Work Package 5: HTA and Medical devices

Tracing methodological and procedural challenges and trends regarding HTA of Medical Devices: an analysis of HTA reports and survey with HTA institutions

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List of Abbreviations

AAZ	Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi / Agency for Quality and Accreditation in Health Care and Social Welfare
AETS	Agencia de Evaluación de Tecnologias Sanitarias/ Agency for Health Technology Assessment
AETSA	Agencia de Evaluación de Tecnologías Sanitarias de Andalucía/ Andalusian Agency for Health Technology Assessment
Agenas	Agenzia Nazionale per i Servizi Sanitari Regionali/ National Agency for Regional Health Services
AOTMiT	Agencji Oceny Technologii Medycznych/ Agency for Health Technology Assessment and Tariff System
AT	Austria
Avalia-t	Galician Agency for HTA
BE	Belgium
CAHIAQ	Agència de Qualitat i Avaluació Sanitaries de Catalunya (AATRM)/ Catalan Agency for Health Information, Assessment, and Quality (CAHIAQ) (former: Catalan Agency for Health Technology Assessment and Research (CAHTA)
CRD	Centre for reviews and dissemination
DACEHTA	Danish Centre for Health Technology Assessment
DE	Germany
DK	Denmark
ES	Spain
FI	Finland
FinOHTA	Finnish Office for Health Technology Assessment
FR	France
G-BA	Gemeinsamer Bundesausschuss/ Federal Joint Committee
HAS	Haute Autorité de Santé/ French National Authority for Health
HIS	Healthcare Improvement Scotland

HRV	Croatia
HTA_HSRDHTA	Folkesundhed og Kvalitetsudvikling (CFK)/ HTA and Health Services Research, Public Health and Quality Improvement, Central Denmark Region (HTA-HSR/DHTA - HTA & Health Services Research)
IQWIG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen / Institute for Quality and Efficiency in Health Care
KCE	Federaal Kenniscentrum - Centre fédéral d'expertise/ Belgian Health Care Knowledge Centre
LBI	Ludwig Boltzmann Institute for Health Technology Assessment
NICE	National Institute for Health and Care Excellence
NIHR_HSC	National Institute for Health Research – Horizon Scanning Centre
NIHR_NETSCC	National Institute for Health Research – Evaluation, Trials and Studies Coordinating Centre
NL	Netherlands
NO	Norway
OGEYI (former GYEMSZI)	National Institute of Pharmacy and Nutrition, Department of HTA
OSTEBA	Servicio de Evaluación de Technologías of the Vasco Country, Department of Health, Basque Government/ Basque Agency for HTA, Department of Health and Consumers Affairs
PL	Poland
SCO	Scotland
SHTG	Scottish Health Technologies Group
SE	Sweden
TLV	Tandvårds och läkemedelsförmånsverket/ The Dental and Pharmaceutical Benefits Agency
UK	United Kingdom
ZIN (former CVZ)	Zorginstituut Nederland/ Dutch Health Care Insurance Board

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Executive Summary

The work carried out in Work Package 5 aimed to structure existing knowledge and improve understanding of the particular challenges characterizing the assessment of MDs. Furthermore, it is intended to set the groundwork for bridging knowledge and implementation gaps and providing best practice recommendations for HTA institutions and policy-makers alike.

It has provided important insights into the suitability of existing HTA assessment tools for medical devices, taking into account similarities as well as differences across different device categories. Moreover, it has clearly identified areas where knowledge and tools are lacking or can be expanded.

In addition to the contribution of the work already presented in Deliverable 1 (taxonomic model and overview of agency practices and methods in Europe), findings detailed in this report show that there are some differences across taxonomic positions with regard to aspects such as acceptable/accepted level of evidence or chosen comparators in current HTA practice.

While a broad range of institutions with different levels of experience participated in the survey, a strong emerging statement was that regulatory changes need to be made in order to facilitate and strengthen their work. Furthermore, that a common understanding on methodological requirements including both the regulatory and the HTA-doers' side is vital.

Introduction

The main goal of Work Package 5 was the advancement of knowledge and understanding of HTA for medical devices (MDs) in a multitude of ways. Furthermore, the work aims to identify areas where knowledge and tools are lacking.

For this purpose, a three-pronged approach was adopted. First, a taxonomy of MDs was developed to identify groups of devices for which different considerations in the context of HTA may be applicable (Task 1, see Deliverable 1, Manuscript accepted for publication (IJTACH)). In a second step, a systematic approach was used to identify institutions involved in HTA in Europe and explore their methods and practices, particularly when specific provisions are in place for the assessment of MDs (Tasks 2a and 2b, see Deliverable 1, Manuscript submitted, within review-process). In a third step, a broad sample of HTA reports published by the identified institutions on specific MDs was filtered on the grounds of their taxonomic position in order to verify the taxonomy's plausibility and to identify areas of particular interest for further analysis (Task 2c, e-poster for presentation at HTAi conference Oslo, 12.06.2015).

Objectives and approach

The three tasks performed so far aimed to gain a deeper understanding about the assessment of MD in European countries, especially regarding methodological challenges or hurdles, but also possible solutions to overcome them.

To identify particularities of current practices and to shed light on how European institutions have been dealing with the assessment of MDs so far, we extracted information from existing HTA reports and analysed their content **(Task 3a)** across specific taxonomic positions (case studies). In more detail we aimed**:**

- to identify if methodological approaches/aspects used by European institutions are specific to certain taxonomic positions (e.g. for diagnostic vs. therapeutic devices),
- to ascertain the extent to which specific tools for the assessment of MDs are lacking, or there are deficiencies in common understanding,
- to formulate recommendations on whether and how existing tools can be modified and,
- to highlight potential areas for further research.

In order to clarify, supplement and expand earlier findings from Tasks 2a and b, to trace methodological and procedural challenges and to capture trends not depicted in the published evidence, we designed and conducted an interview-based survey with HTA institutions **(Task 3b)**. The survey was also used to explore areas for future developments and to test the applicability and relevance of the taxonomy developed in Task 1.

Our recommendations **(Task 4)** for aspects to be taken into account in future assessment of MDs can be found at the end of this report. These are the product from all the research steps described in detail below.

The methods behind the research procedure used here are described in detail below, broken down by task.

Methods

Task 3a: Cases studies - Analysis of HTA reports across different taxonomic positions

The selection of case studies across different taxonomic positions was based on the composed report pool (covering 55 reports from 2004-2014) that was used for the plausibility testing of the taxonomy (see Deliverable 1 and here). Due to feasibility reasons not every taxonomic cell could be analysed. Taking into account the input provided during the partners meeting in Warsaw, we selected six technologies or groups of technologies for analysis.

These include:

1. PET/CT scanners (cell C1/IIb)
2. Devices for hearing impairment (Cells A2IIa, B2IIb, B2III)
3. Joint implants (knee, shoulder, hip; Cell B2/III)
4. Implantable cardioverter defibrillator (ICD; Cells B1/IV and B2/IV)
5. Brachytherapy (Cell C2/IIb)and
6. Devices in Risk class I (Cells A1/I, C1/I).

The intention behind this selection was to include technologies with considerably different characteristics (and therefore, placements in the suggested taxonomy), thus including both diagnostic and therapeutic technologies, technologies used for the same purpose but belonging to different taxonomic positions (case study 2), technologies with a dual function (diagnostic and therapeutic components, case study 4) as well as devices for which our taxonomic model predicted a low relevance for a full evaluation (case study 6).

The corresponding reports from the overall pool created in Task 2c were identified for each case study. An additional search in the database of the Centre for Reviews and dissemination (CRD) revealed no further reports (date of search: 14

April 2015). To provide an overview of current practices, a five-year window (2010-2014) was chosen and the matching reports were selected.

We analysed all selected reports according to an extraction tool we developed based on Drummond et al. (2008). The following aspects were considered during the extraction:

- **EUnetHTA Core Model elements** (e.g. safety)
- **Type of evidence** according to the Cochrane level classification (Ia-IV)
- **Evidence base** (e.g. submission/ independent research)
- **Comparator** (e.g. active/ placebo)
- **Endpoints** (e.g. mortality/ QoL)
- **Quality appraisal** (e.g. appraisal tool used)
- **Stakeholder involvement**
- **Cost and economic evaluation**
- **Objective of report (policy question)**
- **Outcome**
- **Recommendation**

Cost-related aspects were analysed in greater detail using a more comprehensive extraction tool based on the CHEERS checklist (Husereau et al., 2013).

All extractions were carried out by one researcher and checked by a second. The corresponding extraction tables for each report are available upon request and the overview/summarizing tables are presented in the text (Tables 1-11).

Task 3b: Interview survey with HTA institutions

Participant and institution selection

For the participatory approach we conducted interviews with institutions among those identified in Task 2a (Deliverable 1); from the full agency pool, institutions were selected based on the amount of publicly available HTA reports on MDs put together in Task 2c. This approach was adopted based on the assumption that the amount of available reports is associated with the extent of an institution's experience with MD assessment so far. We formed three categories:

- Institutions with no or fewer than 10 available reports: AAZ, AGENAS, AOTMiT, CFK, HIQA, TLV, OGEYI
- Institutions with between 10 and 60 available reports: Avalia-t, DACEHTA, FinOHTA, HIS, KCE, OSTEBA
- Institutions with a more than 60 available reports: HAS, IQWiG, LBI, NICE, ZiN

We consulted both relevant experts and project partners to select the right contact person responsible for MD assessment within the institutions. We sent an email request as well as two reminders in two-week intervals. Participants received the interview guide (see description, below) and the taxonomy developed in Task 1 in advance.

Interview guide

To ensure content validity, each participant was interviewed according to a semi-structured interview guide that was iteratively developed including feedback from members of the research team and experts. The guide consisted of two parts and was structured according to the key principles for conducting HTA set out by Drummond et al. (2008): (i) Structure of HTA programs, (ii) Methods of HTA, (iii) Processes for Conduct of HTA and (iv) Use of HTAs in Decision Making.

Part I of the interview guide aimed at filling information gaps on institutional practices from Task 2 of the Work Package. These answers were used to supplement factual information and were thus analysed in an institution-specific manner. The questions varied depending on the institution's role and the information that was already available from Task 2.

Part II of the interview guide contained questions concerning (i) structural, procedural and methodological challenges characterising the assessment of MDs as perceived by the interviewees, (ii) the usefulness and relevance of the developed taxonomy and (iii) desirable aspects for future developments in the assessment of MDs. The interview guide is attached in the Appendix (page 89). These answers were not presented in an institution-specific manner and were reported anonymously.

Data analysis

Following conventions of qualitative research, data collection and analysis were performed iteratively, aiming *'to validate or extend conceptually a theoretical framework or theory'* (Hsieh & Shannon, 2005, p.1281).

The interviews were transcribed verbatim by external professionals from 2 translation agencies *(Übertrans Tiptoptranskription& Tint Linguistic Services).* Each transcript was checked by one researcher and finally by the corresponding interview partner.

The validated transcripts incorporating participants' comments formed the basis for the analysis. For the **analysis of part I** we created a tabular overview for each institution using summative content analysis (Hsieh & Shannon, 2005).

For the **analysis of part II** we used direct content analysis according to Hsieh and Shannon (2005). To guide the analysis a coding framework was developed and applied based on the major themes and subthemes, which were partially deductive and partially inductive in nature.

The major themes derived from the main questions were used to categorize deductively. Recurrent and significant themes emerged from the raw data that did not fit into these existing major themes were categorized inductively. The unit of analysis was a theme, so text passages ranging from a single word to a whole paragraph were coded.

The software Atlas.ti was used to facilitate the coding process. To enhance the quality and validity of the analysis, two researchers conducted the coding independently. After coding the first 5 transcripts, the coding framework was discussed and further refined. Subsequently, the transcripts of all interviews were coded using the refined framework by two researchers separately. Finally, coding results from both researchers were compared and discussed.

To enhance informative value and illustrate frequencies of the results we used - where appropriate - a categorisation of major themes using the terms *some (10-30%)*, *many (31-65%)* and *most (66-100%)* (Mayring, 2001; Siegel & Schrimshaw, 2000). Where indicated, we also took the institutions' experience into consideration (based on the number of available reports).

Although Individual transcripts were returned to participants for validation and commentary[1], the analysis (results) of the interviews presented here has not been sent out yet. Feedback will be requested from all participants before any scientific articles are submitted for publication.

[1] All interviews except one (CFK) have been validated until now. As a result, slight changes in the analysis presented here might be possible for the publications in scientific journals.

Task 4: Recommendations

Derived from the research steps described above, but mainly from the analysis of the case samples and interviews, we have formulated recommendations to facilitate future assessment of MDs. We also took relevant findings related to non-pharmaceutical technologies as well as other research activities (e.g. KCE recommendations) from EUnetHTA Joint Action 2 into account.

These recommendations entail both overall impulses regarding regulatory issues and processes, but also detailed methodological advice. We will also provide suggestions what should be considered when implementing these recommendations at different levels (e.g. national level).

Results

(a) Case studies

The following paragraphs describe the results of the analysed reports in a tabular overview for each extracted element across all six case studies. The elements sets the focus of the results as we wanted to know if/how the assessment differs between the taxonomic positions and not within one case study.

Report variables of all case studies

Table 1 presents an overview of all included reports and their basic characteristics. Additional details are provided in the notes under the table.

In total, 93 reports published between 2004 and 2014 were included in the initial pool. However, in order to reflect current practice regarding the assessment of MDs, only reports published between 2010 and 2014 (n=55) were included in the analysis. These reports were produced by a total of 15 institutions.

Table 1: Report variables of all case studies

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk class I
Reports 2010-2014 (2004-2014)	19 (31)	4 (8)	7 (12)	3 (7)	8 (10)	14 (25)
Number of Institutions 2010-2014 (2004-2014)	7 (12)	4 (8)	7 (9)	3 (4)	4 (6)	5 (8)
Institutions (reports)	Agenas (1), Avalia-t (1), FinOHTA (1), HIS[1] (4), IQWiG (6), NIHR (5), UETS (1)	AIAQS (1), CVZ[*] (1), NICE[2] (1), NIHR (1)	AETSA (1), CVZ[*] (1), DACEHTA (1), HIS[1] (1), NICE[2,3] (2), NIHR (1)	Agenas (1), KCE (1), NICE[2] (1)	AETSA (1), Avalia-t (4), HIS (2), IQWiG (1)	CVZ[*](3), HAS (2), HIS[1] (2), HVB (5), NICE (1), NICE[3] (1)
Indication (SOCs[**])	16[g] , 3[b,e,f]	4[c]	6[f], 1[k]	3[a]	8[g]	2[d], 3[i], 4[h,j,k,l], 5[f]
Language of full text						
English	3	-	-	2	1	-
Official language	7	2	3	-	5	10
English is official language	9	2	4	1	2	4
Publication type						
Abstract/Summary	1	-	-	-	1	-
Full text	18	4	7	3	7	13
Type of report						
Institutions own HTA report	18	4	6	2	7	13
Update of institutions reports[***]	-	-	1	1	1	1
Adapted HTA through Core-Model	-	-	-	-	-	-
Report from another Institution	1[****]	-	-	-	-	-

Notes: [1] Healthcare Improvement Scotland (HIS): Scoping reports/Evidence notes/Advice Statement used in combination to extract relevant information; [2] includes NICE guidance and the linked full assessment report prepared by an External Assessment Group & corresponding published article in NIHR HTA journal; counted as one, for institution and report; [3] Interventional Procedures Guidance: own assessment done

[*] now ZIN; [**] SOCs according to MedDRA Terminology: [a] Cardiac disorders; [b] Congenital, familial and genetic disorders; [c] Ear and labyrinth disorders; [d] Eye disorders; [e] Infection and infestations; [f] Musculoskeletal and connective tissue disorders; [g] Neoplasms benign, malignant and unspecific (incl. cysts and polyps); [h] Nervous system disorders; [i] Respiratory, thoracic and mediastinal disorders; [j] Skin and subcutaneous tissue disorders; [k] Vascular disorders; [l] Various indications; [***] update considered for reports of institutions where an regular update is not foreseen (as in the case for NICE); [****] FinOHTA based on KCE report

The indications addressed in each report were classified according to the MedDRA® terminology[2] and differed between the case samples. Nevertheless, the most frequent System Organ Class (SOC) was 'Neoplasms benign, malignant and unspecified'. In the case samples 'Devices for hearing impairment, 'ICD' and 'Brachytherapy' only one indication was addressed, whereas MD applications for different indications were evaluated in the case samples 'PET/CT' and 'Implants'. For 'Risk class I' multiple indications were expected all available reports across taxonomic positions (i.e. without focus on a specific technology) were analysed.

The majority of the reports were available as an accessible full text except in the case of FinOHTA (full text available only in Finish) and AETSA (full text could not be identified). The language of full text reports was English in 6 cases, official language in 27 cases and English as official language in 22 cases. Only few reports were updates of the institution's previous reports (n=4) and only one report (FinOHTA) based on a report from another institution (from KCE).

The exploratory approach adopted for 'Risk class I' sought to find out what kind of technologies had been assessed by the institutions. The technologies listed below were included in the analysis (n=14).

- Toric lenses
- Compression stockings
- Mobility devices (4)
- Compression Therapy Products (Orthotic devices)
- Protrusion splints
- Individually calibrated foot-worn biomechanical device
- Mechanotherapy (traction, extansion with device)

[2] MedDRA®: Medical Dictionary for Regulatory Activities terminology is the international medical terminology developed under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).The MedDRA® terminology has a hierarchical structure in which System Organ Classes (SOC) are at the highest level. SOCs provide the broadest concept for data retrieval and are based on etiology, manifestation site and purpose.

- Glasses
- Dynamic elastomeric fabric orthoses
- Wrist splint
- Taping
- Palatal expander
- Debrisoft wound dressing
- Endoscopic balloon dilatation for subglottic or tracheal stenosis

The listed technologies cover a broad range and are mainly from the taxonomic cell 'assistive technologies used by the patients' (A2l).

Assessment variables – EUnetHTA Core Model elements

The first extracted element was the assessment domain with regard to the EUnetHTA Core Model (see table 2). The HTA Core Model from EUnetHTA organises the information within an HTA by dividing it into nine domains. These domains are: Health problem and current use of technology, description and technical characteristics of technology, safety, clinical effectiveness, costs and economic evaluation, ethical analysis, organisational aspects, social aspects and legal aspects.

For the analysis we considered three different options: (1) the domain was addressed and there is an own section or part in the report (marked with ✓), (2) the domain is not addressed (marked with ×) and (3) the domain is touched upon in the report, mostly within the conclusion/recommendations or in the introduction, but there is no own section or part or in depth-analysis (marked with #).

Nearly all institutions addressed in their reports the first domain 'Health problem and current use of technology'. Exceptions are three reports from 'Risk class I' and one report each from 'Hearing impairment' and 'Implants'. This is similar to the domain 'Description and technical characteristics of technology'; however comparatively more reports (n= 9 of 55) did not addressed this domain.

The domain 'Safety' is not addressed by all reports. This is particularly evident for the case studies 'Risk class I' and 'PET/CT'. It can be assumed that for the lower

risk categories safety aspects are not of such a high relevance compared to the high-risk technologies. It has to be taken into account that there are some institutions (e.g. NIHR) who do not necessarily include 'Safety' in the scope of their reports. Since the majority of reports in the 'PET/CT' case study came from such institutions a less frequent assessment of this domain is not surprising.

Table 2: Assessment variables – EUnetHTA core elements

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
EUnetHTA Core Model elements						
Health problem and current use of technology	**19** ✓ 0 × 0 #	**3** ✓ 1 × 0 #	**6** ✓ 1 × 0 #	**3** ✓ 0 × 0 #	**8** ✓ 0 × 0 #	**11** ✓ 3 × 0 #
Description and technical characteristics of technology	**16** ✓ 3 × 0 #	**2** ✓ **2** × 0 #	**6** ✓ 1 × 0 #	**3** ✓ 0 × 0 #	**8** ✓ 0 × 0 #	**11** ✓ 3 × 0 #
Safety	**10** ✓ 9 × 0 #	**2** ✓ 0 × **2** #	**4** ✓ 1 × 2 #	**2** ✓ 0 × 1 #	**8** ✓ 0 × 0 #	6 ✓ **8** × 0 #
Clinical effectiveness	**19** ✓ 0 × 0 #	**4** ✓ 0 × 0 #	**7** ✓ 0 × 0 #	**3** ✓ 0 × 0 #	**8** ✓ 0 × 0 #	**13** ✓ 1 × 0 #
Cost and economic evaluation	**11** ✓ 8 × 0 #	**3** ✓ 1 × 0 #	**5** ✓ 2 × 0 #	**3** ✓ 0 × 0 #	**5** ✓ 3 × 0 #	4 ✓ **8** × 1 #
Ethical analysis/ social or legal aspects	0 ✓ **19** × 	0 ✓ 2 × 	3 ✓ **4** × 	**1** ✓ **1** × 	0 ✓ **8** × 	0 ✓ **11** ×

	0 #	2 #	0 #	**1 #**	0 #	3 #
Organizational aspects/ other MD specific aspects	2 ✓ **16 ×** 1 #	0 ✓ 2 × 1 #	2 ✓ **4 ×** 1 #	**2 ✓** 0 × 1 #	0 ✓ **4 ×** 3 #	0 ✓ **12 ×** 2 #

Notes: ✓addressed, own section/part; × not addressed; # touched upon, but no own section/part, mostly mentioned within recommendation or in introduction part

The domain 'Clinical effectiveness' is addressed by all reports expect one belonging to risk class I.

Cost-related issues, including economic evaluation, are addressed in some way or the other by the majority of the reports (31 out of 55 reports; for a more detailed breakdown of approaches see results on the corresponding variable, below, and Table 11). Out of the 19 reports on 'PET/CT', 11 included these aspects and 8 did not. Interestingly, the majority of reports on 'Risk class I' devices did not consider cost-related elements. It has to be take into account that there are some institutions (e.g. IQWiG), for which economic evaluation does not fall within the scope of standard evaluations.

The domains 'Ethical analysis', 'Social aspects' and 'Legal aspects' are extracted separately but are presented combined into one category in table 2. Fewer reports (n=5) addressed this category. This is most noticeable for case sample 'PET/CT' where none of the 19 reports include ethical, social or legal aspects. As already mentioned for the domain 'Cost and economic evaluation' above, the role/mandate of the institution might be one explanation. 'Hearing impairment' and 'ICD' were the case samples where one of the three aspects was addressed or at least touched upon. It can be assumed that especially for implants (e.g. cochlear implant), these aspects are of higher importance than in comparison to 'Risk class I' devices.

With the aim to capture further information on MD that does not fit into the original domain, we initially expanded the EUnetHTA domain 'Organisational as-

pects' to include 'Other MD specific aspects'. Findings were combined since during the extraction of information we realised that the majority of information was captured by the original domain. In the case sample 'ICD' this domain was addressed — or at least touched upon — mainly within the recommendations. For 'Implants' it was fully addressed three times and one time only touched upon and for 'Brachytherapy' it was touched upon three times. It seems that for the case samples representing use of an MD within a procedure the organizational aspects are more relevant.

Assessment variables – Level of evidence

The extraction of information on level of evidence (see table 3) was based on the hierarchy of evidence according to the Cochrane collaboration (AHCPR, 1992). During the extraction process it became apparent that a distinction had to be made between (1) a priori defined inclusion criteria regarding the level of evidence (LoE), and (2) the LoE of evidence identified and used for analysis. Former relates to preliminary determined study designs/types that would be included for assessment. The latter refers to the actual evidence found through e.g. a systematic literature search.

Table 3: Level of evidence

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Level of evidence						
A priori (e.g. inclusion criteria)						
Ia	7	2	2	2	5	9
Ib	14	4	4	2	5	6
IIa	14	4	2	2	5	6
IIb	9	4	1	2	5	6
III	7	4	2	2	5	6
IV	6	4	3	2	5	9
Not specified/reported	3	-	3*	1*	3	4
Identified data						
Ia	7	-	3	1	2	4
Ib	4	1	5	2	4	7
IIa	4	1	2	1	6	1
IIb	3	1	-	-	3	-
III	5	3	-	1	1	-
IV	7	2	4	1	5	5
Not interpretable/ reported	8	-	1	-	-	2

Notes: Ia- Evidence obtained from meta-analysis and randomized controlled trials, Ib- Evidence obtained from at least one randomized controlled trial, IIa- Evidence obtained from at least one well-designed controlled study without randomization, IIb- Evidence obtained from at least one other type of well-designed quasi-experimental study, III- Evidence obtained from well-designed non experimental study, such as comparative study, correlational studies, and case studies; IV- Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities; *Mostly, NICE documents rather do refer to their general method paper than presenting a detailed description regarding the priori defined inclusion criteria for the LoE

(1) A priori defined inclusion criteria for the LoE

Across all case samples the majority of reports considered all or almost all study types. However, the definition of which LoE was included for analysis was mostly presented in a general manner such as 'we considered all types of studies' or referred to the principles of evidence based medicine (EbM). In addition we identified 14 reports which did not or not sufficiently report inclusion criteria for the study type. In these cases, we were not able to adequately assess the a priori defined study types for analysis and anticipate that all LoE were (automatically) considered.

(2) Identified data

Our findings regarding the reporting of the identified study types were twofold. On the one hand we found differences between the a priori defined inclusion criteria and studies actually identified for the analysis. On the other hand there were differences between case samples. Although that the most a priori definitions for the evidence base referred either to a high LoE (i.e. 'PET') or the inclusion of all study types with a preference for high quality studies, results regarding trials that were actually identified for analysis were heterogeneous. For example, evidence identified was of low(er) quality (e.g. LoE III or IV) within the case samples of for example 'PET/CT' or 'hearing devices'. This illustrated an existing lack of high quality study evidence within the area of MD assessment[3]. In contrast, reports assessing implants frequently identified high quality studies (e.g. LoE Ia and Ib). This result is not surprising, as a lot of research is conducted with respect to e.g. hip and knee prosthetics. Additionally, there are reports e.g. within the case studies of 'PET/CT', 'Brachytherapy' or 'Risk class I 'devices in which studies were identified of both high and low LoE.

[3] This lack was also emphasized by the interviewees in Task 3 (see results survey)

Assessment variables – Type of evidence

Table 4 presents an overview of information on type of evidence included in analysed reports.

Table 4: Type of evidence

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Type of evidence						
Direct	19	4	7	3	8	12
Indirect	1	-	-	1*	-	-
Not interpretable/ reported	-	-	-	-	-	1

Notes: Definition of direct and indirect evidence according to Jansen et al. 2011 and Glenny et al., 2005; *by manufacturer submission

Extraction of this assessment variable was composed of two categories. We distinguished between the considerations of 'direct' or 'indirect' evidence. Usually, direct evidence from well-conducted randomized controlled trials (RCTs) provides the most valid estimates of the efficacy or effectiveness of competing healthcare interventions. However, many interventions have not been directly compared in RCTs. When there is no, or insufficient, evidence from direct comparison trials, it is possible to use results of trials with different comparisons to estimate the effects of compared treatments (Jansen et al. 2011; Glenny et al., 2005)

Our results show that almost all reports, irrespective of the case sample, based their assessment primarily on direct evidence. We identified only one case within the 'PET/CT' sample that clearly states the additional consideration of indirect evidence for evaluation. One additional report also presented indirect evidence for analysis. However, this was induced by the manufacturers' submission of additional data and not due to an explicit criterion for inclusion of indirect evidence.

Assessment variables – Evidence base

Information on the evidence base used in the reports was categorized as follows: 'Independent research', 'Manufacturer submission' and 'Both'. Independent research was again subdivided into 'Primary evidence', 'Secondary evidence' or 'Both'. An overview of extracted information is presented in table 5.

Table 5: Evidence base

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Evidence base						
*Independent research**	19	3	5	2	8	10
Primary evidence	9	1	3	-	1	2
Secondary evidence	3	-	-	1	-	-
Both	7	3	4	2	7	10
*Manufacturer submissions***	-	-	1	-	-	1
*Both****	-	1	2	1	-	2
*No information*****	-	-	-	-	-	1

Notes: * the information from the category *Both* is included in the information to the subcategories of independent research; **only formal submissions of manufacturers were counted; ***includes independent research and manufacturer submissions; **** due to language barrier

Notably, almost all reports were rather based on independent research than on manufacturer submissions. Only reports within the samples on 'Implants' and 'Risk class I' devices conducted independent research in addition to manufacturer submissions. Assessments solely based on manufacturer submission were not

identified in any of the included reports. In comparison to drugs where the assessment based on standardised submissions by the manufacturer (Panteli et al., 2015) this is a remarkable difference. There was only one report for which no information could be extracted, due to language barrier.

With regard to the kind of independent research performed, most institutions include both primary (e.g. RCTs) and secondary evidence (e.g. existing HTAs, SRs). One exception is the case sample 'PET/CT' where 9 reports stated that they were mainly based on primary evidence.

Assessment variables – Comparator included

Information on the comparator included in analysed reports is given in table 6. We clustered the information in three categories: 'Active', Placebo or Sham intervention' or 'None/no treatment'.

Table 6: Comparator included

	PET/CT[a]	Devices for hearing impairment[a]	Implants (art. joints)	ICD	Brachytherapy	Risk I[b]
Comparator included						
Active	16	4	6	3	7	10
Placebo/Sham	1	1	-	-	-	4
None/No treatment	1	-	1	-	1	2
*No information**	2	-	-	-	-	2

Notes: * Due to language barrier or only summary/abstract available; [a] one report included active and placebo as comparator; [b] 4 reports included active and placebo as comparator

The majority of institutions considered active comparators in their reports. Placebo or sham interventions were accepted/included in 6 cases, of which 4 cases derived from reports of 'Risk class I'. In 5 cases "no treatment" was allowed as a

comparator. No information regarding the comparator was found in 4 cases, mainly due to language barriers or because of missing full-text reports.

Thus, based on existing practices, it seems to be feasible to have an active comparator despite discussions about the difficulties of appropriate active comparators for the evaluation of MDs. For the lower risk level devices it seems to have been considered appropriate to use placebo/ sham or none/ no treatment.

Assessment variables – Endpoints

Regarding the endpoints considered by the institution in their reports we focused on outcomes concerning mortality, morbidity, quality of Life (QoL) and safety. We also captured the common terms 'sensitivity and specificity' to evaluate clinical tests, since many MDs serve a diagnostic purpose. Outcomes that could not be assigned to any of these categories were summarized in an additional group termed 'further endpoints'.

Interestingly, in all cases samples, reports considered mortality, morbidity, QoL and safety, except reports referring to the evaluation of 'Risk Class I' MDs. Within this group, mortality was not considered in any report, as was to be expected from a sample of low risk MDs and the indication/purpose they are used for. More frequently addressed outcomes within this sample referred to morbidity (11 out of 13 reports) and safety parameters (7 out of 13 reports). Mortality was also less frequently considered within the sample of 'Implants (hip & knee)' (3 out of 7 reports). In contrast, the consideration of mortality in reports of e.g.' ICDs' seemed to be of more importance. QoL was considered in all reports regarding hearing devices and also frequently considered within the sample of 'Brachytherapy' (4 out of 8 reports). Furthermore, sensitivity and specificity were only taken into account in reports assessing 'PET/CT' and represented the most frequently considered outcomes within this sample (17 out of 19 reports). As 'PET/CT' represents the only case study of a diagnostic procedure, we expected

these findings. We would have expected a consideration of sensitivity and specificity for 'ICDs', which have a diagnostic as well as a therapeutic component. Due to the small sample size in the 'ICD' case study (n=3) this fact has to be investigated further. Outcomes summarized in the category of 'further endpoints' were reported in reports of all case samples, except 'ICD'. Ten out of 19 reports on 'PET/CT' considered such endpoints, compared to three out of four reports on 'Devices for hearing impairment' and six out of 13 reports on 'Risk class I' devices.

Overall, reporting of endpoints was sufficient. Only 3 reports presented no information or lacked specifications in order to make an adequate interpretation.

An overview of results is presented in table 7.

Table 7: Endpoints

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Endpoints						
Mortality	9	2	3	3	7	-
Morbidity	11	1	6	3	7	11
QoL	10	3	6	3	4	3
Safety	9	4	6	2	7	7
Sensitivity and Specificity	17	-	-	-	-	-
Further endpoints	10	3	4	-	3	6
Not interpretable/ reported	1	-	-	-	-	2

Assessment variables – Quality appraisal

The term 'quality appraisal' *'[…] suggests an investigation of the extent to which study authors conducted their research to the highest possible standards' (Hig-*

gins et al., 2011). This includes for us the assessment of methodological quality and/or the assessment of risk of bias.

We clustered the information on quality appraisal according to 4 categories: quality appraisal (1) by using a specific tool, (2) without using a specific tool (reports simply named criteria they considered, e.g. study size), (3) without giving any further details (e.g. 'the quality was assessed') and (4) no quality appraisal done. The first category was further divided into utilization of existing checklists and development of own checklists. Slightly adapted tools by the institution were not considered as a separate subcategory.

The term 'Tool' in this text is used according to the definition by Jüni et al. (2001) who describe it as follows: *'[...] tools are scales, in which various components of quality are scored and combined to give a summary score, or checklists, in which specific questions are asked'.*

Table 8 presents an overview of the methods which the institutions referred to for the critical appraisal of included studies.

Table 8: Quality appraisal

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Quality appraisal						
*Yes, with a tool**	**13**	**3**	1	**2**	**5**	3
Existing checklists	13	3	1	2	5	3
Own checklist developed	6[a]	-	-	-	-	-
Yes, without a specific tool	7	-	**3**	-	1	-
*Yes, but no details given***	5	1	1	1	2	4
No quality appraisal done	-	-	-	-	-	**5**
*No information****	1	-	2	-	-	**2**

Notes: Tools are standardised checklists, instruments to appraise/assess the quality of the evidence, adapted checklists are not considered as a separate subcategory; * Some institutions used existing checklists in combination with no specific tools (n=6); ** For example: institutions only mentioned that the quality assessment based on EbM criteria or that the quality was assessed but without further details on how this happened; *** due to language barrier or only abstract/summary available; [a] IQWiG developed own checklist for prognostic studies (n=6 reports)

Almost all reports from the case samples 'PET/CT', 'Devices for hearing impairment', 'ICD' and 'Brachytherapy' use tools for quality appraisal. No tools used or no specific information given were the most common findings in 'Risk class I' reports.

The majority of institutions utilizing a specific tool relied on existing ones. In six cases (all reports from IQWiG) a new tool for prognostic studies was developed (see table 9). Sometimes institutions used a combination of existing checklist and further, unspecified tools.

In five cases no information could be extracted. For 3 out of these 5 cases we had only the summaries for the analysis, thus the information regarding quality appraisal is might be given in the full text.

With regard to specific tools, table 9 provides an overview of all checklists used by the institutions according to the study design addressed.

For diagnostic accuracy studies the use of QUADAS or its revised iteration (QUADAS 2) seems to be state of the art; however, further instrument were mentioned. Systematic Reviews were mainly assessed by using AMSTAR or criteria based on PRISMA. Drummond et al. (1996) as well as CHEERs seems to be particularly used for economic studies.

The lack of an appropriate checklist for surgical RCTs was raised in the report from NIHR (Carroll et al., 2011):

> '*There is no published surgical RCT checklist, so this review applied surgical-quality assessment criteria outlined in a relevant Cochrane review.'*

IQWiG developed its own instrument for prognostic studies (Wolff et al., 2010) because the use of QUADAS for was considered insufficient:

> *'For the quality appraisal of prognostic studies the adequate consideration of possible confounders in addition to QUADAS as a further quality criterion was foreseen. Within the work this instrument proved to be not suitable for the appraisal. Based on work from Hayden et al. (...)] and Altman et al. (...) an own tool was developed [...]'* (translated from German)

Table 9: Quality assessment: Checklists used according to included study types

STUDY TYPE (DOMAIN)	**TOOL USED FOR QUALITY ASSESSMENT**
PRIMARY STUDIES (CLINICAL-EFFECTIVENESS)	o Criteria used by Centre for Reviews and Dissemination: Systematic Reviews. CRD´s guidance for undertaking reviews in health care. University of York, January 2009. o Criteria from the Cochrane Collaboration: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. o Deeks J, Dinnes J, D'Amico R, Sowden A, Sakarovitch C, Song F, et al. Evaluating nonrandomised intervention studies. Health Technol Assess 2003;7(27). o Thomas BH, Ciliska D, Dobbins M, Micucci S. A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. Worldviews Evid Based Nurs 2004;1:176–84. o Jovell & Navarro-Rubio scale: Jovell AJ, Navarro-Rubio MD. Evaluation of scientific evidence. Med Clin (Barc) 1995;105:740–743 o SIGN: Critical Appraisal: Notes and Checklists
PRIMARY STUDIES (ECONOMIC EVALUATION/ COST-EFFECTIVENESS)	o Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ 1996;313:275–83. o Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. Health Technol Assess 2004;8(36) o Husereau D, Drummond M, Petrou S, Carswell C, Moher D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMC Medicine 2013 11:80. doi:10.1186/1741-7015-11-80 o Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: consensus on health economic criteria. Int J Technol Assess Health Care 2005;21:240–5.
RCTS	o Criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions: Higgins et al., 2011 (see above) o Surgical-quality assessment criteria outlined in a relevant Cochrane review: Parker MJ, Gurusamy KS, Azegami S. Arthroplasties (with and without bone cement) for proximal femoral fractures in adults. [Update of Cochrane Database Syst Rev 2006;3:CD001706; PMID: 16855974.]
INTERVENTIONAL STUDIES	o Cochrane Handbook for Systematic Reviews of Interventions: Higgins et al., 2011 (see above)
CASE SERIES	o Checklist developed by NICE: National Institute for Health and Clinical Excellence. Methods for the development of NICE public health guidance. 2nd edn. London: NICE; 2009.
DIAGNOSTIC ACCURACY/TEST ACCURACY STUDIES	o QUADAS: Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol 2003;3:25. o QUADAS 2: Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JAC, and Bossuyt PMM. QUADAS-2: A Revised Tool for the Quality Assessment of Diagnostic Accuracy Studies. Ann Intern Med 155 (8):529-536, 2011. doi:10.7326/0003-4819-155-8-201110180-00009

	o Criteria suggested by the Cochrane Handbook: Higgins et al., 2011(see above) o Jovell & Navarro-Rubio scale: Jovell et al., 1995 (see above) o OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. Oxford Centre for Evidence-Based Medicine. o Guyatt GH, Oxman AD, Vist G, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, for the GRADE Working Group.Rating quality of evidence and strength of recommendations GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-926
PROGNOSTIC STUDIES	o Wolff R, Westwood M, Scheibler F, Schröer-Günther M, Janßen I, Kleijnen J. Assessment of risk of bias in prognostic studies. Cochrane Database Syst Rev 2010; (Suppl 2010): 23.
DIAGNOSTIC AND THERAPEUTIC IMPACT	o Meads CA, Davenport CF. Quality assessment of diagnostic before–after studies: development of methodology in the context of a systematic review. BMC Medical Research Methodology 9. 2009
SYSTEMATIC REVIEWS	o SIGN (SR/MA): Methodology Checklist 1: Systematic Reviews and Meta-analyses. o Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10 o Critical Appraisal Skills Programme. CASP Checklists. o Following the general principles from PRISMA statement: Moher D, Liberati A Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Int Med 2009;151:264–9.
SYSTEMATIC REVIEW OF DIAGNOSTIC STUDIES	o AMSTAR checklist: Shea et al, 2007 (see above) o PRISMA: Moher et al., 2009 (see above)
EVALUATION REPORTS/ HTAS	o GEVIEC developed by 'Group on Development and Validation of Methods for Quality Assessment of Health Technologies Assessment Reports': Blasco JA, Andradas E. Elaboración y validación de instrumentos metodológicos para la evaluación de productos de las Agencias de Evaluación de Tecnologías Sanitarias. Madrid: Plan Nacional para el Sistema Nacional de Salud del Ministerio de Sanidad y Consumo. Unidad de Evaluación de Tecnologías Sanitarias. Agencia Laín Entralgo; 2008. Report No.: Informes de Evaluación de Tecnologías Sanitarias: UETS Nº 2006/01.
CLINICAL GUIDELINES	o The AGREE Collaboration. Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument 2001.

Notes: * Appropriate quality assessment criteria: There is no published surgical RCT checklist [...] (Carroll et a., 2011; Criteria outlined in Appendix 3, p. 55); ** IQWiG developed own tool based on 2 other articles

Assessment variables – Stakeholder involvement

An overview of information on the involvement of stakeholders identified in analysed reports is presented in table 10.

The majority of reports state that they include stakeholders in the various stages of the assessment (no differentiation was made between different stages e.g. scope, appraisal). These stakeholders include external reviewers, medical or specialist advisers but also other interest groups, such as patient representatives. In comparison to other case samples, 'Risk class I' reports described less stakeholder involvement. In 5 cases no information could be identified for this variable.

Table 10: Stakeholder involvement

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Stakeholder involvement*						
Yes	**15**	**4**	**4**	**3**	**6**	**8**
No	3	-	1	-	1	5
*No information***	1	-	2	-	1	1

Notes: * includes external reviewers, medical/specialist advisers and other interest groups e.g. patients, no further splitting possible; ** due to language barrier or only summary/abstract available

It seems that for the majority of lower risk devices, the institution's own assessment is considered sufficient and does not need to incorporate additional information from stakeholders. However, there are some examples (e.g. HAS, Agenas) where the external stakeholder group plays an essential part for lower risk class devices e.g. due to regulatory criteria/process. Furthermore, it cannot be ruled out that stakeholder involvement did take place during the evaluation process but is not depicted in the HTA report analysed for this work.

Assessment variables – Cost and economic evaluation

The extraction of information on the consideration of costs and/or economic evaluation in included reports was performed in two steps. Initially, a general differentiation was made between reports i) including a general mention of costs related to the use of the technology; ii) reports that used literature review to identify available economic studies and iii) reports wherein an economic analysis was performed de novo and iv) reports where no mention of costs or economic evaluation was identified.

More detailed extraction tables were used to extract information from reports falling under categories ii (data sources, quality of studies) and iii (based on relevant elements from the CHEERS checklist, such as setting; perspective; time horizon; discount rate; endpoints; participatory approach; type of costs; model characteristics; estimation of uncertainty; and consideration of heterogeneity).

Table 11: Cost and economic evaluation

	PET/CT	Devices for hearing impairment	Implants (art. joints)	ICD	Brachytherapy	Risk I
Reports 2010-2014 (n)	19	4	7	3	8	14
Number of institutions	7	4	6	3	4	4
Institutions (reports)	Agenas, Avalia-t, FinOHTA, UETS (each 1); HIS (4), IQWIG (6), NIHR (5)	CVZ, AIAQS, NICE, NIHR (each 1)	AETSA, CVZ, DACEHTA, HIS, NIHR (each 1); NICE (1/2)	Agenas, KCE, NICE (each 1)	AETSA, IQWiG (each 1), Avalia-t (4), HIS (2),	CVZ (1), HIS (2/4), HVB (2/3), NICE (1/5)
Reports (n)	12	3	5	3	2	6
Mention of costs	2	1	-	1	-	5
Literature review of existing studies	9	2	5	2	2*	2
Own economic analysis	4	2	3	2	-	1

Note: *the literature review did not identify any studies

Where there was only a mention of costs, this was usually done as part of the context analysis for the report or when a literature review was attempted but yielded no relevant results. This approach was most frequently employed in reports for Risk Class I devices. For big-ticket devices, it was rather running costs than investment costs that were mentioned. Resource constraints were mentioned in two reports as grounds for not performing a (more) comprehensive budget analysis.

Literature review was used alone or as a source of information for the institution's own economic evaluation. In some cases, institutions used relevant information

from other HTA reports (e.g. HIS from NICE or FINOHTA and HIS from KCE). A literature review of economic evidence was sometimes part of manufacturer submissions (e.g. NICE) or was requested by the agency during the evaluation (e.g. GENAS). Methodologically, literature searches for economic studies were either performed separately (e.g. Agenas, KCE) or integrated in the overall literature search (e.g. HIS). Specialized databases were not always consulted; NHS-EED and EconLit were the ones most frequently included. A priori restrictions regarding perspective and time horizon were not common and the same PICO as for the overall research question was used. Literature searches for economic evidence often yielded no or few relevant studies.

De novo economic evaluations were only included in 12 reports (11 from NIHR and 1 from KCE). A common characteristic was that these analyses focused on direct costs from a payer perspective and used literature and/or participatory elicitation as their information sources. As the vast majority of reports stemmed from the same HTA programme, not much can be said for other institutions. Among the NIHR reports where an economic analysis was carried out, model assumptions and endpoints depended on the type of technology (e.g. diagnostic or therapeutic) while the exact model type chosen varied by indication and the technology's application.

As already mentioned for other assessment elements, the consideration of costs or cost-effectiveness is often outside an agency's remit (e.g. IQWiG). Additionally, they could have potentially been considered during a phase of the evaluation not illustrated in HTA reports. It seems that the approach towards cost-consideration is institution-specific; no clear picture was gained concerning the influence of device type.

To summarise the results, figure 1 provides key findings from the analysis of all case samples.

Key finding from the case samples

- EUnetHTA Core Model elements:
  - For MDs of lower risk categories: safety and economic aspects seem to be of less importance
  - For implants (e.g. cochlear implant, artificial joints) social, ethical and legal aspects seems to be of higher importance
  - Taxonomic positions which entail a MD used within a procedure: organizational aspects seem to be of more relevance
- Level of evidence:
  - Lack of high quality evidence in most cases (although high LoE almost always defined as preferred inclusion criteria for studies)
  - Reports assessing implants frequently more frequently identified high quality studies
  - In some cases both high and low quality studies were included)
- Type of evidence:
  - Almost all reports, irrespective of the case sample, based their assessment primarily on direct evidence
- Evidence base:
  - Almost all reports based assessment on independent research rather than manufacturer submissions
  - Most institutions include both primary and secondary evidence
- Comparator:
  - Majority of the assessments considered an active comparator
  - Placebo or sham interventions were used mainly in reports of 'Risk class I'
- Endpoints:
  - In all case samples reports considered mortality, morbidity, QoL and safety
  - In the evaluation of 'Risk class I' MDs mortality seem to play a minor role, in contrast to reports regarding ICDs.
  - Sensitivity and specificity was solely addressed in reports assessing 'PET/CT' and represented the most considered outcome within this sample
- Quality assessment:
  - Most institutions use existing checklists/tools (e.g. QUADAS 2, AMSTAR or CHEERS)
  - Lack of checklists for surgical RCTs, prognostic studies was mentioned
- Stakeholder Involvement
  - Majority of institutions from reports include stakeholders in the various stages of the assessment, except evaluations of 'Risk class I' MD
  - The types of stakeholders involved vary by agency
- Cost and economic evaluation
  - The type of approach is agency-specific (whether mention of costs, literature review or own economic evaluation) and depends on agency remit and potentially financing streams for MDs
  - A dearth of economic evidence was frequently raised by analysed reports

Figure 1: Key findings from the analysis of HTA reports in the case samples

(b) Survey

Description of Interviewees

Of the 18 individuals approached in this study, 16 responded to our invitation and participated in the survey. All interviews were conducted by telephone, with the exception of two (Agenas, IQWiG), which were conducted in person. The duration of the interviews ranged from 34 to 100 minutes, with the majority lasting approximately 40 minutes. The interviewees represented 16 institutions from 14 countries, among those national Governmental institutions (37,5%), independent research entities with function as governmental institution (31,25%), regional Ministries of Health/Social Affairs including a related department (12,5%) and non-departmental public body with legislative function and independent research entity (each 6,25%), see table 12

Table 12: Overview of institutions included in the interview

INSTITUTION*	COUNTRY	TYPE OF INSTITUTION[1]	ROLE OF INSTITUTION REGARDING HTAS AND MDS
AAZ	HR	4	Provides requested advice and information to decision-makers (MoH, HZZO and management board of hospitals) on drugs and non-drugs
AGENAS	IT	2a	Provides advice and information to decision-maker (MoH) and other stakeholders on yearly predefined number of MDs; prioritizes further MDs in a Horizon Scanning process for assessment and assesses those of high importance
AOTMIT	PL	2a	Provides advice and information to decision-maker (MoH) on public funding of drugs, MDs and specific food supplements
AVALIA-T	ES	3	Provides advice and information to decision-makers (NHS, RHS) on public funding of MDs
CFK	DK	2b	Supports health care policy regarding MDs or drug/device combined products; co-ordinates HTA activities across 5 Danish regions
FINOHTA	FI	2a	Supports decision-making on MDs, surgical interventions and drugs vs. other technologies
HAS	FR	4	Provides requested advice and information to decision-maker (MoH) on public funding of MDs
HIS (SHTG)	UK/ SCT	2a	Provides advice and information to decision-makers on public funding of drugs and non-drugs; SHTG provides technical advice to NHS Scotland in order to support decision-making process based on evidence reviews
IQWIG	DE	4	Provides requested advice and information to decision-maker (G-BA) on public funding of drugs and non-drugs
KCE	BE	4	Provides requested advice and information to decision-makers (MoH, NIHDI) and other stakeholders; prioritizes proposed technologies (drugs and MDs) for assessment and assesses those of high importance
LBI	AT	1	Provides requested advice and information to decision-maker (MoH) on public funding of hospital MDs;

			performs Horizon Scanning and an early assessment of MDs on request of MoH
NICE	UK/ ENG & WAL	5	Provides guidance to the NHS: Evaluations within the diagnostics and medical device tracks are not binding for coverage decisions, they are used as recommendations; technology appraisals on devices have to be adopted within three months (made available by the NHS)
OGEYI**	HU	2a	Provides requested advice and information to decision-maker (HIF) on public funding of drugs and of two categories of MDs
OSTEBA	ES	3	Provides requested advice and information to decision-makers (NHS, Basque RHS) on public funding of health technologies (drugs and non-drugs); performs Horizon Scanning at regional level
TLV	SE	2a	Makes decisions on public funding of medicines, medical devices and dental care treatments; conducts HTAs of MDs on a trial basis
ZIN	NL	4	Provides requested advice and information to decision-maker (MoH) on public funding of health technologies (drugs, non-drugs); ensures quality of care

Notes: *alphabetic order, **former GYEMSZI; Abbreviations- G-BA: Federal Joint Committee, HIF: Health Insurance Fund, HZZO: Croatian Health Insurance Fund, MD: medical devices, MoH: Ministry of Health, NHS: National Health Services, RHS: Regional Healthcare System, RIZIV-INAMI: National Institute for Health and Disability Insurance, further abbreviations of the institutions are listed in Abbreviation list at the beginning of the document

[1] Type of institution (own categorisation): 1. Independent academic research entity, 2. Governmental institutions (a. national, b. regional), 3. Regional Ministries of Health/Social Affairs including a related department, 4. Independent research entities with function as governmental institution, 5. Non-departmental public body with legislative function

First part

The following section shows the results of part I of the interviews about the institutional structures, processes and methods specific for MD assessment (see also methods, page 13/14). As we sought out to update information already captured in Task 2 of WP5 (Deliverable 1), we will mainly present information that is either new or that deviates from what was that identified via the web-based search. Thus, this step goes beyond tracking institutional practices to also reflect the extent to which the institutions' public profiles provide sufficient information to facilitate transparency. Moreover, questions in part I also captured current developments and work in progress within the institutions that might not be publicly available in many cases. A profile for each institution was compiled and can be found in the Appendix.

Role of the institution in the countries HTA system

Table 12, above, presents an overview of the institutions involved and their role in the countries HTA system, mainly regarding MDs.

In comparison to our findings in Task 2, the survey helped in some cases to better understand and classify information on the structures, processes and methods of included institutions. For most institutions, information on role and remit was publicly available. However, due to language barriers, in cases such as AOTMiT and OGEYI, it was helpful to ask the interviewee to give a short overview of the role and main functions of their institution.

Link to MD assessment and coverage decision-making

As HTA aims to help or support the decision-making process it was of great importance to ask about the impact of the institutions assessments in the corresponding health system. This topic was broached twice with two different questions: In the first part of the interviews we were mainly interested in the assess-

ments' link to coverage decision-making (are assessments directly linked to pricing and reimbursement or are they just seen as recommendations). In the second part, the relevant question focused on the interviewee's personal opinion regarding the actual impact. This was primarily interesting for those institutions where assessment results are not binding for decision-makers. Moreover we aimed to identify if and how the institutions themselves try to evaluate their impact.

The assessments of 10 out of 16 institutions are not binding for any kind of decision making, as opposed to those of two institutions which are. In four cases, the bindingness of recommendations depends on either the specific programme (e.g. MTEP within NICE) or the commissioner of the report (NHS, RHS). Interestingly, many institutions where the assessments are not binding, expected that their work will be considered by the decision making body (e.g. MoH).

Definition of MDs used

Considering the taxonomic model developed in Task 1 and considering different categories of MDs, we intended to find out if the institutions themselves used a specific definition or understanding for MDs. Six interviewees referred to the relevant EU Directives (AAZ, Agenas, AOTMiT, IQWiG, KCE, NICE MTEP) while two stated that it is not absolutely necessary to use the directives for their work. Four institutions use no specific definition, three institutions stated that they use their own definition and two use existing definitions (INHATA, HTAi). One important point came from KCE, which pointed out that in documents from Belgium (especially from NIHDI) the terms class I and II refer to their own classification based on Belgian law and not to the EU Directives (see KCE profile, Appendix page 94).
Beside the variable definitions provided by interviewees, there are also differences among institutions concerning which type of devices they assess (scope).

Interestingly, for example OGEYI (Hungary) use a division of devices which is also part of the underlying understanding of the taxonomy developed in Task 1. These divisions are made due to regulatory and funding purposes.

OGEYI separates between (1) medical aids intended for patients to use at their home and in their daily lives (e.g. hearing aids) and (2) other medical devices and diagnostic devices which are mainly intended for physicians to use in hospitals (e.g. PET). Thus the process of assessment differs between these categories:

> *'The process for the first category is much more simplified [...]'* (for more information see OGEYI profile, Appendix, page 104).

Also other institutions use a similar distinction: for example, IQWIG (Germany) assesses medical interventions using a MD, medical aids are assessed by another institution. AOTMiT assesses new devices and the procedure using the device, whereas ZiN assesses either MDs used in the outpatient setting (e.g. hearing aids) or that are used within medical specialist care (e.g. surgical implants). LBI assesses procedures ('Verfahren') in which one or more MDs are involved and TLV distinguishes between "consumables" (included in the benefit package) and MDs that are assessed upon request by the government commission.

The question concerning the use of a specific definition of MDs reveals some deviations from information collected in Task 2, including some corrections (e.g. in the case of Agenas, OSTEBA) but also the addition of new details (e.g. for OGEYI).

Separate department/unit for the assessment of MDs

Most of the institutions interviewed (11 out of 16) have no separate department for MD assessment, mostly due to the size of the institution or staff constraints. One interviewee stressed:

> *'In our case it's impossible because we are five people'*

Due to the fact that some other institutions (e.g. Avalia-t, LBI) focus mainly or solely (Agenas) on MD assessment, no separate/parallel unit exists.

Differences between the process of MD assessment in comparison to other technologies

Seven of the interviewees stated that there is a different process for MD assessment in comparison to the evaluation of drugs. These differences mainly refer to the information retrieval process which is more standardized for drugs and based on formal manufacturer submissions. In contrast, search for information on MDs requires more time and often the institution's own initiative to contact the manufacturer and ask for data and studies.

Three of the interviewees stated the process is nearly the same overall, while differences can be seen mainly between different types of MDs (e.g. diagnostics vs. therapeutics). This latter statement was most frequently expressed by institutions which stated that the process differs.

Only two institutions noted that there is no difference at all between devices and other types of technologies. For four institutions the question was not applicable due to their work mainly or solely focusing on MDs anyway.

Within this context some institutions raised or mentioned new approaches for the assessment of MDs.

> *'Just more recently we have piloted a new product and process whereby we, for five topics... five devices or procedures, we've actually asked the manufacturer for a submission for innovative technology. So, the submissions are very limited, so it still differs quite a lot from medicine assessment in that way.'* (SHTG/HIS).

Derived from the website of the Scottish Health technologies Group the purpose of the Innovative medical technology overview (IMTO)[4] is to afford manufacturers/distributors of non-pharmaceutical technologies the opportunity to submit their clinical and cost effectiveness evidence for independent assessment within NHS Scotland.

NICE mentioned the medical innovation briefings during the interview:

> *'[...] medical innovation briefings. These summaries are written about innovative devices which may not have enough evidence, or get through – gone through the whole evaluation process. And there is just a summary of the technology, what it does, its cost and the evidence that exists. And also some comments from specialist commentators, a clinical expert usually.'*

These MIBs[5] are designed to support NHS and social care commissioners and staff who are considering using new medical devices and other medical or diagnostic technologies (for more information see NICE website and the integrated process statement given in the footnote).

The interviewee from IQWiG mentioned the new German coverage with evidence development approach *'Potentialbewertung (§137e of SGB V)'* but did not describe it in more detail. However, there are two recent publications regarding this new approach that provide further information (Zens et al., 2015; Olberg et al., 2014).

Prioritisation process and specific criteria used for MDs

Answers on this question in most cases deviated from what we had found in Task 2 of Deliverable 1.

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[4] Further details about the innovative medical technology overview (IMTO) process is available here.

[5] More information about NICE's Medtech Innovation Briefings (MIBs) is available here.

In eight cases no standardized prioritisation process exists, because institutions are commissioned mainly by the decision-maker and do not select topics on their own, for example in the case of AOTMiT:

> *'In general our agency works on the order of the Minister of Health. We do not select the subjects of the assessment on ourselves'.*

In six cases the interviewees stated that the entire prioritisation process is different from that used for other technologies, such as drugs. One of the six institutions emphasized that there is more of a difference between new and existing technologies (including drugs). In two cases no differences with regard to the processes was reported.

'Regarding the criteria used for prioritisation, only 5 institutions indicated using different ones for the selection of MDs compared to drugs. However, it is important to mention that among these 5 institutions, two mainly focus on MDs within their work to begin with (e.g. Agenas, SHTG/HIS).
The Scottish Health Technologies Group prioritizes topics depending on

> *'[...] how important they are according to a number of criteria: how does it align with the NHS Scotland strategic position, is there a difference in terms of either uptake or use of the technologies, how big is the likely patient impact, are there likely to be any material resource implications resulting from adoption of the technology or not, is it possible to form an answerable question at this time, is there available evidence of sufficient quantity and quality to address the question purposefully on behalf of the person who sent us the topic [...]'.*

The Agenas prioritisation process for existing technologies is based on an annual agreement with the MoH about a pre-defined number of reports (usually 4 to 5). The technologies are thus selected from multiple sources: through a call to four Italian regions to submit preferred technologies to Agenas and an open call on the website for everyone (e.g. citizens, scientific societies). A small committee

that is composed by representatives from the regions and one representative of the MoH prioritize the technologies to assess according to criteria set out in the national program: cost, impact, burden of disease or inappropriate/improper use of that technology.

Until now, TLVs government commission regarding MD assessment includes no formal prioritisation process (it still operates on a trial basis) but they are currently testing different approaches such as public suggestions via webpage and/or contact with the county councils, governmental institutions and companies. TLV collects suggestions and chooses regarding i) own interest and ii) criteria such as: impact on the health system, size of patient population, disease severity and feasibility of health economic analysis. Based on this step, TLV provides a shortlist with the selected MDs to the County Councils and asks for their input on the MDs most suitable for assessment.

Methodological guidelines and specific methods for MDs

The first search for information performed in Task 2 (Deliverable 1) captured almost all relevant guidelines. Most institutions have their own general guidance or refer to existing ones from other parties (e.g. EUnetHTA, other institutions).

Additional information could be retrieved for institutions where existing guidelines are currently being updated or are under review (e.g. SHTG/HIS HTA manual; NICE DAP, TA, MTEP methods guides) or recent work on new documents has been carried out (e.g. OSTEBAs checklist on organizational aspects, unifying document for Spain or ZiNs guide on introducing cost-effectiveness thresholds).

Most institutions stated that they do not have a methodological document specifically for MDs, confirming findings from Task 2. Two further documents from LBI (Austria) for diagnostics (2010) and bio-markers (2014) were identified (see LBI profile, page 92). Despite the fact that the institutions rarely develop separate documents most of them (n=11) answer the question on whether they use specific methods for specific MDs with 'Yes'. The interviewees stated that they refer mainly to the developed EUnetHTA frameworks (e.g. Core Model™ for diagnos-

tics), use existing guidelines from other institutions or incorporate methodological input from stakeholders. Thus it is not surprising that many institutions report using specific methods while only a limited number of specific documents are available.

Consideration of device specific aspects

Almost all institutions (n=14) consider aspects that are relevant to the assessment of MDs (compared to that of other types of technologies), such as learning curves, device-operator interaction or minimum requirements for e.g. skills of professionals. In most cases these were touched upon the recommendation of the report and interviewees often added that this consideration does not happen within a predetermined intention or framework but rather depends on the type of MD and the research question. Agenas clearly pointed this fact out:

> *'[...] it's a case-by-case strategy. Probably, if you look at the reports, you see that these aspects are being considered but without "a priori" intention. For example, for the endoscopic capsule, a few years ago, we went inside the gastroenterology units to understand how many patients you have to treat for justifying the investment, and in the other reports, no. In some reports we made our national survey, in some others we just limited it to one or two regions [...]'.*

Some institutions use checklists to guide the consideration of organisational aspects (e.g. OSTEBA) or clarify specific questions within a technical report (NICE MTEP).

Answers on these questions confirm findings obtained from the analysis of HTA reports (see results case studies, page 21/22). More detailed information can also found in the subsequent section on results from the second part of the survey.

Availability of HTA reports

Information on available reports per institution was identified in Task 2 and formed the basis for selecting the institutions to survey.

There were some changes in this information following interviewee input, due to the fact that some existing reports were not publicly available, e.g. for Avalia-t:

> *'Some are internal reports. Like I was saying we have specific petitions or maybe you know, not full reports, like we call brief reports. So those are not published online.'*

or due to language barriers (see AOTMiT profile, Appendix page 110).

The number of MD assessments is generally lower than that of drugs, except for institutions who's main line of work revolves around MDs. Links to the reports and information on language used and updated numbers of reports available are provided in each profile table (Appendix).

Research activities on MDs

Not surprisingly, almost all institutions are actively involved in the current EUnetHTA Joint Action 2. Other reported activities concentrating on MDs included, for example, the recent KCE report studying the legally acceptable possibilities for a guided introduction of high-risk MDs (class III and implantable devices) in Belgium after CE-mark has been obtained (Baeyens et al., 2015) and the TLV commission regarding MDs (see TLV profile, Appendix page 116).

Second Part

This section presents results from the second part of the interviews following the major themes and subthemes derived from the analysis. In addition, where appropriate and/or applicable, relevant quotes, categorisations and sub-analyses according to institutions' level of experience are given.

The first question from part II referred to the main differences regarding MDs and drugs within the assessment, reported from the structural, procedural and methodological perspective. Besides these predetermined perspectives, challenges from a regulatory perspective emerged inductively from the material and are presented separately. The answers given addressed mainly challenges which will be illustrated in more detail below.

Challenges specific to MD assessment: (i) from a structural perspective

From 16 interviewees 12 raised points regarding structural challenges in MD assessment. The following subthemes particularly were touched upon by many interviewees:

'Transparency: There is a lack of information about which MDs are entering the market or are currently on it and there are no available registers that could be used for the evaluation. Additionally, detailed data about MDs with a CE mark that are in the possession of notified bodies are not available to HTA institutions. As two interviewees stated:

> *'They (from the drug department) know in advance for the next year which drugs they are looking at and the year after that, they're usually able to plan a year in advance, and fill up all their slots. With the diagnostics and the medical devices, we rely on company notifying the programme.'*

'[We are] legally forbidden to get data from notification/certification body.'

'National legal framework': Due to the existence of different scopes for assessment defined by national law or predefined specific reimbursement criteria, assessors have no flexibility in the way they approach evaluations.

'We have regulatory criteria for reimbursement. This criteria are mandatory – we have to assess medical devices with this regulatory criteria.'

Two further challenges that were mentioned by the interviewees were the absence of a national body for the introduction of MDs into the system and the absence of sufficient capacity (lack of resources for conducting HTA).
These challenges from a structural perspective mostly were raised by institutions with less to medium experiences. Almost all institutions with a high level of experience addressed these issues, mainly the subtheme 'Transparency'.

Challenges specific to MD assessment: (ii) from a procedural perspective

Challenges from a procedural perspective were again raised by 12 out of 16 interviewees. The most frequently cited challenge referred to the *'Coordination of assessment'*. This theme includes the incorporation of stakeholder input at different points during the assessment process in order to expand the limited available evidence.

[...] we tend to create ad-hoc groups, depending on the technology [...] sometimes we can resolve ourselves and sometimes this can lead to a working group where we involve the different parties, the different clinicians that are responsible for managing the patients.

Two interviewees mainly mentioned the stage of the *'Information retrieval'*, as one of the big challenges, particularly requests to manufacturers for additional data/information. Compared to the assessment of drugs, including regularly submission of data to the institution, MD assessment lacks such a standardized process of submitting relevant, as one interviewee clearly pointed out:

'[...] and the assessment evidence is automatically produced by the manufacturers, whereas for non-drug technologies the assessments tend to be at the request of the health system.'

Within the information retrieval process another challenge is that of identifying the most relevant literature given the multiple generations, single products and even classes of MDs.

'Then we discover there are a whole class of products or even one product but multiple generations of devices and that also brings with it some specific aspects in terms of knowing what to focus on and which literature to focus on, those kinds of things because there could be quite big differences between the different generations or iterations of the devices.'

One further challenge mentioned referred to *'Prioritisation'*, which contains the difficulties regarding topic selection, due to the broad spectrum of MDs. Within this context, one interviewee emphasised:

'[...] we do not really know what things might be dangerous and should be evaluated better than others.'

Challenges from a procedural perspective were raised by institutions with less to medium experience with MD assessment. Almost all institutions with a high level of experience addressed these issues, mainly the subtheme 'Coordination of assessment'.

Challenges specific to MD assessment: (iii) methodological perspective

The methodological almost frequently raised by interviewees fell under the theme *'Evidence base'*, encompassing the subthemes 'Weak evidence and limited knowledge', 'Lack of publicly available information' and 'Weak reporting quality of available studies'.

'For me it's the evidence threshold. There are quite often lower levels of evidence, and that gives us challenges in terms of its credibility, but also the assessment of it in terms of the methods of the assessment.'

One further theme raised by nearly half of the interviewees is the *'Broader perspective of the assessment'* including the subthemes 'Evaluation of complex interventions', 'Consideration of other aspects (e.g. organisational aspects)' and 'Diagnostic vs. Therapeutic MDs'. One interviewee gave an example of elements to consider beyond the clinical effectiveness:

'So that for example things that patients use, you need to think about sufficient training and correction of misuse.'

Another theme mentioned concerned *'Methodological approaches'* and included 'Fewer MD-specific methodologies', 'no common definition of PICO aspects' and 'no methodological description of learning curves'.

'Then another issue is choosing the outcomes and for some things, what we have been discussing is, that it would be very important to standardize the outcomes that you measure when you are treating a certain type of disease, [...] that for the O part it would be good to predefine which measures should be used and what would be a clinically meaningful change.'

Moreover, 'Rapid pace of innovation' was raised as one important challenge in e.g. framing the research question, knowing on what to focus and assessing if the findings are transferrable. Two interviewees pointed out:

'And another aspect is, that sometimes the devices go through a very short life cycle until they get an improvement and we sort of have to start the assessment all over again for the updated versions of devices, how do you handle assessments of that, when there is a minor technological change and of course the producer always likes to say that this is a major thing.'

'There's lots of things that we often think about, both in terms of the ways that medical devices change over time, develop over time, and how we can

know whether the evidence is generalisable so that the best version – is it still relevant for the version that you're still looking at.'

Challenges from a methodological perspective were raised by all institutions. With regard to the subthemes, institutions with less experience addressed the theme 'Broader perspective of the assessment' more frequently while experienced institutions mainly mentioned the 'Rapid pace of innovation'.

Challenges specific to MD assessment: (iv) regulatory perspective

Challenges from a regulatory perspective that came up during the interviews encompass two main themes:

'Weak EU regulation regarding licensing of MDs': the existing regulation on licensing of MDs is not as strict and structured as for drugs and does not require (well-established) effectiveness of the device as one interviewee clearly pointed out:

'It's not demonstrating clinical-effectiveness, it's only a demonstration of quality of engineering, and it's not demonstrating that it will work for users.'

'Decentralisation': The notified bodies use different processes and additionally these vary by and also within the countries as one interviewee clearly stated:

'So first of all the regulation it is—I would say in the case of Europe it is a mess. Even in the case of many nations, I would say that even the CE marks that are performed in other nations even. For example in our case […] they almost did not perform any kind of evaluation of and did not give any kind of CE mark. So most of the producers […] are used to go to for example to Germany. They go to, I do not know if I said it correct but they go to TÜV, in terms of obtaining the CE mark […] so the process for confirmation are quite delayed and I think it is much better than going to CE mark notification bodies in other

countries such as Hungary or Romania or whatever, where the processes are not so tight.'

'These themes are strongly linked to the aforementioned structural, procedural and - particularly - methodological challenges, as the majority of issues mentioned are caused/induced in some way by the regulatory framework. As most of the interviewees touched upon these themes, a sub-analysis based on level of experience was not applicable.

Consequences with regard to the assessment and decision making on MDs

The Following findings were derived inductively from the answers given to the question on differences between the assessment of MDs and drugs.
Three subthemes concerning negative consequences were mentioned by more than one interviewee:

- Incremental adoption/use of MDs before evidence is there,
- Difficulty to stop/limit the use of MDs when they are already on the market and
- Many MDs in an experimental stadium on the market.

Further negative consequences emerged but these were only mentioned by one interviewee:

- High rejection rate of MDs for reimbursement based on institutions decision
- Use of MDs due to need while evidence is weak
- No barrier exists between authorization and funding
- Reassessment of MDs becomes a big part of institution's workload

Some positive consequences also emerged from the interview:

- More critical discussion of new MDs
- Professionals are more careful, more critical thinking exists
- Smaller group of stakeholders that need to be informed about MDs

Approaches towards overcoming challenges

One further theme that emerged from the material was the way the institutions try to solve or deal with the challenges described above.

One subtheme mentioned by many interviewees was *'Stakeholder input'*, which encompassed the inclusion of experts groups, clinicians, ad-hoc groups, manufacturers and also scientific societies within the assessment process for example to gather more information due to a lack of high quality evidence. The following quote shows one way of this incorporation:

> *'We have a database of experts. Everyone can send his/her CV and be added to this database.'*

This subtheme corresponds to observation made in the analysis of the reports (see p. 35). Thus, stakeholder involvement seems to be important but also requires considerable time and resources (see also "challenges from a structural perspective").

Further approaches towards solving challenges that emerged from the interviews but were mentioned only by one interviewee were the following:

- Use of Horizon scanning programs
- Set up post-interaction observation/post-introduction monitoring
- Set up patient safety program
- Implementation of new approaches such as coverage with evidence development (CED)
- Creation of a proposal for change at national level: guided introduction of high risk MDs with measures
- Introduction of a national project to address missing data (no further details given)
- Facilitate the conduct of research studies/set up of a register
- Improve flexibility during the assessment process
- Set up own instruction rules (evidence weak -> no full assessment)

- Create own guidance for assessment based on EUnetHTA and own questions

Issues related to the broad variety of MDs

We asked the interviewees which role the broad variety of MDs - ranging from medical aids directly used by patients to big ticket technologies - plays within the assessment process. During the interviews it became apparent that this question was biased by the classification proposed by the taxonomic model developed in Task 1 and thus did not yield the results we expected. In addition, the variability of answers was substantial. Therefore, only the main themes raised by the interviewees will be presented here.

Some interviewees simply agreed that there exists a wide range or heterogeneity of MDs and linked the question to the scope of their institution (overall, mainly high risk MDs were assessed and not smaller products/medical aids). The following quote emphasizes these points:

> *'Yeah it does. We look at what is the kind of – interventions, what we think for what are the indications, how big is the burden for the persons that use it, these are the aspects we look at. We do not have any formal evaluation schemes of all the criteria. But I think we also have – like medical devices are in our law things from, like incontinence material, we call it also medical devices and the PET scans and the proton therapy, it's a wide scheme.'*

Some interviewees stated that it is mainly the difference between diagnostics and therapeutic devices that influences the evaluation and the uncertainties related to MDs were linked to the question about the broad variety of the MDs. That flexibility is required as a result of the variety of MDs was pointed out by some interviewees, as the following quote expresses:

'So I think in the medical devices: [...]we often have to be flexible about, especially in the beginning with the health economic models and things like that [...] often has to do a lot of additional work to do to ensure that the committee has enough information to make decisions.'

Further opinions on the issue (mentioned by one interviewee each) were: variety has no discernible influence, no differentiation is possible due to law, endpoints differ between the MDs, different methodological approaches are needed, involvement of experts is required, not just the type of MD is essential.

Role of device-specific aspects

Aspects that are specific to the assessment of MDs were the subject of one further interview question. We defined "device-specific" as all aspects that are relevant to the assessment of MDs specifically and do not apply for the assessment of other technologies such as drugs. We had already recognized during the analysis of the HTA reports (Task 2c, see page 21) that this definition was not the most useful towards obtaining the relevant information, a fact which was confirmed during the first interviews. As some interviewees did not completely understand what aspects we were referring to, we adapted the question and described with the concept using the example of organisational aspects, and more specifically learning curves.
The three main subthemes that emerged are presented below.

'Extent of consideration': Some interviewees stated that it is crucial to address those specific aspects and to go beyond clinical effectiveness. Others interviewees pointed out that the consideration of such aspects constitutes part of the assessment but clinical effectiveness and safety as well as economic aspects remain the main focus. However, the majority stated, that whether and how these aspects are considered depends on the type of device. Thus this aspect is more or less variable, as one interviewer clearly emphasised:

'Yeah, but it's a case-by-case strategy. Probably, if you look at the reports, you see that these aspects are being considered but without "a priori" intention. For example, for the endoscopic capsule, a few years ago, we went inside the gastroenterology units to understand how many patients you have to treat for justifying the investment, and in the other reports, no.'

Only two interviewees stated that these aspects could not be considered due to the law or due to time or/and resource constraints.

'Purpose of device-specific aspects': The purpose of taking device-specific aspects into consideration mentioned by the interviewees was either general (for 'Informed decision making', 'reimbursement questions') or for formulating 'recommendations/ minimum requirements'. One interviewee expressed stated:

'We're often asked about the volume and outcome relationships as well – that's one of our key questions we get from government, because they want to plan therapy. Again, because we're quite a small country, it's very much about what would be a feasible service? Is it feasible [...] to have a service in a particular area and what is the volume-outcome relationship for this device or procedure?'

'Barriers of addressing device-specific aspects': One important barrier was given by the interviewees. The lack of existing data/studies, for example about learning curves, make it difficult to address these issues even if the intention on behalf of the institutions is there. Thus the lack of available information leads to assumptions that are associated with uncertainties, as one interviewee emphasized:

'Well, we would have access to good quality data regarding this, we could give decision makers a more thorough analysis of all the aspects of the device in question. And yeah, for example learning curves, you mentioned those, they can play an important role when we discuss efficacy or effectiveness or cost-effectiveness, even. But we always go back to this, I wish we had

good quality data regarding this. Certainly we can only make assumptions at that.'

'Device-specific aspects (examples): In their answers to the question on the role of device-specific aspects, most interviewees gave examples of what they look at in more detail. In addition to learning curves, which have already been mentioned above, these were:

- Minimum of patients per year/number of patients required/volume-outcome relationship
- User skills/training for patients
- Patient acceptance
- Feasibility of providing services
- Team work (different professionals) within surgical procedures
- Work and communication protocols
- Technical specifications of different versions
- Kind of hospital to use a certain MD
- Clinical pathways
- Organizational circumstances such as new room in hospital, special infrastructure required
- *Mentioned in general:* social, ethical and organizational aspects

Separate methodological document addressing particularities of MDs

We asked the interviewees if they think a separate methodological document addressing particularities of MDs could be useful or helpful for their work. The institutions that already had a separate document or a document with a separate part for MDs (HAS, IQWiG, LBI, NICE, ZiN) were asked about how useful they found the existing documents.

Overall, most of the institutions including the ones with a separate document see such a document as helpful either for the institution itself or as a training possibility for other parties, as the following quotes pointed out:

> *'Now I realise that it could be better to have also in our guidelines a specific part of MD'*

> '*Companies have little knowledge about health economic analysis [...] it would be good training possibility for them [...]'*

Not surprisingly, those institutions with separate documents found them helpful as such documents mainly entail important steps for the assessment that are different to other technologies such as scoping processes, information sources and methodological approaches. One interviewee add one prerequisite:

> *'Well you have to use it a lot to make it useful...should only make these kind of documents for evaluations you do a lot.'*

Another interviewee also stated that the usefulness of such documents depends on existing experiences. In fact, it was institutions with a higher level of experience with MD assessments (see page 12) that had mostly developed separate documents (e.g. NICE, ZiN).

Some interviewees also stated that separate documents could be helpful but only to some extent:

> *'We never thought about...maybe for things routinely to consider...having a basic understanding of some of those device-specific issues.'*

> *'[...] it is also a matter of how specific can we be because the learning curve might be extremely important for some medical devices, and not so much for others.'*

Some interviewees mentioned that they did not think a separate document would be advantageous (e.g. due to legal or regulatory criteria) or that they were unsure about its potential usefulness.

'Type of document'

We clustered information on the preferred 'Type' of document as it emerged from the answers given to the question above. Three institutions did not elaborate on this, so the following categories refer to 13 interviewees (including the institutions with a separate document).

Most interviewees state that an 'Overall document [for assessments] with additional sections or specific aspects to consider' would be sufficient:

> *'I think it might be useful to have a sort of a basic effectiveness document and then sort of separate additions when considering drugs, when considering vaccines, when considering point of care, point of care diagnostic, when considering imaging, yes, so subcategories but I think it's too heavy if you do a separate document for everything.'*

Some institutions thought that it would be good to have a 'Document for specific types of MDs' such as diagnostics and some other interviewees saw the existing 'EUnetHTA documents' (e.g. for diagnostics) for a standardized approach across European institutions as important guidance that would be/is sufficient for their work.

A document dealing with the full spectrum of MDs was seen as difficult to realise by some of the interviewees, as illustrated by the following statement:

> *'[...] but I think that the devices as a group may be so different, that it would be difficult to develop that kind of document [...] I do not believe in 15 different types of documents.'*

Usefulness of the taxonomic model developed in Task I

In addition to the interview guide, the interviewees received the taxonomy developed in Task 1. The aim was to gather their opinions about its usefulness and applicability in their daily practice. During the interview we shortly explained the taxonomy and its aims and rationale.

Many of the interviewees stated that the taxonomy is useful. However, only four found that it could be used directly by their institutions, while seven stated that it would not be directly applicable for the institution. The main reason behind the latter statements was that the institutions in question lacked the mandate to prioritize technologies for assessment. Four interviewees generally saw the taxonomy as a helpful tool but did not specify for whom:

> *'[...] Generally speaking, yeah, I looked at your work, I find it really interesting [...] I believe that hopefully we in [...] can use your taxonomy.'*

> *'I do agree that it would be very appropriate to deliver a new classification. I am not sure the classification delivered would be used by our organization but it would clearly help to have a unified taxonomy.'*

There were only two interviewees who said that the taxonomy was not useful or that they were unsure about its added value, as one interviewee stated:

> *'Honestly my first reflection, if I see it, in our situation, then I'm asking what is the added value for us to have a different kind of taxonomy, we do an HTA on a specific device, and I do not immediately see that added value of having this taxonomy.'*

Figure 2 summarises the views from the interviewee's regarding the usefulness of the developed taxonomy.

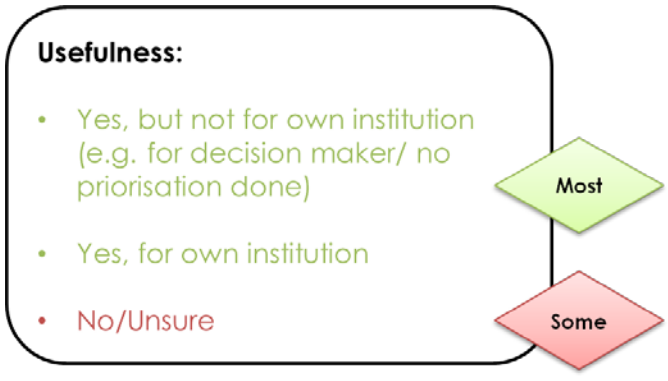

Figure 2: Usefulness of taxonomy

'Helping/crucial aspects and limitations'

Emerging from the answers regarding the taxonomy given above, some interviewees pointed out its helpful or crucial aspects but also its limitations. No specifications in this direction were forthcoming from 6 interviewees.

The four most cited helpful aspects referred to 1) the 'Prioritisation (particularly economic relevance)', 2) the 'Separation between diagnostic and therapeutic MDs', 3) the 'Methodological approaches' depending on taxonomic position and 4) the 'Categorisation of the MDs in 3 groups based on their purpose' (MDs for patients to use directly, artificial body parts and MDs used by medical professionals). The following quote clearly illustrates the prioritisation element:

> *'Yeah, that's pretty much what we have been thinking about over the years. The devices that are to be evaluated should have a really big impact on the healthcare system in some way. So we have pretty much the same reasoning behind that as you have from here. It has to have an economic impact on the healthcare system but it also has to have a big impact on the patient's survival or quality of life, or something like that. We do not try to look at small products...Seems to correlate well to the things that we have been thinking about here'*

One interviewee add that even the yellow cells[6] in the taxonomic matrix make sense:

[6] In the taxonomic model (see Deliverable 1 or e-poster from HTAi conference, Oslo 14.06.2015) yellow cells corresponds to groups of devices for which the relevance of a full evaluation is case-specific.

'[…] for the in-vitro diagnostics, I think you've got pregnancy tests in yellow. That would be – actually that works, because that's case specific […], something like a pregnancy test and over-the-counter test, they would not normally, you wouldn't do an evaluation. But something they've done through IQ tech or something that a patient will use at home, under the guidance of a health professional they would do an assessment on that. So that does actually work with this what you said, it being case-specific.'

One interviewee gave a more detailed explanation on how the taxonomy could be useful for methodological considerations (currently work in progress) from their perspective:

'I can see its use in guiding your thinking about what type of technology you're looking at and therefore what factors you should take into account…have sort of a generic evaluation, what you do with diagnostic things, what you do with therapeutic things and then by the subcategories, directly used by the patients and so and then perhaps by the risk categories, if there are generic things.'

The purpose-based classification of devices in three groups and its helpfulness for considering certain aspects are emphasized by one interviewee:

'So that for example things that patients use, you need to think about sufficient training and correction of misuse.'

Despite the fact that 'Prioritisation' was seen by the institutions as one of the areas where the taxonomy could be helpful, the operationalisation used in the model was at the same time also mentioned as a limitation, as two interviewees pointed out:

'[…] surgical sutures with antibiotics […] this is a device that from a technical point of view, it's really simple, boring maybe for an engineer, but it has huge economic impact.'

Figure 3 gives an overview of all the helpful elements and limitations mentioned by the interviewees and their categorisation based on frequency.

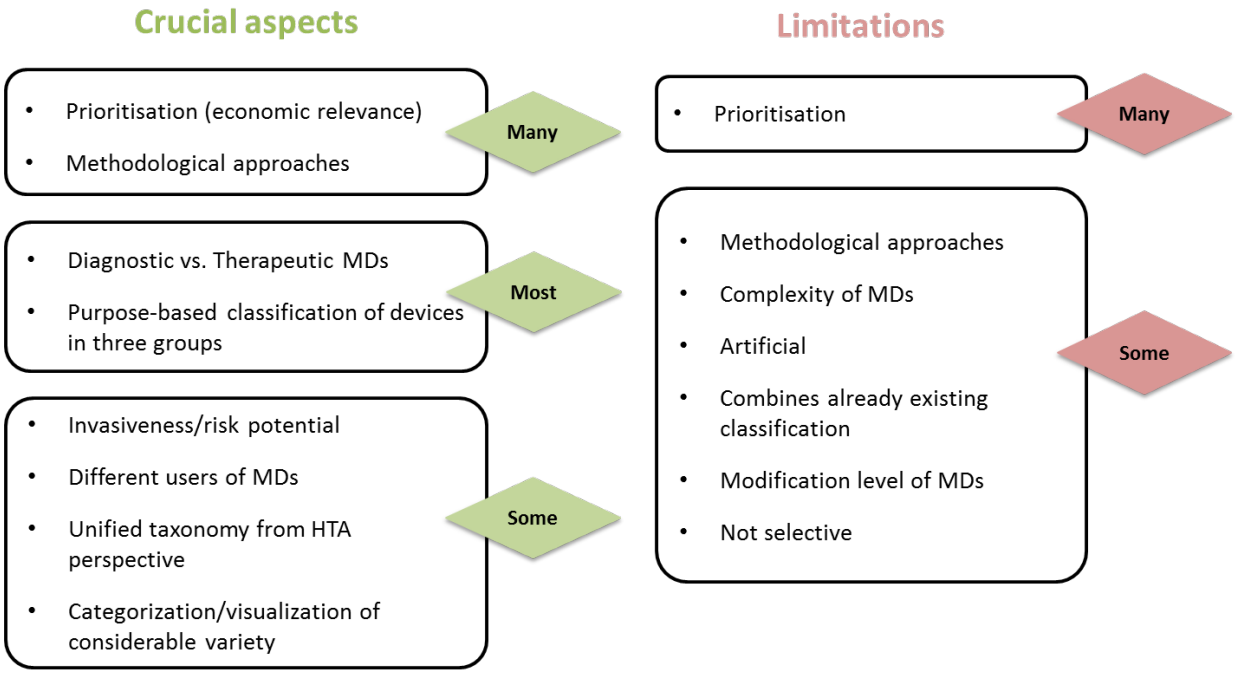

Figure 3: Helpful aspects and limitations of taxonomy by frequency

'Suggestions for refinement of taxonomy'

We asked the interviewees if they had suggestions to refine or improve the taxonomy. Constructive feedback was provided by four interviewees and the following aspects were mentioned:

- A more detailed description of the risk levels
- Additional row/column for prognostic and screening devices within the diagnostic part (A)
- Rename the category 'Artificial body parts' (as it also includes a change of an organ, not only the replacement)
- One row for III and IV or emphasize/make clear that IV is not defined according to the EU directives
- Further test the reliability of the taxonomic model

Impact

To explore how institutions perceived the role of their assessments of MDs within the respective health care systems, we asked interviewees about the impact/influence of their assessments. Given that "impact" can be defined and measured in many ways, we tried to categorise the given views based on verbatim expressions used by the interviewees.

Overall, most of the interviewees thought that their assessments had an impact. Five interviewees confirmed this with a clear *'Yes'*, whereas three added *'Yes, in most cases'*. Another addition was made by one interviewee given a *'Yes, the assessments for reimbursement decisions'* and one further interviewee stated that they have impact *'at various levels'*. That there is an impact to 'some extent' but not always possible to track, was also pointed out by one interviewee. Four interviewees stated that it is *'difficult'* to evaluate their impact without giving more detail. One explanation for this answer is the fact that assessments produced by their institutions are not binding in the decision-making process. Moreover, it was also emphasized that measuring impact/ following up on assessments can be particularly difficult. The latter issue was also pointed out by two of the interviewees who had stated that their assessments had impact (see above).

'Ways to assess impact'

Based on the answers given to the impact question above, 'ways' for assessing it emerged from the interviews. In general, these differ and are institution-specific. As results from the second part of the interviews are reported anonymously, it is not possible to present the impact measures mentioned in a detailed manner. Therefore, the following key points summarise the different approaches towards assessing the impact in a general manner:

- Follow the final decision on implementation (assessments for reimbursement questions)
- Conduct own evaluation/analysis (publicly available/not publicly available) including: e.g. download rate, media presentation, recommendations followed, percentage of assessments translated by the decision maker
- Own impact reports
- After-action reviews (routinely)
- Outcome evaluation framework (in progress)
- Evaluation of assumptions made by the institutions within their reports (in progress, will not be publicly available)
- Work together with an evaluation centre

Future development

The final questions refer to potential future developments and what the interviewees see as desirable aspects to strengthen or facilitate the work for MD assessments. At the end of the interview, participants were asked if they wished to add any further issues not captured until this point. These answers are also presented in this section.

Three main themes emerged from the answers given by all interviewees: 'Changes of the legal framework', 'Methodological requirements' and 'Interaction/discussion'. Two further themes were derived from the answers of three interviewees: 'Early advice to producer/help the companies' and 'Contact to manufactures'.

The subthemes that arose from the three main themes are presented in the following paragraphs.

'Changes of legal framework': Three subthemes could be identified from the interviews concerning desirable changes in the legal framework. These were emphasized by nearly all interviewees and included changes at both the European and the national level, as one interviewee summarised:

> *'I would prefer to have a more harmonized system with changes at the European level, but if the changes at the European level for high risk devices are not going in the direction as checking the added value for the patient then I think that maybe more and more national governments will take their own measures to solve the problems of the European legislation.'*

'Re-regulation of MD licensing process in the EU': A new regulation which is stricter and included evidence-based requirements on effectiveness and safety for receiving marketing authorization (CE mark) was envisioned. Moreover, detailed key points were given by the institutions and provided more detailed insight on what the changes could look like.

- **'Singular/unique, structured and harmonized regulation system':** A singular system across European countries as it exists already for drugs:
  '[...] especially there should be a singular system as for drugs, that when a device is being accepted in one country it also could be transferred to another country [...]'
- **'Data Requirements'**: Data including high quality studies such as RCTs but also studies addressing organizational aspects such as the learning curves:
  '[...] in some areas you get better quality evidence, because in some clinical areas, people are much more used to doing studies and trials and the evidence is better quality than other areas – it varies a lot. So it is a problem.'
- **'Publicly available register':** A transparent system, similar to the FDA database, at the European level including marketing authorization documents, prices, instructions and indications for use as well as other data etc.
  'I think it will be very important to have some publicly open register of medical devices, CE-mark documents at the European level, also with the

prices of these medical devices. For me this publicly available register will be very important at the European level.'

- **'Mandatory study registration:'** Obligation for studies on MDs to be in a central registry.

'Changes regarding national frameworks: Stricter requirements for the introduction of MDs into the market at national level were desired. For this purpose, general changes of the law would be required, as one interviewee pointed out:

'[...] So this is not really working, so we want our Minister of Health to be more visible. Well, all kinds, that we say, if the costs are too high, if you do not get value of money for disease, for intervention we should not pay for it, it's like... But I do not think – I think in a lot of countries there are these kind of discussions, but I do not think any Minister of Health likes to be so specific about healthcare costs.'

'Agreement on evidence in the post-market stage': General agreements at the international level and among stakeholders about which evidence to accept, how to set up evidence generation and when to re-evaluate in the post-market stage would be beneficial, as one interviewee expressed:

'Maybe also some more clue to direction or agreements on what's important in the post-market stage because we have a lot of debates here [...] in terms of the whole development of evidence development, and when is it good enough to try it, and when should you start to collect evidence. Should you continue to collect evidence and then re-review in a period of time and we know that other countries have tried that as well with varying degrees of success. It's quite difficult to do and expensive to set up. While in theory it's a good idea, the practicality of it in terms of ongoing assessment of devices and non-medicine technologies is a much more difficult thing to do and to fund.'

'Methodological requirements': Two subthemes with once more, subdivided elements could be identified from the material depicting in more detail what institutions would wish for with regard to methodological requirements.

'Common understanding/minimum requirements': Have a common understanding concerning general standards for methodological approaches, as one interviewee clearly stated:

> *'I think without doubt there are some challenges in terms of whether the methods for non-medicine technologies have always kept to best. It's just more complexity and therefore more requirements for more nuanced methods.'*

According to the interviewees, this common understanding should encompass:

- **'PICO aspects':** Agreement of an appropriate evidence level/study design for each risk level, predefined comparators, measures to use, the (minimal) clinically meaningful change and patient relevant outcomes as well as clearly defined patient groups.
  'One thing that you might consider, is discussing a little bit the C as well and saying you should think what you compare this device against, so is it, no intervention or no diagnosis or is it the current best practice and how do you do that. So that's, sort of defining what you are comparing it against [...]Then another issue is choosing the outcomes and for some things, what we have been discussing is, that it would be very important to standardize the outcomes that you measure when you are treating a certain type of disease.'
- **'Learning curves':** Clarity on how to consider learning curves.
  'And I haven't actually seen good kind of methodological descriptions that's very sharp of the learning curve.'

'Specific tools/guidelines': Need for specific tools (e.g. GRADE system for prognostic tests) and standardized approaches (e.g. following the 'IDEAL framework').

> *'Also we know that the grading system is not yet accessible for the prognostic test. So this is a different methodological barrier but I hope that in the near future we will have also have grading system for prognostics studies and everything.'*

'Research on methodological approaches': Need for further research on methodological refinements e.g. in the area of health economic approaches.

> *'And then I don't know – I suppose there are a lot research possibilities to develop health economics approaches for devices... we have problems with some economic models because we don't have evidence [...]. Also more research in the use of cost-consequences modelling, because it is not widely used. We often have some queries about how the best way that these models should be developed for certain technologies in terms of the pathway as well. So yes, I think there are many research questions that could be looked at in medical devices.'*

'Interaction and discussion': Three subthemes emerged from the material within this main theme.

'Focus and consciousness on MDs (policy issue)': More attention and focus from decision-makers on device characteristics including a more structured and systematic planning for their introduction to the market. For this purpose, more literacy among decision-makers is required.

> *'So I think it's perhaps a greater appreciation of that both from policy makers but also from the people who purchases and commission services.'*

'Dialogue and interaction between different stakeholders': Interaction of all parties including manufacturers and patients but also between regulatory and re-

imbursement bodies, for example a sharing of existing data. The following quotes clearly illustrate this point:

> *'So we need much more dialogue between the different stakeholders and parts, including patients. Especially in terms of establishing the outcomes of interest for patients, and the requirements of the healthcare system in terms of tailored medical devices and medical device solutions to the requirements of the system.'*

> *'And perhaps if we already have some kind of data, we should improve the way this data is being shared. Perhaps that can be a solution, because maybe the data we are looking for already exists somewhere but we are not aware of it because of several different reasons.'*

'Discussion about prioritisation': More discussion about what needs to be assessed before MDs are reimbursed:

> *'I would definitely say that I would appreciate if we had the same discussions and same coherent thinking about introduction of medical devices. And also much more coherent discussion about the needs for assessment of devices. I think that's a key point from my perspective because I think for some reason drugs – and I think it is also based on the fact that we often have more structured information on drugs.*

> *'So because of the research it's easy to assess drugs, and because it's more difficult we do not think systematically about other kind of technologies, including devices. And I think that a massive policy issue that also could be addressed by the fact that I said I think it could be worthwhile if you could say anything about what kind of technologies we should absolutely test systematically before introduction.'*

Figure 4 provides a summary of the key findings form the interviews.

Key finding from the interviews:

- **Main challenges**
  - Mainly resulting from weak regulation at the European level.
  - Methodological challenges cited the most: weak evidence base and rapid pace of innovation.
- **Methodological document**
  - Agreement on usefulness of considering particularities of MDs in methodological documents.
  - One general document with additional parts or specific aspects to consider would be sufficient.
- **Taxonomy**
  - Usefulness seen in taxonomy but mainly not always for institutions themselves.
  - Prioritisation support aspect seen as the most helpful but also the most critical aspect.
  - Suggestions for refinement were given (e.g. separate row for prognostics).
- **Impact**
  - Most institutions thought that their assessments have impact.
  - Different methods for measuring impact exist; overall, measurement is difficult.
- **Future development**
  - Most interviewees wish to change the EU regulation regarding the licensing process of MDs evidence based requirements
  - Common understanding on methodological requirements and specific tools as well as research needed (e.g. GRADE for prognostic studies).

Figure 4: Key findings from the interviews

(c) Recommendations

(1) Use of developed Taxonomy

Based on the plausibility testing and the interviews with 16 European HTA institutions, we believe that the taxonomy developed in Task 1 can be useful for HTA institutions and decision makers (e.g. MoH, insurers) alike. It can serve as a support tool to *(a)* select topics for assessment and for *(b)* identify certain aspects/particularities that require tailor (methodological) approaches. Detailed recommendation on these aspects are provided below.

(2) Methodological considerations with regard to taxonomy

The following 'pointers' address certain methodological aspects that may be applicable to certain device types (and therefore taxonomic cells) and could/should be considered along with the regular methodological approach adopted by each institution.

EUnetHTA Core Model elements

The EUnetHTA Core Model™ [7] for Diagnostic Technologies was frequently mentioned by the interviewees as a methodological basis. It can serve as a basic understanding on how to assess diagnostics. The Core Model™ iteration specific to Medical and Surgical Interventions and Screening Technologies can also be used as the basis for assessing related technologies.

Based on our findings, the following aspects could be taken into account for specific taxonomic positions:

- For MDs of lower risk categories: safety and/or economic aspects might not be fully touched upon. However, closer inspections of these elements

[7] Available here

maybe of importance for example for low cost MDs broadly used in the healthcare system

- For certain implanted devices and devices that require user skills social, ethical and legal aspects have to be consider in more detail.
- Taxonomic positions which entails a MD within a procedure: organisational aspects have to be consider in more detail (e.g. by using OSTEBAs check-list, see Appendix page 114).

Evidence requirements

The majority of institutions included in this work criticized the lack of high-quality evidence, either in their reports or in the interviews. A regulatory requirement for high-quality clinical trials for market entry that directly compare different interventions, particularly for high-risk products, would constitute a step towards meeting patient safety requirements. At the same time, for some device types (e.g. risk class I devices), it might be appropriate to accept lower levels of evidence/non-randomised studies (NRS) as (part of) the basis for assessment. When RCTs are not feasible due to the type of device or intervention studied, other study designs are required and available; the methodological guide developed by HAS[8] in 2013 provides a detailed and useful overview.

EUnetHTA recently developed a template (available here) regarding additional evidence generation (AEG) for studies in different countries, which could be helpful in order to guarantee standardized reporting of data regarding key methodological elements. In general, we recommend the institutionalisation of new approaches such as coverage with evidence development as some countries already introduced (e.g. Germany).

[8] Methodological choices for the clinical development of medical devices (2013), available here

Evidence base

Independent research (including primary and secondary evidence, as well as published and unpublished data (see also EUnetHTA here) is standard practice for institutions assessing MDs. Manufacturer submissions are used only occasionally and upon request.

Many interviewed institutions pointed out that they use stakeholder input at various stages of the assessment to supplement evidence gaps. Thus, incorporating such input is crucial, not least in order to understand the characteristics of the MD under evaluation. Given the considerable resources associated with such participatory approaches, they can be streamlined.

Comparator

The selection of an active or inactive (placebo/sham intervention) comparator should be considered on a case-by-case basis (see also here). In principle, the use of an active comparator is generally recommended.

Pragmatically, however, there are cases where placebo/sham interventions may be acceptable for comparison. For example, in the assessment of MDs of lower risk classes, placebo or sham interventions can be chosen without major ethical concerns or limitation in the resulting evidence. Similarly, in situations where an active comparator is not ethical and/or feasible, a placebo control arm might also be appropriate. In contrast, high-risk MDs should have active comparators to demonstrate comparative effectiveness and safety.

Endpoints

Based on our findings, outcomes that are likely to be meaningful to clinicians, patients (consumers), the general public, administrators such as mortality, morbidity, QoL and safety for therapeutic MDs are recommended for HTAs. Taking the type of MD under evaluation into consideration, the following observations may be useful:

- For risk class I devices mortality may play a less significant role.
- For devices directly used by patients additional aspects should be given priority such as user skills, compliance and/or quality of life
- For high risk devices such as implants (e.g. ICD), consideration of mortality and morbidity is indispensable.
- Sensitivity and specificity are the most common parameters to be considered when assessing diagnostics

Quality assessment of studies

We identified certain quality appraisal checklists and tools for specific study designs that are used quite often in current HTA practice. These differ mainly between therapeutic and diagnostic technologies.

Based on our results, **QUADAS 2** is indicated for diagnostic studies. Next to STARD, PRISMA and GRADE, QADAS 2 is one of the tools recommended by EUnetHTA (available here).

For the therapeutic studies, the tools vary depending on study type and domain addressed (e.g. effectiveness).

Non-randomized controlled studies (NRS) of lower LoE were often accepted in existing HTA reports. While it is acceptable to take these into account for some types of technologies (see above), we strongly recommend the use of a quality appraisal tool to evaluate NRS studies before they are included in the body of evidence. EUnetHTA, recommends the instrument **'ACROBAT-NRSI'** (draft available here) by the Cochrane Collaboration[9] as the most suitable for this purpose, a recommendation confirmed by the interviews conducted in this work.

[9] Sterne JAC, Higgins JPT, Reeves BC on behalf of the development group for ACROBAT-NRSI. A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI), Version 1.0.0, 24 September 2014. Available here

Further research to expand the scope of existing tools, such as developing a GRADE system for e.g. prognostic studies is indicated to further strengthen the options available to MD assessors.

Methodological guidelines and frameworks

Methodological guidelines have been developed either by individual HTA institutions or by EUnetHTA, which are helpful and can be used as the basis for assessment before additional aspects mentioned above can be considered:

- Meta-analysis of diagnostic test accuracy studies (WP7 SG3 of EUnetHTA JA2; available here)
- Guideline on Methods for health economic evaluations - A guideline based on current practices in Europe (EUnetHTA, available here)
- Methodological guidelines for rapid relative effectiveness assessment (REA) of Pharmaceuticals developed in WP5 of EUnetHTA JA, will be currently adapted for other technologies including MDs (first drafts available here): Clinical endpoints, Composite endpoints, Surrogate endpoints, Safety, Health-related quality of life, Criteria for the choice of the most appropriate comparator(s), Direct and indirect comparison and internal validity (see above)
- Guidelines identified from institutions included in the interviews e.g. HAS, NICE or ZiN (see corresponding profiles in the Appendix)
- The IDEAL framework (available here) for interventional therapeutic innovations (mentioned during the interviews) describes the stages through which such technologies pass, the characteristics of each stage and the study designs possible/indicated for each.

An additional methodological guideline from EUnetHTA on therapeutic medical devices and a model for relative effectiveness assessment for non-pharmaceutical interventions are being currently developed.

(3) Regulatory recommendations

Although WP5 mainly focused on the methodological implications of MD assessment relevant regulatory changes required or suggested by our interviewees also merit attention.

Previous studies have illustrated deficiencies of the regulatory process in Europe and emphasized the need for changes and new requirements (Eikermann et al., 2013; Storz-Pfennig et al., 2013). Given that European regulation is currently being revised, there is an opportunity for insights from our work, which among others incorporate the opinions of 16 HTA institutions, to contribute to the discussions and hopefully help ameliorate the current situation.

Very recently, the Belgian Health Care Knowledge Centre (KCE) published a report (Bayens eta l., 2015) demanding that efficacy requirements be raised to obtain a CE label for high-risk medical devices and transparency on the underlying clinical data. This was an issue unanimously emphasised by our interviewees as well.

Moreover, the KCE report studied which measures can be taken at the national level without contradicting European regulation. The most relevant possibilities are as follows:

> *'1. The routine use of high-risk devices could be limited to a small number of reference hospitals as long as there is no convincing evidence on the intervention's added value for the patient. An appropriate research design could also be demanded. The type of design depends on both the development stage of the device and the research questions.*
>
> *2. Specialists should be encouraged to provide full and understandable information to their patients about the (lack of information on) safety, efficacy*

and costs of new high-risk medical devices as well as the available alternatives. It is only then that patients can give their informed consent.

3. The previous two elements can be integrated in a roadmap, following the Dutch example (3). Specialist should question where the new high-risk device is already used, which information is available on its safety and added value for the patient, what are the medical, organizational and financial risks, is an introduction plan and gathering of data necessary, etc. High-risk devices for which there is no supporting reliable information should only be used in a limited number of reference centres in an appropriate research setting. For high-risk devices, if possible, it is desirable that the added value is tested in a randomized controlled trial before it is widely distributed. Following this roadmap would have a positive impact on specialist's professional liability (and vice versa). This measure has a high probability of being justified, necessary and proportional to achieve a better protection of patients' health.'

(4) Suggestions for implementations of the recommendations

In the following part we will provide some suggestions for implementation of the above mentioned recommendations (1-3) at the different levels.

Regional and National level:

- Consideration of the remit of institutions responsible for evidence based evaluations guiding coverage decisions and the extent to which different device types are included (1).
- Potentially reconsider distribution of responsibility among institutions regarding the evaluation of different device types (1).
- If governments are directly involved in setting methodological requirements, consider differentiation for MDs (and potentially for different device types) (2).

- Competent authorities, be it at national or regional level, should take these findings into account when considering licensing and reimbursement regulation (3).
- If governments are directly involved in setting methodological requirements, consider and/or disseminate 'Pointers' from this WP (2).

Supranational/international level:

- Potentially reconsider distribution of responsibility among institutions in different countries regarding the evaluation of different device types (e.g. REDETSA) (1).
- International networks (e.g. EUnetHTA) could disseminate or promote taxonomic model (1, 2).
- Reconsider regulatory prerequisites for MD licensing at European level. Bringing awareness to the findings of this WP maybe fruitful in this respect (1).
- International networks (e.g. EUnetHTA) could disseminate or promote relevant pointers (2).

Patient level:

- The impact of the implementation would be indirect (potential changes will have influence on patient safety and health):
    - a) through a more explicit consideration of user skills for relevant device types,
    - b) by endorsing patient participation in evaluations particularly for certain device types.

Healthcare professional level:

- Awareness raising among healthcare professionals regrading methodological particularities when conducting clinical trials. Further support on behalf of scientific or professional associations regarding regulatory changes would be beneficial (1, 2).

Procurers of medical technologies:

- If hospitals are involved in or conduct HTA, recommendations 1 or 2 are applicable. Relevant associations could promote idea of hospital base HTA of MDs.

Outlook

The work carried out in Work Package 5 yielded in a better knowledge about the methodological approaches adopted by European HTA institutions and captured impulses for future development.

With the insights described in this deliverable in mind, further work, mostly on detailed methodological recommendations, is needed and planned. In this context, a more direct comparison to HTA of drugs will also be undertaken.

Finally, impulses gained during this work but which go beyond the scope of the project, such as the suggestions for refinement of the taxonomic model or the creation of an interactive database for HTA reports of MDs will be explored further.

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APPENDIX

Interview Guide

Interview guide on 'Medical Devices and HTA' (Advance-HTA)

Introduction

Within Work package 5, our team at the Berlin University of Technology focuses on the evaluation of medical devices (MDs) by selected European institutions that are actively involved in Health Technology Assessment (HTA). In particular, we are interested in the methodological and procedural processes as well as developments within your institution. The main aim of the interview is to clarify and supplement earlier findings from a systematic review and analysis of HTA reports with respect to this area, and to trace methodological and procedural challenges and trends not captured in the published evidence.

The Interview guide is structured according to the key principles by Drummond et al. (2008)[10]: (i) Structure of HTA programs, (ii) Methods of HTA, (iii) Processes for Conduct of HTA and (iv) Use of HTAs in Decision Making.

Please note that this is the full, detailed version of the interview guide. Depending on the information already captured for each institution, some questions will be adapted or only partly asked.

Part I:

Institutional practices

Questions to fill some information gaps from step 2 of work package 5 (systematic review of HTA activities on MD in Europe) regarding institutional structures, processes and methods

Please note that answers from part I will serve to supplement factual information related to agency practices.

- Does your institution use a specific definition of MDs? (e.g. regarding EU-directives)
- Do you have a separate unit/ department, which assesses MDs/ conducts HTAs for MDs?
    - If yes, how many people work in this unit/ department?

[10] Drummond MF, Schwartz JS, Jönsson B, Luce BR, Neumann PJ. Key principles for the improved conduct of health technology assessments for resource allocation decisions. Int J Tech Assess Health Care. 2008;24(3):244-58.

  - If not, how are tasks regarding MD-HTAs distributed?
- Does the process to assess MD in general differ from the assessment of drugs?
- Does your institution use specific criteria to select MDs for an assessment (e.g. high risk, high costs)?
  - If yes, are these criteria different from criteria used for other technologies such as drugs?
- We identified X methodological documents (whereas X are separate documents for MD assessment):
  - Is this number correct, or are there any other unofficial/ unpublished documents that are relevant?
  - Does the methodological paper(s) mirror current practice?
- Does your institution have specific methods for specific MDs (e.g. diagnostics)?
- Does your institution consider device-specific aspects?
  - If yes, can you name them?
  - If yes, how were these aspects considered? (e.g. within recommendations)
- We identified X publicly available reports for MDs on your website, which have been published since 2004 (last search September 2014).
  - Are these (roughly) all the HTAs on MDs which you have done, or are there more which do not appear on the website?
  - How does this number on MD relate to the equivalent for pharmaceuticals?
- Which role does your institution play in the HTA system in your country, especially regarding MDs?
- Are assessments directly connected to coverage decision-making?
- Is your institution currently involved in activities (e.g. EUnetHTA joint actions) or conducts its own research regarding the assessment of MDs?

Part II:

Questions concerning structural, procedural and methodological difficulties and challenges towards the assessment of MDs

Please note that answers from part II will not be presented as results of a specific institution/ country and thus will be handled confidentially and reported anonymously.

- What are the **main differences** between the assessment of MDs and pharmaceuticals …
  - From a structural perspective (indicative examples: scope of agency, awareness of technologies/ horizon scanning)?
  - From a procedural perspective (indicative examples: stakeholder involvement, evidence identification)?
  - From a methodological perspective (indicative examples: level of evidence included)?

- How does the **broad variety of MDs** influence the evaluation (from a methodological perspective)?

- Which role do **device-specific aspects** such as learning curves play within the assessment process?

- *Institutions with a separate document:* How useful do you consider your separate document?

- *Institutions without a separate document:* Do you think it would be useful to **address differences and particularities** of MDs in a separate methodological document?

Questions concerning developed taxonomy/ classification *(please see attached slides)*

- Could your institution use the developed taxonomy as a guidance?
    - If yes, which is/are a helping/crucial aspect(s)?
    - If not, please explain?
    - In general, do you have some suggestions to refine or improve the taxonomy?

Activities, opportunities and closure

- Which impact do your assessment reports have in your country?
- What would be desirable aspects to facilitate/ to strengthen the MD assessment? (e.g. specific tools)
- *In general, not necessarily institution specific:* Which aspects are the most relevant for future developments of MD assessment/evaluation?
- Do you want to add some further information not captured yet in the interview?

Thank you for your participation and help!

All information provided by the interviewee(s) will be used in a confidential manner and for research purposes only. The interview will be recorded. Each participant will receive a full transcript of their interview as well as the analysis of all results before the manuscript is submitted for publication for validation and comments.

Institution Profiles[11]

Austria

Profile of: Ludwig Boltzmann Institut für Health Technology Assessment (LBI)/ Ludwig Boltzmann Institute for Health Technology Assessment

Part I: Institutional structures, processes and methods
Role of institution in the HTA system of the country, especially regarding MDs
- Academic non-profit institute, no national institute - Independent entity for scientific decision-making support in the health sector, founded in 2006* - Works on request of MoH - Remit: mainly MDs (except: horizon scanning of oncological products)
Link between MD assessments to coverage decision-making
- Yes, assessment directly connected to 'hospital catalogue'
Use of a specific definition of MDs/understanding
- No specific definition used - Assessment of procedures *('Verfahren')* in which one or more MDs are involved
Separate unit/ department for assessment of MDs
- Work programme *'Bewertung medizinischer Einzelleistungen'* within resort High-Tech-Medicine - Scientific staff: 12
Differences regarding the process of MD and drug assessment
- No assessment of pharmaceuticals: only Horizon Scanning of oncological products *('Frühbewertung')*
Priorisation criteria for MD selection
- Priorisation done by contractor
Methodological guideline
- External and internal manual: o Wild, C. (2007): Externes Manual. Selbstverständnis und Arbeitsweise. Teil 1. HTA-Projektbericht 03, available here o Gartlehner, G. (2009): Internes Manual. Abläufe und Methoden. Teil 2 (2. Aufl.). HTA-Projektbericht 06, available here - Austrian handbook (developed in cooperation with other Austrian institutions): o Methodenhandbuch für Health Technology Assessment, Version 1.2012, available here - For internal use (not publicly available): instructions with stopping rules for literature search while evidence is too weak to perform a full assessment
Specific methods for specific MDs
- Yes, for diagnostics: o Nachtnebel, A. Evaluation diagnostischer Technologien -Hintergrund, Probleme, Methoden. HTA-Projektbericht 2010; Nummer 36, available here o Kisser, A., Zechmeister-Koss, I. (2014): Procedural guidance for the systematic evaluation of biomarker tests. Decision Support Document 7, available here
Consideration of device-specific aspects
- Yes, aspects such as learning curves, interdisciplinary work, work protocols

[11] Compilation of institution profiles not yet validated: tables will be send to the interviewees for feedback before publication in scientific journals

Publicly available reports for MDs (published since 2004)
- Specialised on MD assessment: 80 reports (9 not yet online)
- All reports publicly available here
Activities regarding the assessment of MDs
- EUnetHTA joint actions: Leader of WP5b HTA of MDs

Notes: * http://www.inahta.org/our-members/members/lbi-hta/

Belgium

Profile of: Federaal Kenniscentrum - Centre fédéral d'expertise (KCE) / Belgian Health Care Knowledge Centre

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- KCE is a government institute (separate federal institute) providing advice to policy makers/specific stakeholders
- KCE is involved in three domains: clinical practice guidelines, health services research (organization of health care funding) and health technology assessment (devices and the drugs)
- Work mainly on request of the MoH, federal public services and RIZIV-INAMI (National Institute for Health and Disability Insurance (NIHDI))
- Perform HTA also for other stakeholders: e.g. individuals, universities, industry *(see priorisation process)*

Link between MD assessments to coverage decision-making

- Not involved in decision-making or implementation process, provide recommendation to various stakeholders
- NIHDI is commissioned for the reimbursement of drugs, devices and implants (based on industry submissions)
    - KCE can make a report if NIHDI need further input

Use of a specific definition of MDs/Understanding

- Refer to EU directives but does not play a role during the evaluation
- NIHDI has two classes of MDs: class I devices with an added value (have to look at all 5 criteria*), class II devices without an added value

Separate unit/ department for assessment of MDs

- No
- Staff: 50 people (30 experts)
- Compile team depending on research question and experiences and methodology of staff
- Can work with sub-contractors (e.g. legal expert)
- Expert meetings (e.g. physicians, industry) for further input

Differences regarding the process of MD and drug assessment

- Same general questions applied
- Where to search and what is available might be very different

Priorisation criteria for MD selection

- For the annual work programme (including all 3 domains) a procedure exist**
- Everybody can submit a proposal
- KCE scores proposals on five criteria:
    - policy relevance, frequency of the disease, its severity, the room for improvements, the importance of the study, possibility to change something and feasibility
- based on these criteria, a rank (league table) will be compiled with the highest scores first
- when something's not feasible or there's no room for improvement, then it's possible that although it has a high score on frequency and severity, and policy relevance, that it will leaved out
- board has to approve the topics (shortlist)
- extra time for very urgent questions

Methodological guideline

- Search for Evidence & Critical Appraisal: Health technology Assessment (HTA), 2007, available here
- Search for Evidence & Critical Appraisal: Health Services Research (HSR), 2007, available here
- Belgian guidelines for economic evaluations and budget impact analyses, second edition, 2012, available here
- Online handbook (process book), available here
- KCE provide additional information to people working with KCE

Specific methods for specific MDs

- No

Consideration of device-specific aspects

- Yes, factor of importance
- Organizational issues: e.g. how many hospitals should provide this procedure, having enough experience with a high risk techniques
- For technology with low volume, very interventional and high risk it's more important to consider

Publicly available reports for MDs (published since 2004)

- All reports are publicly available here
- Amount of KCE reports: 31

Activities regarding the assessment of MDs

- EUnetHTA joint action involvement in JA 2: WP1, WP2 (co-lead partner), WP6 (lead partner), WP7, WP8)
- Own research/recommendations regarding a guided and phased introduction of high-risk medical devices in Belgium available here

Notes: *Specific criteria defined by law in 2014, that should be taken into account in evaluating MDs: 1. therapeutic value, 2. price, 3. importance in medical practice of the medical device, therapeutic and social need, 4. budgetary impact, 5. cost-effectiveness; **more information on the priorisation process is available here

Croatia

Profile of: Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- AAZ established by law in 2007 as a legal, public, independent, non-profit institution and started formal working in June 2009
- According to Act on Quality of Health Care and Social Welfare (Official gazette No. 124/2011), AAZ should*: provide the procedure for HTA and database on HTA at national level, proposing to the Minister of Health Ordinance on HTA process and reporting, providing continuous education in the field of HTA, as well as national and international collaboration in the field of HTA
- Croatian Ordinance on HTA process and reporting is in process from November 2012*
- Legal compliance of the Agency is supervised by the Ministry of Health*
- HTA not mandatory in Croatia (legal framework will be changed**, afterwards ordinance is expected to be in place and HTA will become mandatory)
- HTA on request of the Croatian Ministry of Health, Croatian Health Insurance Fund & the Management board of the main hospitals
- Responsible at national level for pharmaceuticals, medical devices & procedures
- Assessments done by AAZ and appraisal done by National Health Insurance Fund (Committee for drugs as well as medical devices)
- Reimbursement decisions (mainly for drugs and medical devices in connection with procedure according the DRG system) done by Management board of Croatian Health Insurance Fund

Link between MD assessments to coverage decision-making

- Yes, assessment relevant for decision makers but not mandatory*

Use of a specific definition of MDs/Understanding

- According to EU-Council Directives

Separate unit/ department for assessment of MDs

- Three main activities and departments: 'Department for Development, Research and HTA' is dedicated to HTA; no separate unit for assessment of MDs
- Staff: 4 people (HTA Department)

Differences regarding the process of MD and drug assessment

- Not so different but MD assessment rely more on manufacturer information (e.g. CE documents, instruction to use, ongoing studies, unpublished data)

Priorisation criteria for MD selection

- Priorisation done by the contractor *(see Role of institution)*
- AAZ have to assess all requests
- Details about a priorisation process proposed by AAZ for changes of legal framework**

Methodological guideline

- The Croatian Guideline for Health Technology Assessment Process and Reporting, 1st edition, February 2011, available here
- AAZ will develop a document for 'Full economic-analysis' (only BIA is mandatory until now)

Specific methods for specific MDs

- Yes, use appropriate methodological framework according to already published methodological guidelines for assessment of medical devices, for example AHRQ methodological guidelines***

Consideration of device-specific aspects

- Yes, aware of learning curves and connection of MDs with medical procedures
- Asked for data on procedures connected with MDs (e.g. type of approach, technical platforms, easier for patients), on necessary facilities, additional equipment, contrast agents, need for local or general anesthesia, intensive care, rehabilitation, for personnel resources

Publicly available reports for MDs (published since 2004)

- EUnetHTA joint actions 1 & 2: 12 full core HTA or REA on drugs or medical devices (60% on MDs):

full list available here
- National and international work (2011-December 2014): 23 HTA documents finished, 70% of them on MDs (further HTAs in process)
- Most HTA reports (national & international) will be publicly available (in Croatian language) here

Activities regarding the assessment of MDs

- EUnetHTA joint action 2 (WP2, WP4 and WP5 (Strand B: REA on other health technologies)
- Others: FP7-project (EQUIPT), Horizon 2020 (SELFIE)

Notes: *Huic, Mirjana (2015): Croatian experience in health technology Assessment (HTA): National and international view. Vilnius, Lithuania, August 5, 2015 (additional documents sent by mail after the interview); ** Draft proposal Ordinance on HTA process and reporting to Croatian MoH, November 2012 and Proposal of new Act on Quality and Logistics in Health Care, September 2012,*** Sun F, Bruening W, Erinoff E, Schoelles KM. Addressing Challenges in Genetic Test Evaluation. Evaluation Frameworks and Assessment of Analytic Validity. Methods Research Report (Prepared by the ECRI Institute Evidence-based Practice Center under Contract No. HHSA 290-2007-10063-I.) AHRQ Publication No. 11-EHC048-EF. Rockville, MD: Agency for Healthcare Research and Quality. June 2011; Methods Guide for Medical Test Reviews. AHRQ Publication No. 12 EC017. Rockville, MD: Agency for Healthcare Research and Quality; June 2012. (Also published as a special supplement to the Journal of General Internal Medicine, July 2012)

Denmark

Profile of: Folkesundhed og Kvalitetsudvikling (CFK)/ Public Health and Quality Improvement- centre for research and development in social and health services, Central Denmark Region

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Co-ordinate HTA activities across the Danish regions and produce joint HTA projects, commissioned by the 5 Danish regions (do HTA since the national institution closed down)
- HTA activities:
  - No HTA on drugs (own system)
  - Rarely do HTA on a specific devices
  - HTAs for broader disease areas or problems where medical devices (and also drugs) can be one technology
  - Already introduced MDs

Link between assessments to coverage decision-making

- Utilization of already implemented technologies are regulated on the basis of these HTA reports
- Not directly coverage

Use of a specific definition of MDs

- Don't have own definition, refer to EUnetHTAs

Separate unit/ department for assessment of MDs

- CFK has 7 specialist departments: 'Health Technology Assessment and Health Services Research' responsible for HTAs
- Staff: 12 people in the HTA group (not all full-time)
- No specific unit for MDs

Differences regarding the process of MD and drug assessment

- No HTAs on drugs (could be integrate in an assessment, but no specific drugs)
- Comparison not possible (own regulatory system in Demark for assessing drugs)

Priorisation criteria for MD selection

- Selected by the health care planning units in the 5 Danish regions
- General criteria (don't apply rationally): unsolved planning issues, high risk, high cost or ethical issues

Methodological guideline

- Refer to the DACEHTA HTA handbook but will move towards the EUnetHTA core model methods

Specific methods for specific MDs

- No own specific methods developed
- Use EUnetHTA frameworks

Consideration of device-specific aspects

- Yes, such as learning curves

Publicly available reports for MDs (published since 2004)

- Don't have many reports that focus on one specific device, do it in broader disease or problem areas
- Reports in Danish with English summary: *website link (requested per mail)*

Activities/research regarding the assessment of MDs

- EUnetHTA activities in general and 2 people within development and assessment of MDs

Notes: Interview transcript not yet validated

Finland

Profile of: Finnish Office for Health Technology Assessment (FinOHTA)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Part of the technologies and practices assessment unit at the National Institute for health and welfare (THL) and was established in 1995 and incorporated in THL in 2009*
- FinOHTA is the state-funded HTA group that supports important decisions in health care
- Division of labor in Finland:
  - FinOHTA assess devices, operations and surgical interventions as well as evaluations of drugs versus another type of technology (no assessment of soley drugs)
  - FIMEA does HTA of drugs

Link between MD assessments to coverage decision-making

- Two different systems of coverage:
  - decisions to use (e.g. robotic surgery): done by the hospital districts (MUMM project), sometimes even individual hospitals, legislated and guided by the MoH (not a direct link to legislation)**
  - coverage for drugs with its own process
- FinOHTA supply HTA when a legislated decision is made
- Mostly involved in public sector services and they decide themselves

Use of a specific definition of MDs/Understanding

- HTAi definition

Separate unit/ department for assessment of MDs

- No, but main line of work is dedicated to MDs
- Staff: 16

Differences regarding the process of MD and drug assessment

- Not very different to evaluate a drug or a medical device:
  - Basic process/framework is the same: look at the effectiveness, harms, costs and social, legal and organisational, ethical implications
- May differ between different type of devices:
  - Use EUnetHTA principles and separate processes for different types of technologies

Priorisation criteria for MD selection

- Same criteria applied as for any other technology:
  - Is the technology interesting nationally, is it new or being introduced, how large a patient group would be affected, are there safety issues involved, are there other options for use, how large is the expected effect on health and quality of life, are the immediate costs high, are the changes in cost use high, is there scientific information available

Methodological guideline

- Use several different documents for processes to provide HTA information (depending on time)
- Documents e.g. for type of literature search, rapid reviews, systematic reviews
- Use EUnetHTA frameworks

Specific methods for specific MDs

- No own documents for specific MDs but use EUnetHTA frameworks (e.g. for diagnostics)

Consideration of device-specific aspects

- Yes, use EUnetHTA checklist as basic structure (e.g. questions about the learning curve)

Publicly available reports for MDs (published since 2004)

- MUMM project provides brief English abstract, available here
- full HTAs will be published in the Finnish Medical Journal
- Number of reports: 24

Activities regarding the assessment of MDs

- EUnetHTA joint action 2 WP8: refines Core Model for MDs

Notes: * from INHATA website; ** have the traffic light system: green means everybody can use it, red is, either not effective or it has serious harms or the cost effectiveness is not good, no use recommended

France

Profile of: Haute Autorité de Santé (HAS)/ French National Authority for Health

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- HAS provides scientific advice to coverage decision-makers (MoH; Ministre santé
- et sécurité sociale)
    - MoH has to take into account scientific advice but is not obliged to implement the advice into the regulation
- HAS assess all MDs before inclusion on the positive list of reimbursed products
    - Assessment of high-cost devices within the inpatient sector (too expensive for funding within DRG tariffs)and within outpatient sector when used by patients at home
    - Single technology assessment (STAs) on request: application for reimbursement by the manufacturer ('Brand names')
    - Reassessment of MDs:
        - Especially when significant new information is available
        - Review of categories of products ('Generic lines') is also conducted (MTAs)

Link between assessments to coverage decision-making

- Assessments directly linked to reimbursement
- Assessment of clinical added value (link HAS opinion to price)

Use of a specific definition of MDs

- Own 'taxonomy' of MDs: List of products and services qualifying for reimbursement (LPPR) contains 4 categories of MDs

Separate unit/ department for assessment of MDs

- Assessment: Medical devices assessment department (18 project manager)
- Appraisal: National Committee for Medical Devices and Procedures Assessment (CNEDiMTS) within HAS
- Separate department and committee for all reimbursable pharmaceuticals

Differences regarding the process of MD and drug assessment

- General process of assessment: Review of available data (literature and dossier from company) through HAS internal assessors and healthcare practitioners; appraisal through CNEDiMTS
- Generic drugs go through a simplified assessment process

Priorisation criteria for MD selection

- CNEDiMTS works on new medical device plans by selecting new devices into categories and assesses per year one of these categories ('Generic lines')
- Regulatory criteria for reimbursement which are mandatory (ppt for further details)

Methodological guideline

- 'General method for assessing health technologies, 2007', available here
- 'Rapid assessment method for assessing medical and surgical procedures, 2007', available here
- 'Methodological choices for the clinical development of medical devices, 2013', available here
- 'Choices in methods for economic evaluation - a methodological guide, 2012', availablhe here

Specific methods for specific MDs

- No explicit methods for assessment of different types of MDs, refer to their 'General methods'

Consideration of device-specific aspects

- HAS Advices consider organisational aspects (e.g. learning curve)

Publicly available reports for MDs (published since 2004)

- Reports publicly available here
- MD committee assesses six or seven categories, sub categories of MDs per year (MTAs)
- About 200 different MDs through application of manufacturer per year (STAs)

Activities/research regarding the assessment of MDs
- EUnetHTA joint action 2 WP5

Notes: Hubert Galmiche, Deputy Head Medical Devices Assessment Department: HTA for medical devices, power point presentation (additional material received after the interview); *Set of products: common characteristics called "technical specifications", fulfil the same function and have the same indication, reimbursed by health insurance funds at a single tariff, Generic Lines re-assessment process has started, Direct Access to the market, under fixed conditions

Germany

Profile of: Institute for Quality and Efficiency in Health Care (IQWiG)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Since 2004 IQWiG produces independent, evidence-based reports on drugs, non-drug interventions (e.g. surgical procedures), diagnostic tests and screening tests, clinical practice guidelines and disease management programmes*
- IQWiG provides in addition easily understandable health information for the general public*
- Department 'Non-drug interventions' mainly assesses medical interventions that are not solely dependent on the use of drugs (including dental treatments, more complex interventions that consist of various therapy components combined in one procedure, diagnosis methods)*

Link between assessments to coverage decision-making

- Not mandatory

Use of a specific definition of MDs

- No need of a specific definition
- Medical intervention assessment (*'Methodenbewertung'):* assessment of interventions within a MD is used (no specific MDs)
- Following CE mark if required

Separate unit/ department for assessment of MDs

- Department 'Non-drug interventions' *('Nichtmedikamentöse Verfahren'*), exists since 2004
- Staff: 19 people

Differences regarding the process of MD and drug assessment

- Yes, regulatory framework different
- Drug assessment based on dossiers (standardised) whereas medical intervention assessment based on own research and partially request to manufacturers for studies and protocols (not standardised)
- Drug department relies strictly on the authorization of drugs
- More time and effort for MD assessment

Priorisation criteria for MD selection

- No priorisation done (commissionend by G-BA, MoH)
- But IQWIG has a mandate *('Generalauftrag')* to work also on important issues independently

Methodological guideline

- 'Allgemeine Methoden Version 4.2 vom 22.04.2015' [General methods] available here

Specific methods for specific MDs

- Yes, within methodological document separate parts for drug-free therapeutic interventions (section 3.4), diagnostics (section 3.5) and early detection and screening (section 3.6)
- Process of information retrieval different: for medical interventions where the MD is an essential part, manufacturers will be requested

Consideration of device-specific aspects

- Yes, if such aspects could be extracted from studies, these will be considered within 'minimum requirements' determined in Quality Directives *('Qualitätsrichtlinie')* by the G-BA

Publicly available reports for MDs (published since 2004)

- Yes, all reports publicly available here
- Assessments according to §137e *('Potentialbewertungen')* will not be publicly available
- More assessments done for drugs than in comparison to non-drug interventions

Activities/research regarding the assessment of MDs

- EUnetHTA Joint Action 2: WP1, WP5, WP7 (co-lead partner)
- In line with *'Generalauftrag'*: Analysis of clinical evaluation of MDs, details available here

Notes: * general information form IQWiG website

Hungary

Profile of: National Institute of Pharmacy and Nutrition, Department of HTA (OGYÉI ETF), former: GYEMSZI TEI

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- OGYÉIs main task is to support the decision-making process in Hungary
- ETF: Health Technology Assessment Office at OGYÉI
- conduct critical assessments of HTA submissions for pharmaceuticals and for the two sub categories of MDs on request of the Health Insurance Fund (HIF)
- No voting rights at the committee meetings where the evaluation results are presented (members of the committees make the decision)
- Take part in developing domestic or international guidelines

Link between MD assessments to coverage decision-making

- Yes, law e.g. mentions that only those MDs can be reimbursed which are proven to be cost-effective

Use of a specific definition of MDs/Understanding

- Use two sub categories of MDs:
  - (1) Medical aids: devices which are intended for patients to use at their home and in their daily lives (e.g. hearing aids, wheelchairs, bandages)
  - (2) Slightly different procedure regarding other medical devices and diagnostic devices which are mainly intended for physicians to be used in hospitals (e.g. PET)

Separate unit/ department for assessment of MDs

- No
- Staff: 2 people (ETF)

Differences regarding the process of MD and drug assessment

- Process with regard to the 2. sub category of MD is similar to the one of pharmaceuticals:
  - Application from industry to HIF
  - HIF forward submission to medical professional colleagues, to OGYÉI ETF, to a medical research council
  - Critical evaluation of all bodies is discussed within a technology assessment committee meeting
  - Committee makes recommendations to HIF and MoH (decision mostly made by HIF)
- The process for the 1. category of MDs is much more simplified:
  - Few stakeholders involved, without a committee meeting after critical evaluation
- More simplified version when the submission is not aimed to introduce a totally new product to the market for reimbursement (e.g. insignificant aspect of device):
  - HIF deals with the submission on its own

Priorisation criteria for MD selection

- Done by HIF
- No different criteria used in comparison to other technologies

Methodological guideline

- HTA guideline, renewed in 2013 (no English version of the current published guideline available)
- Official translation of old publicly available guideline: Szende A, Mogyorósy Z, Muszbek N, Nagy J, Pallos G, Dózsa C: Methodological guidelines for conducting economic evaluation of healthcare interventions in Hungary: a Hungarian proposal for methodology standards. Eur J Health Econom, 2002, 3:196–206.
- Regulation of the Ministry of Human Resources for healtheconomic analysis [Az Emberi Erőforrások Minisztériuma szakmai irányelve az egészség-gazdaságtani elemzések készítéséhez, 2013], available here: Not a regulation but rather a recommendation of authorities of how any submission should look like

Specific methods for specific MDs

- Guideline tends to cover all areas (from drugs to simple MDs), not specifics for MDs touched

Consideration of device-specific aspects
- Yes, if data is available but submissions lack data and consideration not possible
Publicly available reports for MDs (published since 2004)
- Evaluations not publicly available (for MDs as well for drugs) - Amount of MD evaluations in comparison to drugs nearly the same (but evaluations of pharmaceutical submissions since 2004, evaluations of MDs intended for patient use since 2007 and critical assessment of MDs which are intended for physicians to use since 2010 but actually the first submissions was in 2011) - Nowadays: 80 pharmaceutical submissions annually and work with a higher number of medical aids intended for patient's use
Activities regarding the assessment of MDs
- Part in EUnetHTA joint action 2: WP5 (applying the HTA core model for rapid assessment, some cases of MDs), WP7 sub group (develop methodological guidelines) and sub group 4 (create a uniform data template for submissions, for pharmaceutical and for MD submissions) - SEED consortium

Italy

Profile of: Agenzia Nazionale per i Servizi Sanitari Regionali (AGENAS) / National Agency for Regional Health Services

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Agenas is the only national agency in Italy that is appointed by the MoH for HTA of MDs
- Agenas is kind of a national hub for HTA for all the 17 regions (*regional network for HTA, RIHTA*), they can assess technologies that are of interest for many regions *(common-interest technologies):*
    - In some regions there are HTA units that are very experienced, they perform HTA on a regular basis and produce HTAs for their local context but also in collaboration with Agenas and with other regions

Link between MD assessments to coverage decision-making

- All reports provide recommendations, but these are not mandatory to decision-makers

Use of a specific definition of MDs/Understanding

- Yes, 'health technology' definition according to EUnetHTA network* ; 'medical device' definition provided by the Italian MoH (=EU Council Directives)

Separate unit/ department for assessment of MDs

- No
- Staff: 12 people but part-time (have several activities, e.g. horizon scanning for new and emerging technologies)

Differences regarding the process of MD and drug assessment

- No comparison possible: Italian medicines agency (Agenzia Italiana del Farmaco, AIFA) exclusively appointed for drugs

Priorisation criteria for MD selection

(1) Priorisation process for existing/mature technologies:

- Annual call: agreement with the MoH about a pre-defined number of reports (usually 4/5), includes different kind of outputs (e.g. SRs, Rapid HTAs)
- Technologies therefore are selected from multiple sources:
    - call to four** regions: submit preferred technologies to Agenas which they identify in their context in several ways
    - open call on the website via a form: everyone can submit a technology (e.g. citizen, scientific society, manufacturer)
- Small committee that is composed by four regions and one representative of the MoH will prioritize the technologies to assess according to the national program***
- Criteria could be: cost, impact, burden of disease or inappropriate/improper use of that technology
- MoH has also the right to vote or to sponsor one technology over one other (e.g. due to urgency)

(2) Priorisation process for new and emerging technologies:

- All the regions are invited to submit and prioritize new or emerging technologies
- No committee for the prioritisation

Methodological guideline

- Guideline 'Manuale delle procedure HTA, 2014' (refer to publications, guidelines from other institutions), available here (only in Italian)
- Follow the Cochrane 'instructions' for the systematic reviews
- Use EUnetHTA frameworks

Specific methods for specific MDs

- Yes, considered different kind of devices and technologies but without a pre-defined framework
- Use EUnetHTA Core Model structure for national reports that are clustered according to different types (e.g. for diagnostic)

Consideration of device-specific aspects

- Case-by-case strategy, considered but without 'a priori' intention
- Within recommendations: e.g. utilization rate and limit the use of a technology, institute registries

Publicly available reports for MDs (published since 2004)

- All reports publicly available here, most in English and Italian
- Numbers: 11

Activities regarding the assessment of MDs

- EUnetHTA joint actions: leader of WP4

Notes: *http://www.eunethta.eu/about-us/faq#t287n73; **selected four regions that have more skills and experiences because the level of knowledge about HTA is different across the 17 regions; ***The other technologies will stay on the list: if some regions have independent resources and they want to assess these technologies, they can do that, but this is outside from the agreement with the MoH

Netherlands

Profile of: Zorginstituut Nederland (ZiN)/ Dutch Health Care Insurance Board (former: CVZ)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Involved with reimbursement questions for the benefit package (MDs, pharmaceuticals etc.)
- Tasks regarding the quality of care
- Open system:
  - no need for an assessment (e.g. most of the hospital care)
  - only assess part of interventions (e.g. when different parties ask ZiN to do it or when ZiN think it would be a good e.g. due to high risk)
  - only criteria of effectiveness, cost-effectiveness assessment not mandatory
  - if it meets the criteria of effectiveness but ZiN don't want it in the package: ZiN advices on exclusion, the MoH decides
  - if it doesn't meet the criteria of effectiveness: HIF decides on reimbursement
  - pharmaceuticals with a budget impact over 2.4 million should also be reimbursed
- Closed system:
  - need always an assessment (e.g. outpatient pharmaceuticals)
  - ZiN advise MoH who makes a decision

Link between MD assessments to coverage decision-making

- Yes, for both systems
- Open system: criteria in the law that ZiN is mandated to decide whether an intervention meets the requirements or not

Use of a specific definition of MDs/Understanding

- No specific definition
- Part of extramural MD (e.g. helping aids in case of hearing problems, walking problems) or of medical specialist care (e.g. surgical implants)

Separate unit/ department for assessment of MDs

- Different departments for pharmaceutical care, hospital care, outpatient care
- Staff: ~400, ~150 dedicated for the quality of healthcare and for the evaluations, ~100 of them are involved in assessments (no full FTAs)

Differences regarding the process of MD and drug assessment

- Yes, due to the divided system
- Closed system: more criteria, thus more strict, guidelines for the research to follow, based mostly on manufacturer applications
- Open system: own research, deal with more incomplete data

Priorisation criteria for MD selection

- Own decisions on what to evaluate (open system)
- Questions from patient organizations, professionals, etc.:
  - criteria: e.g. try to indicate whether it's an important problem or question, is there a lot of money involved, is there a risk that patients get these treatments while there insufficient information whether it's safe or effective
  - don't have to answer all requests: risk-based selection of the topics ZiN want to address
  - do assessment in a certain amount of time (four or five months)

Methodological guideline

- 'Kosteneffectiviteit in de zorg: Op weg naar een genuanceerd en geaccepteerd gebruik van kosteneffectiviteitsgegevens in de zorg, 2013' (Cost-effectiveness in health care: Towards a nuanced and accepted use of cost data in healthcare), available here
- 'Conditional reimbursement of health care, 2012', available here
- 'Medical tests: assessment of established medical science and medical practice, 2011', available here
- 'Established medical science and medical practice, Update 2015', available here
- In progress: working on a document on cost-effectiveness

Specific methods for specific MDs
- Differences between normal care and diagnostic tests
Consideration of device-specific aspects
- Depends on what issue ZiN is working on - Try to identify all the relevant aspects and address them all - Report published that addressed a lot of relevant items ZiN addressed in their assessments, available here
Publicly available reports for MDs (published since 2004)
- Different types of documents available here: Advices to MoH and answers to requests of different stakeholders (e.g. HIF want a new intervention be reimbursed, not sure about effectiveness) - Most of the evaluations are on pharmaceuticals - ~20 assessments a year for the hospital care
Activities regarding the assessment of MDs
- EUnetHTA Joint Action 2: WP1, WP2, WP5 (lead partner), WP7

Poland

Profile of: Agency for Health Technology Assessment and Tariff System (AOTMiT)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- AOTMiT was established in 2005 as an advisory body to the MoH to inform decisions on public funding of health technologies, particularly those that are included in the basic benefits package
- Since 2009 AOTMiT is defined as a legal entity
- Assessment of drugs, medical devices or specific food supplement

Link between MD assessments to coverage decision-making

- AOTMiT provide recommendations to MoH
- Two steps of providing recommendations that both goes to the MoH, who makes the decision:
  - statement done by the Transparency Council *(assessment)*
  - recommendation provided by the president of AOTMiT *(appraisal)*

Use of a specific definition of MDs/Understanding

- Polish legislation is in line with the EU directives (Act from 2010, setting this directives in Polish legislation)
- AOTMiT don't have a specific definition
- Assessment of new devices and the procedure using the device

Separate unit/ department for assessment of MDs

- No, it's the same person who deals with drugs, as well as the application for reimbursement of devices

Differences regarding the process of MD and drug assessment

- No, the requirements are the same and the analysis look similar

Priorisation criteria for MD selection

- AOTMiT works on the order of the MoH and thus don't select the subjects of the assessment
- In general two ways of starting the process taking drugs as well as devices into reimbursement:
  - Unified process: starts with the application from the producer and is highly regulated by law
  - Initialization by the MoH: process is similar to (1) but not so highly regulated
- In every case the process is more or less the same

Methodological guideline

- 'Guidelines for conducting Health Technology Assessment (HTA), April 2009' developed by the Polish community (Experts in HTA field), available here
- Guideline (above) transposed into the 'Regulation of the Minister Of Health of 2 April 2012 on the minimum requirements to be satisfied by the analyses accounted for in the applications for reimbursement and setting the official sales price and for increasing the official sales price of a drug, a special purpose dietary supplement, a medical device, which do not have a reimbursed counterpart in a given indication', delivered in compliance with the Act of May 12th, 2011 on the reimbursement of medicinal products, special purpose dietary supplements and medical devices, in force from January 1st, 2012, available here
- Regulation of the MoH is AOTMiTs actual Guideline

Specific methods for specific MDs

- No

Consideration of device-specific aspects

- No

Publicly available reports for MDs (published since 2004)

- 2007-2014*: 26 assessment of MDs and procedures using MDs; 2015: none
- 2014: 10 assessments of MDs among 320 total assessments (less than 3% counted for MDs assessment)
- Not all assessments are on the website

Activities regarding the assessment of MDs
- EUnetHTA joint actions: take part in reviews of rapid reports, two were for MDs

Notes: * based on a tabular overview provided by AOTMiT after the interview

Spain

Profile of: Axencia de Avaliación de Tecnoloxías Sanitarias de Galicia (AVALIA-t) / Galician Agency for HTA

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- Main activity of the agency is related to the assessment of MDs
- Work for the National Healthcare System (NHS) and on demand for the Regional Healthcare System (RHS)*
- 60-70 % of all assessments of MDs are for the NHS, 30-40 % of all assessments of MDs are for the RHS
- RHS: provide input to the commission responsible for reimbursement
- Horizon Scanning (RHS)

Link between assessments to coverage decision-making

- Assessment of medical devices and procedures is mandatory: all MDs (when there is a major modification) have to be assessed for decision-making purposes before they go into the health care system
- Manufacturer apply for reimbursement after they get CE certification
- Specific commission decides on reimbursement and relies therefore on HTA reports

Use of a specific definition of MDs

- No definition but have regulated the MDs that have to undergo a HTA assessment: "*Medical devices used for the prevention, diagnosis, treatment or rehabilitation of diseases. These include: 1. In vitro diagnostic, prognostic or predictive genetic tests, 2. Diagnostic medical devices, 3. Therapeutic medical devices (includes medical devices implanted in body and those used for assisting medical interventions/procedures), 4. Screening tests, 5. Assistive medical devices used by patients (excludes categories not covered by NHS)*"

Separate unit/ department for assessment of MDs

- No, because MD assessment main line of work
- Staff: 14

Differences regarding the process of MD and drug assessment

- Main line of work concentrates on MD

Prioritisation criteria for MD selection

- Work for NHS: annual plan, priorisation done at national level and distributed among the agencies, for more information:
    - Varela-Lema, L.; Fuente-Cid de la, R.; López-García, L. (2014): Developing a prioritized list of innovative technologies: The Spanish experience. International Journal of Technology Assessment in Health Care; 30(6):626–633. doi: 10.1017/S0266462314000774.
- Work for RHS: no priorisation done, Priorisation might be in relation to the ones that will be assessed first by Avalia-t
- PriTec Tool: decision support tool on which MDs will go on for post-introduction of observational or conditional studies

Methodological guideline

- Internal document
- In progress (end of 2015): unifying methodological document for Spain (within Spanish network)
- Further publications:
    - Varela-Lema L, Ruano-Ravina A, Mota TC, Ibargoyen-Roteta N, Imaz I, Gutiérrez-Ibarluzea I, Blasco-Amaro JA, Soto-Pedre E, Sampietro-Colom L. Post-introduction observation of healthcare technologies after coverage: the Spanish proposal. Int J Technol Assess Health Care. 2012 Jul;28(3):285-93. doi: 10.1017/S0266462312000232. PubMed PMID: 22980706

Specific methods for specific MDs

- Yes, there are different methods for assessment of different types of MDs (e.g. diagnostic, in-vitro)
- Follow EUnetHTA and other guidelines, own scales

Consideration of device-specific aspects

- Yes, e.g. make recommendations regarding the type of hospital (or centre) and on the minimum number of treated patient, that the hospital (or centre) can have

- Go into applicability, accessibility and appropriateness of use indications
- Have published indications for use of consensus documents with clinicians & other stakeholders

Publicly available reports for MDs (since 2004)

- ~30 reports publicly available here
- Brief reports (no full reports) not publicly available

Activities/research regarding the assessment of MDs

- Associated partner in EUnetHTA 2006-08 (WP4, 6, 7, 8)**
- Collaborating partner in EUnetHTA Joint Action 1 (WP4, 7) and Joint Action 2 (WP2 ,4, 5,7)**

Notes: *In Spain exist a common healthcare basket (that's covered and reimbursed for all Spanish) and a complimentary basket within the regions (the regions can add to that if they want); ** http://www.eunethta.eu/organisation/avalia-t

Profile of: Servicio de Evaluación de Technologías of the Vasco Country, Department of Health, Basque Government/ Basque Agency for HTA, Department of Health and Consumers Affairs (OSTEBA)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- No HTA unit devoted to the MoH on the Spanish level
- From 2006 on: network of regional agencies (7 regions) work together, coordinated by a secre-

tariat in Madrid, the presidency is rotatory
- Topics to be assessed are distributed among the regional HTA units
- OSTEBA works for the National Healthcare System (NHS): MoH distributed topics among regional HTA units and works also for the Regional Healthcare System (RHS), the Basque Country
- OSTEBA assess medical devices, pharmaceuticals, public health interventions, vaccines and screening programs and procedures, surgical procedures and also organizational technologies so those related to the structural services

Link between assessments to coverage decision-making
- Not mandatory, but from 2011 on they were much more related to the decisions on the benefit package of the national level (decisions on reimbursement on certain technologies)

Use of a specific definition of MDs
- Use the definition that has been agreed by INAHTA on the HTA glossary, translation from English to Spanish and Basque

Separate unit/ department for assessment of MDs
- No, just a unit devoted for new and emerging technologies, mostly assess MDs but also other technologies
- Staff: 5 people for regional level task and 7 for national level tasks and other projects

Differences regarding the process of MD and drug assessment
- Similar in terms of the clinical aspects: consider efficacy, safety and economic aspects
- Different structures for ethical, social or organisational issues: use different kind of checklists
- Separation between diagnostics and therapeutic devices *(see specific methods)*

Prioritisation criteria for MD selection
- Proactive process:
  - For different kind of technologies, provided mostly by the Basque Health Service and the Department of Health at the Basque Country
  - Horizon Scanning System: identifying possibly technologies that could impact the system, especially focused on the areas of priority of the Department of Health at the regional level
- Reactive process:
  - Yearly performed for the MoH at the Spanish level *(see also profile of Avalia-t)*
  - MoH asks the different regions for topics to be assessed at the national level: list is prioritized and according to the capacity of the regional bodies

Methodological guideline
- Ibargoyen-Roteta N, Gutiérrez-Ibarluzea I, Asua J. Report on the development of the GuNFT Guideline.i Guideline for Not Funding existing health Technologies in health care systems . Madrid: Plan de Calidad para el SNS del MSPS. Servicio de Evaluación de Tecnologías Sanitarias del País Vasco (Osteba); 2009. Informes de Evaluación de Tecnologías Sanitarias: OSTEBA Nº 2007/11
- Ruano Raviña A, Velasco González M, Varela Lema L, Cerdá Mota T, Ibargoyen Roteta N, Gutiérrez Ibarluzea I, et al. Identification, prioritisation and assessment of obsolete health technologies. A methodological guideline. Quality Plan for the National Health System. Galician Health Technology Assessment Agency; 2007. HTA Reports: avalia-t No. 2007/01. *(Action of all the Spanish agencies, coordinated by the Galician agency)*
- Other evidence-based reports available here *(e.g.how to structure a report when you want to produce a clinical protocol),* it was coordinated by the Aragon Institute of Health Sciences
- Methodological guidelines agreed by all the Spanish agencies on how to develop the clinical practice guidelines, updating, adapting them and disseminating, available here(only in Spanish)
- Work together with the different Spanish agencies and develop also a checklist on ethical and organisational aspects: OSTEBA CHECKLIST EN ASPECTOS ÉTICOS Y ORGANIZATIVOS *(only in Spanish, Basque available)*
- Working on a checklist in collaboration with the INAHTA group on ethics: Osteba Checklist on Ethical aspects in HTA (2013)

Specific methods for specific MDs
- No, mostly similar

- In the case of diagnostics: use a specific checklist for particular organisational aspects

Consideration of device-specific aspects

- Yes, use checklist on organisational aspects (refinement of EUnetHTA core model) *(see methodological guideline)*
- Consider life cycle of technologies

Publicly available reports for MDs (since 2004)

- In general, focusing more on MDs and the production of clinical guidelines
- Produce around 7 reports (blue reports) per year (more than 70% of the blue reports are on MDs), plus two clinical practice guidelines for the NHS
- Produce around 12 reports a year for the RHS (including all types of technologies)
- Reports for RHS** on devices: 18, procedures: 5
- Untill 2010, number of reports for RHS** on diagnostics: 2, devices/procedures: 1, device/diagnostics: 5, diagnostic/public health intervention: 2, diagnostic/devices/drugs: 3, diagnostic/procedures: 3

Activities/research regarding the assessment of MDs

- EUnetHTA joint action 2: WP4, WP5, WP7 (related to MDs)
- involved in methodological guidelines on MDs

Notes: * Spanish health care system is quite decentralized because the provision of health is done at the regional level, decisions are taken at the regional level; common benefit package at the national level; ** List with HTA reports from 2004 on provided by OSTEBA

Sweden

Profile of: Swedish Dental and Pharmaceutical Benefits Agency (TLV)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- TLV is a central government agency whose remit is to determine whether a pharmaceutical product or dental care procedure shall be subsidized by the state*
- TLV has two roles regarding the assessment of MDs:
    - Consumables (e.g. syringes), that are included in the benefit scheme
    - Government commission regarding assessment of MDs on a trial basis:
        - First commission in 2012, second commission in 2013
        - Trial ends December 2015 (permanent commission will be decided)
        - Background: Medications have been evaluated well and not the same thing has been done for MDs
        - Aim: initiated to aid the county councils in making more informed decisions regarding MDs**; possibility to do this and how it works
        - Another objective was to, at the national level, perform HTA's, which would enable uniformity and equal health care**

Link between assessments to coverage decision-making

- Consumables: 100% included
- Government commissions: TLV assess MDs but the County Councils make the decision, not mandatory

Use of a specific definition of MDs

- *Requested by mail*

Separate unit/ department for assessment of MDs

- No, but 3 people commissioned with the governmental task
- Consumables staff: 2

Differences regarding the process of MD and drug assessment

- No

Priorisation criteria for MD selection

- Government commission: no formal priorisation process exists yet (trial basis), test different approaches:
    - Public suggestions via webpage; contact County Councils, governmental institutions and companies for suggestions
    - Collection by TLV and choice regarding i) own interest and ii) different criteria such as: impact on health system, size of patient population, severity of disease, feasibility of health economic analysis
    - Provide shortlist of collected MDs to County Councils and ask for most suitable MDs

Methodological guideline

- 2 Final documents of governmental commissions available here
- Four-step-approach for the evaluation of MDs (Swedish, will be translated in English), some information is available here

Specific methods for specific MDs

- No

Consideration of device-specific aspects

- Yes, discuss all kind of aspects of the new treatment and the introduction of the new treatment for medical devices
- beside the health economic evaluation, there is a second part in the assessment which take into account ethical dilemmas, budget impact analysis, organisational aspects such as the need of changes in order to accommodate the new product (e.g. new kind of room in the hospital), also legal aspects

Publicly available reports for MDs (published since 2004)

- Government commission: 5 assessments available here
  - Distribution via representative in County Councils (contact person)
- Due to the trial starting in 2012, number of assessments for medications (since 2002) is much higher

Activities/research regarding the assessment of MDs

- SEED consortium

Notes: * Additional information retrieved from website and from ** Final report available here

United Kingdom/ England &Wales

Profile of: National Institute for Health and Care Excellence (NICE)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- NICE within the UK provides guidance to the NHS
- Different programmes for different technologies *(see separate unit)*
- Goal in each case is the production of guidance which is available on the website and is used in the NHS

Link between MD assessments to coverage decision-making

- Pharmaceuticals and technology appraisals have a funding direction: has to be adopted within three months
- Diagnostics and the medical devices: don't have a funding direction; recommendations for commissioners and people working within the NHS to provide services, or clinicians, and procurement managers and people within the health care service who are commissioning services and are making decisions about treatment care per patient; helpful for building business cases to provide new services and to adopt innovate devices
- Actual decisions are made at local-hospital level

Use of a specific definition of MDs/Understanding

- Within Method guide of MTEP definition of medical technologies which refer to EU Council Directives (p.5)

Separate unit/ department for assessment of MDs

- Yes, separate programmes
- Medical Technologies Evaluation Programme (MTEP), set up in 2010 to look specifically at medical devices, surgical procedures
- Diagnostic Assessment Programme (DAP), set up in 2010 to looks specifically at diagnostic technologies
- Technology Appraisal Programme (TA) looks at pharmaceuticals and devices
- Interventional Procedures Programme (IP) look mostly on procedures

Differences regarding the process of MD and drug assessment

- The medtech (devices and diagnostics) and the pharmaceuticals programmes are hard to compare really, because they work in a different ways
- All programmes have slightly different methodological approaches and ways of operating
- Separate system of submission and assessment (DAP, MTEP), e.g. in the MTEP guidance development process, the company, have to do a submission to NICE which is the clinical and cost evidence for their case for adoption
- Each programme has its own methods and process guide *(see methodlological guideline)*

Priorisation criteria for MD selection

- For each programme there are different criteria
- Selecting and routing process described in detail in the process guides *(see methodlological guideline)*
- Within medical devices and diagnostics: independent Medical Technologies Advisory Committee do the topic selection

Methodological guideline

- 'Guide to the multiple technology appraisal process, 2009'*, available here
- 'Guide to the single technology appraisal process, 2009'*, available here
- 'Guide to the methods of technology appraisal, 2013', available here
- 'Diagnostics Assessment Programme manual, December 2011', available here
- 'Medical Technologies Evaluation Programme, Methods guide, 2011', available here
- 'Medical Technologies Evaluation Programme, Process guide, 2011', available here
- 'Interventional Procedures Programme, Methods guide, 2007', available here
- 'Interventional Procedures Programme, Process guide, 2009', available here
- Medtech Innovation Briefings (MIBs): integrated process statement on how NICE select topics

and prepare the documents available here
- Updates on TA, DAP and MTEP guides (expected by end of 2015)

Specific methods for specific MDs
- Yes, for DAP, MTEP and IP

Consideration of device-specific aspects
- Yes, varies and depends on the technology (e.g. training and learning curves)
- Task of the External Assessment Center (e.g. for MTEP)
- Particular questions identified at selection meeting
- Technical reports could be compiled

Publicly available reports for MDs (published since 2004)
- Yes, all guidances as well as the full assessment reports produced by EAC are publicly available here
- Number (including all programmes): 295
- Medtech Innovation Briefings (MIBs): 36

Activities regarding the assessment of MDs
- EUnetHTA joint actions

Notes: *There is a new guide to the technology appraisal process that incorporates both multiple and single technology appraisal processes, available here

United Kingdom/ Scotland

Profile of: Scottish Health Technologies Group (SHTG) from Healthcare Improvement Scotland (HIS)

Part I: Institutional structures, processes and methods

Role of institution in the HTA system of the country, especially regarding MDs

- HIS has the legal remit within Scotland to undertake technology assessments of medicines and non-medicines on behalf of NHS Scotland
- HIS is a broader umbrella organisation and house the Scottish Intercollegiate Guidelines Network (SIGN) of the Scottish Medicines Consortium (SMC)
- SHTG is a group that came from government and was transferred to HIS to provide advice on technologies – anything that isn't a medicine
- SHTG has a broad remit: cover anything from typical definitions of technology up to methods of service delivery and organisation
- Offer advice to NHS Scotland to help in decision-making based on evidence reviews (follows a rapid review end of the spectrum)
- SHTG is independent and impartial of government

Link between MD assessments to coverage decision-making

- Each individual board has local discretion of what it chooses to purchase or provide on behalf of its local resident population
- SHTG reviews produce advice (Status of evidence product is 'required to consider'), these are not mandatory but expected to inform them

Use of a specific definition of MDs/Understanding

- No
- General agreement that MD is any healthcare technology other than medicine

Separate unit/ department for assessment of MDs

- HIS: about 300 people
- SHTG: about 15 people full-time equivalent (including health services researchers, health economists, information scientists, secretariat, clinical appointments)
- Staff generic and work across a range of different technologies

Differences regarding the process of MD and drug assessment

- SMC looks at medicines based on submissions from manufacturers
- SHTG looks at already published evidence (IMTO process works with submissions, limited)
- SMC reviews all new license applications
- SHTG responds to the services requirements round about topics (open topic referral form)

Priorisation criteria for MD selection

- Open topic referral form: topics could be add by the service, clinicians or policy makers or health board personnel
- Prioritise them depending on which topics come in and how important they are according to a number of criteria:
    - how does it align with the NHS Scotland strategic position, is there a difference in terms of either uptake or use of the technologies, how big is the likely patient impact, are there likely to be any material resource implications resulting from adoption of the technology or not, is it possible to form an answerable question at this time, is there available evidence of sufficient quantity and quality to address the question purposefully on behalf of the person who sent us the topic

Methodological guideline

- 'Standard operating procedure' (technologies scoping, evidence notes, advice statements, innovative medical technology overviews) available here
- Health technology assessment manual (not actually up on the website, review in progress)

Specific methods for specific MDs

- No specific guide or manual
- Follow own procedures

- For extra advice or input on assessing diagnostics: look to other guides from other people
- Can make us of a national diagnostics steering group for input
- Some people from staff attend specific training about differences and the nuances in terms of diagnostics assessments as opposed to other aspects

Consideration of device-specific aspects

- Yes, on occasion
- A number of the questions to SHTG have been about volume and outcome relationships
- thought about learning curves and other topics of interest to the people who put the topic to SHTG

Publicly available reports for MDs (published since 2004)

- Key products: evidence note and following advice statement
- Sometimes undertake full healthcare technology assessments
- Undertake about 20 pieces of advice a year
- 2008-2014: about 100 published outcomes, including working papers and procedural things
- All outputs publicly available
    - technologies scoping reports available here
    - IMTO reports available here
- For pharmaceuticals it's different: SMC reviews every new license application for new medicines, approximately 70 to 100 medicines a year
- Elements of device assessment undertaken by SIGN (look at devices and their use within the guideline)

Activities regarding the assessment of MDs

- EUnetHTA joint action 2 WP5, WP7
    - o reviewers on two of the pilots in WP5 strand B on medical devices
    - o WP7 work with pilots of templates for submission for non-medicine technologies