EUnetHTA WP7: Implementation report November 2018

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Contents

Abbreviations

AAZ: Agency for Quality and Accreditation in Health Care
AEMPS: Agencia Española de Medicamentos y Productos Sanitarios
AETSA: Andalusian Agency for Health Technology Assessment
Agenas: The National Agency for Regional Health Services
AIFA: Agenzia Italiana del Farmaco
AOTMiT: Agency for Health Technology Assessment and Tariff System
AQuAS – Agència de Qualitat i Avaluació Sanitàries de Catalunya
ASSR-RER: Agenzia Sanitaria e Sociale Regionale-Emilia-Romagna
AVALIA-T – Galician Agency for Health Technology Assessment
CE: Conformité Européenne (European Conformity)
CGM: Continuous glucose monitoring
DEFACTUM: Social & Health Services and Labour Market
EC: European Commission
EPAR: European Public Assessment Report
EUnetHTA: European Network for Health Technology Assessment
EU REA: EUnetHTA Relative Effectiveness Assessment
FOPH: Federal Office of Public Health
GOeG: Gesundheit Österreich GmbH
GRADE: Grading of Recommendations Assessment, Development and Evaluation
HAS: Haute Autorité de Santé
HIFU: High-intensity focused ultrasound
HILA: Pharmaceuticals Pricing Board
HIS: Healthcare Improvement Scotland
HIQA: Health Improvement and Quality Authority
HTA: Health Technology Assessment
HTW: Health Technology Wales
INFARMED: National Authority of Medicines and Health Products
ISPOR: International Society for Pharmacoeconomics and Outcomes
JA: Joint Action
JA2: Joint Action 2
JA3: Joint Action 3
KCE – Belgian Health Care Knowledge Centre
LBI: Ludwig Boltzmann Institute
NCPE: National Centre for Pharmacoeconomics
NHS: National Health Service
NICE: National Institute for Health and Care Excellence
NIPHNO: Norwegian Institute of Public Health
NIPT: Non-Invasive Perinatal Testing
NIPN: National Institute of Pharmacy and Nutrition
NSPHMPD: National School of Public Health, Management & Professional Development
NOMA: Norwegian Medicines Agency
OSTEBA – Basque Office for Health Technology Assessment
PICO: Population, Intervention, Comparator, Outcome
PICOTS: Population, Intervention, Comparator, Outcome, Timing, Setting
POP Database: Planning and Ongoing Projects Database
PT: Pharmaceutical Technologies
PTJA: Pharmaceutical Technologies Joint Assessment

OT: Other technologies
OTCA: Other Technologies Collaborative Assessment
REA: Relative Effectiveness Assessment
rTMS: Repetitive Transcranial Magnetic Stimulation
SBU: Swedish Agency for Health Technology Assessment and Assessment of Social Services
SHTG: Scottish Health Technologies Group
SMC: Scottish Medicines Consortium
SmPC: Summary of Product Characteristics
SNHTA: Swiss Network for Health Technology Assessment
SUKL: State Institute for Drug Control
TLV: Dental and Pharmaceutical Benefits Agency
UCSC: Università Cattolica del Sacro Cuore
UNIBA: Comenius University in Bratislava
UK: United Kingdom
VASPVT: State Health Care Accreditation Agency, Lithuania
WCD: Wearable Cardioverter Defibrillator
WP: Work Package
ZIN: Zorginstituut Nederland

Foreword

As of November 2018, EUnetHTA has published 10 assessment reports in Joint Action 3 (JA3), 3 pharmaceutical technology (PT) assessments and 7 other technology (OT) assessments). Agencies report 104 examples of use, 45 uses of the PT assessments and 59 uses of OT assessments. Of the 104 uses, 64 describe use in assessment procedures and 40 in dissemination activities. Compared with Joint Action 2 (JA2) the number of uses of EUnetHTA assessments has improved.

The range of countries using the assessments is encouraging. For PT assessments 16 countries report using at least one JA3 assessment. Similarly for OT assessments 14 countries now report using of at least one JA3 assessment.

Partners report using EUnetHTA assessments to:

- support evaluation of company submissions or as background or additional information for their assessments
- extract elements of the EUnetHTA assessments into existing agency report structures
- replace agency documents and processes with EUnetHTA outputs

Partners identify benefits from using EUnetHTA assessments, including time and cost savings and improved quality of and confidence in the agency's assessments. Unsurprisingly, agencies who are able to replace their documents and processes with those from EUnetHTA report the biggest resource benefits.

Factors that support agencies to replace their documents and processes with EUnetHTA outputs include (1) historical involvement in EUnetHTA, (2) taking part in joint production activities, (3) an agency remit to prepare HTA as opposed to evaluate company submissions, (4) alignment of EUneHTA tools and methods with those of the agency and (5) where multiple agencies are involved in resource allocation, the HTA agency has procedural freedom of the HTA aspects of the process. These factors are likely to support development of trust in EUnetHTA outputs and an easier ability to incorporate EUnetHTA outputs into existing agency processes. Agencies assessing other technologies are more likely to possess more of the characteristics that support most efficient implementation.

For users of assessments of other technologies, reasons for not using EUnetHTA assessments primarily relate to issues of timing and relevance. The implementation issues prioritised by partners for EUnetHTA to resolve focus on topic selection including mechanisms to identify topics that align with the priorities of multiple agencies, to develop a scope for the joint assessment that reflects the needs of all interested agencies and to carry out assessments in a timely manner.

Users of assessments of pharmaceuticals report a varied range of issues that prevent or limit their use of EUnetHTA assessments. Users suggest a varied range of (sometimes contradictory) solutions to these issues reflecting the wide range and often very prescribed HTA needs of users of pharmaceutical assessments.

Looking to increase implementation, feedback suggests that to fully understand and overcome implementation issues, agencies must be able to see how EUnetHTA assessments fit within the broader context of decision-making in which there are important dependencies between clinical effectiveness analysis and non-clinical aspects such as economic analysis, and between assessment, appraisal and decision-making processes. Users of pharmaceutical assessments need to be able to develop a familiarity with the outputs, to evaluate the impact of using EUnetHTA assessments and to identify changes needed to their processes. Partners identified the following activities to support implementation:

- production of a greater number of assessment reports,
- involvement of the widest range of partners in production activities
- improved predictability and standardisation of assessment contents.

Issues of timing and scope relevance for users of PT assessments are less frequently reported now than in JA2. However, these issues remain a problem that impacts on implementation for some agencies.

Looking to the future, partners identified that a permanent model of HTA cooperation should be underpinned by a set of principles:

(1) different HTA approaches are required for different health technologies and decisions that HTA informs

(2) relative effectiveness assessment is only one aspect of HTA, HTA cooperation needs to work alongside and support these other aspects

(3) the model of HTA cooperation must be able to respond to the continuously changing environment in which HTA is carried out

(4) to plan to use joint assessments and reduce duplication, agencies need to know clearly what they will receive in what timeframe

(5) broad involvement of agencies in joint assessment processes is a key enabler of uptake and change

Partners identified the following activities outlined in the EC proposal for a regulation in HTA that EUnetHTA could usefully test and evaluate further in JA3 because of their importance to developing a permanent model of HTA cooperation:

(1) Topic identification, selection, prioritisation and timing (particularly for OT);

(2) Stakeholder and Member State engagement;

(3) Review and maintenance of joint assessments;

(4) Role of the coordination group and governance structures; and

(5) Definition of ‘acceptable use’ to be used to monitor and evaluate any permanent model of HTA cooperation.

Introduction

This is the second Work Package 7 (WP7) implementation report. The first implementation report was published in May 2018.

This report focuses on the uptake and implementation of joint and collaborative assessments published under JA3, providing comparisons with the data in the first implementation report and with JA2 data where appropriate or feasible.

This implementation report is divided into the following sections:

- Section 1 – Update of implementation data on use of JA3 assessments.
- Section 2 – Thematic analysis of qualitative interviews on use of JA3 assessments.
- Section 3 – Case study on use of joint EUnetHTA relative effectiveness assessments (REAs) to inform economic evaluation – thematic analysis (with supporting appendix 2).
- Section 4 – Summary of WP7 focus groups held to support development of the scientific and technical mechanism for a sustainable model of health technology assessment (HTA) cooperation.

Each section of the report provides: i) a summary of key findings; ii) a statement of methods used; and iii) results.

Section 1 – Implementation Data

Key findings

- The implementation data shows an increasing use of EUnetHTA assessments. 104 examples of use of JA3 assessments have been reported to date (November 2018), 45 for PT assessments and 59 for OT assessments. Of the 104 uses, 64 were in assessment procedures and 40 were in dissemination.
- For PT assessments 16 countries reported using a JA3 assessment as of November 2018, rising from 10 in May 2018. Similarly for OT assessments 14 countries have now reported use of a JA3 assessment, rising from 9 in May 2018.
- Despite the increasing use, agencies identify a range of issues that limit their ability to use EUnetHTA assessments. For PT assessments the biggest issues are: language, reporting, relevance and timing. Users of OT assessments are much less likely to identify factors limiting use.
- Some agencies carried out work on the topic EUnetHTA assessed, but did not use the EUnetHTA JA3 assessment (n = 43 for OT; n = 15 for PT).
- For OT assessments timing was the main factor preventing use. For PT assessments the factors preventing use were more varied, and related to timing, relevance, reliability, evidence and methodology and awareness.

Methods

Implementation data is collected by WP7 for all published EUnetHTA joint and collaborative assessments. Agencies provide data through completion of an implementation survey (intranet version for EUnetHTA partners, internet version for non-partners). The implementation survey is sent out after the publication of each assessment. The survey is predominately multiple choice but with some free-text responses (questions ask about whether assessment was used, if so how it was used, and factors that prevented or limited use). Respondents are expected to revise / update responses if their status changes.

Implementation data is downloaded, 'cleaned' and analysed by WP7 every 2 to 3 months. Implementation data is included in the WP7 implementation report published bi-annually (see section 1 – results). Selected survey responses are followed-up by implementation leads for qualitative interview and findings incorporated into implementation reports (see section 2).

The implementation data in this report is as reported on 16th November 2018.

Results

Published assessments

To date 10 joint or collaborative assessments have been published under JA3, 7 OT assessments and 3 PT assessments. Implementation data on each of these assessments is presented in this section of the report.

Table 1 below details the date when each assessment was published. The publication date should be born in mind when considering the data presented. For example, at the time of writing this report assessment OTJA08 has been published for less than 6 months. This will not be enough time to fully capture implementation data on the use of the assessment.

Table 1: Publication dates for JA3 assessments

Assessment	Publication date
OTCA01 (Wearable cardioverter-defibrillator)	Nov-16
OTCA02 (Antibacterial-coated Sutures)	Apr-17
OTCA03 (NIPT)	Feb-18
OTCA04 (MammaPrint)	Jan-18
OTCA05 (Magnetic stimulation)	Apr-17
OTJA08 (Glucose Monitoring)	Jul-18
OTCA09 (HIFU Ablation)	Apr-18
PTJA01 (Midostaurin)	Nov-17
PTJA02 (Regorafenib)	Oct-17
PTJA03 (Alectinib)	Jan-18

Response rates

Table 2 details the response rate by agency for all JA3 assessments[1]. The response rates by agency are high for PT ranging from 80% (PTJA03) to 85% (PTJA01, PTJA02). The response rates for OT are also good ranging from 61% (OTJA08) to 79% (OTCA01). OTJA08 is the most recently published assessment (July 2018) with less than 6 months follow-up data available. The response rate for this assessment can also be expected to increase over time.

[1] Calculated based on 38 agencies currently using HTA to assess non-pharmaceutical technologies and 46 using HTA to assess pharmaceutical technologies. Data on use of HTA was collected by WP7 in their research and analysis of HTA and reimbursement processes in EUnetHTA partner countries and from partners in the implementation network

Table 3 below details the response rate by country for JA3 assessments[2]. Response rates by country for PT are very high ranging from 86% (PTJA03) to 97% (PTJA01). Response rates for OT are also good ranging from 71% (OTCA03, OTCA09) to 79% (OTCA01, OTCA02, OTCA04, OTCA05).

The data in table 3 also shows that country response rates have improved across all assessments since May 2018 (where comparable data is available).

Table 2: Response rate by agency – JA3 assessments

Assessment	Responses from expected agencies	
	Number (N)	Percentage (%)
OTCA01 (Wearable cardioverter-defibrillator)	30 of 38	79 %
OTCA02 (Antibacterial-coated Sutures)	26 of 38	68 %
OTCA03 (NIPT)	28 of 38	74 %
OTCA04 (MammaPrint)	27 of 38	71 %
OTCA05 (Magnetic stimulation)	28 of 38	74 %
OTJA08 (Glucose Monitoring)	23 of 38	61 %
OTCA09 (HIFU Ablation)	25 of 38	66 %
PTJA01 (Midostaurin)	39 of 46	85 %
PTJA02 (Regorafenib)	39 of 46	85 %
PTJA03 (Alectinib)	37 of 46	80 %

Table 3: Response rate by country – JA3 assessments

Assessment	Responses from expected countries - May 2018		Responses from expected countries - November 2018	
	Number	Percentage (%)	Number	Percentage (%)
OTCA01 (Wearable cardioverter-defibrillator)	17 of 24	71%	19 of 24	79%
OTCA02 (Antibacterial-coated Sutures)	16 of 24	66%	19 of 24	79%
OTCA03 (NIPT)	N/A	N/A	17 of 24	71%
OTCA04 (MammaPrint)	N/A	N/A	19 of 24	79%
OTCA05 (Magnetic stimulation)	17 of 24	71%	19 of 24	79%
OTJA08 (Glucose Monitoring)	N/A	N/A	18 of 24	75%
OTCA09 (HIFU Ablation)	N/A	N/A	17 of 24	71%
PTJA01 (Midostaurin)	25 of 29	86%	28 of 29	97%
PTJA02 (Regorafenib)	25 of 29	76%	27 of 29	93%
PTJA03 (Alectinib)	N/A	N/A	25 of 29	86%

[2] Calculated based on 24 countries currently using HTA to assess non-pharmaceutical technologies and 29 using HTA to assess pharmaceutical technologies. Data on which countries use different types of HTA was collected by WP7 in their research and analysis of HTA and reimbursement processes in EUnetHTA partner countries and from partners in the implementation network

Topic relevance

As with the May 2018 implementation data, the data for November 2018 continues to show that EUnetHTA is generally choosing topics that are within an agency's remit. As shown in table 4 below, agencies indicating that topics were not within remit ranged from 0% (OTJA08) to 16% (PTJA03).

For a number of agencies, although the topic area chosen by EUnetHTA is within their remit, the agency is not currently planning to assess the technology meaning the EUnetHTA topic is not aligned with their agency priorities. This group of agencies continues to remain the biggest group of non-users of EUnetHTA assessments.

The assessment topics for OT show higher levels of topics being within an agency remit but not in the work programme compared to PT. For OTCA01, OTCA02 and OTCA05 over 60% of responses indicated the topic to be within remit, but with work not currently planned.

Table 4: Work status in the topic area subject to EUnetHTA assessment

Assessment	Work on this topic is……			
	Not in our remit*	In our remit but not currently planned	Planned but not started	Ongoing or complete
OTCA01 (Wearable cardioverter-defibrillator)	2 (7%)	19 (63%)	1 (3%)	8 (27%)
OTC02 (Antibacterial-coated Sutures)	4 (15%)	16 (62%)	0 (0%)	6 (23%)
OTCA03 (NIPT)	3 (11%)	13 (46%)	1 (4%)	11 (39%)
OTCA04 (MammaPrint)	2 (7%)	12 (44%)	1 (4%)	12 (44%)
OTCA05 (Magnetic stimulation)	2 (7%)	17 (61%)	0 (0%)	9 (32%)
OTJA08 (Glucose Monitoring)	0 (0%)	7 (30%)	2 (9%)	14 (61%)
OTCA09 (HIFU)	3 (12%)	11 (44%)	1 (4%)	10 (40%)
PTJA01 (Midostaurin)	6 (15%)	12 (31%)	3 (8%)	18 (46%)
PTJA02 (Regorafenib)	6 (15%)	15 (39%)	3 (8%)	15 (39%)
PTJA03 (Alectinib)	6 (16%)	7 (19%)	4 (11%)	20 (54%)
Total	**34 (11%)**	**129 (43%)**	**16 (5%)**	**123 (41%)**

Overview of use of EUnetHTA assessments

Table 5 below and figure 1 overleaf illustrate the use of all published JA3 assessments[3]. As shown 104 examples of use of JA3 EUnetHTA assessments have been reported to date, 45 for PT assessments and 59 for OT assessments. Two principal types of use are reported:

1. Support for or as an alternative to the agency's existing HTA procedures – 64 examples in total (37 for PT and 27 for OT).

2. Dissemination to support awareness of EUnetHTA assessments and/or evidence informed decision making – 40 examples in total (8 for PT and 32 for OT). Examples of reported dissemination activities included: dissemination to decision makers and stakeholders; publication of assessment, supporting documents and news items on agency websites and social media; and indexing in national evidence databases.

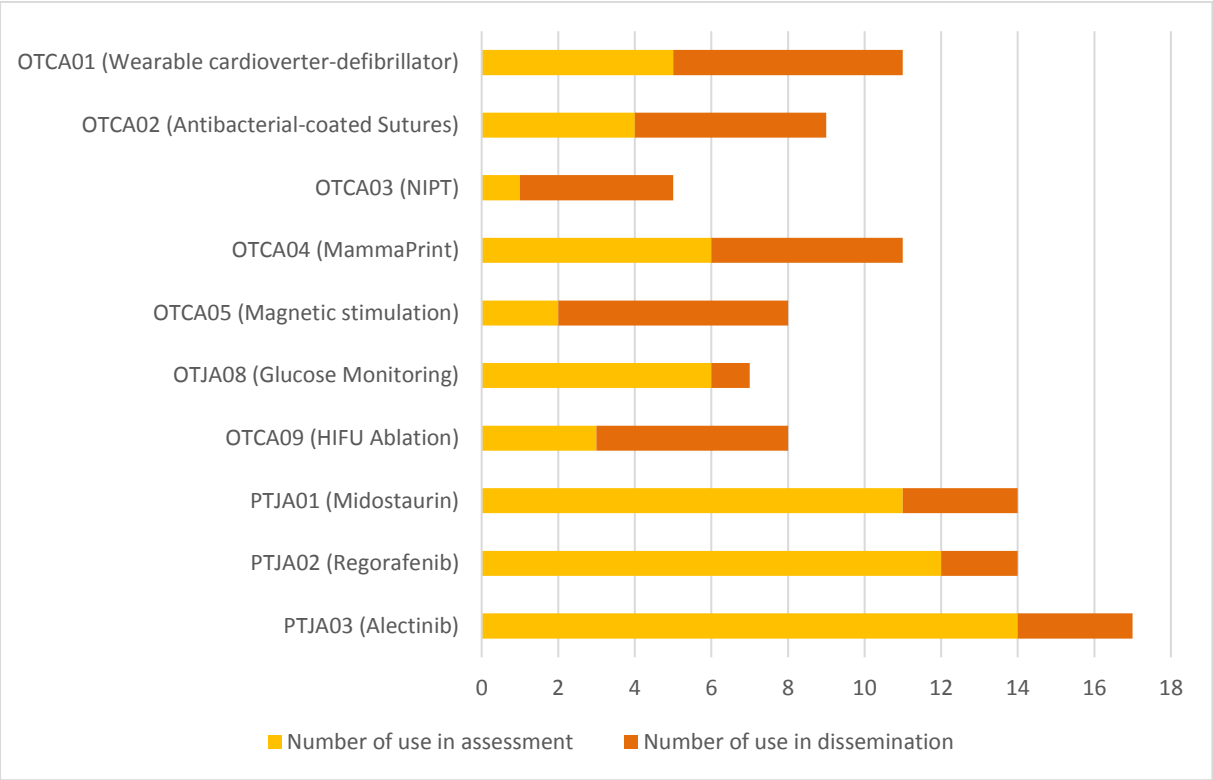
Fifty-nine agencies responded to the survey question on whether the use of assessments were national or regional, 54 (92%) were reported to be national and 5 (8%) were reported to be regional. The EUnetHTA assessment most commonly informed an agency procedure used for reimbursement. However, this was more likely for PT than other OT.

Table 5: Use of the EUnetHTA JA3 assessments

	Number of uses in assessment	Number of uses in dissemination	Total number of uses of the EUnetHTA assessment
OTCA01 (Wearable cardioverter-defibrillator)	5 (45%)	6 (55%)	11
OTCA02 (Antibacterial-coated Sutures)	4 (44%)	5 (56%)	9
OTCA03 (NIPT)	1 (20%)	4 (80%)	5
OTCA04 (MammaPrint)	6 (55%)	5 (45%)	11
OTCA05 (Magnetic stimulation)	2 (25%)	6 (75%)	8
OTJA08 (Glucose Monitoring)	6 (86%)	1 (14%)	7
OTCA09 (HIFU Ablation)	3 (38%)	5 (62%)	8
PTJA01 (Midostaurin)	11 (79%)	3 (21%)	14
PTJA02 (Regorafenib)	12 (86%)	2 (14%)	14
PTJA03 (Alectinib)	14 (82%)	3 (18%)	17
Total	**64 (62%)**	**40 (38%)**	**104**

[3] In the count of use each agency is only counted once for each assessment. Agencies reporting both use and dissemination for an assessment are counted once under use only.

Figure 1: Use of the EUnetHTA JA3 assessments



Countries reporting use of EUnetHTA assessments

The maps overleaf (figure 2 for PT assessments and figure 3 for OT assessments) illustrate the countries reporting use of JA3 assessments. Red shading represents countries that reported use in assessment activities, yellow shading represents use in dissemination activities only.

For PT assessments 16 countries reported using a JA3 assessment. All 16 reported use in assessment activities and 5 of those countries also reported use in dissemination activities. This demonstrates an increase in countries using JA3 assessments from the May 2018 implementation report when 10 countries reported using JA3 assessments (9 in assessment activities and 1 as part of dissemination only).

For OT assessments 14 countries reported using a JA3 assessment. Of those 14 countries, 12 reported use in assessment activities and 5 of those countries also reported use in dissemination activities. A further 2 countries reported use in dissemination only. Again this demonstrates an increase in countries using JA3 assessments from the May 2018 implementation report when 9 countries reported using JA3 assessment (6 in assessment activities and 3 as part of dissemination only).

Figure 2: Countries reporting use of at least one PT assessment

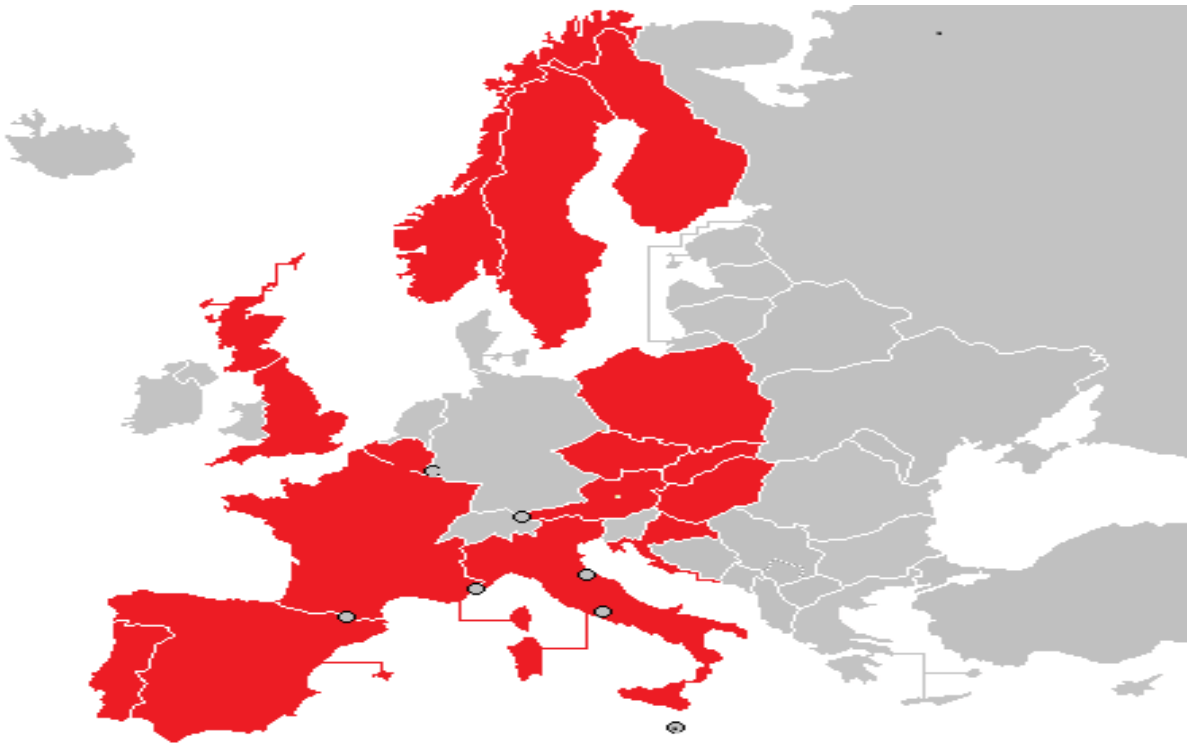
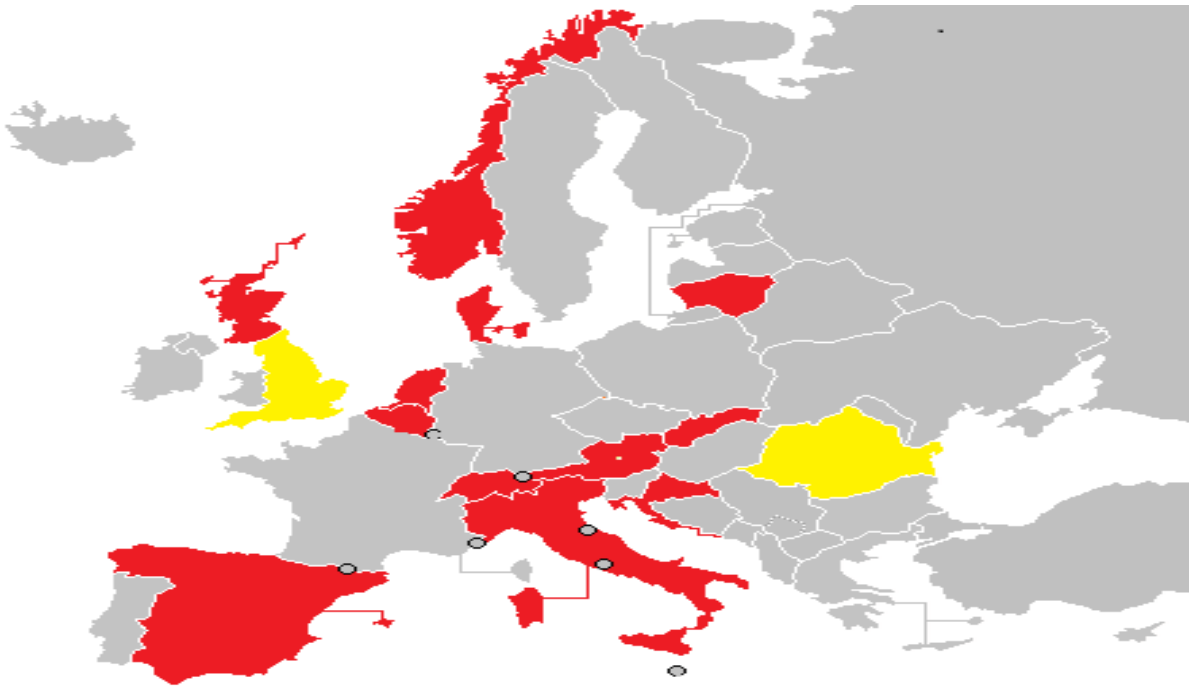


Figure 3: Countries reporting use of at least one OT assessment

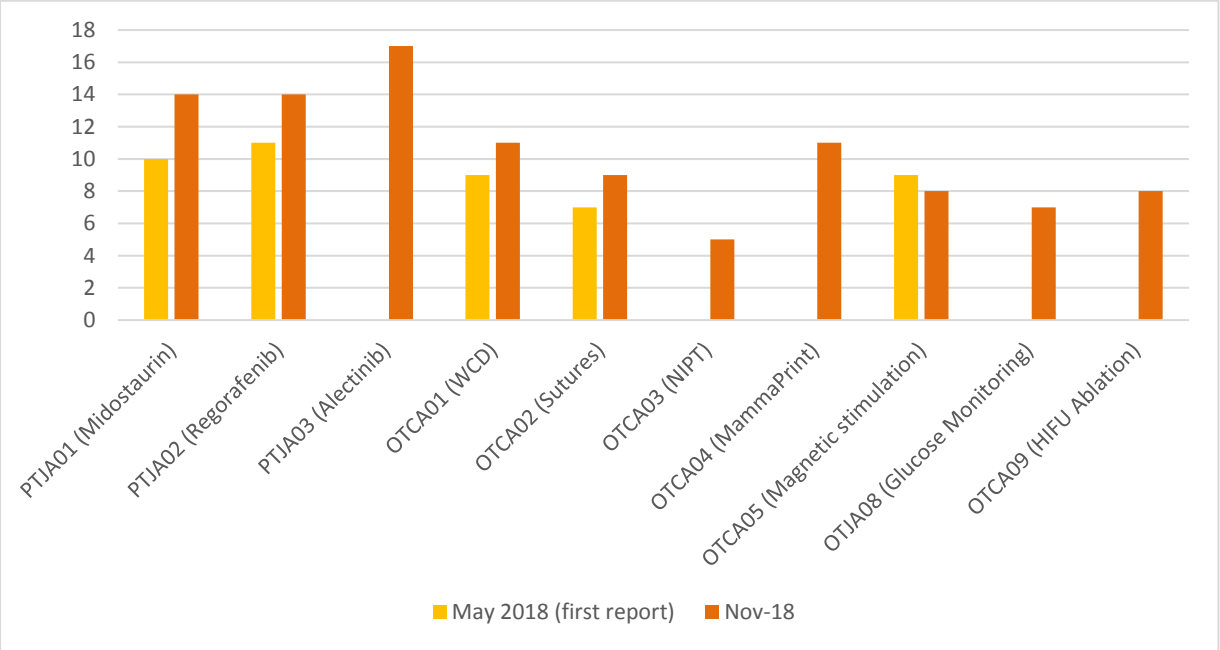


Red = reported use in assessment activities, Yellow = reported use in dissemination activities only

Comparison of use of JA3 assessments – May and November 2018

Figure 4 below details the total number of uses of JA3 assessments, comparing reported use in May 2018 with November 2018. All of the assessments where data was available for the two time points (May and November) show an increase in usage, with the exception of OTCA05 where one agency amended a survey response to report non-use (having previously reported an assessment was ongoing).

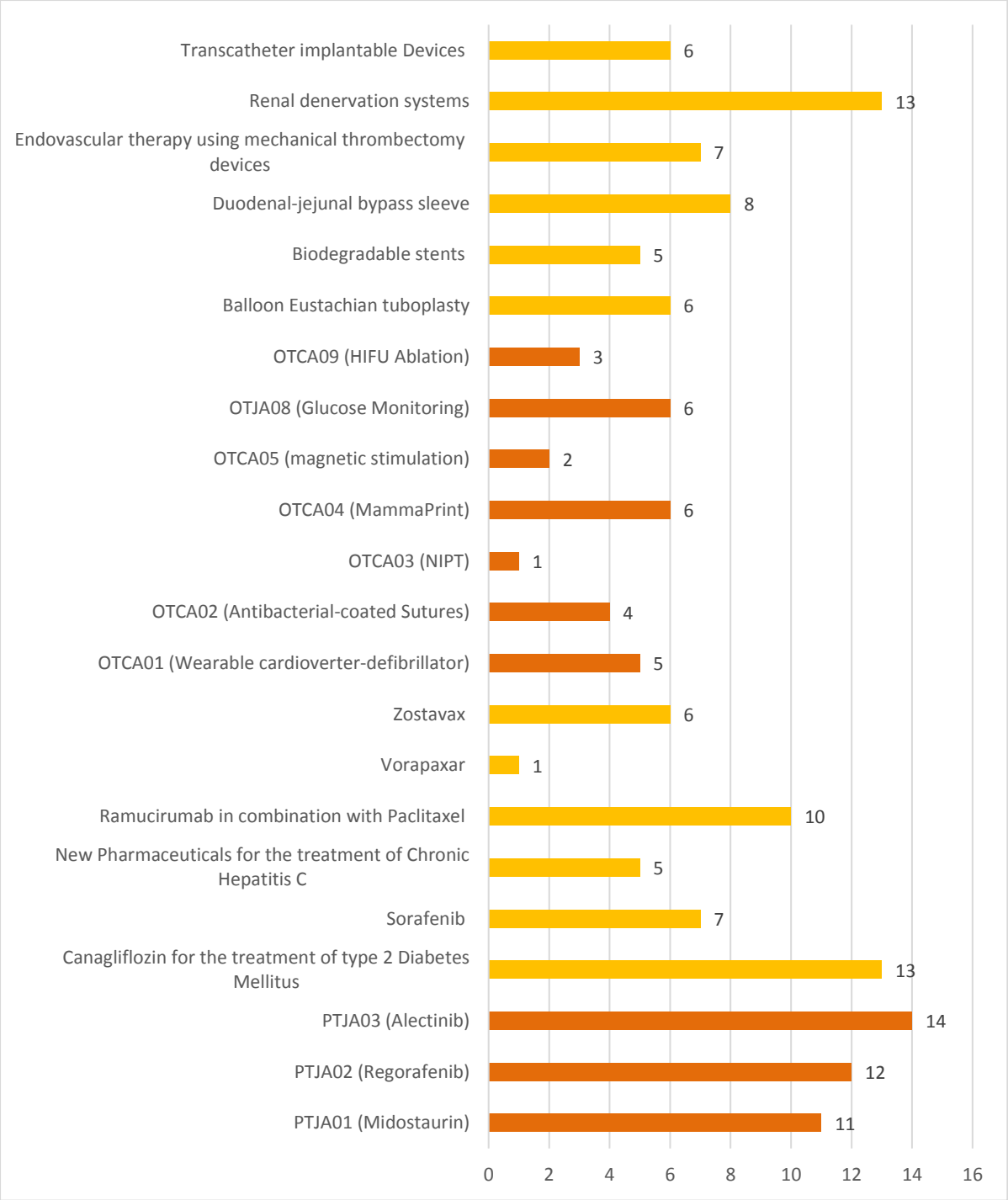
Figure 4: Use of JA3 assessments – May and November 2018



Comparison of use of JA3 assessments in assessment procedures with JA2

Figure 5 overleaf compares the number of reported uses of JA3 assessments in assessment procedures (dark orange) with JA2 assessments (light orange). Comparison is only made on use in assessment procedures (rather than total use) because JA2 data was predominately focussed on use in assessment procedures (not dissemination). Data for use of JA3 OT assessments is now starting to show comparable use with JA2, while use of JA3 PT assessments has increased from the reported use in JA2. Data on use of both JA3 and JA2 assessments is as reported at November 2018.

Figure 5: Use of EUnetHTA joint assessments in national assessment procedures – Comparison between JA3 and JA2

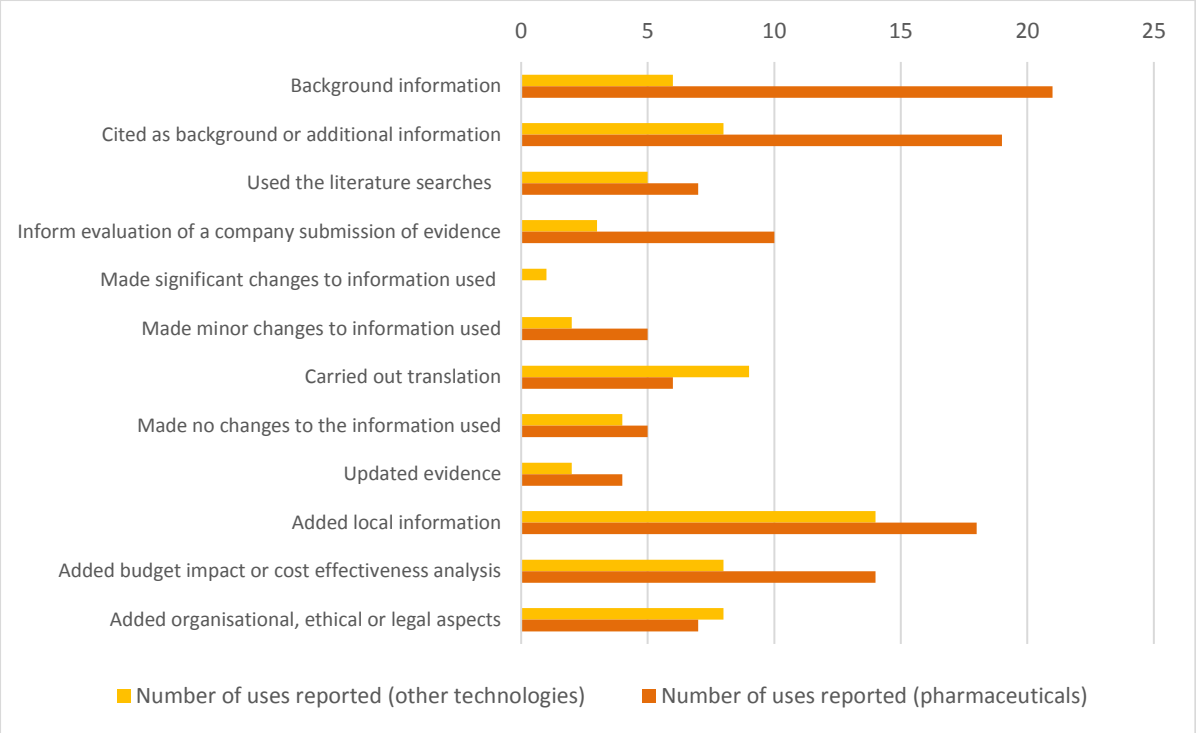


In figure 5 JA3 assessments are shaded dark orange, JA2 assessments are light orange.

Type of use of JA3 assessments

Figure 6 below details the type of use of assessments published under JA3. As shown both PT and OT assessments are used for a wide range of different purposes. Most frequently the assessment is read for background information or cited in the agency report as background or additional information. Agencies also frequently reported using the assessments and adding local information, budget impact or cost-effectiveness analysis, and organisational, legal or ethical aspects. PT assessments are also frequently used to inform the evaluation of a company submission.

Figure 6: Type of use of JA3 assessments



Sections of the assessments used

Where agencies have used EUnetHTA joint assessments in national assessment procedures, they were asked to report which sections of the assessments they have used. Where specific sections were used, 39 agencies (65%) reported they have used all sections of the assessment and 21 (35%) used specific sections (4 agencies did not respond to this question). Where agencies did use specific sections, the sections used most frequently were:

- Clinical effectiveness – 20 (PT = 15, OT = 5)
- Safety – 15 (PT = 10, OT = 5)
- Health condition and use of technology – 9 (PT = 6, OT = 3)
- Description of technology 8 (PT = 5, OT = 3)

Limiting Factors

Agencies that used a JA3 assessment in their assessment processes were asked whether there were any factors that had affected their ability to use the assessment (see figure 7 overleaf). Agencies using assessments of other technologies frequently reported that there were no limiting factors affecting their use (n = 16).

For PT assessments the most frequently identified limiting factors were:

- the requirement to prepare reports in their national language (n = 16)
- the requirement to use a specified report structure (n = 13)
- the timing of the availability of the EUnetHTA assessment (n = 9).

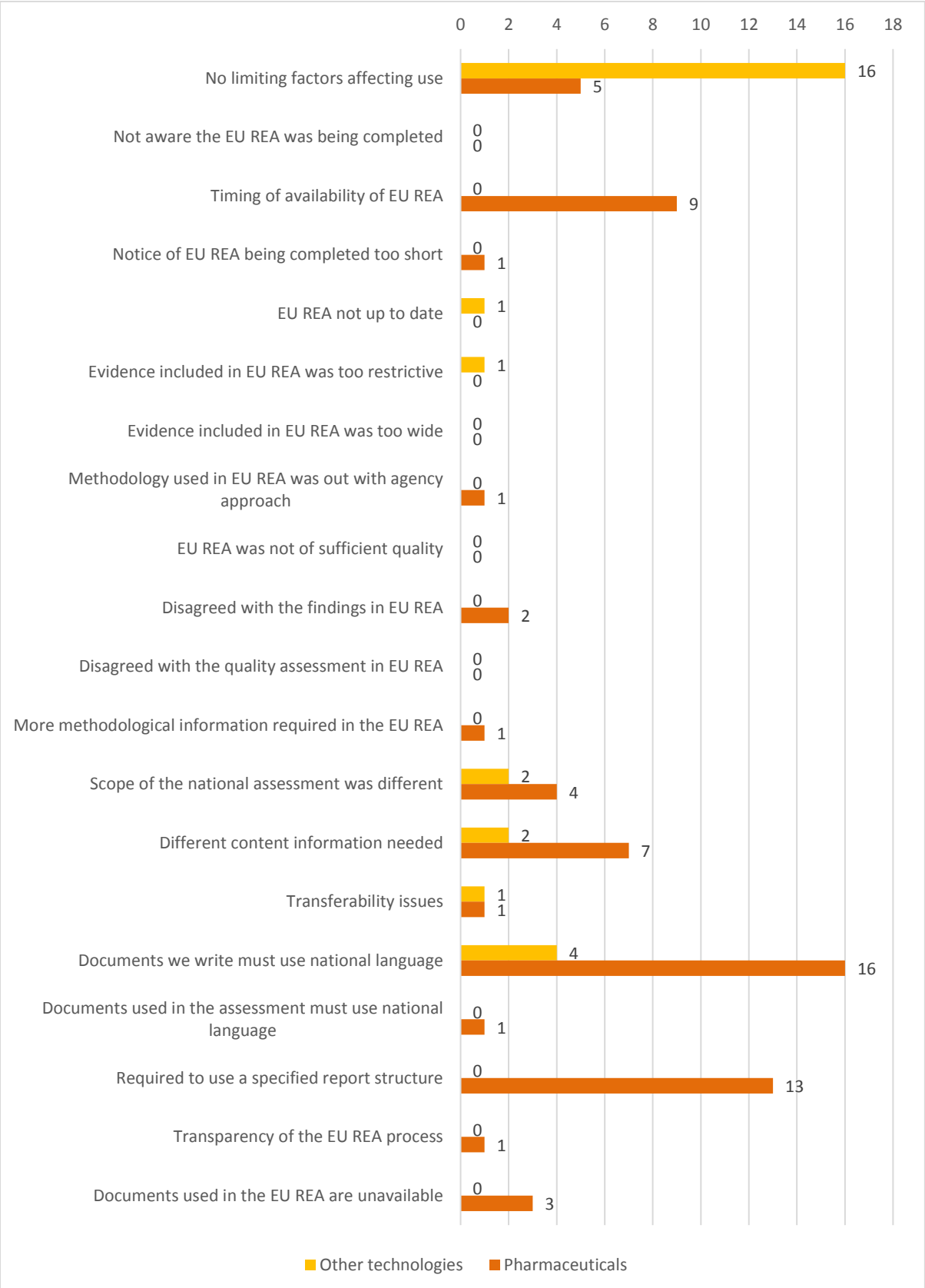
Users of OT assessments were much less likely to identify factors limiting use than users of PT assessments. For other technologies the most commonly identified limiting factor was the requirement to prepare reports in their national language (n = 4).

Figure 8 (PT) and figure 9 (OT) 19 categorise the limiting factors reported into the following groups: awareness; timing; evidence and methodology; reliability; relevance; transferability; language; reporting and accountability.

The limiting factors identified by users of PT assessments are quite varied. The most commonly identified limiting factors were: language (28%); reporting (22%); relevance (18%); timing (17%).

The main limiting factors identified for other technologies are language (36%) and relevance (37%). However, this data is from a much smaller sample (n=11).

Figure 7: Factors limiting use of JA3 Assessments (n)



Limiting factors (grouped)

Figures 8 and 9 below categorise the limiting factors into the following key groups: awareness; timing; evidence and methodology; reliability; relevance; transferability; language; reporting and accountability.

Figure 8: Factors that limited use of PT assessments (%)

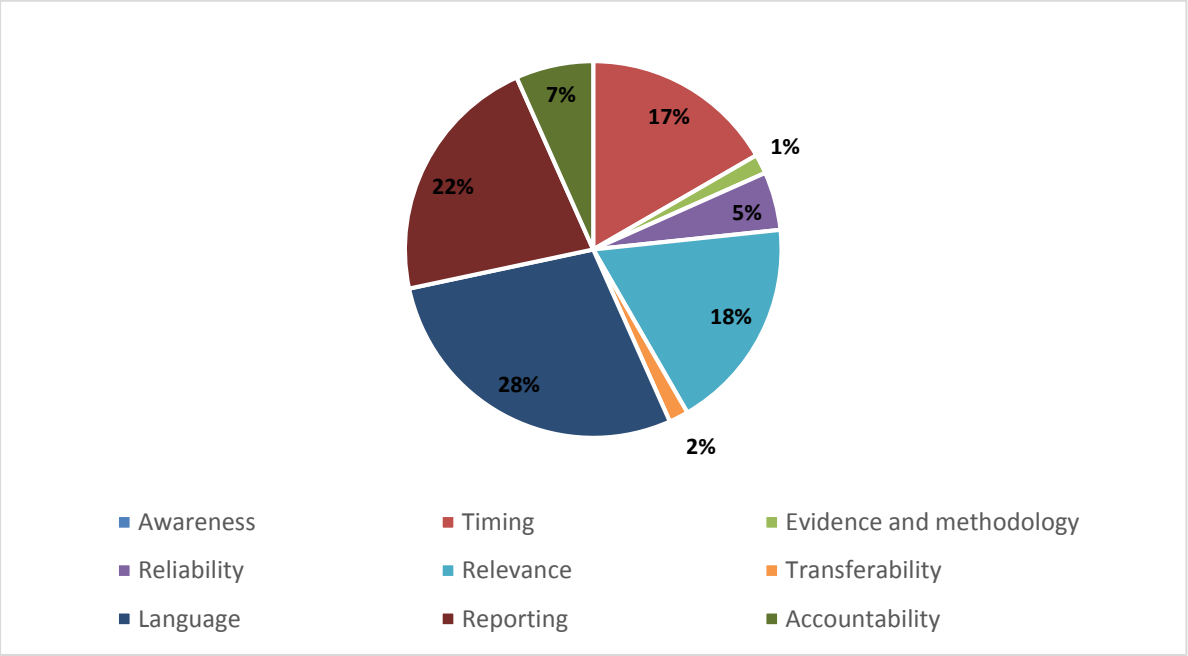


Figure 9: Factors that limited use of OT assessments (%)

Non-use of assessments

The implementation data shows some agencies carried out work on the topic EUnetHTA assessed, but did not use the EUnetHTA assessment (see table 6 – below).

For the 7 OT assessments published under JA3 there were 43 cases of an agency working on the topic but **not** using the EUnetHTA assessment, ranging from 2 examples for OTCA02 to 10 examples for OTCA03.

For the 3 PT assessments published under JA3 there were 15 cases of an agency working on a topic but not using the assessment, ranging from 3 examples for PTJA02 to 7 examples for PTJA03.

Table 6: Non-use of assessments by agencies working on topic area

	Worked on the topic but did not use the EUnetHTA assessment
OTCA01 (Wearable cardioverter-defibrillator)	3
OTCA02 (Antibacterial-coated Sutures)	2
OTCA03 (NIPT)	10
OTCA04 (MammaPrint)	6
OTCA05 (Magnetic stimulation)	7
OTJA08 (Glucose Monitoring)	8
OTCA09 (HIFU Ablation)	7
Total	**43**
PTJA01 (Midostaurin)	5
PTJA02 (Regorafenib)	3
PTJA03 (Alectinib)	7
Total	**15**

Preventing factors

Agencies who didn't use the EUnetHTA assessment were asked about the factors that prevented them from using the assessment. As shown in figure 10 below for OT assessments the timing of the availability of the EUnetHTA REA (n = 32) was overwhelming identified as the main factor preventing use of assessments. For PT assessments the timing of the availability of the EUnetHTA REA was also identified as the main preventing factor (n = 8).

Figure 10: Factors that prevented use of assessments

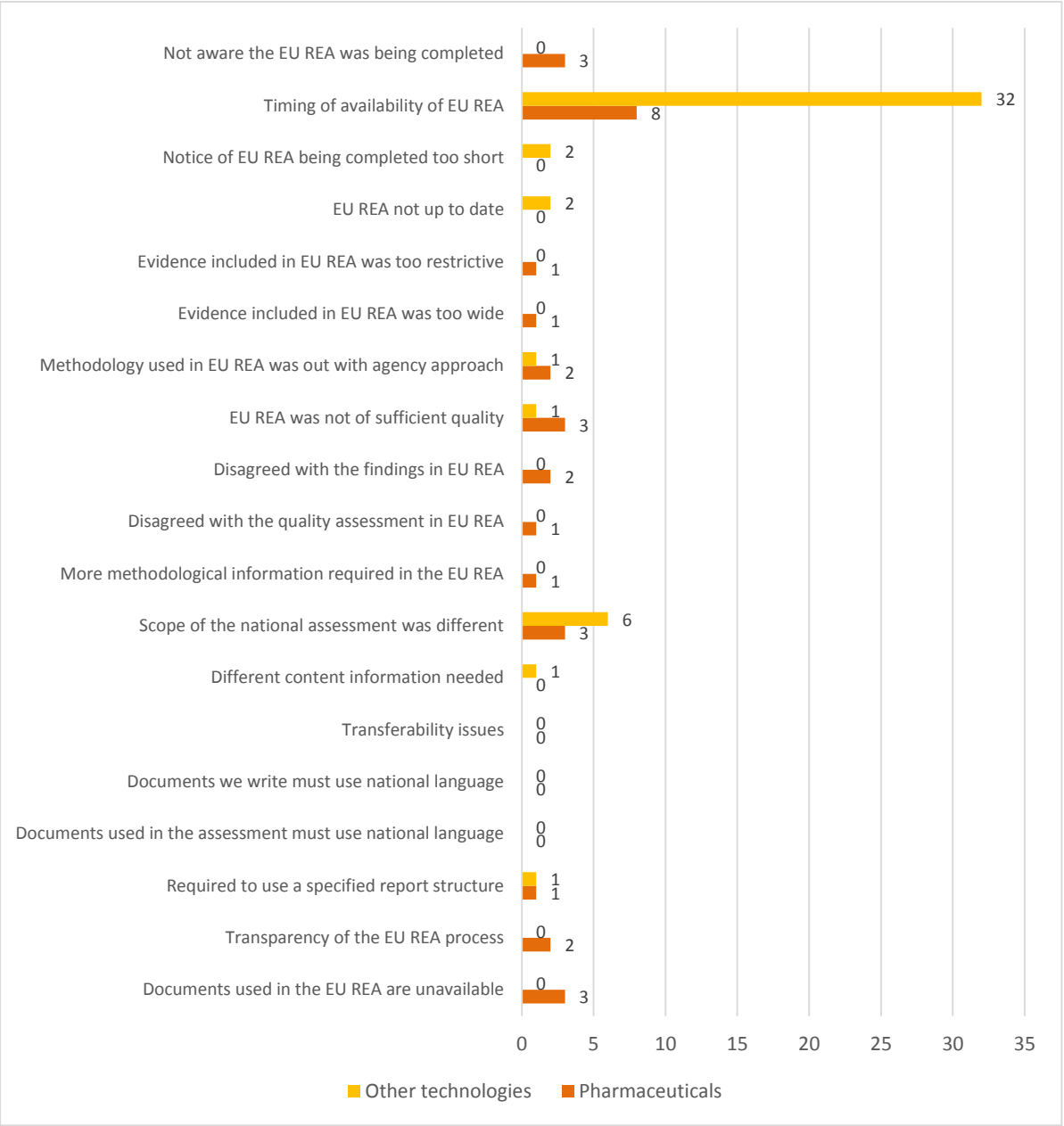
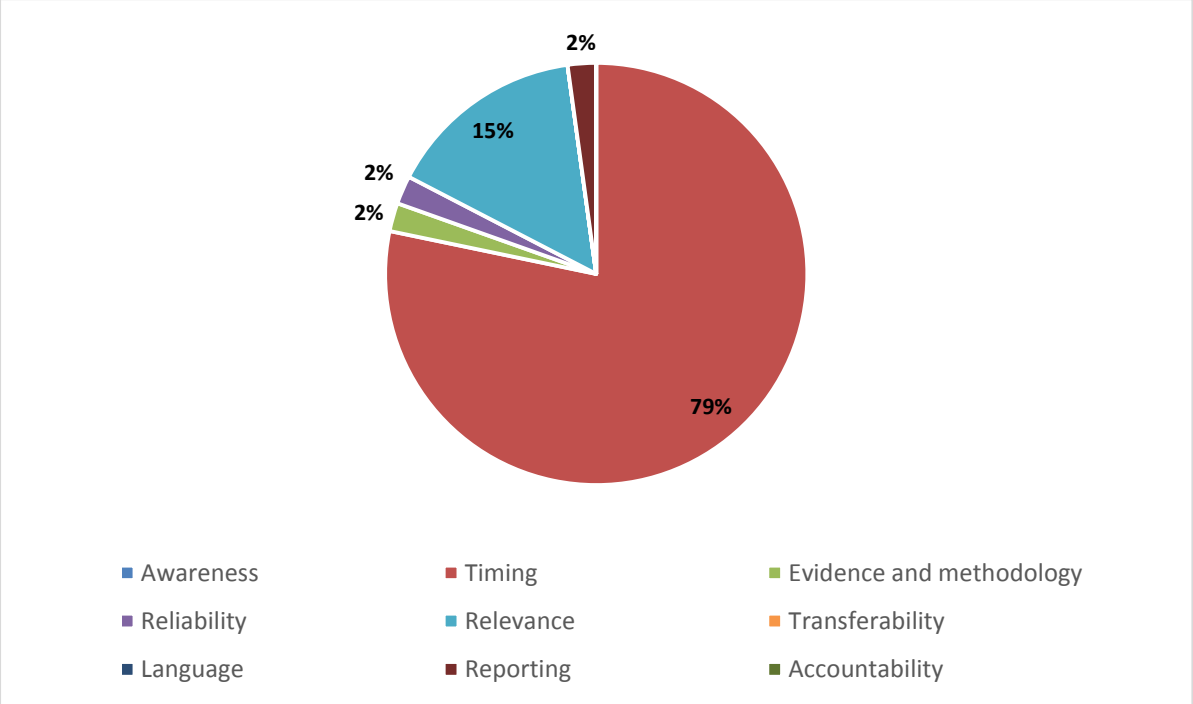


Figure 11 (PT) and figure 12 (OT) categorise the factors preventing the use of JA3 assessments and present them in percentage (%) terms. For PT assessments the most commonly identified factors were: timing (26%); reliability (22%); accountability (16%); and evidence and methodology (13%). For OT assessments the main preventing factors identified were: timing (79%); and relevance (15%).

Figure 11: Factors that prevented use of PT assessments (%)

Figure 12: Factors that prevented use of OT assessments (%)



Section 2 – Thematic analysis of qualitative interviews on use of JA3 assessments

Key findings

Themes were analysed from the free text responses to the implementation feedback survey and interviews carried out through the implementation network.

Eight themes were identified. These are:

- Benefits from using a EUnetHTA assessment
- The value of involvement
- Importance of timing
- Maximising relevance
- Accessibility of EUnetHTA assessments
- Completeness of included information
- The need for standardisation
- Complexities of contextualisation

Methods

Partners completing the implementation surveys are asked whether they are happy for their responses to be followed by a representative of the WP7 implementation network. The responses from these partners are checked by WP7 to identify responses and agencies to follow up in a short semi-structured telephone interview.

An interview template is circulated in advance of the interview and covers areas in the implementation survey in further detail. After the interview the person conducting the interview prepares notes and these are sent to the interviewee to check and amend.

Interviews for 13 partners are included in this analysis. These are augmented by free text responses from the implementation survey.

Results

Benefits from using a EUnetHTA assessment

Agencies identified benefits from using a EUnetHTA assessment in terms of (1) time or cost savings and (2) improved quality or confidence in the findings. Benefits were more likely to be reported for assessments of other technologies.

> *"Greater confidence in national decision making as drawing on work Europe-wide".* **(OT)**
>
> *"Reduced the time needed for the evaluation considerably".* **(PT)**
>
> *"Time savings, resources savings, and quality".* **(PT and OT)**
>
> *"The main benefits are: time and resource saving and reliability of evidence reported in JAs".* **(PT and OT)**

Perceived benefits were not always realised using the current processes of joint assessment, most often because of issues with timing, relevance and content. It was most often (but not exclusively) users of pharmaceutical assessments who saw perceived benefits, but for whom these were not currently realised.

> *"The assessments were used as a source of information and evidence. This utilization did not have a relevant effect on resources or time savings for the time being. However, provided we can find a time frame and adjusted content that make assessments timely and applicable, both kind of savings may be anticipated".* **(PT)**

> *"The use of the assessment did not result in time or resource savings. However, it could have if the assessment had been of more relevance to the national context (e.g. covered extrapolation of clinical efficacy, and if it had investigated and discussed uncertainties in detail)".* **(PT)**

The value of involvement

Being involved in the process of preparing EUnetHTA assessments has a positive impact in terms of providing familiarity with the report, access to data, trust in the contents and speeding up the adaptation process. Users of pharmaceutical assessments were more likely to indicate that having a report did not save time and resources unless there was also involvement in the production process.

> *"The researcher involved with the Freestyle Libre project had previously been involved with adapting other EUnetHTA assessments and was familiar with the structure."* **(OT)**
>
> *"When the agency is part of the assessment team with access to the assessment report in earlier stages of the process, we will probably be able not only to couple both processes but also to make it more efficient".* **(PT)**

Importance of timing

Three types of timing issues were mentioned: (1) issues with when the EUnetHTA assessment are carried out, (2) issues with the amount of time to carry out the EUnetHTA assessment, and (3) the need to be able to plan agency work around EUnetHTA assessments becoming available.

For other technologies timing is a common factor for not using the EUnetHTA assessment. HTA accumulates over a long time span and some agencies may have already assessed a topic a number of years ago and might not be planning to review their assessment and/or decision.

> *"The EUnetHTA assessment was not used due to an inadequate timing. The topic was selected as one of the national priorities a couple of years before the EUnetHTA assessment were carried out".* **(OT)**

For pharmaceuticals, although assessments are now available at the time of the EPAR, timing remains a limiting factor for some agencies.

> *"Our national reports are normally started before the EUnetHTA assessments are made publicly available through the website which limits its usefulness in the national context".* **(PT)**
>
> *"The national assessment was almost finished when EUnetHTA JA was published. If EUnetHTA assessment was available earlier (latest at the time of marketing authorisation), it would be more useful".* **(PT)**
>
> *"Some JAs were published too late. We recognize efforts make to improve timing of JAs. Timing and coverage (number of assessed technologies) are relevant to improve EUnetHTA impact".* **(PT and OT)**

A tension is revealed between rapid decision making and early access to EUnetHTA assessments required by some agencies versus time required to do a comprehensive assessment required by other agencies.

> *"EUnetHTA assessments usually take 30% longer compared to national assessments".* **(OT)**
>
> *"Too little time for the assessment to ensure high quality".* **(PT)**

Unsurprisingly, the different perspectives lead to different solutions. Some agencies suggest that the EUnetHTA process and product should be made more responsive and some want to maintain the product and change the mechanisms in which EUnetHTA assessments are used by agencies. The differing perspectives highlight the need to balance different health systems requirements through discussions about HTA needs, the functions of HTA in different countries and to deliver clarity to agencies around the aims and expectations of joint assessment.

Agencies also highlighted their need to be able to plan to use EUnetHTA assessments which required advance notice of assessments being available and once timelines are available that these are adhered to by authors of EUnetHTA assessments. Where there is insufficient advance notice or timelines are not adhered to these have a negative effect on uptake and resource savings.

"*Assessment proposals arrive in parallel but not soon enough for assessment planning. Therefore, assessments are positively received but most often do not coincide with the needs of the agency".* **(OT)**

"Timelines for EUnetHTA and our agency were closely aligned. Therefore delay to EUnetHTA assessment publication was a problem as we were unable to re-schedule our meeting" **(OT)**

Maximising relevance

Relevance of scope

Relevance can either prevent use of a EUnetHTA assessment or limit the use an agency can make of an assessment. Where an agency used a EUnetHTA assessment, but the scope was not relevant this meant that either the agency had to remove or disregard information in the EUnetHTA assessment or they had to add further information to the local assessment. Agencies underlined the need for broad involvement of users in the early stages of planning the assessment to determine the most relevant scope.

"Only the Freestyle Libre flash glucose monitoring product was relevant to our scope. Therefore the parts of the EUnetHTA assessment relating to other products were not used". **(OT)**

"Midostaurin: the EUnetHTA assessment led to very minor resource saving mostly because midostaurin has 2 indications and only one was included in the EUnetHTA report". **(PT)**

Relevance of methodology

In general there were few comments about the relevance of methodology used in the assessments and individual aspects of methodology such as literature searching, application of GRADE and critical appraisal methods. The limited number of comments about methodology may reflect that for pharmaceuticals many agencies use them to support their work rather than to replace their work. As more agencies begin to use the reports to replace their work, issues about methodology may increase.

"Parts on methods (systematic literature search and selection) and GRADE assessments were not used as this is generally not of relevance in relation to how we conduct national assessments" **(PT)**

"The availability of an indirect comparison in EUnetHTA assessments is generally attractive (if the comparator is relevant) as it will provide a critique of these data, where usually they are unpublished." **(PT)**

"Naïve comparisons were not used because we do not accept these kind of analysis (too much uncertainty)". **(PT)**

Completeness of REA information included in the report

Agencies identified additional generic information relevant to the REA domains of the EUnetHTA assessment that they needed to add to inform the local assessment. In some instances agencies required further detail for their local assessment (e.g. more methodological information about an outcome reported in the EUnetHTA assessment) and in other instances agencies required different information (e.g. a different clinical outcome or a different analysis such as extrapolation). The requirement to add additional generic (e.g. not context specific) REA information meant that the EUnetHTA assessment was incomplete for some agencies.

"The alectinib report documented Quality of Life outcome measures which were not available from other publicly available sources. This was helpful, however more methodology information was required to enable interpretation of these results. Therefore an alternative source (clinical study report) was also used". **(PT)**

"Health economics / cost effectiveness is the main aspect in our assessments. Therefore, it would have increased the usefulness of the report if it had included extrapolation of the clinical efficacy data from the clinical study, as well as a discussion related to this part." **(PT)**

"With respect to brain metastases, two different operationalizations were used in the study (RANO, RECIST). The validation of both of them can be questioned. The authors use (CNS progression according to) RECIST criteria without justifying their choice". **(PT)**

"Information about time to off treatment would be appreciated". ***(PT)***.

These comments underline the need to work with a range of agencies to define the scientific content, methodological criteria and level of detail that needs to be included in the evidence submission and assessment report, in order to ensure that EUnetHTA assessments can be used as an alternative to agency reports.

Accessibility of reports

Views on the accessibility of the reports varied. In general users of the pharmaceutical assessments had more difficulties with accessibility and structure than users of the assessments of other technologies. A number of users of pharmaceutical assessments noted issues with accessibility may stem from a lack of familiarity and the need to be able to get used to using the reports in their processes.

For pharmaceuticals, the length of the report and the number and clarity of sections was an issue for some users.

> *"The EUnetHTA assessments are not always reader-friendly because they usually are exceedingly exhaustive, and that makes the integration of the information in other type of assessments difficult. Although the methodology is irreproachable and the organization is good, the applicability is not easy due to the large amount of information given".* **(PT)**
>
> *"Orientation is difficult because the reader does not know where to find, for example, information on overall survival. Information is scattered and there is no complete overview. Authors don't follow the order of research questions….those inconsistencies affect the comprehensibility and quality of the report"* **(PT)**

Some agencies, particularly other technologies, had positive feedback

> *"We found the report easy to read, with a logical order of sections and chapters and with a suitable structure in general".* **(OT)**
>
> *"The logic of the report structure was easy to use, the language was understandable".* **(PT and OT)**

Other agencies thought the reading flow and ease of interpretation could be improved.

"Assessments are not easy to read (not a good reading flow)." **(PT and OT)**

"The large extension of the assessments often makes the communication of the main results difficult". **(OT)**

"The summary is too long and the tables are not understandable for non-statisticians." **(PT and OT)**

"As authors/reviewers of some JA, we know how to move in the JA's structure. When we show it to a less EUnetHTA expert audience, the main issues are on complexity and redundancy of some sections". **(PT and OT)**

Standardisation of reports

EUnetHTA reports vary in terms of their content and the lack of standardisation can limit the extent to which agencies can predict how reports will need to be implemented and the procedures put in place to reduce duplication.

"The three REA performed within the JA3 are very different. This highlights the lack of a clear scientific guidance on what should be the methodology, the objective and the aim of common assessment. There has been no scientific coordination that leads to heterogeneity of the reports and no common arbitration on certain choices made by authors. This has been source of inequity in the assessment which is what we would like to avoid every days….the heterogeneity together with the lack of scientific coordination limit the national implementation of these reports." **(PT)**

Complexities of contextualisation

For many agencies the EUnetHTA assessment goes through a process of contextualisation before use in decision making. This can include adding: (1) non-clinical content, (2) local clinical content (usually clinical management, technology use or epidemiology), (3) support for decision making and (4) additional processes designed to validate the adapted report or to inform local appraisal and decision making.

Additional non-clinical content

Non-clinical information that agencies most frequently mentioned was economics. Some agencies use cost-effectiveness as a key criteria in their decision making and for such agencies a key function of information included in a clinical assessment is to inform the economic analysis that informs decision making. Some felt that consideration should be given to including economic analysis / information in joint assessments.

> *"The literature search included in EUnetHTA assessment did not include a review of existing economic evaluations. This would have been useful as structure could have been used/adapted in conjunction with local inputs".* ***(OT)***
>
> *"We are interested in a health economic analysis in order to be able to use larger parts of the report".* **(PT)**
>
> *"From our perspective, the missing domains in JAs are relevant. At local level, economical and organizational aspects are crucial to make available and sustainable a health technology and integrate it in the NHS".* **(OT and PT)**

One agency specifically made the point that REA information could be used in their assessment, but only if it was consistent with data supplied by industry in the cost-effectiveness analysis.

> *"It could be used for example for analysis of OS and PFS results and relative effectiveness. However, this is only possible if the company submits similar material to EUnetHTA and national agency."* **(PT)**

Additional local clinical information

Local information relating to the condition and clinical management was also added by some agencies.

> *"The less used sections were those related to the epidemiology and current health problem because regional/ national/ local sources of information were more likely to be chosen for our national report".* **(PT)**
>
> *"Local information was added to the summary including the use of the technology in the country".* **(OT)**

Support for decision making

Some agencies would also value having more direction in the assessment in terms of the conclusions being made and for which groups.

> *"Conclusions are mainly not very courageous and there are no recommendations included. Use GRADE for defining recommendations."* **(OT and PT)**
>
> *"Sometimes it is not easy to make a conclusion and having a summary, agreed by a trusting committee would be more suitable for some forms of adaptation*" **(PT)**

Additional procedures

Some agencies also need to carry out additional procedures to validate the contextualised assessment, or as part of stakeholder consultation or evidence submission to inform appraisal and decision making.

> *"No changes were made but some additional work (e.g. economic model, patient group submission and consultation with national clinical experts)."* **(OT)**
>
> *"An adaptation would take some months to at least (1) validate all the references, (2) make an external validation with clinicians (especially if the external expert was not from our country), (3) make an allegation process with industry, (4) add the budget impact analysis and (5) see the clinical adaptability (the patient profiles and way to treat are not the same around Europe). The lack of time undoubtedly affects the availability to include an adaptation in the agenda"* **(OT)**

Section 3 – Case study on use of joint relative effectiveness assessments (REAs) to inform economic evaluation

Key findings

- Most agencies participating in the case study reported that they have used joint REAs for the purposes of clinical assessment, rather than economic evaluation. Most commonly the EUnetHTA joint REAs were reported to have been used to check clinical data and to validate company submissions and national assessments / appraisals.
- A number of agencies were keen to emphasise that they felt EUnetHTA joint assessments could be used to inform both clinical assessments and economic evaluation and that they will consider using them in future, but identified some key challenges / barriers to use.
- The biggest challenge identified in this case study was timing. Some agencies cited examples where they had planned to use a EUnetHTA joint REA, but reported that there were either unable to use it or the extent to which it could be used was limited by delays to publication. For others the timelines of the EUnetHTA work did not fit with national timelines for undertaking economic evaluation, again limiting or preventing use of joint REAs.
- Agencies identified a number of key benefits of using joint REAs to inform economic evaluation, including significant potential for saving time / resources and the credibility and confidence given to national assessments when using work undertaken at a European level to a known high quality / standard.
- Agencies made a number of proposals on how joint REAs could be improved to make them more useful for economic evaluation, including: giving guidance in the joint REA in key issues for consideration when undertaking economic modelling on the health technology (based on the REA results); information on long term clinical modelling to support validation of the economic model (where the company is often extrapolating); and expanding the scope of REAs to include certain economic aspects such as costs and resource use.

Methods

Under activity 2 of WP7 case studies are being undertaken to support implementation of joint assessments. Case studies provide an opportunity to explore in detail the experiences of joint working, the use of jointly produced products and the context in which HTA cooperation will have to be implemented.

The aim of this case study was to explore how joint REA can inform and support economic evaluation of health technologies. The selection of this topic for a case study recognizes that economic evaluation is often thought of as separate from REA when

in reality the two are closely linked, and also that many HTA agencies struggle with health economic capacity, expertise and resources.

The case study was undertaken using the methods / stages described below:

- EUnetHTA partners that use health economics as part of their procedures were contacted to establish if they wished to participate in the case study. 9 agencies responded to confirm they wished to participate in the case study.
- A semi-structured interview pro forma was developed to undertake the interviews. This included key areas / themes to be covered in the interview, but with flexibility to enable discussion and generation of new ideas where possible.
- The interview pro forma was piloted through undertaking face to face (F2F) interviews (4 interviews with agencies in 2 countries).
- The interview pro forma was then revised and finalised in line with feedback received from the pilot F2F interviews.
- Virtual interviews were undertaken with the other case study participants. All interviews took between 1 and 2 hours to complete and were audio recorded. One agency submitted a written response (received via e-mail).
- The case study interviews were written up and sent to each participating agency for comments and changes, before finalising.
- The findings were analysed thematically and summarised into results / key findings for inclusion in this implementation report (see results).
- An appendix to this implementation report provides a narrative summary for each interview conducted.

Results

This section of the report details the results of the case study and is divided into 5 main sections:

i) **Summary of agencies participating in the case study** – This section provides a summary of the HTA agencies that participated in the case study, providing information on their role, function, remit and size.

ii) **Use of EUnetHTA joint REAs** – This section of the report explains how agencies participating in the case study have used EUnetHTA joint REAs at a national level.

iii) **Benefits of using EUnetHTA joint REAs** - This section explores the benefits and opportunities that agencies identify in using EUnetHTA joint REAs to inform economic evaluation

iv) **Challenges / barriers to using EUnetHTA joint REAs** - This section explores the challenges and barriers that agencies identify in using EUnetHTA joint REAs to inform economic evaluation

v) **Proposals for EUnetHTA** – This section details proposals, made by case study participants, on how joint REAs could be improved to make them more useful for economic evaluation.

Summary of agencies participating in the case study

As shown in table 7 below, 9 agencies from 7 countries participated in the case study.

Table 7: Agencies participating in the case study

Country	Agency
Hungary	NIPN
Ireland	HIQA, NCPE
Netherlands	ZIN
Norway	NOMA
Scotland	SHTG, SMC
Sweden	SBU
Wales	HTW

The agencies participating included both users and producers of HTA. The case study participants included: agencies with a remit covering PT only (SMC, NCPE and NOMA); OT only (e.g. HIQA, SHTG and HTW); and some with a remit covering both (ZIN, NIPN and SBU). The remit of all of the agencies in the case study was national. Some of the agencies cover all stages of HTA whilst others focus on appraisal only.

The agencies participating in the case study varied significantly in size, ranging from ZIN employing approximately 60 HTA staff through to HIQA with 6 HTA staff. Notwithstanding the size of the agency, the majority of case study participants identified health economic capacity as a challenge within their agency.

Describing their working practices, the agencies interviewed most often used carried out clinical effectiveness and health economic analysis in parallel, but used separate staff. The staff will work together to support the evaluation.

All of the agencies participating in the case study have been involved in EUnetHTA for some time, and some since EUnetHTA was established. This is with the exception of HTW which was only formed in November 2017, too late to join JA3. HTW, does, however, have staff that has previously participated in EUnetHTA in previous roles and so was able to draw on this experience when answering the interview questions.

All of the agencies have experience of working on EUnetHTA assessments published under JA2 or JA3, either as authors or reviewers (or both). This is with the exception of SBU which has not been involved in any joint assessments, but has been involved in the development of various EUnetHTA tools and guides.

Use of EUnetHTA joint REAs

Eight of the nine agencies interviewed for the case study reported that they have used EUnetHTA joint REAs. Most agencies reported that they have used joint REAs for the purposes of clinical assessment, rather than economic evaluation. Most commonly the EUnetHTA joint REAs were reported to have been used to check clinical data and to validate company submissions and national assessments / appraisals.

A number of respondents to the survey were keen to emphasise that they felt EUnetHTA joint assessments could be used to inform both clinical assessments and economic evaluation. The agencies stated that they will consider using them in future, but identified a number of key barriers to use (in particular timing) which are explored in detail later in this section.

Benefits of using EUnetHTA joint REAs

A number of benefits of using EUnetHTA joint REAs were identified by the agencies interviewed. It was recognised that a well undertaken REA is important for economic modelling and it is hoped that more EUnetHTA joint REAs can be utilised for economic modelling in future. One agency commented:

> *"A good REA that you can trust gives you the core information and 'engine' for your model and also good information for long term extrapolations…. It would be great if we could have lots of European joint REAs that we could plug into economic models*" **(PT and OT).**

A number of agencies feel that the use of EUnetHTA joint REAs offers significant potential benefits in terms of time and resource saving.

> *"It (the joint REA) can help with capacity constraints as running searches, reviewing the clinical effectiveness and summarising this takes a lot of time / resource. When this is done as part of EUnetHTA assessment it can save time / resource for economic modelling".* **(OT)**

Another key benefit of EUnetHTA joint REAs is the confidence that agencies and decision makers at a national level can draw upon when utilising work undertaken at a European level that they know will be of a high standard / quality.

"The joint REA gives HTA assessors at a national level confidence because you know it has been developed and reviewed at a European level and the clinical effectiveness review will have been undertaken to a good quality". **(PT and OT)**

Agencies also highlighted specific types of information and data included in joint REAs that they feel to be particularly beneficial / helpful for clinical and economic evaluation. This included: relative effectiveness data (versus comparators); relative safety data; morbidity and quality of life data; point estimates of effect; information on end points; information on the comparator(s); and description of the health technology.

Challenges / barriers to using EUnetHTA joint REAs

The challenges and barriers identified to using joint REAs to inform economic evaluation are similar to the issues identified as preventing / limiting use of EUnetHTA assessments in the qualitative interviews (section 2). The biggest challenge identified in this case study was timing. Some agencies cited examples where they had planned to use a EUnetHTA joint REA, but reported that there were either unable to use it or the extent to which it could be used was limited by delays to publication. For others the timelines of the EUnetHTA work did not fit with national timelines for undertaking economic evaluation, again limiting or preventing use of joint REAs. One agency remarked in general terms that a significant challenge was ensuring there was sufficient time after obtaining the clinical evidence to undertake a good cost-effectiveness analysis.

"For OTJA08 the initial intention was to use the clinical assessment in the REA to inform the economic evaluation and model inputs. However, in order to stick within national timelines the economic evaluation had to be conducted in parallel with the REA assessment…. The evidence was validated at a later stage with the evidence included in the REA when the first draft became available. Going forward, we will consider using REA assessments to inform both their national clinical assessments and economic evaluation, but this depends on the national timelines specific to each topic". **(OT)**

"We often need to have to have completed our assessment to meet national timelines before the EUnetHTA joint work starts" **(PT)**

A further key challenge identified by agencies is the relevance / applicability of the joint REA to local practice, in particular whether the comparator and outcomes are relevant and whether the health systems and clinical pathways are sufficiently similar.

"Clinical pathways in countries often differ from the trial and the estimate of relative clinical effectiveness may not be applicable" **(OT)**

Further key challenges identified were:

- Language – in some countries reports have to be translated into national language.
- Documents – how to incorporate joint REAs into national reports and templates.
- Confidentiality - access to confidential data for modelling.
- Methods – whether EUnetHTA methods are in line with national methods.

Proposals for EUnetHTA

The agencies participating in the case study interviews made a number of proposals on how joint REAs could be improved to make them more useful for the purposes of economic evaluation. One agency suggested that HTA including REA and an economic model would be most helpful.

> *"Consider including the economic model in the joint assessment alongside the clinical assessment".* **(OT)**

Some agencies proposed that the scope of REAs should be expanded to include certain non-clinical economic aspects such as cost and resource use data and resource impact or a review of studies of economic evaluations.

> *"Resource use and cost data across various European health systems linked to the technology assessed and comparators would be nice to have. Maybe something that can be collected as part of a questionnaire that is sent to EUnetHTA partners (or agencies collaborating in the joint assessment)".* **(OT)**
>
> *"It would be helpful to have an outline of resource implications in the REA in terms of what is needed to implement the technology".* **(OT)**

Other agencies identified specific changes or additions that could be made to the information included in joint REAs. Specific proposals included:

- Guidance on considerations for economic modelling

> *"After completing the clinical effectiveness reviews you will often have a good idea about the requirements for and parameters of the economic model, so it would be helpful to give general guidance on key issues for consideration in the economic model".* **(OT)**

- Inclusion of long term clinical modelling

> *"Include long term clinical modelling. Often the company is extrapolating, so would be good if we could use this information to validate the model".* **(PT)**

- Description of treatment pathways in the clinical trial and in practice

> *"Clinical pathways in countries often differ from the trial and the estimate of relative clinical effectiveness may not be applicable. Perhaps this could be addressed through a much more detailed description of the trial, the setting and the clinical pathways. More detail on clinical pathways could also be collected through standardised questionnaires"* **(OT)**

- More information on quality of life data and data collection instruments. **(OT)**
- Sub-group analysis for comparators. **(PT and OT)**

Section 4 – Summary of WP7 focus groups on technical support to develop the scientific and technical mechanism for sustainable HTA cooperation

Key findings

- WP7 held focus groups to start to bring together implementation issues identified so far and the implications from these for supporting increased uptake in JA3 and developing a sustainable model of HTA cooperation
- Participants identified 5 principles that should underpin development of a model of HTA cooperation:
    - Different approaches are required for different health technologies and decisions that HTA informs
    - Relative effectiveness assessment is only one aspect of HTA and it would be positive if mechanisms of HTA cooperation could also support other aspects
    - A permanent model of HTA cooperation must be able to respond to the continuously changing environment in which HTA is carried out
    - To plan to use joint assessments and reduce duplication, agencies need to know more clearly what they will receive in what timeframe
    - Broad involvement of agencies in joint assessment processes is seen as a key enabler of uptake and change
- Participants identified 5 areas of the proposal for a regulation in HTA that could benefit from increased exploration in EUnetHTA activities
    - Topic identification, selection, prioritisation and timing
    - Stakeholder and Member State engagement
    - Review and maintenance of joint assessments
    - Role of the coordination group and governance structures
    - Definition of ‘acceptable use’ to be used in the future

Methods

One objective of EUnetHTA JA3 is to support voluntary cooperation at scientific and technical levels between Health Technology Assessment Bodies by providing a sustainable model for the scientific and technical mechanisms of a permanent European cooperation on HTA (objective 1.2 in the Grant Agreement).

WP7 support this objective by providing technical support for WP1 as WP1 develop the scientific and technical mechanism for sustainable HTA cooperation.

At the end of September 2018 WP7 held focus groups with partners to start to bring together the implementation issues identified so far and to prioritise the issues and solutions so as to support increased implementation in JA3 and the longer term development of a sustainable model of HTA cooperation.

The meeting was organised into 3 topics for discussion with partners (N = 24) divided into groups based on interest in PT and OT. Partners received preparatory documents including a copy of the proposal for a regulation on HTA from the European Commission, implementation feedback survey data about the use of EUnetHTA assessments and a thematic analysis of interviews with partners about the experience of using or the decision not to use EUnetHTA assessments.

Results

Principles that should underpin development a model of HTA cooperation

Five key principles were identified that should underpin a permanent mechanism of HTA cooperation:

Principle 1: Different HTA outputs and mechanisms for HTA cooperation are required for different types of health technologies and decisions that HTA can inform

The way in which the EUnetHTA assessments are used varies between agencies and countries depending on their health system, ways of working and the decision the assessment informs. Different outputs, methods and procedures can be required for different types of health technologies and for the different types of decision HTA informs.

Principle 2: EUnetHTA activities in JA3 should actively seek to enable agencies to prepare or future HTA cooperation

For agencies carrying out pharmaceutical assessments, limited output from EUnetHTA means that many agencies still have challenges understanding how the clinical assessment report outlined in the EC proposal will fit into the larger Member State decision making procedures, and changes needed to be able to incorporate the reports into Member State procedures.

EUnetHTA activities should enable partners to prepare for permanent HTA cooperation. Partners identified the following facilitating activities:

1. Increased output of joint pharmaceutical assessments (PT)

2. Involvement in production processes to support a practical understanding of how to use assessments – JA3 should support the widest possible range of agencies to gain experience in production processes. (PT, OT)

3. Topic selection should actively align with national priorities and aim to ensure that by the end of JA3 all agencies have had the opportunity to use a EUnetHTA assessment of a topic with national relevance (PT, OT)

4. Supporting capacity development by pairing experienced and less experienced agencies in production processes and providing a range of training opportunities as part of production processes (PT, OT)

Principle 3: Agencies must be able to plan to use EUnetHTA assessments and to know in advance what information and analyses will be in an assessment.

Standardisation and transparency of approach in EUnetHTA assessments are fundamental to support agencies to develop procedures that will avoid duplication, to define how the assessments will be used and which contextual elements will need to be carried out by the agency. EUnetHTA can support this process by:

- Clearly defining the content of reports

- Ensuring standardisation of report contents

- Defining the boundary between assessment and appraisal

- Defining the boundary between clinical analysis for REA and clinical analysis used to inform non-clinical economic evaluation (PT, OT)

Partners proposed that a working group could be set up in JA3 who would oversee consistency across reports and help support best possible standardisation.

Principle 4: HTA is a scientific process of which relative effectiveness assessment is only one aspect

For many agencies REA is not the only aspect of HTA that informs decision making. Economic analysis, resource use and budget impact are areas where agencies may struggle with resources and benefit from cooperation with other agencies. Although, in JA3 it is appropriate to focus on REA, in the longer term support for other aspects of collaborative HTA are important. JA3 should be used to explore how such collaborations could work in the future either through voluntary cooperation or through other resources such as ISPOR, or an independent task force.

Principle 5: The scientific and technical elements of HTA cooperation must be sufficiently flexible to be able to respond to continuous changes in the environment in which HTA is carried out

HTA systems are not static and the regulation proposed by the EC, as well as the scientific and technical elements of a model of HTA cooperation developed by EUnetHTA must be able to respond to changes in the environment in which HTA is produced and used. (PT, OT)

Scientific and technical elements of the proposal from the EC to test and evaluate in EUnetHTA

Partners identified 5 key scientific and technical aspects of the proposal from the EC that would benefit from further exploration and evaluation by EUnetHTA as part of the work to develop a permanent model of HTA cooperation

1. Topic identification, selection, prioritisation and timing (OT)

Topic identification, selection, prioritisation and timing is seen a priority for other technologies but less of an issue for pharmaceuticals.

For other technologies, elements of the EC proposal to explore during JA3 include:

- The role of the coordination group - JA3 should test wider partner engagement in topic identification and selection processes
- The extent to which the criteria for prioritising topics in the EC proposal for an HTA regulation will identify and align with Member State priorities
- Timing of the process – if timing should follow CE marking or evidence accumulation and how such information can be identified, tracked and shared with partners to support decisions about assessment timing
- The extent to which existing tools such as the POP database and the REQUEST tool can support topic identification and selection procedures and are aligned with the EC proposal
- Earlier planning and notification of assessments – use of fixed timescales between topic selection and assessment to support agency planning
- Validation of PICOTS by a wider group of agencies than the assessment team so as to determine relevance to a large group of agencies.
- Explore whether it might be possible to incorporate greater harmonisation in timing of local assessments across Member States through centralised planning and broad involvement of decision makers in topic selection

- Resourcing required to support the process

2. Mechanisms of engagement (PT, OT)

The proposal from the EC outlines a procedure for Member State and stakeholder engagement that is currently not taken into account in EUnetHTA activities. For both pharmaceuticals and other technologies further work in JA3 is required to explore these. Specific elements mentioned included:

- Defining the appropriate mechanisms of engaging marketing authorisation holders and comparator companies e.g. consultation, fact checking
- Identifying where in the process stakeholder consultation is best placed e.g. after preparation but before finalisation, or during preparation
- Which stakeholder groups are best engaged at a Member State level and which at a European Union-level to inform preparation of the assessment
- The impact of stakeholder involvement on procedural aspects such as timing
- Involvement of Member States in reviewing or approving draft reports
- How stakeholders should be involved in defining processes for assessment
- Mechanisms for involving national decision makers in selection and prioritisation of topics for assessments of other technologies

3. Procedures for updating and maintaining the joint outputs (PT, OT)

Updating assessments is an activity that can challenge agency resources and could benefit from closer HTA cooperation. The review procedures in the proposed HTA regulation are resource intensive and not reflected in EUnetHTA activities. In JA3, review procedures need further exploration to identify when updates should be done and how to coordinate between countries so that updates add value. Specific elements mentioned for pharmaceuticals included:

- Appropriate timing of updates when a pharmaceutical has a staggered market entry across Europe and fast accumulation of evidence.
- Whether updates of EUnetHTA assessments carried out by a single agency can be used by other partners (e.g. mutual recognition systems)
- Feasibility of updating pharmaceutical assessments as multiple technology assessments.
- Resourcing for update procedures.

For other technologies a different set of issues were identified mainly focusing on identifying when an update of an assessment would add value to multiple agencies. Suggestions for solutions to explore during JA3 included:

- Technical solutions to monitor for new studies relevant to the assessment, possibly through existing EUnetHTA tools such as the POP database
- Establishing a committee to discuss and decide when each joint assessment needs reviewing and updating
- Assessing whether the assessment team that undertook joint assessment could also be responsible for reviewing / updating that assessment
- Identifying a key outcome measure and following it up through collection of real world data to determine when the assessment needs to be reviewed / updated
- A formal 'surveillance' review process similar to clinical guideline development to determine when the assessment needs updating

4. Governance structure (PT, OT)

The role of the coordination group and subgroups and their responsibilities (e.g. in topic selection, preparation, approval) outlined in the EC proposal should be subject to testing and evaluation. However, resources may not be sufficient to do this in JA3 and this may need to be considered during any transition period.

5. Definition of use (PT, OT)

In the timeframe of JA3 it is important to maintain a flexible definition of use and it is not possible to have a restrictive list of uses. However, JA3 should be used to test definitions of use with partners, understand the resource savings associated with different types of use and put in place the indicators by which use will be measured in the future.

Content development to support uptake

Pharmaceuticals

Partners mentioned the following content areas as needing development in JA3:

- Level of detail in the first 2 domains of the HTA CORE model some elements may be better added as part of local contextualisation.
- Transparency of the methodology and justification of the choices made by authors. Transparency is important for decision making so that choices made in the HTA can be critiqued.
- The level of methodological reporting and investigation - aspects such as choice and measurement of outcomes and direct and indirect comparison methods can be fundamental for appraisal and decision making.

- Subgroup analysis. There is a need to understand whether these analyses can be identified in consultation with partners before assessment starts.

- The boundary between clinical analysis for REA and for health economic evaluation and which analyses will be available in an REA.

- The nature of the conclusions that will be available in the report and the boundary between assessment and appraisal.

For some agencies length of the current reports is a barrier for use. Agencies suggested:

- Including methodological aspects in appendices to shorten the main report

- A comprehensive summary for agencies who would be able to use this instead of the main report.

There was disagreement about how far clinical analysis in REA reports should go. On the one hand reports that focus on more complex statistical methods address areas where agencies most often struggle. On the other hand in JA3 it is equally important that EUnetHTA focusses on agreeing what should be in an REA report which may be harder if the REA report is expanded to also include analyses that will be included in cost-effectiveness analysis. It was agreed that in the longer term it is important that HTA cooperation supports capacity development and shared understanding of areas such as statistical modelling used in economic evaluations, but in JA3 the focus should be on clearly defining the REA content. Additional clinical analysis informing economic evaluation may be carried out locally.

Other technologies

Content issues reflected as priorities for assessments of other technologies:

- Procedures for ensuring relevance of the scope and PICOTS of the assessments to partners

- Standardisation of the evidence and methodology

- Accessibility of content

- Reliability, increasing quality

- Non-clinical aspects and in particular economics

Relevance of the scope of the EUnetHTA assessment to the local context is a key barrier to uptake. Involving a greater number of partners in scoping assessments of other technologies (as for pharmaceuticals) was seen as an appropriate mechanism to help maximise relevance. Specific aspects of relevance mentioned:

- Assessments need to include range of comparators (though it is recognised that this is resource intensive).

- For other technologies where assessments are most frequently multiple technology assessments, there is variation in how Member States may group technologies for joint / collaborative assessments.

- Study design: clarity about the study designs to be included in the report as assessments may more frequently need to draw on non-randomised data than assessment of pharmaceuticals.

Partners identified and prioritised some issues relating to the accessibility of content:

- Lengthy, un-itemised and, in general, unstructured conclusion sections make it difficult for decision makers to use them. Key findings and results should be summarised in a short, concise and easy to read summary.

- Translating the executive summary into national languages would make them more accessible and usable by decision makers. This was compared to the translation into all EU languages done for SMPC in pharmaceuticals.

- As with pharmaceuticals there is a need for a clear line separating assessment from appraisal and decision making

In addition, in JA3 EUnetHTA needs to work on:

- Moves in HTA towards making better use of real world evidence, defining how such data may be used in its assessments.

- Support reliability and quality by determining a consensus through discussion on methods and procedures to be used and then once agreed by providing training on these methods.

As with pharmaceuticals, for many agencies REA is not the only aspect of HTA that informs decision making. Economics, resource use and budget impact are areas where agencies may struggle with resources and benefit from cooperation with other agencies. For other technologies agencies may still develop their own economic models rather than obtaining these from companies, therefore the issues about collaborative working in economics may be different between technology types.