper.

Reflection

All the above-mentioned value frameworks are operational and the impact of their application is publicly available and used in resource allocation decisions in the selected jurisdictions.

With regard to Table 1, we remark that comparison with the situation in 2013 is complicated due to the fact that some aspects were considered to be missing by HTA organisations. However, it becomes clear that several HTA-agencies have adapted their value frameworks, especially in terms of broadening the scope of health technologies to be assessed and aspects of value to be considered (especially Quality of clinical evidence, Clinical uncertainty, and Quality of clinical and economic modelling evidence).

Finally, multiple stakeholders have been included in reviewing/developing the value frameworks (i.e. ZIN in the Netherlands, TLV in Sweden, EUnetHTA HTA Core Model and ICER in the US), which have led to some changes to their original frameworks.

Recent and new developments

This observation is in line with the more recent discussions that indirect (unintended) outcomes should also be considered to allow for value based decisions.⁴¹ After all, decision-makers need assessments that are contextualised, involve a range of stakeholders, take interdependence and interactive aspects into account, and consider varying patient characteristics in addition to effectiveness, economic, ethical, legal and social aspects. Current HTA-methodologies and decision-making informed by HTA (appraisal) only partly respond to these issues.⁴²

For this purpose, **new methodological approaches** have been developed including:

ADVANCE-HTA

ADVANCE-HTA is a FP7 project including academic/scientific organisations, patient and professional NGOs, HTA organisations, international organisations; experts from a wide range of disciplines and professional backgrounds. The overall aim is to improve methods and practices regarding the application and implementation of HTA, including value assessments.⁴³ The project that finished in December 2015 aimed to:

- understand the parameters of value in HTA appraisals from an international perspective;
- explore how factors such as disease severity, burden of disease, distinguishing between levels of innovation, and the quality of the available evidence can be incorporated more explicitly – and in a quantifiable way, in the HTA process;
- explore how alternative analytical frameworks, such as MCDA, can be used to elicit value;
- conduct case studies in the field of orphan drugs as well as colon cancer by using alternative analytical tools and by explicitly incorporating all identified parameters of value.

The findings show that "if HTAs include criteria which relate to (low) prevalence and severity of distress and other exceptional burdens that rare diseases can impose on entire families/specific ethnic/racial minorities, then they are more likely to be judged affordable than if more general assessment methodologies or processes are used. Patient access is also likely to be affected by the existence or otherwise of additional HTA evaluation modifying factors. These could relate to not only the value of demonstrating social solidarity in situations where only relatively small numbers of people are involved, but also the social fact that at given points in history some disease may be popularly seen as deserving greater investment than others. Such prioritisation judgement may be driven by subjectively perceived

⁴¹ Tanios, N., Wagner, M., Tony, M., Baltussen, R., van Til, J., Rindress, D., Kind P., Goetghebeur, M.M., and the International Task Force on Decision Criteria. (2013). Which criteria are considered in healthcare decisions? Insights from an international survey of policy and clinical decision makers. *International Journal of Technology Assessment in Health Care*, 29(4), 456-465. doi:10.1017/S0266462313000573 [doi].

⁴² Facey, K. (2015). Improving the effectiveness and efficiency of evidence production for HTA in the light of current trends in drug and device development, health system funding, regulation and HTA. Background Paper Policy Forum, 2015. Available at: http://www.htai.org/index.php?eID=tx_nawsecuredl&u=0&g=0&t=146055570&hash=bbaca56cdf06b3e64996c72012feebc0860afee7&file=fileadmin/HTAi_Files/Policy_Forum_Public/publications/15019_HTAi_BackgroundWeb.pdf

⁴³ <http://www.advance-hta.eu/wp2.php>

fears or objectively based beliefs that some sorts of innovation are more likely to prove viable than others, despite having equal potential 'worth'."⁴⁴

INTEGRATE-HTA

INTEGRATE-HTA is another innovative, three-year FP7 project that ended in December 2015. Using palliative care as a case study, this project aimed to develop concepts and methods for a comprehensive, patient-centred, and integrated (as opposed to side-by-side) assessment of complex technologies. The INTEGRATE-HTA model includes and considers the 'traditional' criteria used in HTA value frameworks (i.e. effectiveness and economic, sociocultural, ethical, and legal issues) as well as additional criteria including patient preferences, patient-specific moderators of treatment⁴⁵ and context and implementation issues. The INTEGRATE-HTA model is developed in 5 steps which are translated into guidances that are available on the website⁴⁶: In step 1, stakeholders (e.g. professionals, voluntary workers, patients, and relatives) are involved in the HTA process to elicit needs, topics, and outcomes. In step 2, groups of patients with different preferences and treatment moderators are identified. Then an initial logic model is developed to provide a structured overview of participants, interventions, comparators, and outcomes including context and implementation aspects in order to assess the health technology. In step 3, the evidence assessment (effectiveness, economic, ethical, socio-cultural, and/or legal aspects) is conducted; this might also include focus group discussions with patients. In step 4, the assessment results are then structured using the logic model to visualise the results as well as the interactions between them. It also allows consideration of different scenarios depending on the variation in context, implementation and patient characteristics. Finally, in step 5, the HTA results feed into a decision-making process in a way that is meaningful to decision-makers. For this purpose, a tool to structure a deliberative discussion (in cooperation with the decision committee) will be selected. This may be quantitative (e.g. MCDA) or qualitative (e.g. consensus methods) decision support tools.⁴⁷

The concepts and methods developed within INTEGRATE-HTA have been applied in a case study on palliative care in England.⁴⁸ The lessons learned included: a) Make stakeholders part of the assessment; b) Identify and model relationships between the intervention under study, patient characteristics, implementation issues, and context; c) Integration of all relevant aspects needs to start from the beginning. Recently, CADTH used the guidance in a case study on dialysis modalities. Their experiences with applying the guidances were presented during an INAHTA-webinar on the INTEGRATE-HTA project (September 2016).⁴⁹

⁴⁴ <http://www.advance-hta.eu/wp7.php>

⁴⁵ These are theoretical variables in a causal model that can be studied via subgroup or regression analysis in epidemiological studies, randomised controlled trials (RCTs) or between-study comparisons in meta-analysis. Source: Van Hoorn, R., Tummers, M., Kievit, W., Van der Wilt, G.J. (eds.) (2016) Guidance on the assessment of treatment moderation and patients' preferences [Online]. Available from: <http://www.integrate-hta.eu/downloads/>

⁴⁶ <http://www.integrate-hta.eu/downloads/#results>

⁴⁷ Wahlster, P., Brereton, L., Burns, J., Hofmann, B., Mozygamba, K., Oortwijn, W., Pfadenhauer, L., Polus, S., Rehfuess, E., Schilling, I., van Hoorn, R., van der Wilt, G.J., Baltussen, R., Gerhardus, A. (2016). Guidance on the integrated assessment of complex health technologies - The INTEGRATE-HTA Model [Online]. Available from: <http://www.integrate-hta.eu/downloads/>

⁴⁸ Brereton, L., Wahlster, P., Lysdahl, K.B., Mozygamba, K., Burns, J., Chilcott, J.B., Ward, S., Brönneke, J., Tummers, M., van Hoorn, R., Pfadenhauer, L., Polus, S., Ingleton, C., Gerdiner, C., van der Wilt, G.J., Gerhardus, A., Rowher, A., Rehfuess, E., Oortwijn, W., Refolo, P., Sacchini, D., Leppert W., Blazeveciene, A., Spagnolo, A.G., Preston, L., Clark, J., Goyder, E. (2016). on behalf of the INTEGRATE-HTA project team (2016). Integrated assessment of home based palliative care with and without reinforced caregiver support: 'A demonstration of INTEGRATE-HTA methodological guidances' – Executive Summary [Online]. Available from: <http://www.integrate-hta.eu/downloads/>

⁴⁹ <http://www.inahta.org/2016/09/new-inahta-webinars/>

MedtechHTA

This FP7 project,⁵⁰ finalised in December 2015, was focused on advancing methods of HTA for medical devices. For this purpose, the project consisted of four components: 1) regulatory process of medical devices and the impact on the uptake and diffusion of medical devices; 2) current methods used for HTA of medical devices and whether these differentiate from other technologies (i.e., medicines), including comparative effectiveness of medical devices; 3) value of information and uncertainty surrounding the development of new medical devices; and 4) drivers of diffusion of medical devices. One of the conclusions of the project is that a medical device related intervention should be considered a complex intervention. It is recommended to include the intervention's components and the relation between intervention, modifying factors and outcome in the formulation of the research question. Furthermore, factors driving adoption of medical devices should be addressed in HTA reports to estimate the impact of the interplay of physician characteristics, organisational, regional, and environmental factors, and manufacturers' actions⁵¹ (see also INTEGRATE-HTA).

Besides these new methodological advances in value frameworks, other types of **value frameworks targeting specific countries/regions or health technologies** have been found in the literature, including:

Balanced Assessment System (BAS) targeting middle-income countries⁵²

In 2014, Danko published an article, emphasising that the current HTA systems for assessing the value of drugs may not be suitable for middle-income countries. In several Central and Eastern European (CEE) countries, HTA has no formal role in decision-making regarding pricing and reimbursement of new health technologies. Most often, therapeutic value and health care priorities are used as criteria in the decision-making process. Cost-effectiveness evidence is requested only in those countries with a more advanced HTA infrastructure. Moreover, budget impact is increasingly used in countries with very limited resources. Danko has the opinion that 'light' assessment (using economic criteria, therapeutic added value and ethical and health policy considerations), in which pragmatic and resource-saving methodologies are applied on the basis of available information, is more fit for purpose than the traditional economic evaluation paradigm (cost per QALY). 'Pragmatic' means that it is sufficient to use secondary assessments, as well as to rely on earlier conducted international assessments and checklists in formulating recommendations. Also, the use of MCDA could be considered. The final choice of the approach is context-dependent, taking into account local priorities. The analysis of Danko concerning the use of HTA in CEE countries has been confirmed by others. For example, Kaló et al (2016) mentioned that current HTA frameworks can not be fully used for decision-making without taking into account country-specific aspects, such as country size, gross domestic product per capita, major social values, public health priorities, and fragmentation of healthcare financing.⁵³ Several of these aspects are also part of the **framework developed by the World Health Organization (WHO) in determining universal health coverage**. The criteria used in determining coverage include a combination of population coverage, service coverage, and financial coverage or financial protection. Furthermore, considerations of equity and fairness are recommended to be taken into account and addressed locally. For example by giving priority to services which are most cost-effective, those which benefit the poorest and which offer financial risk protection; expand universal coverage to the country's high-priority services and safeguarding disadvantaged groups, such as rural populations.⁵⁴ The WHO mentions that the process of moving towards universal coverage can be facilitated by mechanisms for ensuring public accountability and participation, such as the accountability for reasonableness framework.⁵⁵ This viewpoint is recently acknowledged by other authors as well.⁵⁶

⁵⁰ <http://www.medtehta.eu/wps/wcm/connect/site/medtehta/home>

⁵¹ Drummond, M. MedtechHTA. Summary of project, recommendations. Final conference, 2015. Available via: <http://www.medtehta.eu/wps/wcm/connect/5ca9f321-192c-4f71-b3c6-97463acdbebc/10+Final+recommendations+Drummond.pdf?MOD=AJPERES>

⁵² Danko, D.(2014). Health technology assessment in middle-income countries: recommendations for a balanced assessment system. *Journal of Market Access & Health Policy*, 2: 23181 - <http://dx.doi.org/10.3402/jmahp.v2.23181>

⁵³ Kaló, Z., Gheorghe, A., Huic, M., Csanádi, M., Boerlum Kristensen, F. (2016). HTA implementation roadmap in Central and Eastern European countries. *Health Economics*; 25, S1:179–192. DOI: 10.1002/hec.3298

⁵⁴ http://www.who.int/health_financing/topics/benefit-package/UHC-choices-facing-purchasers/en/

⁵⁵ http://www.who.int/choice/documents/making_fair_choices/en/

⁵⁶ Baltussen, R., Jansen, M.P., Mikkelsen, E., Tromp, N., Hontelez, J., Bijlmakers, L., Van der Wilt, G. Priority setting for universal health coverage: We need evidence-informed deliberative processes, not just more evidence on cost-effectiveness. *International Journal of Health Policy and Management*, 2016; 5(x), 1–4. doi 10.15171/ijhpm.2016.83.

Value framework for complementary diagnostics⁵⁷

In 2016, the Office of Health Economics (UK) and the European Personalised Medicine Association presented a general value framework with regard to complementary diagnostics. They used the following definition of complementary diagnostics: “using biomarkers for the purposes of risk assessment, diagnosis, prognosis, monitoring, and guiding therapeutic decisions; and they are used in the sense of economic complements, that is, medical products or technologies that are used in combination to produce a synergistic effect.” The framework was developed as the common value frameworks applied in the field of drugs and medical devices (focusing on health gains, cost savings in the health care system and productivity – mainly cost-effectiveness) were not considered the best fit. Through literature search additional ‘new’ elements were identified that could be used to adapt or augment the cost-effectiveness of complementary diagnostics: reduction in uncertainty, real option value, value of hope, value of insurance, scientific spill overs. As these elements are considered to be largely independent, they can be aggregated at the societal level. The developed framework was tested in three case studies regarding evaluations performed by NICE (UK) and HAS (France), but should be seen as a first step in determining the value of complementary diagnostics. Since 2010, MSAC and PBAC in Australia have an evaluation framework in place for this type of co-dependent⁵⁸ (investigative) health technologies. The framework includes criteria such as net clinical benefits, cost-effectiveness and financial implications of the joint use of the health technologies.⁵⁹ Furthermore, MSAC (Australia) has recently developed an evaluation framework in the field of **genetic and genomic based health technologies**, consisting of a Clinical Utility Card.⁶⁰ This card is based on the clinical utility gene cards developed and updated in EuroGentest2, a project funded by the European Commission to harmonising the process of genetic testing across Europe. The cards are disease-specific guidelines regarding the clinical utility of genetic testing, which is defined as “the ability of a genetic test to significantly affect the clinical setting and patient outcome”. The cards provide guidance to all relevant stakeholders, including clinicians, geneticists, referrers, service providers and payers⁶¹. Clinical utility cards are based on the ACCE framework, originally developed by the US Centers for Disease Control and Prevention and the Foundation for Blood Research during 2000-2004. The ACCE framework enables the evaluation of data on genetic tests using four criteria: Analytic validity, Clinical validity, Clinical utility and associated Ethical, legal and social implications.⁶²

EDMA - value framework for in-vitro diagnostics

The European Diagnostic Manufacturers Association (EDMA, part of MedTech Europe) is in the process of developing a value framework for in-vitro diagnostics.⁶³ The focus will be on the value of diagnostic information in which a broader concept of value for diagnostics will be taken into account, as well as the total care pathway. Currently, they are in the conceptual phase, working with an international multi-stakeholder platform including experts from leading institutions and key opinion leaders (from the US, New Zealand, Australia, and EU countries). The aim is to include different stakeholder groups, such as patients, payers, HTA organisations in the development of the framework.

⁵⁷ Garrison, L., Mestre-Ferrandiz, J. and Zamora, B. (2016). The Value of Knowing and Knowing the Value: Improving the Health Technology Assessment of Complementary Diagnostics. White Paper. Office of Health Economics and EPAMED. Available from: <https://www.ohe.org/news/value-knowing-and-knowing-value-improving-health-technology-assessment-complementary>

⁵⁸ Defined as: patient health outcomes related to the use of one health technology (e.g. a medicinal product) are improved by the use of another health technology (e.g. a pathology test or an imaging technology).

⁵⁹ <https://pbac.pbs.gov.au/product-type-4-codependent-technologies.html>

⁶⁰ Australian Government. Department of Health. Medical Services Advisory Committee. Clinical Utility Card for heritable mutations which increases the risk in [disease area]. Proforma, June 2016. Available via: [http://www.msac.gov.au/internet/msac/publishing.nsf/Content/OBD63667C984FEEACA25801000123AD8/\\$File/CUC-proforma-assessment-genetic-testing.pdf](http://www.msac.gov.au/internet/msac/publishing.nsf/Content/OBD63667C984FEEACA25801000123AD8/$File/CUC-proforma-assessment-genetic-testing.pdf)

⁶¹ <http://www.eurogentest.org/index.php?id=668>

⁶² <http://www.cdc.gov/genomics/gtesting/ACCE/>

⁶³ <http://intranet.edma-ivd.eu/index.php/component/content/article/7-about-in-vitro-diagnostics/468-health-technology-assessment>

Value frameworks in the field of medical devices

Currently, there are several initiatives to develop value frameworks for medical devices; these initiatives are at different stages of development. Among these are:

- **ISPOR Medical devices and diagnostics special interest group⁶⁴**

This group, initiated in 2014, aims “to provide a definitional and methodological framework for the challenges facing the value assessment of medical devices and how these challenges can be overcome.” There is literature about assessing individual medical devices, but there is not yet a standardised approach (value framework) regarding which core elements should be evaluated/assessed. E.g. which aspects of medical devices should be assessed by health economics, outcomes research? Multiple stakeholders are considered including: payers, HTA agencies, procurers / commissioners, policy makers, manufacturers & designers (industry), health care practitioners / providers / implementers, and patients and society. The focus lies on the difference between drugs and medical devices and on the diversity of medical devices. The group organised a workshop on the challenges of value assessment regarding medical devices during the ISPOR conference in Rome, 2016. The case studies presented included insulin pen needles and mechanical thrombectomy.⁶⁵ The results of this workshop serves as input to two scientific articles that the group is preparing (members of ISPOR were able to review draft papers) and that will be available by the end of 2016. ISPOR also has an initiative on US Value Assessment Frameworks⁶⁶ (mainly targeting drugs – see Section 4).

- **AdvaMed initiative on assessing the value of medical technology and diagnostics (US)**

The Advanced Medical Technology Association (AdvaMed), a trade association with over 300 members globally⁶⁷, is in the process of developing a value framework for medical technology and diagnostics. For this purpose, they include the views of several stakeholders (payers, providers, patient groups and industry) as their perspectives impact the assessment and ultimately the coverage/reimbursement decision. It is noteworthy that HTA-organisations are not mentioned as a key stakeholder in the development of the value framework. AdvaMed has identified four broad categories of criteria to be considered in the assessment of a medical technology: clinical impact, non-clinical patient benefits (e.g. patient-related outcomes), care delivery economics, and societal benefits (population health impacts, employer impacts and systemic changes). AdvaMed aims to present the framework in early 2017.⁶⁸

- **Medical Device Innovation Consortium (MDIC), a public-private partnership (US)**

In 2015, the MDIC presented a framework for incorporating patient preferences into regulatory assessments of medical technology. The framework consists of two parts: a) how to incorporate patient preferences into benefit-risk assessment, and b) a “catalogue of methods” to collect and analyse patient preference information. The aim is to improve the understanding of industry, FDA staff, and others of how the patient’s perspective might be incorporated into this process. The framework was developed by a group of MDIC’s member organizations, experts in decision science and preference assessment methods from academia and other organizations. The work was funded by FDA. The framework is considered to be a working document that needs to be updated when stakeholders have more experience with collecting and using patient preference information in the regulatory process.⁶⁹

⁶⁴ http://www.ispor.org/sigs/MedDevicesDiag/Value_assessment_MD.aspx

⁶⁵ www.ispor.org/Event/GetReleasedPresentation/856

⁶⁶ <http://www.ispor.org/ValueAssessmentFrameworks>

⁶⁷ <http://www.advamed.org/about-advamed>

⁶⁸ Information provided by a Policy Forum Member.

⁶⁹ Medical Device Innovation Consortium (2015) Medical Device Innovation Consortium (MDIC) Patient centred benefit-risk project report. A framework for incorporating information on patient preferences regarding benefit and risk into regulatory assessments of medical technology.

- **European Coordination Committee of the Radiological, electromedical, and healthcare IT Industry (COCIR)**

COCIR released a position paper at the end of 2014, emphasising that there are important differences between health technologies and that these need to be taken into account when performing HTA. They propose the following value elements to be considered by HTA agencies:

- a. Flexibility and pragmatism combined with acceptance of different types of evidence: Adopt different methodologies to assess whole healthcare system benefits appropriate to the medical technology and the need that is being addressed (e.g. clinical application, productivity, access); Recognise that different levels of benefit/risk exist for medical technologies and adopt a pragmatic approach to incorporate different types of evidence into effectiveness assessments
- b. Broad scope of benefits considered: Recognise healthcare system benefits as well as patient benefits; actively encourage input of different perspectives from multiple stakeholders (patients, carers, clinicians, payers, et al); Develop mechanisms for facilitating recommendations for further research - both through early dialogue activities before HTA to develop appropriate evidence, and following an HTA to develop study protocols to fill evidence gaps.⁷⁰

Value-frameworks in early access and patient access schemes

Explicitly (or implicitly), decision-makers are using value frameworks in early access and patient access schemes. Such schemes are alternative agreements between healthcare payers and manufacturers for conditional coverage of promising health technologies, where there are concerns with their effectiveness or cost-effectiveness⁷¹ or to manage its adoption in clinical practice in order to maximise effective use, and/or limit the budget impact.⁷² An example is the 'Early Access to Medicines' scheme (EAMS) introduced by the UK government in 2014. The scheme is targeting medicines with a "potential to be of value in areas of unmet medical need". This means that drugs can already be used in clinical practice in parallel with the later stages of the regulatory process. This process will provide an opportunity to make products available to patients 1-1.5 years before formal marketing authorisation.⁷³ A similar framework has been introduced by the Australian Government in 2011,⁷⁴ which is currently in the process of being updated.⁷⁵ Patient access schemes are most often targeted towards a minority of drugs (most often anti-cancer and immune modulating agents).⁷⁶ Recently, some stakeholders, including payers, expressed concerns regarding such schemes - principally from a patient safety viewpoint in addition to making funding decisions based on considerable uncertainty.⁷⁷ Future research is warranted to evaluate the performance of patient access schemes⁷⁸ as only few studies explored their impact.^{79,80,81}

⁷⁰ COCIR position paper. Assessing the value of Medical Imaging and Health ICT The role of Health Technology Assessment (HTA), 29 October 2014.

⁷¹ Garrison, L. P. Jr., Towse, A., Briggs, A., et al. Performance-based risk-sharing arrangements—good practices for design, implementation, and evaluation: report of the ISPOR good practices for performance-based risk-sharing arrangements task force, *Value in Health*, 2013, 16(5): 703-719.

⁷² Klemp, M., Fronsdal, K.B. and Facey, K. What principles should govern the use of managed entry agreements?, *International Journal of Technology Assessment in Health Care*, 2011;27(1):77-83.

⁷³ National Institute for Health and Care Excellence. Centre for Health Technology Evaluation. Note to describe procedures at NICE to support the Early Access to Medicines scheme. EAMS – procedure at NICE. January 2016.

⁷⁴ <http://www.pbs.gov.au/info/publication/factsheets/shared/framework-for-introduction-of-managed-entry-scheme-for-PBAC-submissions>

⁷⁵ <http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/pbac-outcomes/2015-03/march-2015-other-matters-managed-access-programme-framewk>

⁷⁶ Godman, B., Oortwijn, W., De Waure, C., Mosca, I., Puggina, A., Specchia, M.L., Campanell, P. Van der Tuin., J. Links between pharmaceutical R&D models and access to affordable medicines. European Parliament. Directorate General for Internal Policies. Policy Department a: economic and scientific Policy. European Union, PE 587.321 EN. IP/A/ENV/2015-06, October 2016. Available via: [http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU\(2016\)587321](http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU(2016)587321)

⁷⁷ Ermisch, M., Bucsis, A., Vella Bonanno, P., Arickx, F., Bybau, A., Bochenek, T. et al. Payers' views of the changes arising through the possible adoption of Adaptive Pathways. *Frontiers in Pharmacology* 2016; 7 Article 305; 1-9. <http://dx.doi.org/10.3389/fphar.2016.00305>

⁷⁸ Lu, C.Y., Lupton, C., Rakowsky, S., et al. Patient access schemes in Asia-pacific markets: current experience and future potential *Journal of Pharmaceutical Policy and Practice*, 2015;8:6 DOI 10.1186/s40545-014-0019-x

⁷⁹ Ferrario, A., Kanavos, P., Dealing with uncertainty and high prices of new medicines: a comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden, *Social science & medicine*, 2015; 124: 39-47. doi: 10.1016/j.socscimed.2014.11.003

⁸⁰ Garrison, L. P. Jr., Towse, A., Briggs, A., et al. Performance-based risk-sharing arrangements—good practices for design, implementation, and evaluation: report of the ISPOR good practices for performance-based risk-sharing arrangements task force, *Value in Health*, 2013, 16(5): 703-719.

⁸¹ Eijkenaer, F., Emmert, M., Scheppach, M., Schöffski, O. Effects of pay for performance in health care: a systematic review of systematic reviews, *Health Policy*, 2013; 110(2-3):115-130. doi: 10.1016/j.healthpol.2013.01.008

Reflection

Most of the frameworks presented in this Section are recently developed and have to testify their applicability in practice. What most of these developments show is an increased focus on stakeholder involvement in developing value frameworks, that value is considered a broad concept (beyond economic considerations, i.e. also including indirect effects), that there is a need to contextualise the evidence/information and that there is no single value framework that fits all purposes.

4. Value frameworks and clinical decision-making

US value frameworks

Value frameworks to inform treatment decisions are proliferating, especially recently in the US. These are mainly geared towards health care professionals and patients but their decisions will definitely affect other stakeholders (e.g. guideline developers, payers).

Examples of such frameworks include those from:

American College of Cardiology and American Heart Association (ACC-AHA)

In 2014, the ACC-AHA presented their approach to explicitly include value assessments (cost-effectiveness) when developing guidelines and performance measures.⁸² The increase in health care cost and the value of care to patients were the key drivers for this initiative. A committee of experienced clinicians and specialists in cardiology, health economics, and methodological experts developed the framework, which was subject to peer review.

The framework includes the following criteria: clinical benefit versus risk and value (cost-effectiveness). When the cost-effectiveness of a treatment or diagnostic strategy has been adequately evaluated using scientific evidence, a rating of the level of value is given according to the following categories: high value (H), intermediate value (I), low value (L) – with the possibility to adapt the level where appropriate according to the uncertainty surrounding the evidence (U), and value not assessed (NA). The level of value (high or low) is assigned following the recommendations of the World Health Organisation: “poor value” (L) when the cost per life year gained is greater than three times the gross domestic product (GDP) per capita of the country (this would be US \$150,000/QALY or more for the US), and “good value” (H) if the cost per life year gained is less than one times the GDP per capita of the country.

The framework is to be considered a guideline and the category of value should be presented in addition to the level of effectiveness (which is the traditional approach). Target audiences include decision-makers, health care providers, and practice guideline developers to assure that clinical guideline recommendations results in value for money.⁸³ However, it is also mentioned that the value provided is only one of several factors used in resource allocation decisions.

American Society of Clinical Oncology (ASCO)

In June 2015, ASCO presented its conceptual framework to assess the value of cancer treatment options.⁸⁴ The aim is to “provide a standardized approach to assist physicians and patients in assessing the value of a new drug treatment for cancer as compared with one or several prevailing standards of care”. The initiators also explicitly mention the increase in health care cost as main drivers to develop the framework. In addition to using the framework in clinical decision-making, ASCO also mentions that the framework can be used at the societal level: “the assumption underlying this effort is that the cost of a given intervention should bear a relationship to the beneficial impact it has for the patients who receive that treatment”.

The framework compares the clinical benefit (overall survival, progression-free survival response rate), toxicity, and cost of cancer therapies (per month) as well as additional criteria: symptom palliation and time off due to treatment.⁸⁵ A “Net Health Benefit (NHB)” score is calculated based on clinical

⁸² Anderson, J.L., Heidenreich, P.A., Barnett, P.G., Creager, M.A., Fonarow, G.C., Gibbons, R.J., Halperin, J.L., Hlatky, M.A., Jacobs, A.K., Mark, D.B., Masoudi, F.A., Peterson, E.D., Shaw, L.J. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;63:2304–22.

⁸³ <http://www.acc.org/latest-in-cardiology/articles/2014/03/27/12/44/accaha-to-include-costvalue-assessments-in-guidelines-and-performance-measures>

⁸⁴ ASCO Special Article by Schnipper et al. American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options. *Journal of Clinical Oncology*, 2015;10.1200/JCO.2015.61.6706

⁸⁵ Neuman, P., Cohen, J. (2015). Measuring the Value of Prescription Drugs. *The New England Journal of Medicine*; 373;27 December 31, 2015

benefit and toxicity using evidence from high-quality prospective clinical trials. Value is determined by comparing benefit to cost. The framework includes drug acquisition cost and cost to the patient.

The framework is developed by a multidisciplinary group of physicians and other representatives of the oncology community, taking the perspective of the patients into account when determining the NHB score.⁸⁶ After the initial development of the framework, ASCO asked input from an advisory committee including oncologists, patient advocates, payers, industry after which they have requested public comments on it. This led to a revised framework that was published in May 2016. The main revisions are modification of the NHB score to better reflect true differences between treatments by using hazard ratios, when available; and to consider all side effects. The latter was instigated by feedback from patients that mild side effects can also have a major impact on quality of life.⁸⁷

National Comprehensive Cancer Network (NCCN)

The value framework of the NCCN is called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) with NCCN Evidence Blocks. The framework is focused on oncology drugs and "intended as a visual representation of five key measures that provide important information about specific recommendations contained within the NCCN Clinical Practice Guidelines in Oncology. The goal is to provide the health care provider and the patient information to make informed choices when selecting systemic therapies, based upon measures related to treatment, supporting data, and cost."⁸⁸ The five key measures are efficacy, safety, evidence quality, evidence consistency and affordability. Each of these measures can be scored on a scale of 1 (least favourable) to 5 (most favourable). The scores are separately presented and the synthesis should be done by the user (provider/patient).

The framework was developed by NCCN staff and disease specialist clinicians and they accept public comments.

An overview of the value assessment frameworks has been presented in several documents, including a report of the National Pharmaceutical Council that was published in June 2016.⁸⁹ The following tables (Table 4 and Table 5) are taken from this publication, summarising the main elements of value frameworks in the US:

⁸⁶ <http://wp.vcu.edu/nvcarroll/2015/06/26/asco-releases-value-framework-for-assessing-value-of-cancer-drugs/>

⁸⁷ <http://www.asco.org/advocacy-policy/asco-in-action/asco-value-framework-update>

⁸⁸ National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN Guidelines®) with NCCN Evidence Blocks™. NCCN website. <http://www.nccn.org/evidenceblocks/>.

⁸⁹ Westrich, K. Current landscape: value assessment frameworks, National Pharmaceutical Council, June 2016.

Table 4. Overview of US value assessment frameworks

	ACC-AHA	ASCO 2.0	DrugAbacus ⁹⁰	ICER ⁹¹	NCCN
Target audience	Physician/ patient	Physician/ patient	Payers, policy makers, physician/ patient	Payers, policy makers, physician/ patient	Physician/ patient
Services addressed	Treatments, primarily drugs	Drug regimens	Drugs	Primarily drugs, has been extended to devices and delivery system programs	Treatment regimens, primarily drugs
Conditions addressed	Cardiovascular	Oncologic	Oncologic	All conditions particular focus on new drugs anticipated to be high impact	Oncologic
What is the "Value" Output?	Level of value assessment (high, medium, low, uncertain, not assessed)	Numerical net health benefit score; drug regimen cost	Value-based price	Value-based price benchmark; assessment of care value (high/ intermediate/ low)	Score (1-5) for each of 5 evidence blocks: efficacy, safety, quality of evidence, consistency of evidence, affordability
Evaluations to date	1 guideline includes concept, but makes no assessment	10 examples using initial draft frameworks; 4 examples using updated framework	Tool includes 54 drugs approved from 2001-15	8 topics have been completed; 5 are in process	12 guidelines include evidence blocks
Selection Process for Future Evaluations	As guidelines are updated, value assessments will be added	Undetermined at this time	Will eventually include other cancer drugs and other indications	Selected by ICER and three advisory boards informed by horizon scan and payer input	As clinical practice guidelines are updated, evidence blocks will be added

⁹⁰ See also Section 3 for more information on DrugAbacus

⁹¹ See also Section 3 for more information on ICER

Table 5. Development of US value assessment frameworks

	ACC-AHA	ASCO 2.0	DrugAbacus	ICER	NCCN
Who developed it?	Writing committee (primarily physicians); still underway	ASCO Value in Cancer Care Task Force (physicians)	Peter Bach/ Real Endpoints	ICER	NCCN staff in consultation with disease specialist clinicians
How inclusive was development?	Unknown	Advisory committee including oncologists, patient advocates, payers and biopharmaceutical industry provided input	Unknown	Advisory committee of payers, patient organizations, physician organizations and biopharmaceutical industry provided input	Restricted to NCCN members per NCCN regulatory requirements
Was there a public comment period?	Unknown	Yes	Unknown	No	NCCN accepts comments on an ongoing basis
Was it user tested?	Unknown	Software tool will be user tested prior to release	Unknown	Payers, providers, patient groups, and clinical societies provided feedback ⁹²	Beta testing underway
How often will the framework be updated?	Unknown	To be determined	Unknown	Annually ⁹³	Continuously, as needed

Another issue concerns the use of these frameworks in (clinical) decision-making. In 2015, Neuman and Cohen presented an overview of the main US value frameworks (ACC–AHA, ASCO, ICER, MSKCC, and NCCN). The authors state that the frameworks are mainly targeting oncology drugs, use different concepts of value and that this will lead to different outcomes.⁹⁴ This viewpoint was also presented during a recent conference on these value frameworks.⁹⁵

During this conference,⁹⁶ a case study on multiple myeloma was presented by Goodman, comparing four value frameworks (ASCO, DrugAbacus, ICER and NCCN) in order to identify reasons for the differences between them and to determine which reasons make sense and which may be concerning. It appeared that even when frameworks targeted the same patient populations, applied the same treatments, as well as used the same evidence, their clinical outputs varied; moreover, cost-related outputs or measures of affordability represented different types of costs/economic impacts. The varying results were mainly due to methodological differences in applying the value frameworks. An important observation made was that multiple myeloma patients value outcomes that may not be fully captured in the frameworks; e.g. health-related quality of life, ease of use, management of toxicities and side effects and financial burden. Looking at the result of this case study, the presenter recommended amongst others “to reach out to patients and clinicians early and ongoing to better understand patient-centred and clinically relevant outcomes; to choose comparators that are relevant to therapeutic options for patients and clinicians; and to be sensitive on how patients, clinicians, and others who are not the primary target audiences of an assessment may be affected directly or indirectly by how stakeholders will use the results of those assessments.”⁹⁷

⁹² Information provided by a Policy Forum Member.

⁹³ Refers to budget impact calculations, but wholesale changes will be more periodic (information provided by a Policy Forum Member).

⁹⁴ Neuman, P., Cohen, J. Measuring the Value of Prescription Drugs. *The New England Journal of Medicine*, 2015;373:27 December 31.

⁹⁵ Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016.

⁹⁶ Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016.

⁹⁷ Goodman, C. Why Four Frameworks (Should) Arrive at Different Conclusions Multiple Myeloma Reviews. Presentation at Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016

ISPOR Initiative on US Value Assessment Frameworks⁹⁸

This recent initiative from ISPOR on US Value Assessment Frameworks aims to “1) identify and discuss key methodological and process issues in defining and applying value frameworks to health care resource allocation issues; and 2) convene a Special Task Force that will collaborate to produce a white paper that advises on the appropriate definition and use of high-quality value”, with 3) input and assistance from leading experts and key stakeholders in the health economics and outcomes research community.⁹⁹ The development of several value assessment frameworks during the last few years, resulting in diverging outcomes, was the starting point for this Initiative. Before the Task Force started its policy work in July 2016, the Initiative focused on theoretical frameworks and background information. The Task Force expects to deliver the white paper on the appropriate definition and use of value frameworks in early 2017. In addition, the Initiative will publish separate papers on value frameworks in the official journal of ISPOR (Value in Health).

European value framework

In Europe, a value framework in the field of oncology drugs was presented by the European Society for Medical Oncology (ESMO) in 2015. The initial work began in 2013 by leading clinicians that formed a Task Force. The value framework assesses the magnitude of clinical benefit for cancer medicines (ESMO-MCBS) in curative or non-curative settings. The initial draft was reviewed by more than 200 clinicians and more than 50 biostatisticians. The final draft was validated by a field testing of 77 cancer medicines across 10 cancer types. The framework can be applied to assess the “relative benefit of treatments using outcomes of survival, quality of life, surrogate outcomes for survival or quality of life or treatment toxicity in solid cancers”.¹⁰⁰ Some European payers and their advisors have recently criticised the use of the ESMO criteria in practice.¹⁰¹ According to Wild, costs are not taken into account, because of the high variability of prices across European countries.¹⁰²

ESMO described the framework as “a tool to assist oncology clinicians in evaluating the most effective anti-cancer medicines for their patients”. ESMO mentions that it can also be used in public policy decision-making and to develop and/or improve clinical guidelines. The framework is intended to be prospectively applied to new drugs that will be approved by the EMA. Those drugs that obtain the highest scores will be highlighted in the ESMO Clinical Practice Guidelines.¹⁰³ Although ESMO intended their framework to identify and highlight the most promising new cancer therapies, it was reported (by the Guardian) as a tool to identify and remove the ‘useless drugs’.¹⁰⁴

Reflection

The frameworks presented are all evolving, using the feedback from external stakeholders, as testified for example by the different versions of the ASCO framework (ASCO 2.0) and the EUnetHTA Core Model. Although the views of patients is increasingly considered to be important, there is room for improvement as most of the frameworks do not yet include factors that might be considered important to them (see case study on multiple myeloma). Furthermore, as mentioned by the INTEGRATE-HTA project, it is beneficial to include relevant stakeholders from the beginning.

The application of the frameworks remains a challenge. The only framework(s) presented in this Section that has been formally applied in practice is the NCCN Evidence Blocks framework, in the development or updating of guidelines (and ICER – see Section 3). The other frameworks have not yet been formally used for a value assessment;¹⁰⁵ this means that the proof of the pudding is in the eating.

⁹⁸ <http://www.ispor.org/ValueAssessmentFrameworks>

⁹⁹ ISPOR. Announcement. ISPOR announces establishment of new initiative on value assessment frameworks. May, 2016. Available from: <http://press.ispor.org/index.php/new-initiative-on-value-assessment-frameworks/>

¹⁰⁰ Cherny, N.I., Sullivan, R., Dafni, U., Kerst, J.M., Sobrero, J., Zielinski, C., de Vries, E.G.E., Piccart, M.J. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Annals of Oncology*, 2015; 26 (8): 1547-1573. doi: 10.1093/annonc/mdv249

¹⁰¹ Wild, C., Grössman, N., Vella Bonanno, P., Bucsics, A., Furst, J., Gulbinović, J., Godman, B., Jones, J., Pomorski, M.K., Emprechtinger, R.. Utilisation of the ESMO-MCBS in practice of HTA. *Annals of Oncology*, 2016;27(11):2134-2136.

¹⁰² Wild, C. Effectiveness comparison of international assessments and policies of/for new cancer medicines. Presentation at the Piperska Meeting, 30 June 2016, Leiden, the Netherlands.

¹⁰³ <http://www.esmo.org/Press-Office/Press-Releases/ESMO-Announces-a-Scale-to-Stratify-the-Magnitude-of-Clinical-Benefit-of-Anti-Cancer-Medicines>

¹⁰⁴ Information provided by a Policy Forum Member.

¹⁰⁵ Westrich, K. Current landscape: value assessment frameworks, National Pharmaceutical Council, June 2016.

5. Value frameworks and decision-making to purchase a health technology at provider level¹⁰⁶

Value-based procurement

Recently, more attention is being paid to value-based procurement due to increasing health care costs and variations in health outcomes, and the potential of medical technology to address these challenges. Traditionally, most systems, including hospitals, purchase medical technology using up-front purchase costs.¹⁰⁷ Value-based procurement means that in addition to minimising the cost, other quality-based factors (e.g. technical merit, accessibility, patient needs, and innovative characteristics) need to be considered. In Europe, this has already led to important changes in public procurement directives. Currently, the most economically advantageous tender is selected. This means that the selection is based on cost and quality assessment criteria that might be given different weights in the final score.

In some countries around the globe (e.g. Sweden, UK), and more recently in Canada (e.g. Ontario), there have been developments to move towards value-based procurement.¹⁰⁸ The frameworks aim to facilitate innovations that "promote health and well-being, improve access to health and health services, and deliver effective, efficient, and quality care. The Ontario Health Innovation Council specifically aims "to better support development and adoption of innovation, a broad range of key stakeholders, including procurement officials, but also patients, industry, health care providers and health professionals will need be engaged in defining health care procurement priorities and strategies on an early and ongoing basis. Stakeholders will focus on addressing health system priorities and population needs rather than the day-to-day purchasing of specific goods and services. In addition, individual health care providers will work with shared service organizations to efficiently procure innovative technologies. Finally, the health system will need to invest in the skills, knowledge and competencies needed to enable strategic procurement."¹⁰⁹ The framework proposed by the Ontario Health Innovation Council explicitly mentions that value is a broad concept and is assessed according to social impact (e.g. healthier lifestyles, healthier populations), health system benefits (e.g. improved patient experience and engagement, better access to health) and economic benefits (increased economic development, increased R&D). Value-based procurement seems to be evolving quickly in Canada, as more jurisdictions are developing strategies.

¹⁰⁶ The majority of providers in the US are incurring at least some financial risk for patients and therefore engaging in value appraisal that is identical to that of the payer (information provided by a Policy Forum Member)

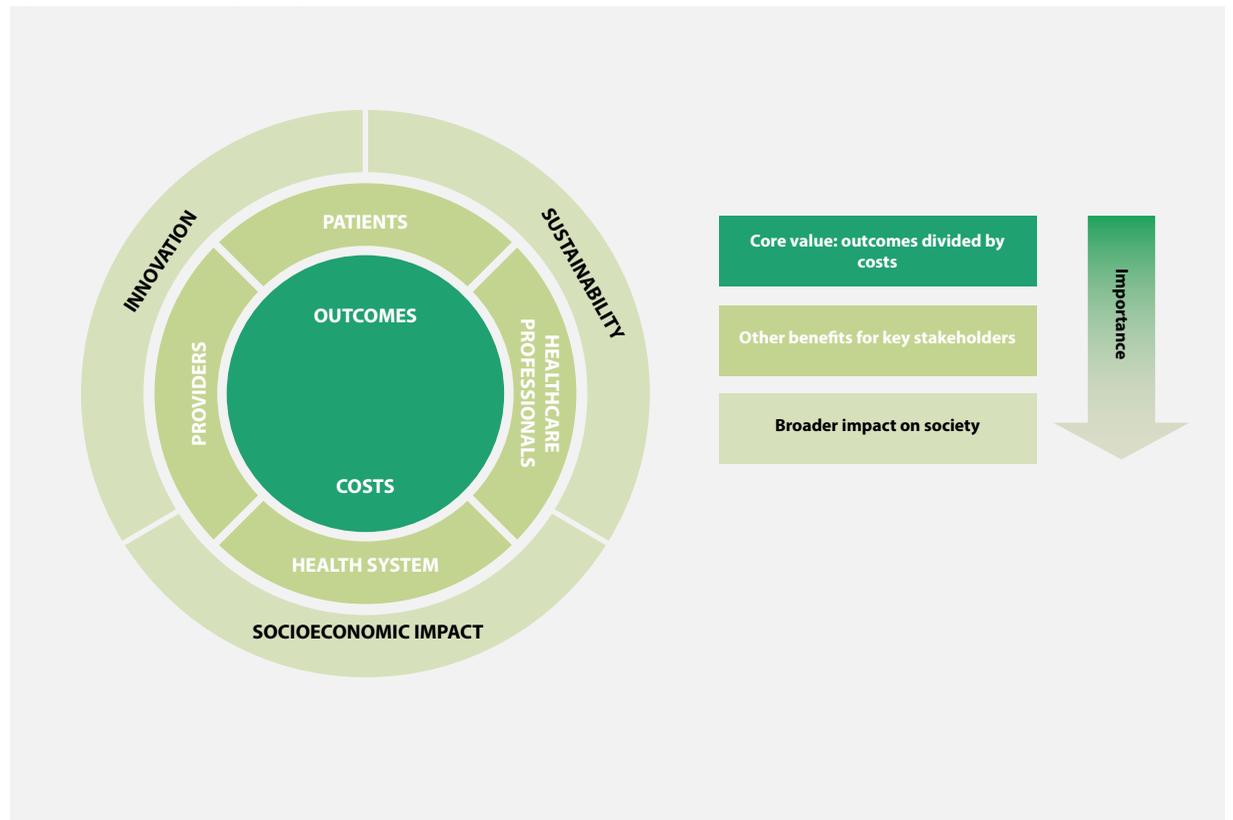
¹⁰⁷ <https://www.bcgperspectives.com/content/articles/medical-devices-technology-sourcing-procurement-unexpected-driver-value-based-health-care/>

¹⁰⁸ http://www.conferenceboard.ca/commentaries/healthcare/default/16-03-15/value-based_procurement_the_new_health_care_imperative-481875798.aspx

¹⁰⁹ <http://www.ohic.ca/sites/default/files/Ontario%20Health%20Innovation%20Council%20Report.pdf>

In addition, Eucomed (part of MedTech Europe) together with the Boston Consulting Group (BCG) developed a framework for value-based procurement in the field of medical technology (see Figure 2; taken from the website of BCG).¹¹⁰

Figure 2. A value-based public procurement framework



Source: BCG Analysis.

Note: Costs include the costs of care delivery.

In this framework the traditional (purchase) cost-only procurement model is replaced by a broader concept of value, including total cost of care delivery and relevant outcomes for different stakeholders, including patients (e.g. patient-reported outcome; comfort of wearing catheters), health care providers (e.g. improved care pathways), health professionals (improved user-friendliness of products), and health systems (reduced societal costs). Each element is operationalised by criteria that can be used by contracting authorities in developing a specific tender and by manufacturers in preparing their offer, using a pragmatic approach (i.e. fit-for-purpose). The framework offers the possibility to assign a monetary value to each criterion by the contracting authority. The system is based on the procedure used by the Stockholm County Council in Sweden (coordinating most of the hospitals in the city), which used the WTP approach for valuing an incremental improvement in outcome measures (e.g. safety for users).¹¹¹

In developing the framework, procurement experts, manufacturers and health care providers were involved. The framework is considered to be a first step, as it still needs to be fully tested and adapted to specific product categories. Currently, the developers are further refining the framework, in close collaboration with decision-makers and procurement bodies at national and regional level.

¹¹⁰ <https://www.bcgperspectives.com/content/articles/medical-devices-technology-sourcing-procurement-unexpected-driver-value-based-health-care/?chapter=3>

¹¹¹ <https://www.bcgperspectives.com/content/articles/medical-devices-technology-sourcing-procurement-unexpected-driver-value-based-health-care/?chapter=3#chapter3>

Hospital based HTA

Hospital-based HTA aims to provide hospital decision-makers with relevant, comprehensive, objective, reliable information with regard to the effects and implications of introducing a new health technology into the hospital.¹¹² Many hospitals around the world (e.g., in the US, Spain) have “value assessment committees”, using more or less structured value frameworks.

Worth mentioning is the AdHopHTA project, another FP7 project that ended in 2015 and in which more than 385 people from 20 different countries were involved. The handbook that resulted from the project provides information on how to improve decision-making on investments for new health technologies in hospitals through the use of HB-HTA. Its target audiences are: hospital managers and healthcare sector executives, healthcare professionals, HB-HTA units, health authorities and national or regional HTA agencies, producers of potentially innovative health technologies, international organisations dealing with hospital care, patients and the general public, and the worldwide HTA community. One of the drivers for this project was “to improve the sustainability and efficiency of social and healthcare systems”.

The results from the project shows that value criteria at hospital level somehow differs from those traditionally used by HTA agencies when assessing health technologies (see Figure 3).¹¹³

Figure 3. Comparison of EUnetHTA core model and hospital-based HTA core model

Domain	HTA Core model	HB-HTA Core model
	EUnetHTA	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
D5.1 Societal point of view	✓ relevant	
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

Reflection

Value-based procurement is quickly evolving, and adopts a broader concept of value, in which patient outcomes, as well as outcomes for health professionals, providers and social impact, health benefits and economic benefits (at health system level/population level) are taken into account.

With regard to HB-HTA, it becomes clear that a different approach (compared to EUnetHTA Core Model) is needed when advising decision-making at the hospital level on the appropriateness of introducing a new health technology.

¹¹² Adophta handbook. http://www.adhophta.eu/sites/files/adhophta/media/adhophta_handbook_website.pdf

¹¹³ Adophta handbook. http://www.adhophta.eu/sites/files/adhophta/media/adhophta_handbook_website.pdf

6. Assessing value and its impact in decision-making in practice

The different characteristics of value frameworks used across organisations and countries determine its use in coverage decision-making and can ultimately impact the decision for reimbursement.

The case of multiple myeloma presented in Section 4, has clearly indicated that different frameworks lead to different conclusions. In this particular case, the differences were considered to be of methodological nature. However, ethical and political considerations used by health systems / stakeholders can also determine the extent to reimburse a health technology (see also Section 2). This is probably due to the fact that health care is developed under diverse national or local circumstances, which are influenced by historical, political and cultural factors.¹¹⁴

The role of ethical and political considerations in making reimbursement decisions

In Sweden, the WTP for a QALY depends on three principles: 1) equal human value/dignity (equity); 2) need and solidarity; and 3) cost-effectiveness. These are jointly used and cannot be separated although there is a hierarchy among them: the principle of equity constitutes the main framework and the need and solidarity principle determines how cost-effectiveness can be used. This means that the WTP for a QALY is not fixed to a specific value but differs depending on the medical need; patients with more severe conditions are given priority. This raises a number of issues which need further consideration and may be subject to political and cultural influence: a) does the duration of a condition alter the need (i.e. do young patients have precedence over older patients)? b) should WTP be higher for patients with rare diseases? c) Is treatment to prevent future diseases as important as treatment of on-going diseases and if so, is the magnitude of the risk important; d) Is the size of the effect important (in addition to its impact on the ICER)?¹¹⁵ The approach taken in Sweden is different from other countries, also from Norway, a Nordic country that might be culturally close to Sweden.^{116,117}

Furthermore, in Poland the government decided to use a differential approach to reimburse treatments for disease with high prevalence (using utilitarian approach – cost per QALY), rare diseases (750<7.000 patients; a combination of utilitarian approach and egalitarian approach) and ultra-orphan diseases (<750 patients; using the egalitarian approach – price justification).^{118,119} The incremental cost-effectiveness ratio used in Poland is less than or equal to three times the gross domestic product per capita¹²⁰ for all medicines including orphan medicines. Its use is supported by narrowing indications and risk-sharing schemes.¹²¹

The use of end-of life-criteria and the Cancer Drugs Fund (i.e. separate budget for oncology indications that were not approved by NICE and were not routinely available) in England (UK) are other examples of political considerations that play a role in resource allocation decisions. For example, in a study on societal values conducted by NICE, it appeared that citizens in the UK were willing to allocate more resources to treatments of severe diseases that address unmet medical need, provided that they resulted in substantial health benefits.¹²² However, the citizens did not support the Cancer Drugs Fund, which was

¹¹⁴ Oortwijn, W. (2015). Moving towards a process of fairer HTA. <http://www.icpublicpolicy.org/conference/article/article.php?conference=2&article=65>

¹¹⁵ Input from a Policy Forum Member.

¹¹⁶ Nord, E., Johansen, R. Concerns for severity in priority setting in health care: a review of trade-off data in preference studies and implications for societal willingness to pay for a QALY. *Health Policy*, 2014;116(2-3):281-8. doi: 10.1016/j.healthpol.2014.02.009. Epub 2014 Feb 28.

¹¹⁷ Input from a Policy Forum Member.

¹¹⁸ Borski, K. Economic aspects of rare diseases. *Developmental Period Medicine*, 2015;XIX,4: 528-532 <http://medwiekurozwoj.pl/articles/2015-4-21.pdf>

¹¹⁹ Landa, K. Health Technology Assessment – right and wrong use of HTA for treatment of ultra rare diseases http://ec.europa.eu/chafea/documents/health/prague-rd-landa_en.pdf

¹²⁰ PLN 119,600; Euro 29,200 (2015 figures)

¹²¹ Matuszewicz, M., Godman, B., Bak-Pedersen, H., Fürst, J., Gulbinovič, J., Mack, A., Selke, G., Timoney, A., Warmińska, E., Malmström, R.E. Improving the managed introduction of new medicines; sharing experiences to aid authorities across Europe. *Expert Rev Pharmacoecon Outcomes Res.* 2015;15(5):755-758.

¹²² Godman, B., Oortwijn, W., De Waure, C., Mosca, I., Puggina, A., Specchia, M.L., Campanell, P. Van der Tuin., J. Links between pharmaceutical R&D models and access to affordable medicines. European Parliament. Directorate General for Internal Policies. Policy Department a: economic and scientific Policy. European Union, PE 587.321 EN. IP/A/ENVI/2015-06, October 2016. Available via: [http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU\(2016\)587321](http://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL_STU(2016)587321)

installed by the government in 2011.¹²³ This Fund was closed earlier this year, after which a new approach to the appraisal and funding of (all new licenced) cancer drugs, including a new Fund was adopted at the end of July 2016.¹²⁴ The new approach has been developed by the NHS, NICE, Public Health England and the Department of Health and was informed by public consultation and engagement with patient groups and industry.

A case study on how value frameworks of different health systems (with views from different stakeholders) may result in different outcomes is presented below.

Use of value frameworks: the case of Hepatitis C treatment

The recent launch of new high-priced products, such as medicines to potentially cure patients with the hepatitis C virus, has emphasised the role of severity of the disease and budget impact in value frameworks for reimbursement decisions across countries around the globe. As there are considerable price variations across countries, taking existing prevalence rates, a standard treatment with Sofosbuvir (Solvaldi) could potentially quadruple the total health care budget in certain countries.¹²⁵ This has led to an increase in price negotiations between payers and manufacturers with regard to these treatments. However, price negotiations appeared to be difficult in the UK due to the existing procurement law. The NHS is not allowed to negotiate with individual companies. Therefore, the role of the NHS (as payer) seems to be focused towards rationing health care, while other relevant stakeholders, such as HTA bodies (NICE), clinicians and patients have a different view based on the evidence provided in the HTA report and experiences from practice. The way in which the NHS in England/Wales (UK) is limiting high-priced medicines in treating patient with the hepatitis C virus (through rationing) has been described in detail by Gornall et al.¹²⁶ By contrast the Australian payer/government decided to provide access to Sovaldi across all genotypes (for equity reasons). The government was able to do this via special budget allocation, taking the view that this would be a short-term increase in expenditure with a long term gain in eradication of the disease (and negotiated a low price in December 2015).¹²⁷ Furthermore, a recent study¹²⁸ on decision-making regarding reimbursement of new hepatitis C medicines suggests that decision-makers need to be receptive to views of the public, patients and clinicians in the appraisal process; this implies a broader view on the concept of value (compared to cost-effectiveness) as well.

¹²³ Linley, W.G. and Hughes, D.A. Societal views on NICE, cancer drugs fund and value-based pricing criteria for prioritising medicines: a cross-sectional survey of 4118 adults in Great Britain, *Health Economics*, 2013; 22(8), p. 948-964.

¹²⁴ <https://www.england.nhs.uk/cancer/cdf/>

¹²⁵ Brennan, T. and Shrank, W. New expensive treatments for hepatitis C infection, *JAMA*, 2014; 312(6), p. 593-594.

¹²⁶ Gornall, J., Hoey, A., Ozieranski, P. A pill too hard to swallow: how the NHS is limiting access to high priced drugs. *British Medical Journal*, 2016; 354:i4117 doi: 10.1136/bmj.i4117 (Published 27 July 2016)

¹²⁷ Input from a Policy Forum Member.

¹²⁸ Kieslich, K., Ahn, J., Badano, G., Chalkidou, K., Cubillos, L., Hauagen, R.C., Henshall, C., Krubiner, C.B., Littlejohns, P., Lu, L., Pearson, S., Rid, A., Whitty, J.A., Wilson, J. Public participation in decision making on the coverage of new antivirals for hepatitis C, *Journal of Health Organization and Management*, 2016; 30, Issue 5.

7. Summary

The discussion of the Policy Forum in January 2017 will focus on the use and challenges of existing and new value frameworks for decision-making in the allocation of health care resources.

The Policy Forum meeting will be framed around case studies covering two main themes:

1. **Elements of value frameworks.** The focus lies on the level of novelty of new/emerging value frameworks, including the impact of a participatory process in developing value frameworks, as well as the reasons and challenges of considering different value criteria (or parameters) for technological and/or contextual reasons.
2. **Use of value frameworks to inform decision-making.** Examples of the use of value frameworks by different countries resulting in diverging recommendations/decisions given the same health technology assessed will be presented and discussed. In addition, the risk and opportunities to properly transfer value across multiple indications will be explored. Furthermore, the need to quickly transfer to market innovations with potential high value to ensure quick access to patients with unmet need will be addressed, using examples on how well available value frameworks can be used for early access schemes. Finally, considering presentations and discussions on updated and new value frameworks, the need for a new/updated conceptualization of value will be discussed and if so, how this should be determined.

Discussions will seek to address the following key areas, with the understanding that context matters:

Development of value frameworks:

- Why is there a proliferation of value frameworks? Why are new frameworks currently emerging?
- Are emerging value frameworks really “new”?
- Should the development of (more elaborated) explicit value frameworks be encouraged? For example is the use of criteria, quantitatively or qualitatively (e.g. by means of MCDA) the best way to deal with values or are other approaches needed, e.g. ethical analysis?
- The majority of the current and new value frameworks focus on drugs and biologics. Does the lack of value frameworks in devices, surgical procedures and programmatic interventions bias the basis of informed health care decision-making?¹²⁹ How to overcome this challenge?
- Should the parameters and/or its metrics differ in value frameworks when addressing different types of technologies (drugs, medical devices, genetic tests, etc.). If yes, how to balance pragmatism and HTA resource availability with the need to develop technology specific value frameworks?

Defining value:

- Whose values are at stake and how to weigh the values of different stakeholders involved?
- Who is legitimate to define value?

Linking theory and practice

- Do value frameworks reflect wider health care and social considerations?
- What parameters are worth to take into account when assessing value? Should they be the same for the diverse perspectives that could be taken into account?
- What are the elements that differ across traditional value frameworks and should these be addressed (in practice) in all value frameworks? If so, how?
- Some value frameworks include more criteria than others? Are “more” criteria necessarily “better” than fewer criteria?
- How to consider the “time” aspect in value frameworks? (stepwise vs. breakthrough innovations)
- Are value frameworks fit for purpose to allow for continual/adaptive assessment (RWD/RWE infrastructure and capabilities)?
- What lessons can be learnt to improve the current or future frameworks?
 - Implications beyond primary target audiences
 - Increased transparency

¹²⁹

Based on: Goodman, C. Why Four Frameworks (Should) Arrive at Different Conclusions Multiple Myeloma Reviews. Presentation at Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016

- Stakeholder input and responsiveness throughout the development (but clearly from the start)
- Are the core key elements in value frameworks and other aspects context-based? If yes, which ones and how?
- Sourcing evidence to address the assessment
- Roles and standards for cost-effectiveness thresholds
- Roles and standards for budget impact analysis
- Need for monitoring and evaluating the use of the framework?
- Toward unified methods?¹³⁰
- Acknowledging and explicitly addressing value judgments to improve the accountability of HTA and related decision-making processes?¹³¹

How are value frameworks used by decision-makers?

- How well do the frameworks work in practice? Are they useful for decision-making? Do they have any impact?
- How are cultural and contextual characteristics influencing final decisions? How shall we deal with this?
- Decision-making includes a mix of explicit and implicit sources for assessing value. Is there a way to minimise the risk of an unbalanced view and emphasis towards explicit sources?
- Should there be a "one-size fits all" approach to value frameworks or is there space for more pragmatic approaches? If so, in what kind of situations (e.g. high-income vs. middle and low income countries)?
- How to deal with – maybe implicit – conflicting aims of value frameworks and/or stakeholders views (e.g. patient-doctor vs. payer)?
- Are there unintended consequences of using value frameworks?
- How well are existing value frameworks informing decisions for early access of valuable emerging technologies (especially disruptive health technologies)?

¹³⁰ Based on: Goodman, C. Why Four Frameworks (Should) Arrive at Different Conclusions Multiple Myeloma Reviews. Presentation at Assessing value: promise & pitfalls. National Pharmaceutical Council. Washington DC: 29 September 2016

¹³¹ Hofmann, B., Cleemput, I., Bond, K., Krones, T., Droste, S., Sacchini, D., Oortwijn, W. Revealing and acknowledging value judgments in HTA. *International Journal of Technology Assessment in Health Care*, 2014 Dec;30(6):579-86. doi: 10.1017/S0266462314000671;