EUnetHTA WP7:
Deliverable 7.2 - Final Report

Contents

Abbreviations

CA	Collaborative Assessment
CHMP	Committee for Medicinal Products for Human Use
COI	Conflict of Interest
CRP	C-Reactive Protein
CUR	HTA Core model: Health Problem and Current Use of Technology Domain
DNA	Deoxyribonucleic acid
DOI	Declaration of interest
EC	European Commission
EUnetHTA	European Network for Health Technology Assessment
EVAR	Endovascular aneurysm repair
EPL	EUnetHTA prioritisation list
FLACS	Femto-Laser Assisted Cataract Surgery
HIFU	High intensity focused ultrasound
JA	Joint Assessment
JA2	Joint Action 2
JA3	Joint Action 3
JA/CA	Joint or Collaborative Assessment
MD	Medical Devices
NIPT	Non-invasive prenatal testing
PICO/PICOS/PICOTS/PICOD	Population, intervention, comparator, outcome, timeframe, study design
POCT	Point of care testing
PT	Pharmaceutical
OT	Other technology
REA	Relative Effectiveness Assessment
SOP	Standard operating procedures
TAVI	Transcatheter aortic valve implantation
TEC	HTA Core model: Description and Technical Characteristics of the Technology
TEVAR	Thoracic Endovascular Aortic Repair
WP	Work Package

1. Executive Summary

In this report we describe:

- Use in Joint Action 3 (JA3) of joint assessments (JA) and collaborative assessments (CA) and compare this with use in Joint Action 2 (JA2).
- How changes in JA and CA processes have affected implementation.
- The extent to which structures, methods and processes being implemented are “fit for purpose” in terms of awareness, timeliness, relevance, scientific rigour, evidence and methodology, usability, transparency and independence.
- Recommendations for structures to support implementation in a future model of Health Technology Assessment (HTA) cooperation based on the JA3 experience.

We do this using survey data about JA2 use collected in JA2 and followed up in JA3, and survey data about JA3 use collected in JA3. The survey data are complemented with interview data, responses to email questions and records about agency involvement in JA2 and in JA3.

Implementation data are available for 27 JA/CA published under JA3. 298 examples of use have been reported. In total there have been 89 uses of the 7 pharmaceutical (PT) assessments and 209 uses of the 20 other technology (OT) assessments. Most uses of the PT assessments (n= 60) are in assessment procedures, with only 29 examples of sharing via dissemination. In contrast, for OT there have been 209 examples of use, with 85 of those in assessment procedures and 124 examples of sharing via dissemination. Use of PT assessments is usually as part of a reimbursement and/or pricing procedure, while use of OT assessments is varied including assessment procedures but also decisions to assess, decisions to review and targeted and non-targeted dissemination to support local decision making.

For PT there has been increased production and use of JA/CA in JA3 compared to JA2. For OT there has been increased production of JA/CA, but there is currently less use of JA/CA in JA3 compared to JA2. For both PT and OT there is an increased number of countries that have used JA/CA in JA3 compared to JA2.

Changes in JA3 processes are seen to have improved implementation. Changes made to awareness, timeliness and relevance have allowed greater use. Changes in scientific rigour, evidence and methodology, usability, transparency and independence have improved the confidence with which agencies use JA/CA.

Most agencies still report factors that can prevent or limit the extent to which JA/CA are used. The most frequent factors identified are timeliness and relevance. In addition, for PT assessments requirements to use a specified report structure and national language can limit use.

The tables overleaf make recommendations for key scientific and procedural features that if put in place would help maximise implementation of JA/CA in a future model of HTA cooperation. It makes recommendations for 3 groups:

1. the entity responsible for JA/CA in a future model of HTA cooperation (table 1),

2. agencies and countries participating in future HTA cooperation (table 2), and

3. the PT industry (table 3).

This latter group is included in the recommendations because of the role that industry plays in initiating PT assessments in many countries and providing the evidence submission for these assessments. Different groups have the primary responsibility for resolving different issues. Agencies and countries participating have primary responsibility for addressing language barriers to uptake, while the entity producing JA/CA in a future model of HTA cooperation has primary responsibility for creating timely, rigorous, usable and transparent reports. For areas such as awareness, relevance and evidence and methodology groups have a shared responsibility for overcoming barriers.

Support for implementation is needed in a future model of HTA cooperation. The level of implementation support required will differ by agency and country and will depend on how developed HTA systems are in individual countries and the levels of HTA experience and expertise within these countries. Once the details of a future model of HTA cooperation are known, agencies still establishing HTA systems should be prioritised and offered early, individualised, facilitative support at a country level (that is, encompassing HTA agencies, and also commissioners and decision makers) to put in place the capacity, expertise and processes to implement future ways of working. Modalities of support proposed included online resources and implementation advisers. The use of audit and monitoring provoked mixed opinions as to whether these tools were appropriate.

Table 1: Recommendations for the entity responsible for JA/CA in a future model of HTA cooperation

Awareness	• Identify the target user group and ensure target users are engaged in the network • Develop a formal outreach strategy to individuals and groups who are not part of the network as well as to networks and organisations working in related areas • Offer advice and support for developing or scoping HTA capacity for countries who are still establishing HTA programmes. • Implement an alert system within and outside of the network using multiple media channels to proposed JA/CA, JA/CA starting, project plans publishing and JA/CA publishing. • Provide regular activity updates through newsletters • Facilitate breadth of involvement in activities to develop familiarity and trust among agencies • Regularly repeat training and knowledge sharing activities to respond to high staff turnover in agencies

Timeliness	• Support planning by agencies to use JA/CA:
	  o Early information sharing about the JA/CA scope and contents
	  o Early notice of publication dates and alerts to delays
	  o Sharing of draft documents
	• For PT, publication close to marketing authorisation
	• For OT, collaborate with Medical Device (MD) regulators to develop an anchor for OT HTA timing in the future

Relevance	• Link to horizon scanning initiatives to identify innovative topics early in their lifecycle • When selecting topics for OT JA/CA consider the number of local assessments already available • Develop a clear definition of what agencies can expect in a 'European' scope (that is, population, intervention, comparator, outcomes, timeframe and study design (PICOTS)) for JA/CA • Require authors to author with a European perspective in mind • Provide an opportunity for agencies to feedback and influence scope of the JA/CA • Target the PICO survey to individuals and groups who define the scope for the JA/CA in a country
Scientific rigour	• Clearly define the methodological expertise required by JA/CA authoring teams • Put in place a programme to ensure that methodological expertise required is available e.g. through internal capacity building and/or external expert support • Allocate sufficient time in the JA/CA process for authoring • Define a mechanism acceptable to agencies that ensures published reports do not contain factual errors
Evidence and Methodology	• Include consideration during OT scoping of the study designs available to respond to the question and evidence availability and consequent suitability of the topic for JA/CA • Develop mutual agreement of methodology to be applied and the extent of the interpretation of the evidence • Ensure consistent application of methodology across JA/CA to support planning by agencies

	• Put in place a regular programme of maintenance, updating and extending of methodological guidance • Put in place a programme of capacity building to support development of methodological expertise • Further development of guidance on how to incorporate patient and clinical expert evidence into JA/CA
Usability	• Provide guidance to authors about using templates and expectations for information to be included in JA/CA • Broker an agreement about JA/CA length and depth to meet the needs of a majority of agencies • Agree common phrases for use in JA/CA • Avoid use of terminology and language peculiar to the network • Include an editing procedure for JA/CA to support clarity of language • Ensure any new templates are given enough time for agencies to get used to them before they are changed • Develop a monitoring and evaluation system to capture the impact of HTA cooperation over time and support ongoing changes to improve usability
Language	-
Transparency and Independence	• Publish company evidence submissions used to develop JA/CA • Monitor conflict of interest (COI) procedures to ensure that rules of involvement do not detrimentally affect the engagement of the most knowledgeable experts

Table 2: Recommendation for agencies and countries participating in HTA cooperation

Awareness	• Where feasible create an opportunity in standard operating procedures (SOPs) to allow priority topics to be proposed for JA/CA and for JA/CA topics to be circulated to decision makers • Implement a communication procedure to raise awareness of JA/CA to relevant external groups and organisations using and commissioning HTA in the country • Include an alert in agency procedures for assessors to check for ongoing or published JA/CA • Include a question in company applications for reimbursement or evidence submissions about whether JA/CA is being prepared or is already available • Develop a standardised agency process for adapting JA/CA
Timeliness	-
Relevance	• For HTA systems that define the topics for assessment, consider how priorities for assessment can be collected in advance through horizon scanning or notification systems • Allocate dedicated agency resource to input into PICOTS surveys for JA/CA • Develop an agency procedure for gathering PICOTS information to inform JA/CA • Embed sufficient flexibility in processes to extract relevant content material and ignore other content material in JA/CA
Scientific rigour	• Ensure staff have the skills to participate in JA/CA assessment teams by allowing participation in training courses and webinars
Evidence and Methodology	• Identify and resolve any areas of methodology where agency methodology actively hinders use of JA/CA • Promote awareness of JA/CA methodology and processes within the agency through staff training and knowledge transfer
Usability	-
Language	• Adjust procedures and legal regulations to allow technical documents to be prepared in English
Transparency	-

Table 3: Recommendations for PT Industry

Awareness	• Disseminate from a global level to a local level the availability of JA/CA • Highlight in local evidence submissions the availability of JA/CA
Timeliness	• Coordinate local launch strategies with publication of JA/CA
Relevance	• In scenarios where industry define the scope used in local reimbursement applications, ensure this scope is incorporated into the JA/CA evidence submission • Use local submission requirements to justify the scope of the JA/CA evidence submission
Scientific rigour	• When preparing JA/CA evidence submission follow submissions guidelines and methodological guidelines
Evidence and methodology	• When preparing JA/CA evidence submission follow submissions guidelines and methodological guidelines
Usability	-
Language	-
Transparency and independence	• Allow publication of company submission files • Allow publication of all relevant data for the assessment

4. Introduction and Objectives

Introduction

There are two main objectives of the European Network for Health Technology Assessment (EUnetHTA) JA3:

> 1.1 To increase the use, quality and efficiency of joint HTA work at European level to support evidence-based, sustainable and equitable choices in healthcare and health technologies and ensure re-use in regional and national HTA reports and activities.
>
> 1.2 To support voluntary cooperation at scientific and technical level between HTA agencies by providing a sustainable model for the scientific and technical mechanism of a permanent European cooperation on HTA

This report supports these objectives. The report describes use of JA3 JA/CA and compare this with use in JA2 and makes recommendations for structures to support implementation in a future model of HTA cooperation based on the JA3 experience.

Objectives

This report answers the following research questions:

1. Compared with JA2, has there been an increase in JA3 in the number and uptake of JA/CA?
2. What is the relationship between changes in uptake and changes in JA/CA processes, including:
    a. changes that were implemented between JA2 and JA3, and
    b. changes that were implemented in JA3?
3. To what extent are the structures, methods and processes being used fit for purpose meeting the individual needs of agencies?
4. What are the key scientific and procedural features that need to be put in place by the individuals, groups, and agencies coordinating and participating in future HTA cooperation to maximise implementation of JA/CA?
5. What support for implementation (e.g. implementation advisers, mechanisms for shared learning, measurement and evaluation of implementation) should be built into a future model of HTA cooperation?

5. Methods

Data collection

At the start of JA3, EUnetHTA developed a feedback tool to capture use of JA/CA (see appendix 1). The tool was developed collaboratively by Work Package (WP) 1, WP3 and WP7 to support monitoring and evaluation by WP3 and WP7. The draft tool was subject to consultation with EUnetHTA WP7 partners.

The final tool is available on the EUnetHTA intranet and EUnetHTA partners are asked to complete the feedback survey after publication of each JA/CA and update their survey entry if their work status changes. A password protected version is available on the EUnetHTA internet so that non-EUnetHTA agencies can also provide feedback on their use of JA/CA.

The data used in this analysis were downloaded June 29th, 2020.

The data from the WP7 implementation survey is supplemented in this report by the findings from an e-mail survey sent to selected agencies (N=38) to identify reasons for patterns of use and changes in use between JA2 and JA3. We received 22 responses to the email survey.

Additionally, semi-structured qualitative interviews were undertaken with 12 selected agencies to collect more detailed information, specifically on:

- their perceptions of the changes made to the production processes and the impact of these on implementation
- their ability to participate in process stages requiring user engagement (for example topic identification, selection and prioritisation pilots, scoping and authoring)
- the extent to which the structures, methods and processes being implemented are considered "fit for purpose" in meeting their needs. Areas of discussion focussed on awareness, timeliness, relevance, scientific rigour, evidence and methodology, usability, transparency and independence.

WP7 also updated the JA2 evaluation results to capture examples of use of JA2 assessments that had occurred after the end of JA2. The JA2 implementation data in this report includes follow up to April 2018. Further details of the JA2 data used in this report are available in the implementation report published in May 2018[1].

[1] https://eunethta.eu/wp-content/uploads/2018/06/May-2018-Implementation-report_website_FINAL.pdf

Methods of Analysis

Stage 1: Identification of procedural changes

In stage 1 of the work WP7, WP4 and WP6 lead and co-lead partners developed a list of changes in JA3 assessment processes to be evaluated. Changes evaluated were those perceived to have an effect on implementation either in terms of the absolute level of implementation (e.g. number of agencies using JA/CA) or on the implementation experience (e.g. trust in the JA/CA or ease of JA/CA adaptation). The changes were grouped into key themes for analysis, for example: changes aimed to improve timeliness, relevance, scientific rigour and awareness.

Differences in production processes for PT and OT assessments means that this report evaluates a different set of changes for PT compared with OT assessments.

Stage 2: Relationship between existing procedures, procedural changes and uptake

In stage 2 of the work the relationship between changes in JA3 procedures and uptake of JA/CA was explored. In this stage of the work the quantitative and qualitative data from the implementation feedback survey, records of partner involvement, email survey and interviews were thematically analysed. The themes for analysis were the effect of changes on (1) awareness of reports, (2) report timeliness, (3) scope and content relevance, (4) reliability and scientific rigour, (5) appropriateness of evidence and methodology applied, (6) usability in terms of report structure and language, (7) transparency and independence.

Stage 3: Definition of uptake processes

The final stage of the work sought to make recommendations for the scientific and procedural features that need to be in place to maximise uptake of JA/CA in a future model of HTA cooperation. These recommendations were developed from the outcomes of the stage 2 work and additionally areas where agencies identified that further improvements were needed.

6. Report structure

The results and recommendations are presented in the following order:

Section 5 presents a summary of the implementation data reported in JA3

Section 6 addresses the first research question:

1. *Compared with JA2, has there been an increase in JA3 in the number and uptake of JA/CA?*

Section 7 explores the relationship between reported use in JA2, participation in production processes in JA3 and reported use in JA3.

Sections 8-14 address the second, third and fourth research questions:

2. *What is the relationship between changes in uptake and changes in JA/CA processes, including:*

    a. *changes that were implemented between JA2 and JA3 and*

    b. *changes that were implemented in JA3?*

3. *To what extent are the structures, methods and processes being implemented "fit for purpose" meeting the individual needs of agencies?*

4. *What are the key scientific and procedural features that need to be put in place by the individuals, groups, and agencies coordinating and participating in future HTA cooperation to maximise implementation of JA/CA?*

These sections are structured around the following key themes

- Awareness
- Timing
- Relevance and transferability
- Reliability and scientific rigour
- Evidence and methodology
- Usability and reporting structure
- Language

- Transparency and independence

Section 16 addresses the final research question:

> *What support for implementation should be built into a future model of HTA cooperation?*

7. Results: Overview of the JA3 use of JA/CA

This report includes 27 JA/CA that have been published under JA3 up to the end of April 2020 for which implementation data are available, 20 OT assessments and 7 PT assessments. An 8th PT assessment sotagliflozin (PTJA04), has been published but as yet no implementation data are reported because it is not launched in Europe.

To accurately capture the implementation of JA/CA a follow up period of approximately 18 months to 2 years is needed for PT and of approximately 3 years for OT. At the time of writing this report, 4 OT assessments (OTCA17, OTCA18, OTCA20 and OTCA22) and 3 PT assessments (PTJA06, PTJA08 and PTJA09) have been published for under 6 months. An additional 3 OT assessments (OTCA10, OTCA14 and OTCA19) and 1 PT assessment (PTJA07) have been published for less than 1 year. Data reported for these JA/CA will be affected by an inadequate follow-up period.

Response Rate

The agency response rate to the survey is high with similar levels for OT and PT. For JA/CA published over 6 months ago the response rate ranges from 43-86% (see appendix 2 for a breakdown). As expected, response rates increase over time as companies submit applications for reimbursement and/or agencies make decisions to complete or not to complete work on a topic. The highest response rates are for assessments with the longest follow-up period.

Shortly after publication of JA/CA responses to the implementation feedback survey are usually from agencies who know they will not or are unlikely to work on a topic e.g. it is out of remit or work has already been carried out. In addition, earlier responders to the survey tend to be (1) agencies in countries where companies launch their PT products earliest, (2) from authors of OT JA/CA where the topic is already in their work programme and from (3) agencies who are able to choose their own work areas and have identified the topic as relevant to their context. Agencies responding early on to the implementation feedback survey are not a representative sample of all JA/CA users and this should be considered when interpreting the implementation feedback survey data from recently published assessments.

Topic relevance

As shown in table 4, EUnetHTA is usually selecting topics that are within an agency's remit. There are slightly higher levels of PT topics being out of remit than OT topics. In their responses agencies indicated that they may (1) only do certain PT products e.g. inpatient or outpatient products, (2) have additional criteria to select PT topics for HTA such as likely budget impact or (3) only do specific types of PT HTA e.g. multiple technology assessments.

In contrast OT topics are more often within remit but not in the work programme. From interviews there was mixed feedback about JA3 OT topic relevance, for some agencies, topics were more relevant than for others:

> *"The topics, for the most part, have also been relevant to our work"*

> *"Agency also sees a potential for using (parts of) OT assessments in our own assessments, but so far we have not been commissioned to do an assessment for a technology that already has been evaluated by EUnetHTA".*

For all topics there is relatively little planned activity reflecting that agencies often react to requests for assessments and work with little notice of an assessment being needed.

Table 4: Work status in the topic area subject to JA/CA

JA/CA	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 (6%)	23 (64%)	1 (3%)	10 (28%)
OTCA02 (Antibacterial-coated Sutures)	5 (16%)	20 (65%)	0 (0%)	6 (19%)
OTCA03 (NIPT)	2 (6%)	17 (50%)	1 (3%)	14 (41%)
OTCA04 (MammaPrint)	1 (3%)	14 (45%)	2 (6%)	14 (45%)
OTCA05 (Magnetic stimulation)	3 (9%)	21 (64%)	0 (0%)	9 (27%)
OTCA06 (TAVI)	2 (8%)	9 (36%)	3 (12%)	11 (44%)
OTCA07 (FLACS)	1 (5%)	17 (77%)	0 (0%)	4 (18%)
OTJA08 (Glucose Monitoring)	0 (0%)	10 (34%)	1 (3%)	18 (62%)
OTCA09 (HIFU)	3 (10%)	15 (52%)	1 (3%)	10 (34%)
OTCA10 (Stool DNA testing)	2 (11%)	13 (70%)	0 (0%)	4 (21%)
OTCA11 (3D Implants)	2 (10%)	14 (70%)	0 (0%)	4 (20%)
OTCA12 (CRP POCT)	2 (7%)	14 (52%)	1 (4%)	10 (37%)
OTCA14 (Robot assisted surgery)	3 (13%)	12 (52%)	1 (4%)	7 (30%)
OTCA15 (Irreversible electroporation)	2 (9%)	14 (64%)	0 (0%)	6 (27%)
OTCA16 (Stents)	1 (4%)	17 (68%)	0 (0%)	7 (28%)
OTCA17 (Lithium triborate)	*2 (15%)*	*6 (46%)*	*0 (0%)*	*5 (38%)*
OTCA18 (Regional hyperthermia)	*3 (20%)*	*7 (47%)*	*1 (7%)*	*4 (27%)*
OTCA19 (Screening for osteoporosis)	4 (21%)	12 (63%)	0 (0%)	3 (16%)
OTCA20 (EVAR / TEVAR)	*2 (17%)*	*8 (67%)*	*0 (0%)*	*2 (17%)*
OTCA22 (POCT: D Dimer and Troponin)	*3 (21%)*	*7 (50%)*	*0 (0%)*	*4 (29%)*
PTJA01 (Midostaurin)	6 (14%)	13 (31%)	3 (7%)	20 (48%)
PTJA02 (Regorafenib)	7 (17%)	16 (39%)	1 (2%)	17 (41%)
PTJA03 (Alectinib)	6 (15%)	8 (20%)	2 (5%)	24 (60%)
PTJA06 (Polotuzumab)	*4 (27%)*	*4 (27%)*	*2 (13%)*	*5 (33%)*
PTJA07 (Ustekinumab)	6 (29%)	6 (29%)	2 (10%)	7 (33%)
PTJA08 (Siponimod)	*5 (33%)*	*3 (20%)*	*4 (27%)*	*3 (20%)*
PTJA09 (Brocilizumab)	*3 (30%)*	*3 (30%)*	*2 (20%)*	*2 (20%)*

Gray shaded cells are the most recently published JA/CA <6 months

Use of JA/CA

Under JA3 implementation data are collected on two principal types of use:

1. Support for or as an alternative to the agency's existing HTA procedures
2. Dissemination of JA/CA to support awareness of the availability of JA/CA and/or evidence informed decision making

As shown in figure 1[2], 298 examples of use of the 27 published JA3 JA/CA have been reported. In total there have been 89 uses of the 7 PT assessments and 209 uses of the 20 OT assessments. The majority of uses of the PT assessments (n= 60) are in assessment procedures, with just 29 examples of sharing via dissemination. In contrast, for OT there has been 209 examples of use, with 85 of those in assessment procedures and 124 examples of sharing via dissemination.

For PT assessments the total number of uses ranges from 22 (PTJA03) to 6 (PTJA08). For OT assessments the total number of uses ranges from 15 (OTCA06) to 5 (OTCA17). The examples of lowest use are in recently published JA/CA where use is expected to increase further over time.

For PT use of JA/CA is usually part of a reimbursement and pricing process that occurs after regulatory authorisation. For OT, a much more varied range of uses are reported. One OT agency commented that in JA3 they had thought much more about the different ways in which JA/CA could be used:

> *"we have been thinking more laterally about usage, and realising that we don't have to either take or leave a report; rather we can use parts of it, and at the very least, we can disseminate it to appropriate people"*

Examples of OT use include:

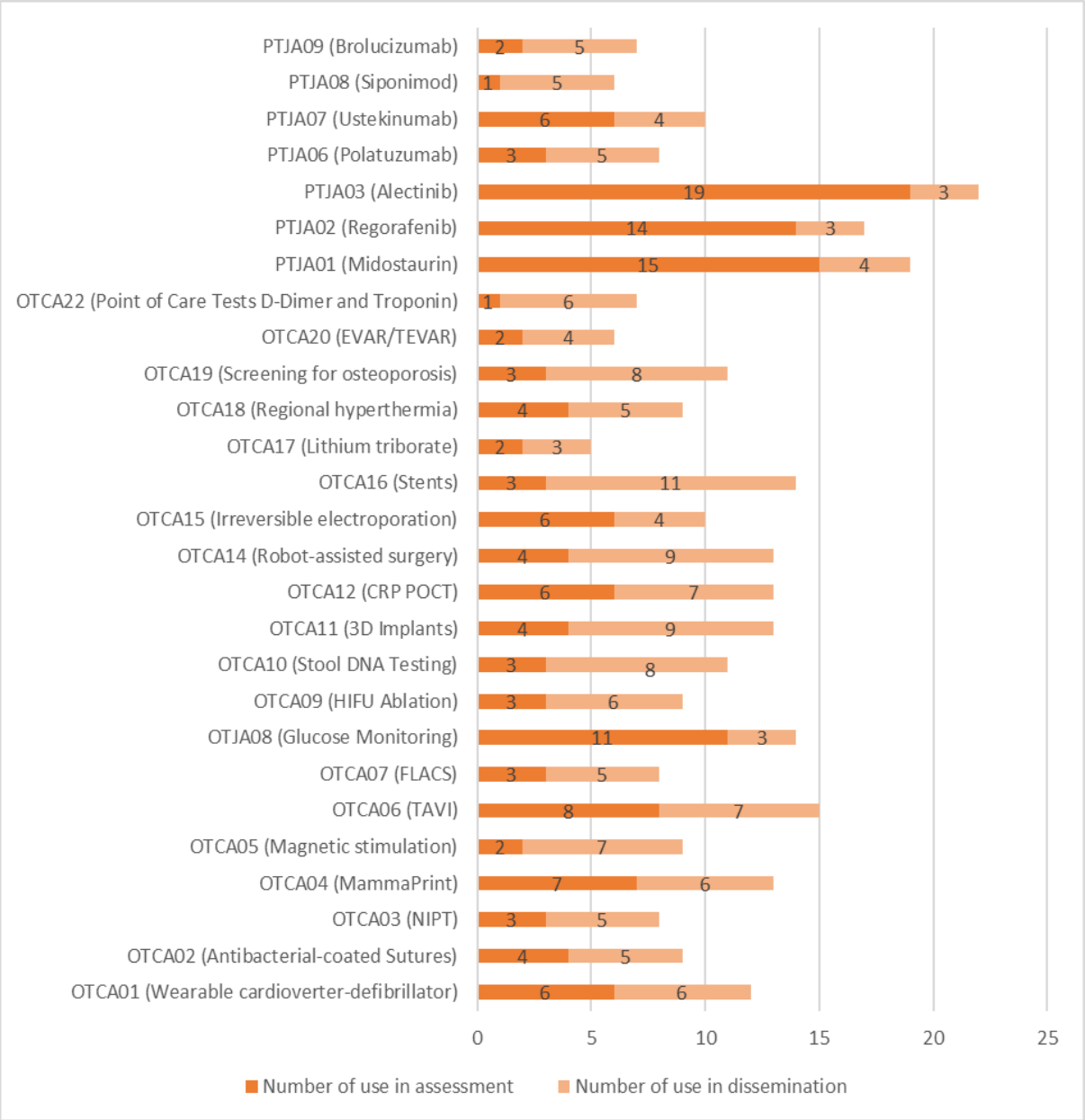
- use in agency HTA assessment procedures
- use to monitor the need to review an existing assessment
- use to decide if an assessment should be carried out
- use to inform data collection protocols for evidence generation activities.
- targeted dissemination to decision makers or clinical networks

[2] In the count of use each agency is only counted once for each JA/CA. Agencies reporting both use and dissemination of the same JA/CA are counted once under use in assessment only.

- non-targeted dissemination in newsletters and on websites

Targeted dissemination to decision makers and clinical networks sometimes included an explicit decision about whether a topic should proceed for agency assessment, or if an existing agency assessment should be reviewed. In other cases, the JA/CA was shared for information only.

Figure 1: Use of the JA3 JA/CA



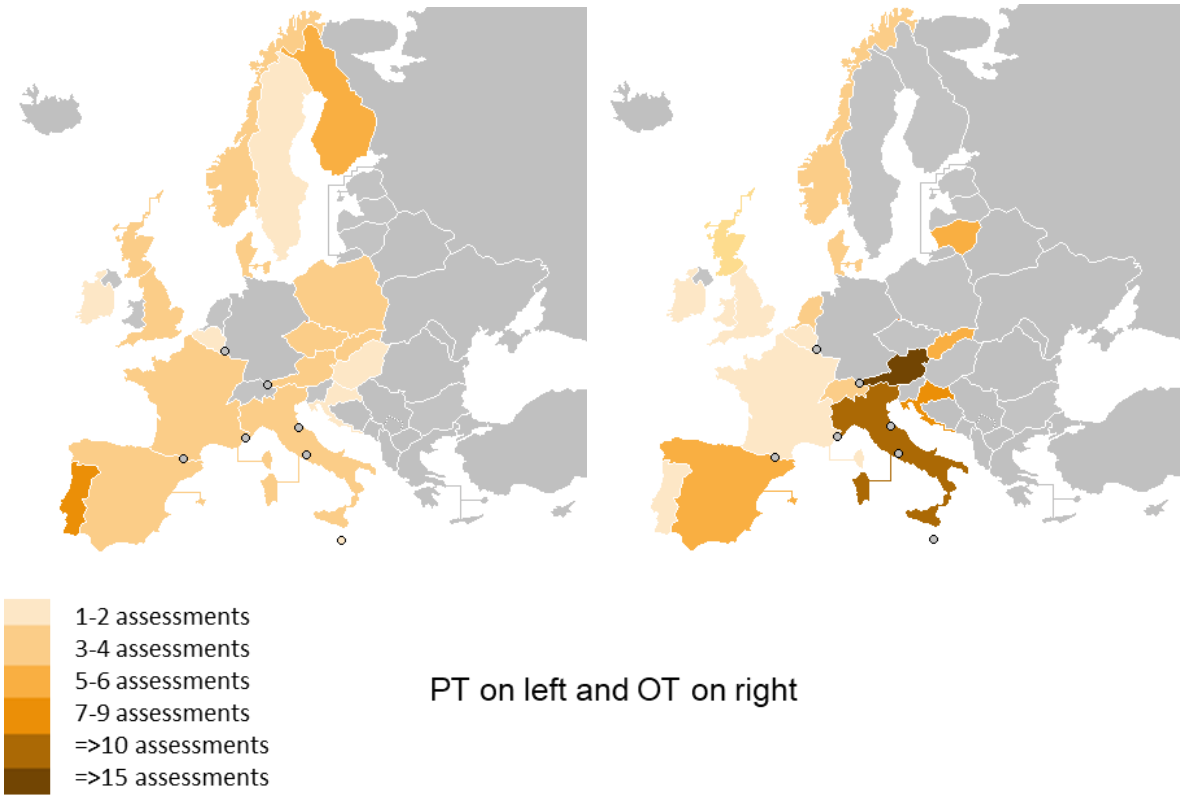
Countries reporting use of JA/CA

For PT assessments 19 countries report using a JA3 JA/CA. All 19 countries report use in assessment activities. Countries using PT assessments in their assessment activities report using between 1-7 JA/CA. Six countries report using 1-2 JA/CA, 11 countries report using 3-4 JA/CA and 2 countries report using 5 or more.

For OT assessments 20 countries report using a JA3 JA/CA. Of those, 17 report use in assessment activities and 3 countries report dissemination of reports only (Germany, Romania and Sweden). Six countries report using 1-2 JA/CA in their assessment activities, 5 countries report using 3-4 JA/CA, 3 countries report using 5-6 JA/CA and 3 countries report using 7 or more JA/CA. The highest use is reported by Austria.

Figure 2 below provides colour coded maps illustrating the number of uses of JA/CA in assessment activities. The darker the shading indicates the more reported uses.

Figure 2: Number of uses of JA/CA – analysis by country

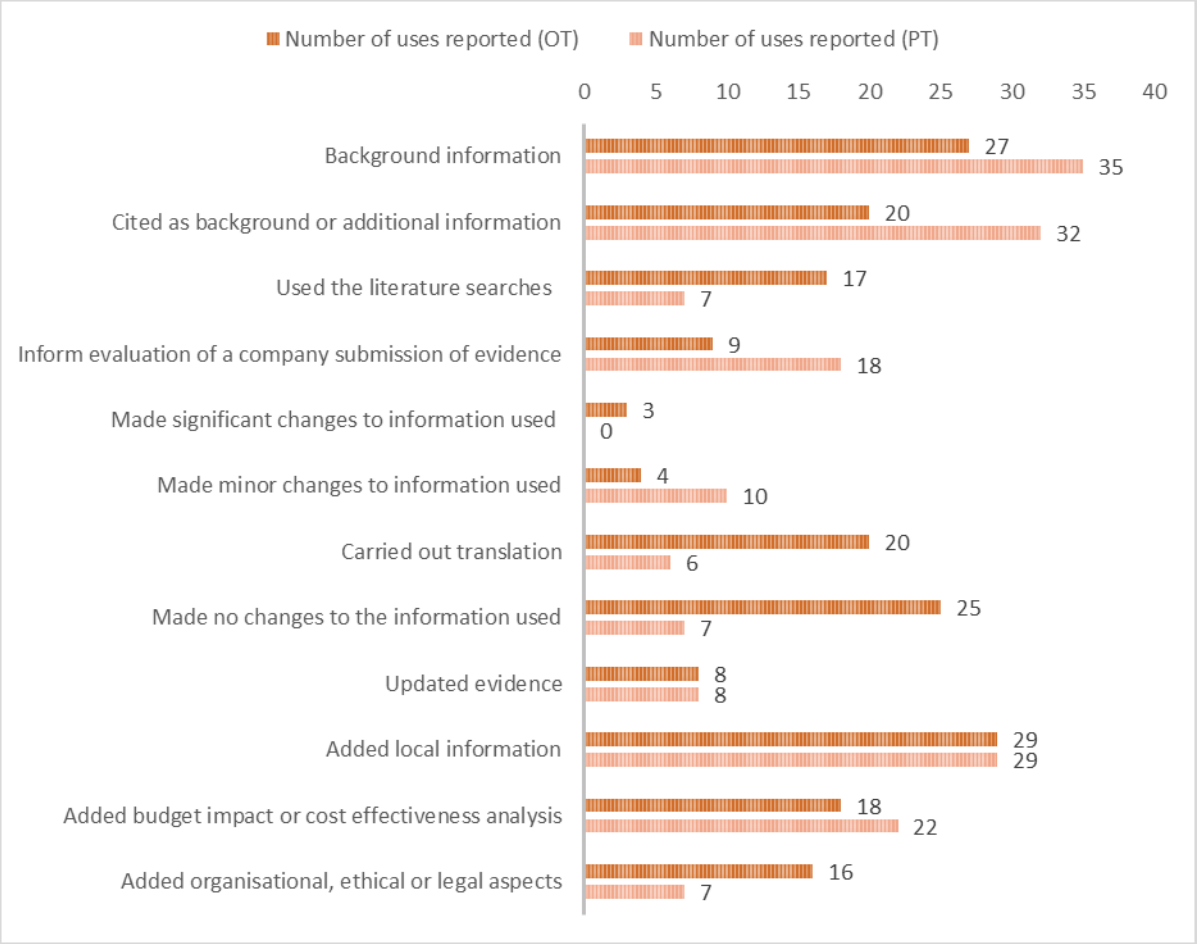


Type of use of JA/CA

Figure 3 below details the type of use of JA/CA published under JA3. Most frequently the JA/CA is read for background information or cited in the agency assessment as background or additional information. Agencies also frequently reported using the JA/CA and adding local information and budget impact or cost-effectiveness analysis. PT assessments are also frequently used to inform the evaluation of a

company submission. The data show that more agencies use OT assessments with no changes or carry out translation only compared to PT assessments.

Figure 3: Type of use of JA/CA



Throughout JA3, agencies assessing OT have more frequently reported using JA/CA to replace agency work. This observation was explored in a question added to the implementation feedback survey that asked agencies if they used the JA/CA to support or replace their work. The responses to this survey question are only available for the most recently published JA/CA. Data show that JA/CA are more likely to support agency work for PT, but that they replace agency work in a majority of OT cases (figure 4).

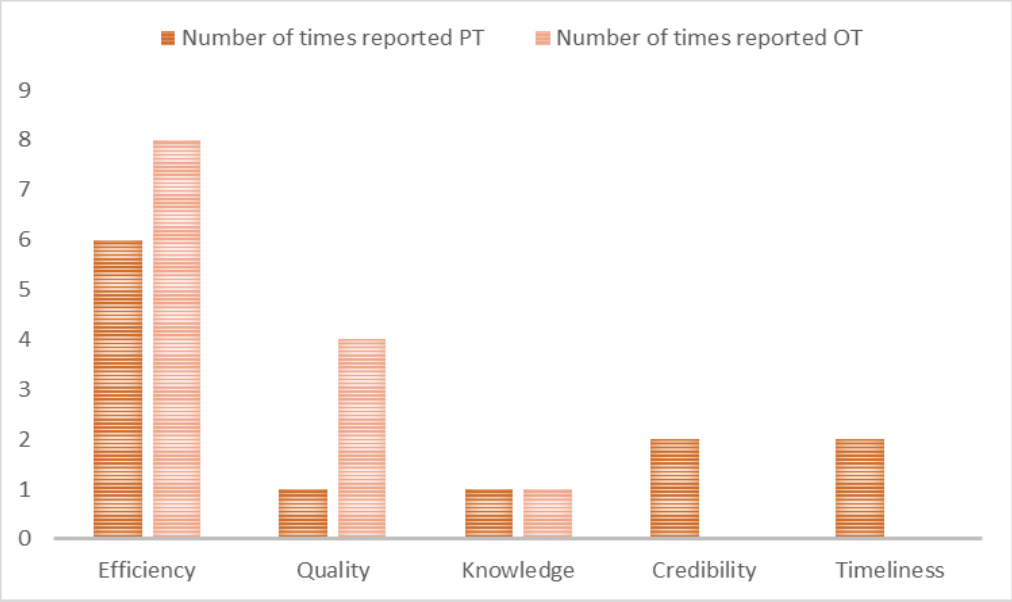
Figure 4: Reported use to support or replace agency work (%)

Data for this question are available for the 12 most recently published OT assessments and 3 most recently published PT assessments.

Benefits of use

The implementation feedback survey collects data about the benefits of using a JA/CA. Initially these data were collected with free text questions. The question was revised part way through JA3 to be a question with categorical response options based on the free text answers given previously.

Figure 5: Reported benefits



Data are only available for the 8 most recently published JA/CA

For the 8 most recently published JA/CA for which use is reported (PTJA06 and 07, OTCA10, OTCA22, OTCA15, OTCA17-18) the benefits identified are shown in figure

5. The data show that the main benefit identified was efficiency, namely that the JA/CA saved agency staff resources or time. Agencies using OT assessments also reported that the JA/CA improved the quality of their work, while agencies using PT assessments reported a range of other benefits. Timeliness was reported as a benefit when an agency was also an author of a JA/CA.

For the 3 PT assessments published at the start of JA3, the free text answers suggested variable efficiency gains for these PT assessments. Responses ranged from no efficiency gains because the JA/CA became an additional part of the evidence package, to considerable savings because the JA/CA replaced the agency assessment and only a national language summary was needed. For these 3 PT assessments 12 agencies reported no savings or limited savings, while 6 reported greater savings. Greater savings came from being able to use the report without any changes, adding only a local summary and from being part of the authoring team and therefore being able to use the knowledge gained from the JA/CA and transfer that to the agency assessment.

For the 14 OT assessments published before the revised question was implemented in the feedback survey free text answers again suggest variable efficiency gains. Responses ranged from no savings and additional workload to a saving of 6 person months. Of the 32 responses to this question 8 reported none or limited savings and 24 suggested greater savings. OT assessment users are more likely to report savings in efficiency from using JA/CA than PT assessment users.

Non-use of JA/CA

As shown in table 5 for the 20 OT assessments published to date under JA3 there have been 62 cases reported of an agency working on the topic but **not** using the JA/CA. The highest recorded count was 11 examples for OTCA03 (NIPT). For the 7 PT assessments published under JA3 there have been 15 cases of an agency working on a topic but not using the JA/CA. The highest recorded count was 4 examples each for PTJA01 and PTJA03.

Table 5: Non-use of JA/CA by agencies working on topic area

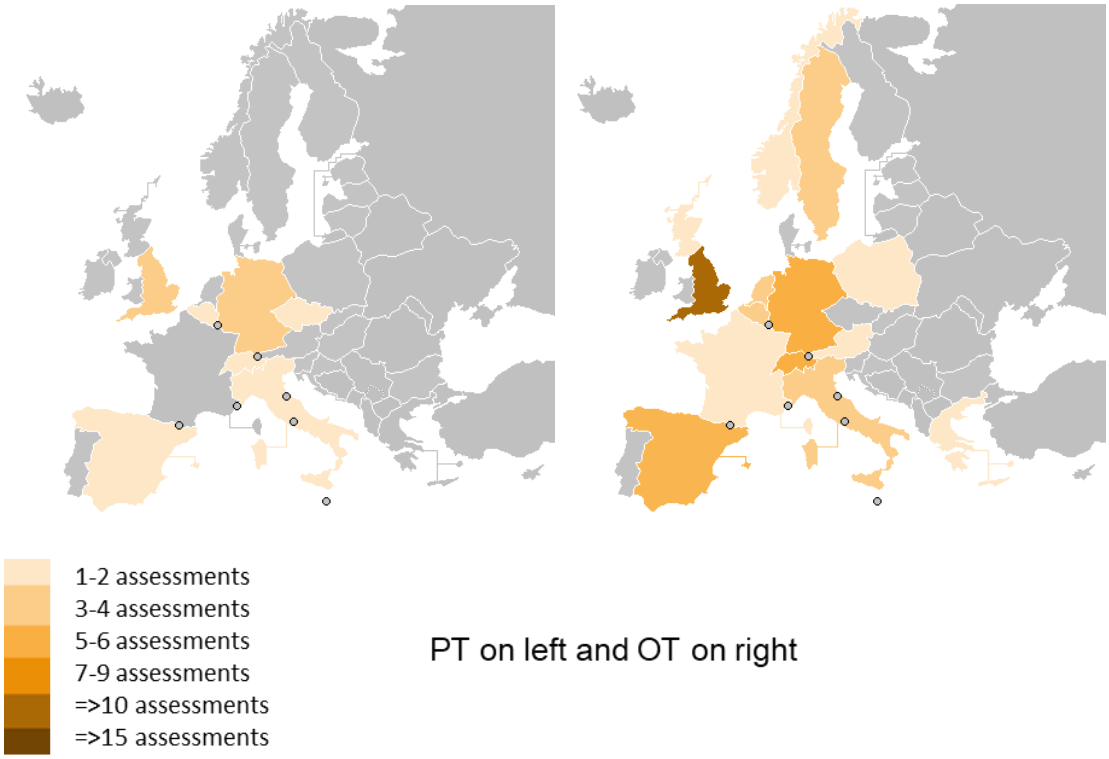
	Worked on the topic but did not use the JA/CA
OTCA01 (Wearable cardioverter-defibrillator)	4
OTCA02 (Antibacterial-coated Sutures)	2
OTCA03 (NIPT)	11
OTCA04 (MammaPrint)	7
OTCA05 (Magnetic stimulation)	7
OTCA06 (TAVI)	2
OTCA07 (FLACS)	1
OTJA08 (Glucose Monitoring)	7
OTCA09 (HIFU Ablation)	7

OTCA10 (Stool DNA Testing)	1
OTCA11 (3D Implants	1
OTCA12 (CRP POCT)	2
OTCA14 (Robotic Surgery)	2
OTCA15 (Irreversible electroporation)	0
OTCA16 (Stents)	2
OTCA17 (Lithium triborate)	3
OTCA18 (Regional hyperthermia)	0
OTCA19 (Screening for Osteoporosis)	0
OTCA20 (EVAR/TEVAR)	0
OTCA22 (Point of Care Tests D-Dimer and Troponin)	3
OT Total	**62**
PTJA01 (Midostaurin)	4
PTJA02 (Regorafenib)	2
PTJA03 (Alectinib)	4
PTJA06 (Polotuzumab)	2
PTJA07 (Ustekinumab)	1
PTJA08 (Siponimod)	2
PTJA09 (Brocilizumab)	0
PT Total	**15**
Total (PT and OT)	**76**

Figure 6 overleaf provides colour coded maps detailing which countries report doing HTA on the topic area but not using the JA/CA. The data are presented by country and the darker shading indicates higher levels of non-use. For Spain and Italy higher levels of non-use are observed for OT because there are multiple HTA agencies in these countries; a JA/CA may be used by one or two agencies but not used by others depending on context and work programme.

It is underlined that non-use rarely arises because an agency has made a conscious decision not to use a JA/CA. Reasons for non-use are explored in more detail in sections 8-15 of this report.

Figure 6: Number of non-uses of assessments – analysis by country



Summary of limiting and preventing factors

Most countries report at least some factors that limit or prevent the use of JA/CA. Two countries (Austria and Croatia) report use of PT assessments and no factors that limit or prevent their use. Four countries (Lithuania, Denmark, Ireland and Wales) report use of OT assessments and no factors that limit or prevent their use.

Table 6 shows that users of PT assessments report more limiting factors than users of OT assessments. Users of OT assessments report more preventing factors than users of PT assessments.

Table 6: Number of preventing and limiting factors reported

	Limiting	Preventing	**Total**
PT	95	33	**128**
OT	51	77	**128**
Total	**146**	**110**	**256**

Figure 7 shows that no single factor limits use, a variety of factors are reported. In contrast figure 8 shows that for OT challenges with timing is an overriding factor that prevents use. Very small numbers of other preventing factors are reported.

Figure 7: Number of limiting factors reported by category

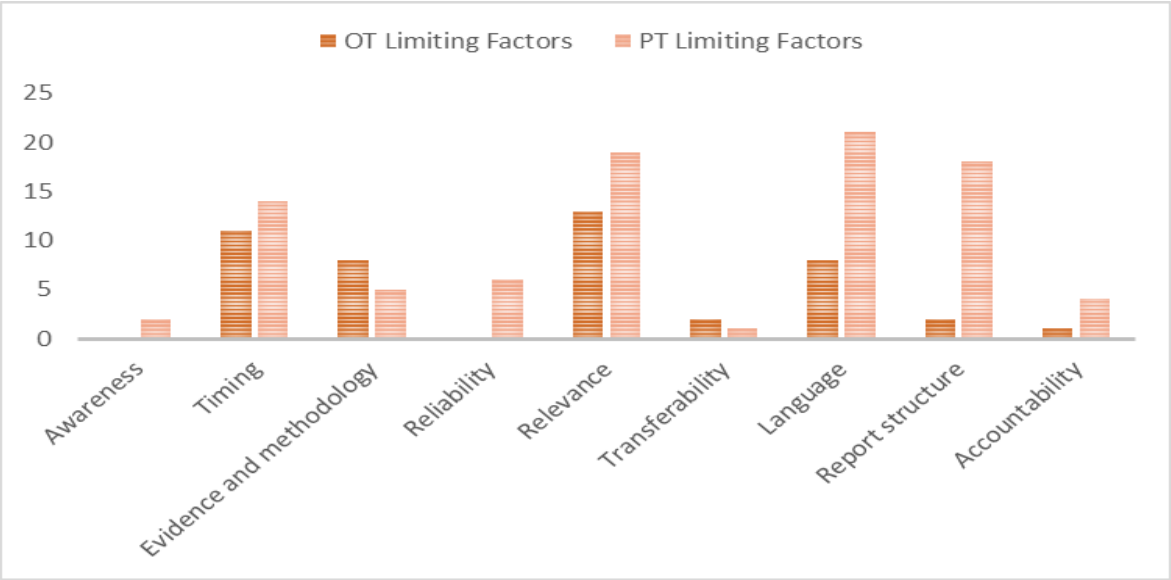
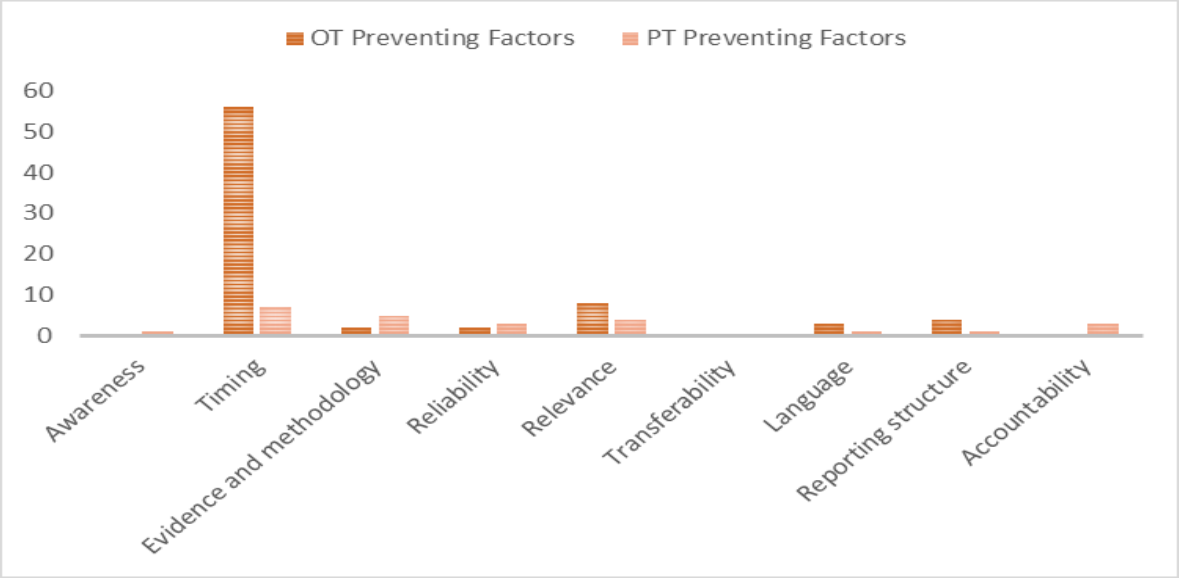
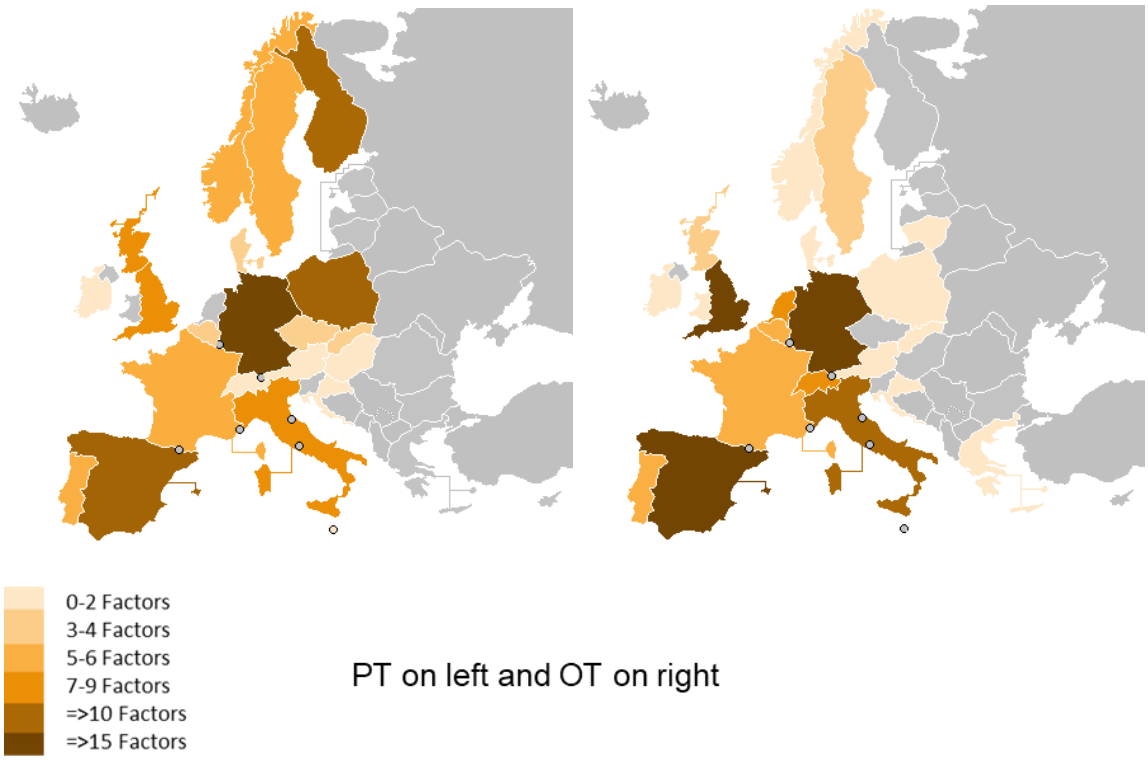


Figure 8: Preventing factors reported by category



The maps (figure 9) below show the number of factors reported to limit or prevent use of JA/CA by country. In each map the darker the shading indicates that a country reports more limiting and preventing factors. When interpreting these data, the data will in part be related to the number of assessments that were used or not used e.g. a country reporting more use or non-use of JA/CA also has more opportunities to report factors that either prevent or limit the use of the JA/CA. However, the maps show that not all countries have the same level of challenges.

Figure 9: Total number of limiting or preventing factors by country



Note: For OT Spain and Italy report high levels of limiting and preventing factors. This because there are multiple HTA agencies, each reporting a small number of challenges.

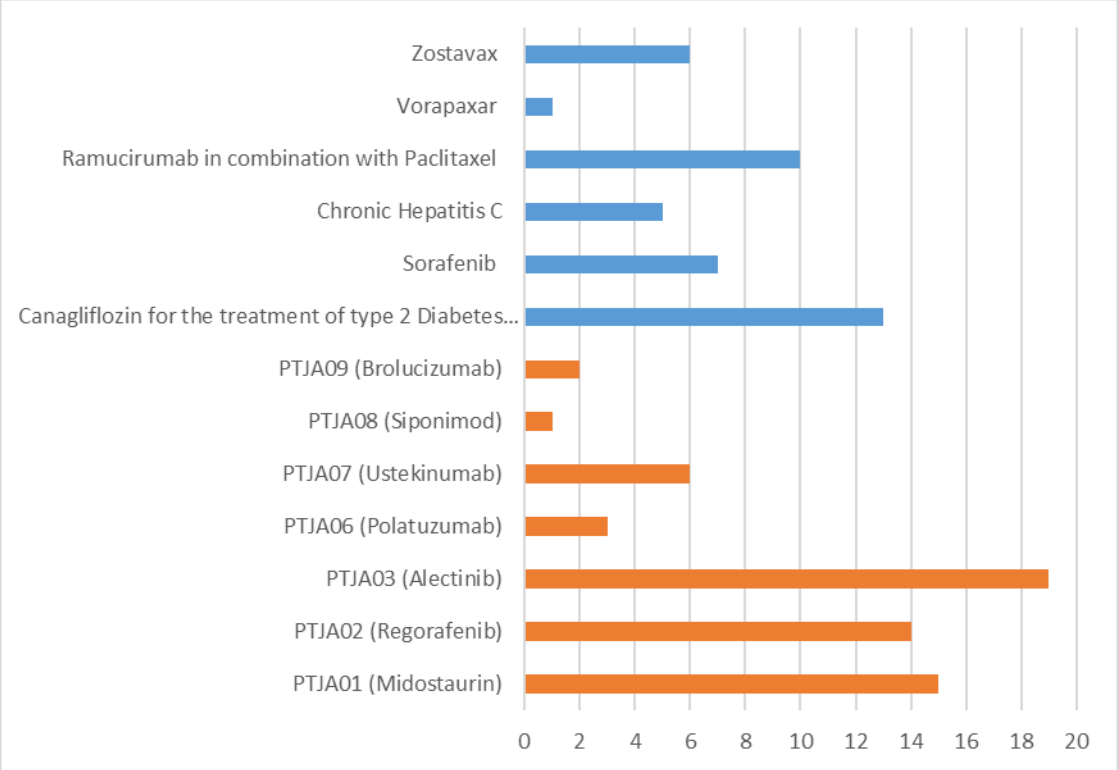
8. Results: Comparison of use in JA2 and JA3

The results of the analysis presented in this section of the report draw primarily on findings from the JA3 implementation feedback survey and data on use of JA2 relative effectiveness assessments[3]. In JA2, both full Core HTA and rapid relative effectiveness assessments were produced, but for this analysis only JA2 rapid relative effectiveness assessments are used as this is similar to the JA3 output.

Pharmaceutical Assessments

In figure 10 below the use of PT assessments published in JA2 and JA3 is compared, JA2 assessments are denoted in blue and JA3 assessments are denoted in red. Comparison is only made on use in assessment procedures (rather than total JA3 use) because JA2 data was predominately focussed on use in assessment procedures. For the 4 assessments (PTJA01-3 and PTJA07) published for 6 months or longer the median number of uses of the 4 PT assessments is 14.5. This compares with a median number of uses of 6.5 for the 6 PT assessments published in JA2.

Figure 10: Use of PT assessments in JA2 and JA3

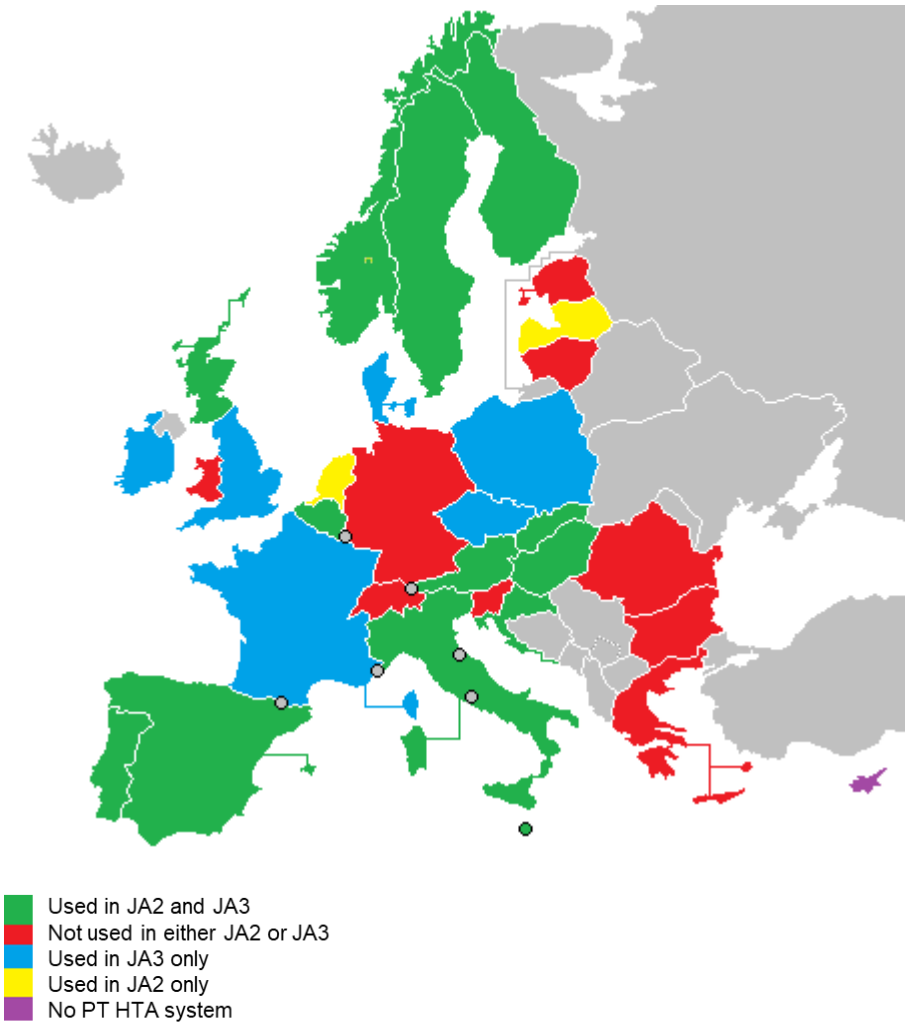


[3] A list of agencies taking part of the JA3 is here: https://eunethta.eu/about-eunethta/eunethtanetwork/
A smaller different set of agencies took part in JA2

Country change in use from JA2 to JA3

Data were analysed to explore changes in the number of countries reporting use of relative effectiveness JA/CA in JA2 and JA3. The results for PT assessments are presented in figure 11 below. In JA3 more countries are using PT assessments than in JA2 as shown by the additional countries shaded in blue. A small number of countries reported using JA2 assessments but not JA3 assessments. This is primarily because of topic relevance (Netherlands) and limited and/or delayed company submission for reimbursement (Latvia). Some countries do not report using either JA2 or JA3 assessments, reasons for this include topic relevance (Wales, Slovenia), lack of alignment with the timing of decision making (Switzerland) and HTA systems still becoming established over the JA3 period (Romania, Greece).

Figure 11: Changes in use JA2 and JA3 – PT

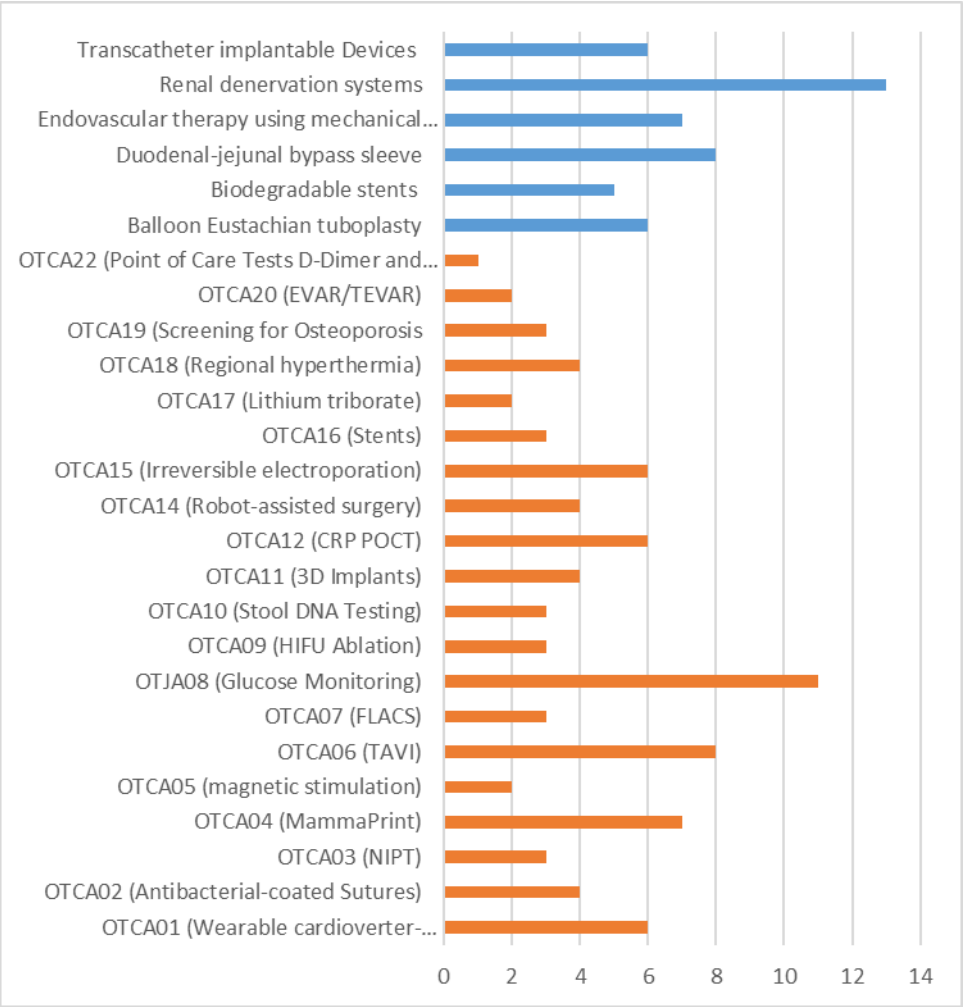


Other Technology Assessments

Figure 12 compares the use of OT relative effectiveness JA/CA published in JA2 and JA3. JA2 assessments are denoted in blue and JA3 assessments are denoted in red. Again, comparison is only made on use in assessment procedures (rather than total use) because JA2 data was predominately focussed on use in assessment

procedures. Excluding the 4 recently published OT assessments, the median number of uses for the 16 JA3 OT assessments is 4. This compares with a median number of uses of 6.5 for the 6 JA2 OT assessments. The data show more variation in use than in JA2 (5-13 reported uses in JA2 and 1-11 reported uses in JA3).

Figure 12: Use of OT assessments in JA2 and JA3

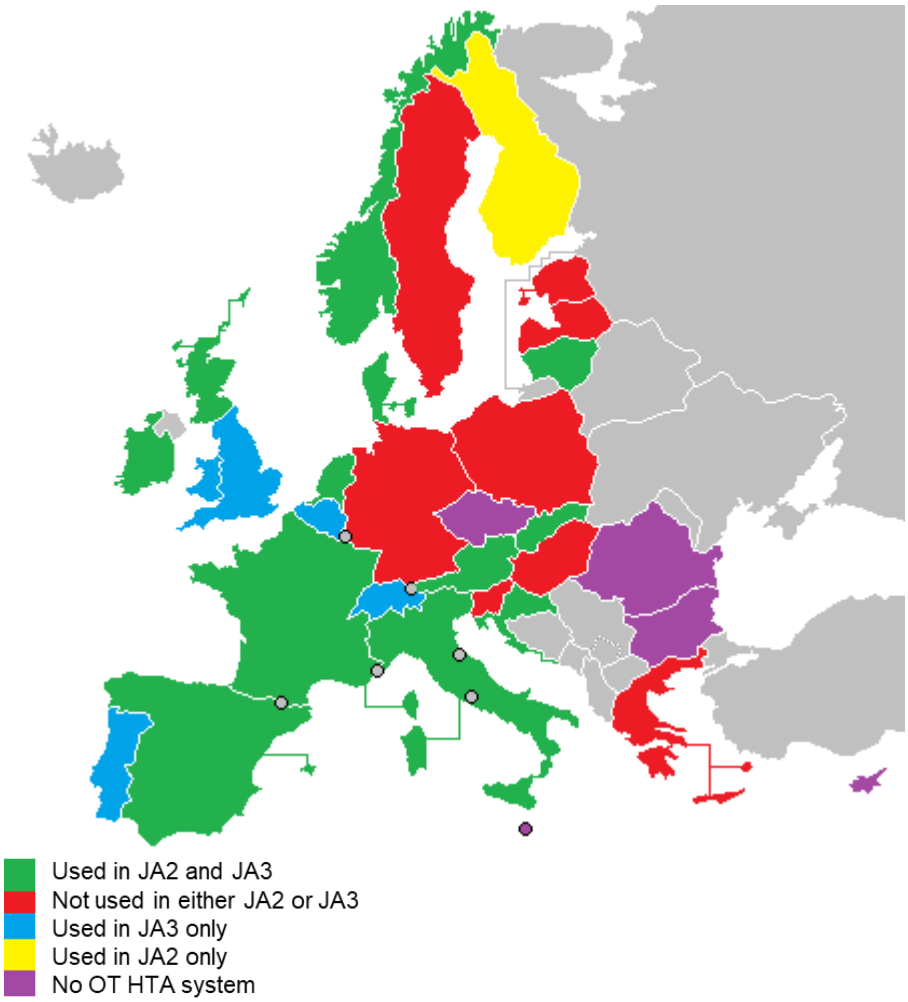


Country change in use from JA2 to JA3

The data were analysed to explore whether the number of countries using OT relative effectiveness JA/CA has changed between JA2 and JA3. The results are presented in figure 13 below. As can be seen in JA3 there are an additional 5 countries using OT assessments for the first time (denoted in blue). There are still a number of countries yet to report using OT assessments in either JA2 or JA3 (denoted in red), in some of these instances this is because the remit of OT HTA is still very limited (Latvia, Slovenia), developed during the JA3 period (Greece), responds specifically to company applications (Hungary) or must follow a required procedure (Germany). One country used JA2 assessments but because of HTA reorganisation has not reported use of JA3 assessments (Finland). It is noted that in JA2 both REA and full Core HTA were produced. Five countries: Sweden, Estonia,

Romania, Switzerland and Slovenia reported using JA2 full Core HTA but not the JA2 relative effectiveness JA/CA.

Figure 13: Changes in use JA2 and JA3 – OT



In the agency e-mail survey, we explored the reasons why agencies felt that use of OT assessments was currently lower in JA3 than in JA2. Some agencies identified issues with assessment timing, relevance and evidence availability that meant that OT assessments were not prioritised for implementation.

> *"All EUnetHTA OT assessments have been carefully assessed…Generally, the assessment either did not have a clear result (certainty of evidence high or moderate), was not timely or were not prioritized due to other available assessments. Another reason was that it was not relevant for our context".*

It was also highlighted that although the much higher number of OT assessments produced in JA3 was positive, limited agency capacity means that agencies can only adapt a certain number of assessments and in JA3 have had to prioritise to a greater degree which JA/CA were used.

> *"We do not have the resources to make use of all the produced EUnetHTA assessments, which means that we have to prioritise in relation to the relevance to our context"*

Other agencies reflected that their low use of OT assessments arose from the fact that their own OT HTA processes were still developing:

> *"The OT assessment process is under improvement in our Agency".*

In addition, it was noted that for some countries the recipient of an OT assessment was not always very clear which affected the ability to use:

> *"The processes in the pharmaceutical field are more established. For example, there has been a clear recipient of PT assessments, as opposed to OT assessments".*

Other agencies noted environmental factors and the challenges that arise because there is no regulatory timetable for other technologies:

> *"PT assessments are linked to the regulatory timetable and are on products that are expected to be evaluated by all or most agencies…. Other technologies have their own unpredictable way and timing of coming to the attention of decision makers"*

And other agencies noted there may simply have not yet been sufficient follow-up:

> *"this could be due to several reasons: 1) Assessments from JA2 are done a long time ago, so HTA agencies have an opportunity to use them longer; 2). It takes a while for a technology to come into some small countries and into their reimbursement systems, so maybe older technologies currently became more relevant for some parts of Europe".*

Conclusions

- For PT there has been increased production and use of JA/CA in JA3 compared to JA2
- For OT there has been increased production of JA/CA, but there is currently less use of JA/CA in JA3 compared to JA2, reasons for low uptake of OT assessments include:
    - Limited agency capacity and increased output in JA3 means agencies have had to prioritise which JA/CA they use
    - The characteristics of access to OT across Europe means that OT can be introduced and come to the attention of decision makers in different countries at very different time points

  - OT HTA processes are not fully established in some countries and the process of linking OT HTA to decision making often less clear than for pharmaceuticals
  - Short follow up time for some JA/CA

- For both PT and OT there is an increased number of countries that have used JA/CA in JA3 compared to JA2

9. Relationship between participation and implementation

In this section we explore the influence that participation in previous joint actions and in JA3 assessment procedures has had on implementation.

A much larger number of agencies have been involved in EUnetHTA JA3 than were involved in JA2. Summarising the possible reasons for increased uptake of PT assessments in JA3, one agency commented that they felt that the increase in the number of PT agencies participating in JA3 positively contributes to PT implementation.

> *"Timeliness, increased awareness of the product and EUnetHTA collaboration, relevance of the topics, higher number of published JAs, easy access, publicity, involvement of many HTA [agencies] as partners in EUnetHTA".*

In addition, several agencies highlighted the positive role that participation in JA/CA processes and activities have on uptake:

> *"[the agency] became an active member in the Assessments (as a DR, co-author and author) and more involved in the different EUnetHTA working parties"*

Other technologies

Figure 14: Reported use of OT REA in JA2 and JA3

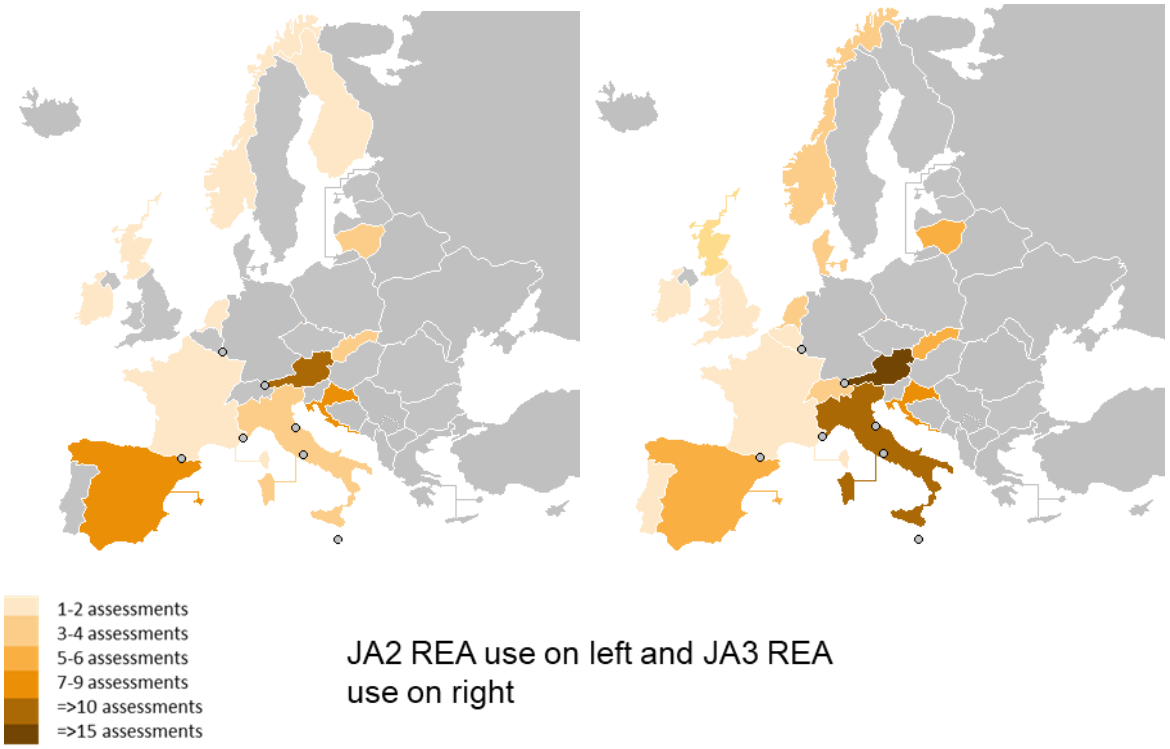


Figure 14 above shows the reported use of JA2 OT REA and JA3 OT REA. Darker shades indicate more reported use. The figures are in broad alignment. Countries who reported using more JA2 REA assessments also report using most JA3 REA assessments.

For OT, project management can be decentralised to activity centres (shown in figure 15) who commit to producing JA/CA. For the 20 published OT assessments most topic proposals (15 topics (75%)) have come from agencies who are activity centres or the WP4 OT co-lead partner. Further, just under half (39 of 85 (46%)) of reported OT uses in assessment procedures come from the agencies who are the WP4 OT co-lead partner or activity centres.

Figure 15: Countries with OT Activity Centres in JA3

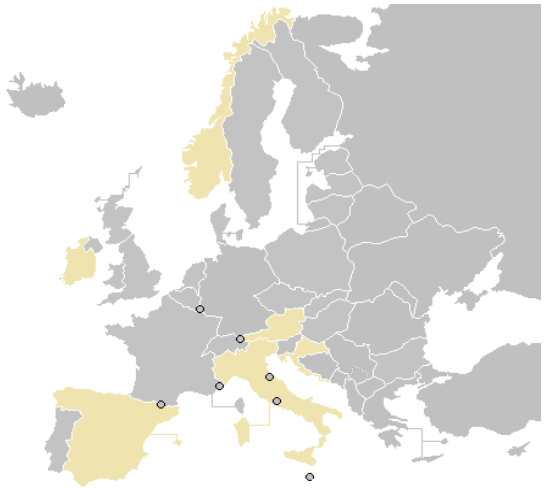
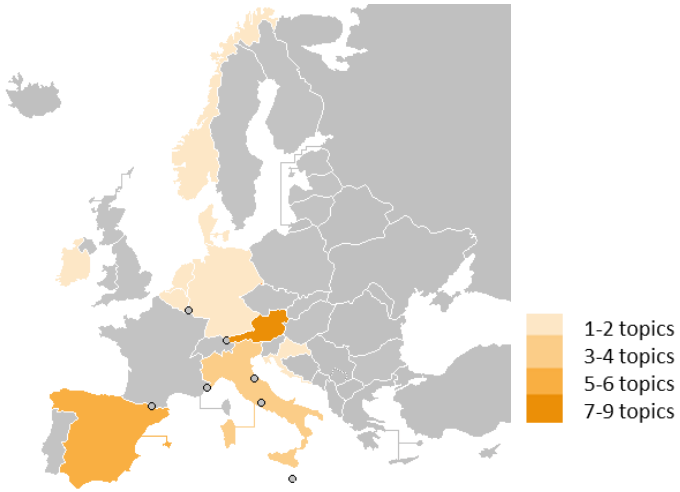


Figure 16: Countries who have proposed OT topics in JA3

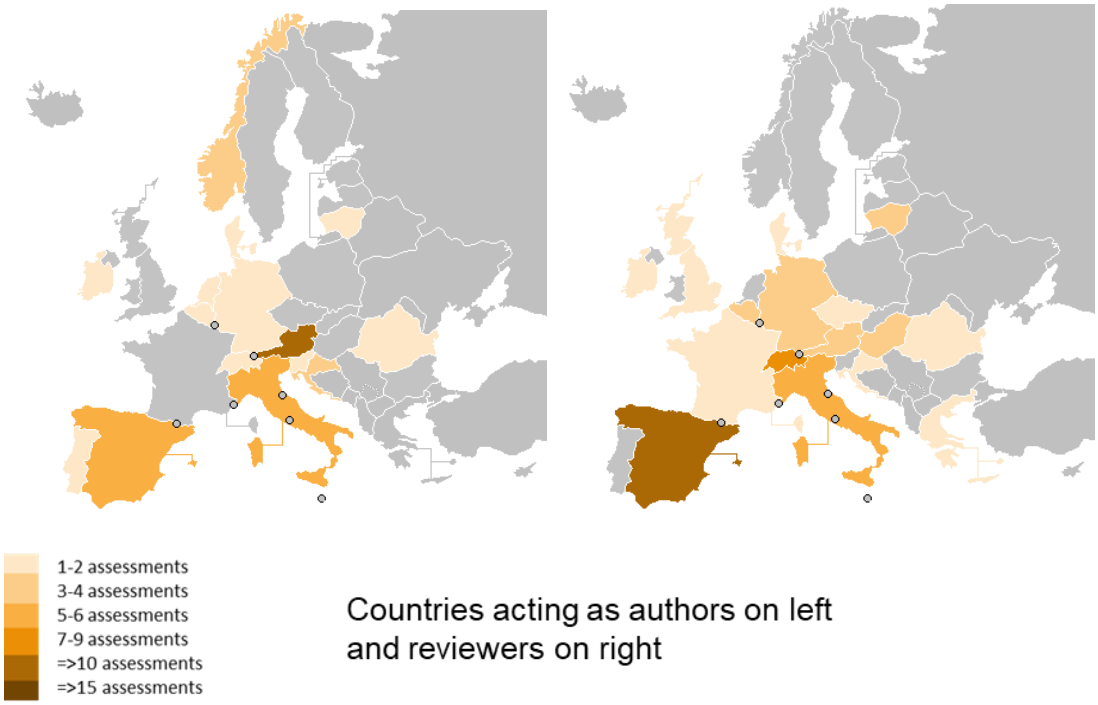


The 20 published assessments were proposed by a total of 14 agencies in 10 countries (figure 16). 53 out of 85 (62%) reported uses of OT assessments come from agencies who have proposed topics for assessment.

Figure 17 shows the countries that acted as OT JA/CA authors and reviewers. 24 authors or co-authors of OT assessments report using the assessment they

authored (out of 44 (55%)). It is noted that for recently published assessments some authors may not yet have used or reported using the report, so this figure is expected to go up in the future. Nine reviewers report using the assessment they reviewed (out of 56 (16%)). Six agencies report being involved in an assessment (all as reviewers) and working on the topic area and not using the JA/CA. This was usually because the agency previously worked on the topic area and were using their involvement in the JA/CA to understand whether new evidence that would affect their original HTA or decision had been published. Twelve out of 85 (14%) reported uses of OT assessments in assessment procedures were from agencies who have not been involved in any OT assessment production (either as authors or reviewers).

Figure 17: Countries who were OT JA3 authors or reviewers



Pharmaceuticals

Figure 18 shows the reported use by countries of JA2 and JA3 PT assessments. Darker shades indicate more reported use. For PT in JA3 there is less variation in use of assessments – in JA2 a small number of countries made most use of assessments, whereas in JA3 use is more evenly spread. Agencies who reported using more JA2 assessments are not reporting most use of JA3 assessments.

Figure 18: Reported use of PT REA in JA2 and JA3

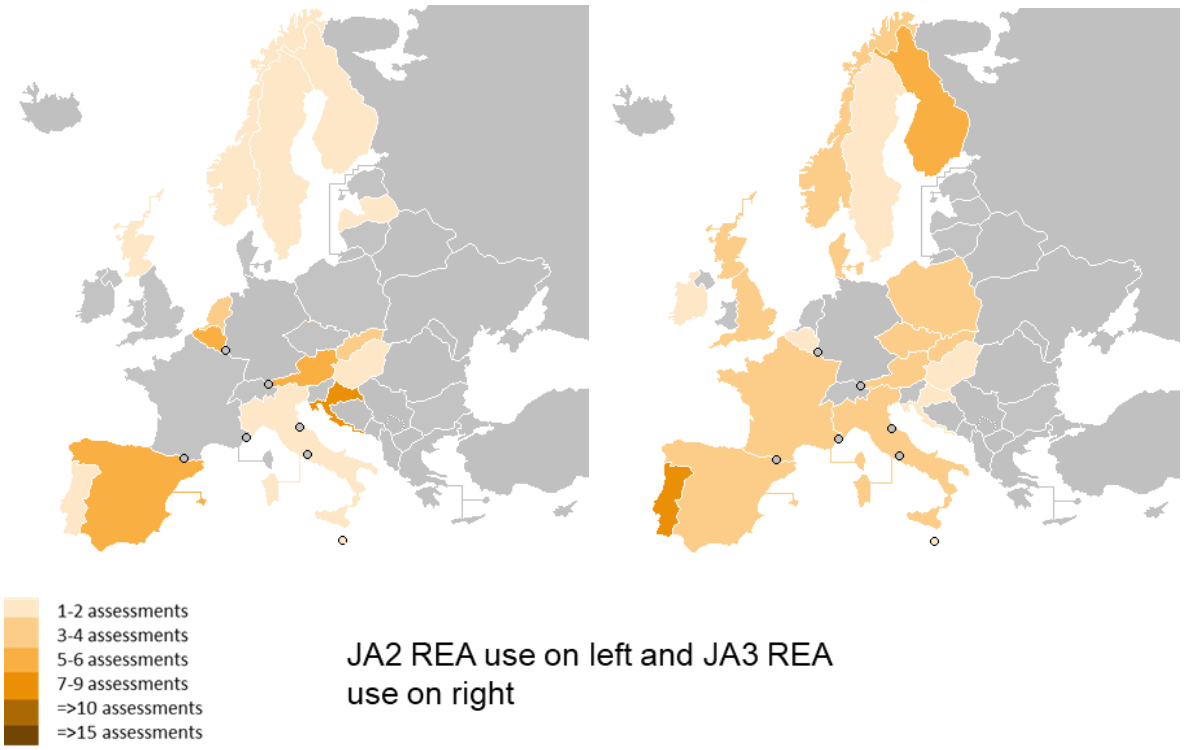


Figure 19: Countries who were PT JA3 authors or reviewers

Figure 19 shows the countries who acted as PT authors and reviewers for the PT assessments for which implementation data are available. For PT seven authors or co-authors of assessments report using the assessment they authored (out of 18 (39%)). Eleven reviewers report using the assessment they reviewed (out of 30

(37%)). It is noted that for recently published assessments some authors and reviewers may not yet have received company applications for reimbursement, so this figure is expected to go up in the future. Only 1 agency reports being involved in an assessment (as a reviewer) and working on the topic area and not using the JA/CA (reason given timing – JA/CA was not available at the time of agency assessment). Where authors or reviewers have not used the JA/CA reasons for this include:

- the topic was not subsequently prioritised for HTA
- the topic was found to be in the remit of an alternative agency in the country
- the company has not (yet) asked the agency to assess the product at the time of the cut-off date for this analysis.

Eleven out of 60 (18%) reported uses of PT assessments in assessment procedures come from agencies (n=4) who have not been involved in any PT assessment production (either as authors or reviewers).

Conclusions

- Engagement of a larger number of agencies in JA3 compared with JA2 is seen to have positively influenced awareness and uptake
- Participation in production processes is seen to support subsequent uptake.
- OT agencies who reported more use of JA2 REA assessments are also more likely to report higher use of JA3 REA assessments. For PT reported use in JA2 appears to be less related to reported use in JA3.
- The model of topic identification and selection used in OT supports use of assessments by activity centres, authors and co-authors, but appears less successful at consistently identifying topics that also gather significant use from agencies acting as reviewers and agencies outside of the assessment team.
- Involvement in PT assessments is less related to uptake than OT involvement, this is because the PT assessment team is identified before an agency knows whether a company will apply for reimbursement in their country and therefore whether they will need to carry out HTA.

10. Results: Awareness

Fitness for purpose of procedures

Figure 20: Countries reporting awareness as a limiting or preventing factor

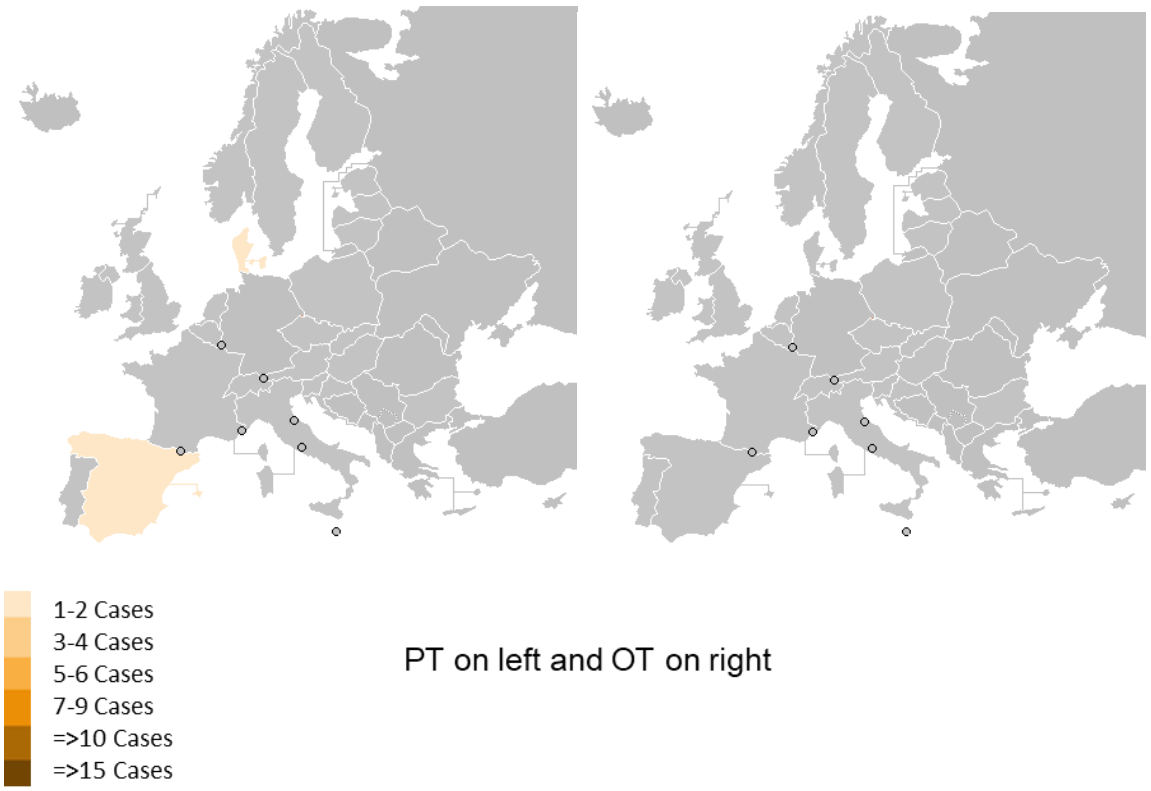


Table 7: Limiting and Preventing factors reported about awareness

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Not aware of the assessment being produced	1	0	2	0	**3**

Number of agencies reporting

The data in figure 20 and table 7 do not show issues reported about JA/CA awareness in JA3. The challenges reported are for PT assessments and in two cases are reported by an agency who is not a EUnetHTA partner and so has access to fewer communication channels and alert systems than other agencies.

Agency perceptions of changes introduced in JA3

During JA3 EUnetHTA has made the following changes to its procedures to improve partner awareness of JA/CA:

- Publication of the project plan at CHMP opinion (PT)
- Publication of the project plan as soon as it is final (OT)

- Alerts for JA/CA starting and publication of project plans and assessments (PT and OT)

Most agencies interviewed were aware of these procedural changes to improve awareness of JA/CA.

The earlier publication of the project plan was felt to be helpful for PT and OT assessments and expected to improve use in the future. The notification systems and publicity of assessments in JA3 was considered to have improved compared with JA2 and generally felt to have improved awareness of JA/CA and uptake in JA3. The recent introduction of a monthly newsletter by WP4 for PT assessments was identified as being particularly helpful.

> *"Better information about the timelines for planned and ongoing assessments".*

Agency recommendations for the future

A need for further improvements to internal communication with partners was highlighted. An extension of the PT newsletter to OT would be welcomed. In addition, the following areas were mentioned:

- Regular and routine updates of distribution lists (as staff turnover is high in many agencies)
- Enhanced use of e-mails and social media (felt to be particularly important given varying levels of use of the intranet in different agencies)
- The list of assessments on the intranet and internet should list the phase and timescales of each assessment stage e.g. scoping, assessment.

Agencies reporting higher use of JA/CA were able to add JA/CA topics into agency topic selection processes and were able to take topics from their agency topic selection processes and put them into JA/CA topic selection processes.

> *"The basic reason [for our increased use] is that EUnetHTA topics have been included as part of the list of topics to be prioritized by the Ministry of Health. If they are selected, they are included as part of the Work Plan for translation/adaption".*

> *"Now we are better in coordinating proposals of topics relevant to our Commissioning Forum with selection/suggestions of topics in JA3"*

This level of awareness of JA/CA with commissioners and decision makers outside of partner organisations is still being put in place in some countries.

> *"in the future, [agency] aims to notify health insurance companies about the EUnetHTA reports if we do not have the topic on our internal agenda"*

> *"OT assessments could also be relevant for the regions. We are in contact with the regions in order to increase awareness of the EUnetHTA reports".*

While some awareness raising activities must be undertaken at an agency or country level, it was also suggested that EUnetHTA could do more to raise awareness in other organisations and networks, for example support for JA/CA could be improved by engaging more with Cochrane Groups and the Guidelines International Network to develop strategic relations and build relationships:

> *"what I am missing in this discussion is the possibility to strengthen the support for EUnetHTA products and processes by reaching out to two particular communities: Cochrane and Guidelines International Network, both doing assessments often on the very same topic".*

There was agreement that at an agency level inclusion of the reuse of JA/CA in agency SOPs and procedures is imperative if joint work is to be properly embedded.

> *"Key first area is to have procedures in place to support inclusion…important to embed this infrastructure".*

> *"It is important that this is noted down in national procedures, so that it is not only dependent on EUnetHTA "ambassadors"*

> *"We have developed a standardised way of using the assessments as well, which has also made it easier to use the assessments".*

Conclusions

- A lack of awareness of JA/CA among HTA users is not a key factor preventing or limiting use of JA/CA.
- The following changes to notification systems have been positively received:
    - More alerts for planned, ongoing and published assessments
    - Earlier publication of OT and PT project plans
- Agencies recommend:
    - The implementation of a robust information and communication system
    - Internal communication mechanisms that use a wide variety of channels without relying on any single channel
    - Contacts lists require regular updating because of staff turnover

- Extension of the PT newsletter to OT
- Greater dissemination to and collaboration with people, groups and organisations who are not part of the network or not directly involved in the production work
- Formal inclusion in agency procedures of an alert to check for ongoing or published relevant joint work to support improved awareness of JA/CA across agency staff not directly connected to EUnetHTA
- Agency communication strategies to ensure relevant HTA users and commissioners in a country are aware of JA/CA

11. Results: Timing

Fitness for purpose of procedures

Figure 21: Countries reporting timing as a limiting or preventing factor

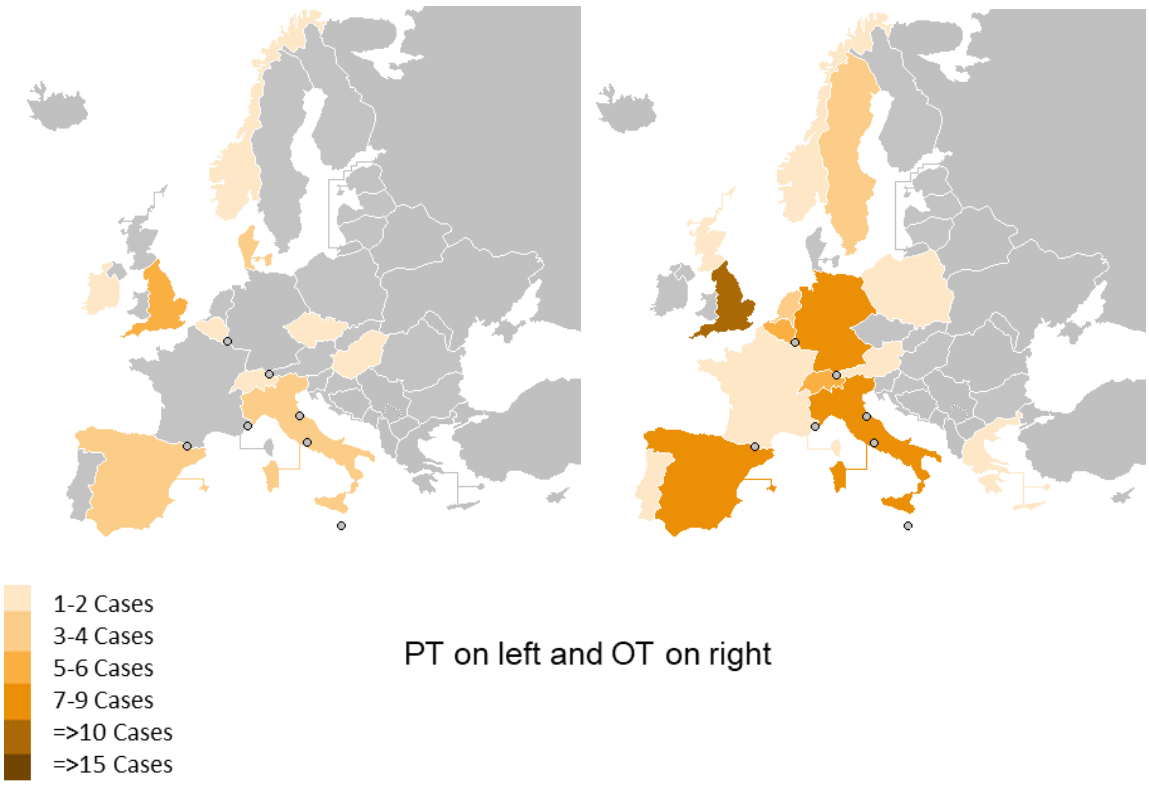


Table 8: Limiting and Preventing factors reported about timing

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Assessment not available	7	54	12	7	**80**
Notice too short	0	3	2	2	**7**
Not up to date	0	1	1	2	**4**
Total	**7**	**58**	**15**	**11**	**91**

Number of agencies reporting

The implementation data (figure 21 and table 8) suggest that for some countries PT assessment timing remains an issue. This is usually because agency assessment processes can start at or before CHMP opinion and so an agency may have already started work when the PT assessment is published. In the interviews one of the agencies highlighted that delayed launch in some countries means that if a PT assessment is carried out too early then it may no longer be up to date when a company submits its application for reimbursement. However, in only 1 instance was this given as a factor limiting use of a PT assessment.

For OT assessments the implementation data show that timing is, by some margin, the biggest factor reported to prevent the use of JA/CA.

It was noted that in countries with later adoption of an OT having a JA/CA is of value and can be used even if it needs updating, although opposite views were expressed as to how resource intensive updating is:

> *"when the topic actually crops up at the national level, a OT assessment is extremely useful, even though it has become out of date, because update is generally quite quick and a lot of background work has already been done, saving time and resources"*

> *"if use EUnetHTA assessment and it is 6 months old you then have to update on searches etc.so whilst you cut down work you won't eliminate it or replace work."*

However, the key barrier for OT timing was when agency work had already taken place before the JA/CA became available, in some cases some years before EUnetHTA produced their assessment.

> *"Some reports were in principle useable but too late".*

Agency perceptions of changes introduced in JA3

The main procedural change made by EUnetHTA in respect of timeliness for PT assessments were changes made at the start of JA3 allowing the publication of PT assessments closer to marketing authorisation.

All agencies interviewed viewed changes to PT timing as either positive or neutral in supporting them to use PT assessments. Among respondents the main reason for increased use of JA3 assessments compared to JA2 assessments was identified to be improved timing, assessments often came too late in JA2.

> *"Timing – all reports are published close to EPAR which is in line with our national procedure".*

> *"The key reason for the change [in use of assessments] is timing. PT EUnetHTA assessments in JA3 have been available at the time [agency] receive a submission".*

The main procedural change made by EUnetHTA in respect of timelines for OT assessments was the sharing of draft assessments. In September 2019 it was approved that draft assessments would be shared with partners outside of the assessment teams, with this to become operational from OTCA23 onwards.

A number of agencies interviewed were not aware of this change and because the change has yet to be implemented agencies were unable to comment definitively on the impact of the change, but many felt that it will be positive and will help agencies to plan to use OT assessments.

> *"It will be really helpful to support early adaptation work and plan at an earlier point to plan and determine whether they will use the assessment nationally".*

Agency recommendations for the future

To further improve the timeliness of PT assessments it was suggested that agencies could benefit by having the PICO made available to them earlier, rather than an at CHMP opinion as currently. It was suggested that it may be possible to achieve this through making the PICO available internally to partners on the intranet and not publicly on the internet.

Whilst the findings from the interviews confirmed OT timing as a key barrier to use, partners identified no obvious solutions to solve the challenge of timing. It is, however, hoped and anticipated that going forward the new medical devices regulations in Europe will help to provide an anchor to ensure less spread out and variable uptake across Europe for OT.

Conclusions

- Earlier publication of PT assessments close to marketing authorisation has supported increased use of these assessments. However, for agencies who can start work at CHMP opinion, timing of the joint PT assessment remains a limiting factor in the ability to use EUnetHTA assessments.

- There are ongoing challenges to identify the best possible timing to carry out OT assessments so they are of value to the largest number of agencies. It is hoped that EU MD regulations will help create an anchor that will allow for greater alignment of timing of OT HTA across Europe.

- Early sharing of information about PICO and draft assessments supports better planning and use of JA/CA. The improvements in JA3 are welcomed, but partners suggest it would be helpful if more PICO information can be shared earlier.

12. Results: Relevance and transferability

Fitness for purpose of procedures

Figure 22: Countries reporting relevance as a limiting or preventing factor

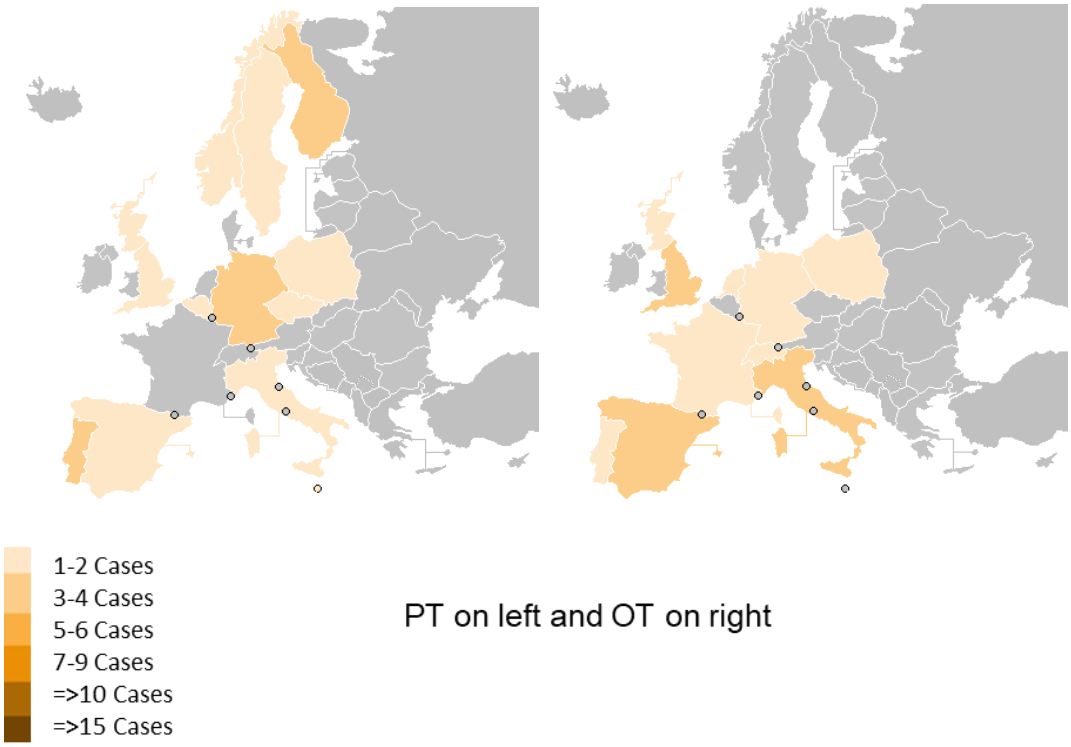


Table 9: Limiting and Preventing factors reported about relevance

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Scope Relevance	4	7	7	11	**29**
Content Relevance	0	1	14	7	**22**
Transferability	0	0	1	2	**3**
Total	**4**	**8**	**22**	**20**	**54**

Number of agencies reporting

Respondents to the implementation feedback survey are asked if the following factors either prevented or limited use of JA/CA.

- Differences in the scope of the JA/CA and agency assessment ("scope relevance")
- Differences in the content of the JA/CA and agency assessment ("content relevance")

Implementation data (figure 22 and table 9) show that relevance remains a key issue limiting and preventing use of both PT and OT assessments.

The data show that a lack of alignment of the scope more often prevents use, but a lack of alignment of content does not. For PT assessments fewer agencies report

issues with alignment of scope and more report issues with requiring different content information. For OT assessments more users report issues with scope relevance and fewer report issues with content alignment.

Issues of content alignment in PT arise in part from the use of economic information in agency assessments and need to analyse clinical data to inform and interpret economic analyses. In contrast, OT assessments have more heterogenous objectives and PICOs which create more challenges with creating a European scope. Giving reasons for non-use of OT assessments one agency commented:

> *"In some other cases the PICO was not in line according to ours (different place of OT in the therapy, which we scope at the professional societies)"*

The challenge of adaptation when there was a lack of alignment of scope was illustrated by one agency:

> *"for those reports that were chosen to be adapted (which means not only translated in their summaries and published on our websites) we usually found that the PICOD did not fit our context (relevance) and in some cases we needed to basically re-run literature searches, re-make systematic reviews and rewrite CUR and TEC chapters".*

Agency perceptions of changes introduced in JA3

Several procedural changes have been implemented by EUnetHTA to improve the relevance of **PT** assessments, including:

- Formal request to partners for interest in topic
- EUnetHTA prioritisation list (EPL) for topic selection
- PICO Survey
- Early access to confidential information in the draft regulatory assessment report allowing citation of the CHMP assessment report in PT assessments

Most agencies were aware of these changes. Agencies identified PICO surveys as being important in improving relevance and supporting engagement of agencies early in the assessment process.

> *"PICO survey is very useful, and we always participate in this".*

> *"The PICO surveys were able to involve our Agency from the beginning of the process"*

However, not all agencies found taking part in the PICO survey easy:

> *"PICO surveys are difficult to answer as often the populations are more limited / focussed to limit budget impact".*

> *"But difficult to input to the PICO at the stage it is undertaken – but have tried to do so to ensure that the report is of relevance when it comes through".*

The EUnetHTA prioritisation list (EPL) was also identified by PT users as being helpful in improving relevance for some agencies. However, several agencies commented that the prioritisation had little impact nationally either because they assess all new medicines in that country or because the identification and selection of topics is industry led.

For OT, the key procedural change implemented to improve the relevance of JA/CA was the EUnetHTA Prioritisation List (EPL) for topic selection. This was published on 2nd July 2019 for OT.

Reactions to the OT EPL were mixed, some agencies considered that it had been helpful for their own topic selection processes, but for the most part it was not considered to have been very useful for OT assessments.

> *"Would be good to have a shorter more focussed prioritisation list that gives more detail such as the PICO".*

> *"An administrative burden but of limited use for OT. As in most instances - authors will only act as authors if they have been asked to review the topic at a national level".*

> *"Helpful document and we shared it very widely but feedback now is that a topic is prioritised but then it does not start, and we get questions as to why"*

Some agencies considered that a greater use of horizon scanning would help better alignment of topics for JA/CA with agency priorities, while other agencies proposed sharing lists of agency priorities before work had been started.

Agency recommendations for the future

For PT it was identified that the PICO survey has been particularly helpful in improving relevance.

> *"Keep emphasis on PICO development (PICO survey and adherence to PICO in report) to support relevance"*

It was suggested that further work on the PICO would be helpful to establish who defines the PICO in different partner countries and that the PICO survey should be

specifically targeted at these people to ensure the best and most informed feedback is obtained from the PICO survey.

It was also suggested that a teleconference would be helpful after the PICO survey, in order to allow the authors of the assessment to respond to any questions on how survey comments have been addressed in the final PICO.

Reflecting on the challenges of creating a JA/CA to suit multiple agency requirements, it was noted that it was unlikely that JA/CA could have a scope that would suit everyone, therefore agencies will need to have sufficient procedural flexibility to extract information relevant to their context. However, EUnetHTA should ensure that authors adopt a European perspective.

> *Do not limit content to have a report that suits every country 100%. Rather, allow for a report with more PICO's or outcomes if necessary, so that every country can pick what they need. (NB: authoring teams should author with this European perspective in mind.)*

Further suggestions to improve relevance for OT assessments focussed on the need for better scoping, particularly at the pre-scoping stage to ensure that topics coming through are well defined. It was suggested that the PICO survey should be extended to cover OT assessments. This is currently being considered by WP4 and a pilot PICO survey for OT assessments is being undertaken.

Conclusions

- Relevance is a factor that prevents or limits the use of JA/CA. However, the challenge for OT and PT differs, for OT alignment of scope is a bigger challenge, whereas for PT alignment of content is the bigger challenge.
- The PICO survey introduced for PT assessments is perceived to have had a positive impact on assessment relevance and implementation.
- The EPL lists are perceived to have been less useful for implementation. For OT there remains a need to work further on topic identification and alignment of topics for JA/CA with agency priorities.
- Agencies need to ensure there is sufficient procedural flexibility to allow them to extract relevant information from JA/CA and ignore irrelevant elements.
- Authoring teams should adopt a European approach to authoring JA/CA

13. Results: Reliability and scientific rigour

Fitness for purpose of procedures

Figure 23: Countries reporting reliability as a limiting or preventing factor

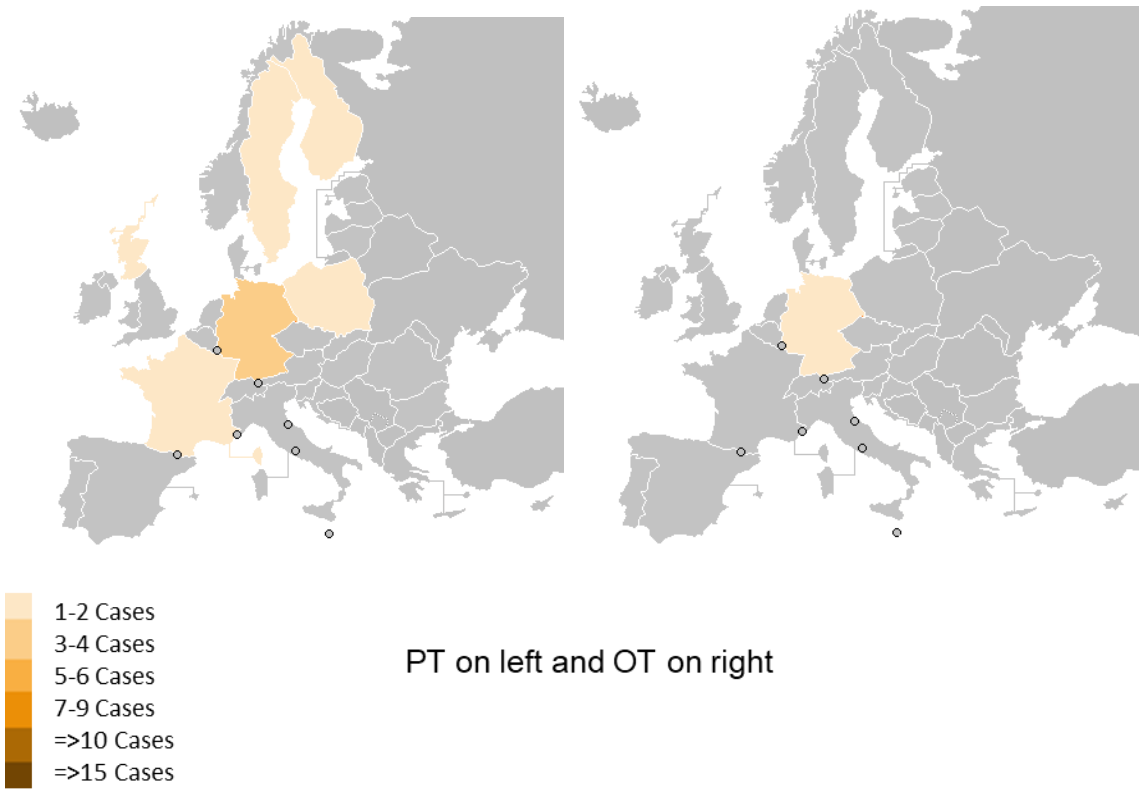


Table 10: Limiting and Preventing factors reported about reliability

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Not sufficient quality	3	2	0	0	**5**
Disagreed with findings	2	0	2	0	**4**
Disagreed with quality assessment	1	0	0	0	**1**
Needed more methodological information	1	0	2	0	**3**
Total	**7**	**2**	**4**	**0**	**13**

Number of agencies reporting

Respondents to the implementation feedback survey are asked if the following factors either prevented or limited use of the JA/CA.

- The JA/CA was not of sufficient quality
- The agency disagreed with the findings of the JA/CA
- The agency disagreed with the assessment of quality in the JA/CA

- The agency needed more methodological information to make a judgement about quality

The data (figure 23 and table 10) show that factors relating to reliability are more apparent for PT assessments than for OT assessments, and most often prevent use. No single reliability factor is identified as a bigger issue than the others.

In general, the data show that the scientific rigour of JA/CA was felt to be fit for purpose, though one agency commented that quality of OT assessments was variable. In addition, quality remains an important factor limiting use of assessments in a small number of locations:

> *"agency has not used the EUnetHTA PT assessment reports….as they did not meet the requirements of transparency, standardization, completeness, independence and methodological quality which are prerequisites for the use in our country".*

Agency perceptions of changes introduced in JA3

The procedural changes made to improve scientific rigour were common across PT and OT assessments and were:

- Implementation of the Companion Guide
- Submission requirements documents
- Optional factual accuracy checks

In JA3 EUnetHTA has implemented a quality management system through the Companion Guide to support production of JA/CA. The Companion Guide was largely viewed positively for both PT and OT, but agencies were equivocal about whether it has or will improve implementation of assessments. One agency viewed the benefits mainly to be in providing more confidence in assessments while another commented that the decision makers did not have that level of knowledge and so would not really consider it in detail when choosing to use an assessment

> *"Absence of quality management system was not stopping the agency using EUnetHTA assessments previously…although the presence may give users more confidence".*

> *"Not sure if changes will improve uptake as our commissioner is not at that level of knowledge of procedures when undertaking HTA and considering use of EUnetHTA assessments".*

The introduction of a submission requirements document was again viewed positively by the agencies that were aware of it, although not all were aware that it has been introduced. For OT it was recognised that some companies, particularly

smaller companies, do not always fill in the submission file. There was, therefore, uncertainty about how beneficial it would be in this context.

The optional factual accuracy check by manufacturers on draft documents was welcomed by some, with this being an important additional step to allow companies to check and if necessary, get corrected assessment errors. Some agencies were, however, not in favour of company involvement in this stage.

> *"Factual accuracy check by manufacturers is of great interest and should be mandatory, to increase scientific rigour and transparency".*

> *"Addition of factual accuracy checks is particularly helpful for complex devices or where there are issues around the CE mark*".

Agency recommendations for the future

Several agencies underlined that there was a need to ensure that authoring teams had sufficient methodological expertise to undertake JA/CA through internal training and internal or external expert support.

In addition, it was noted that authoring teams need to have sufficient time allocated to undertake JA/CA using the procedures that have been defined.

Finally, it was noted that while the implementation of the quality management system was useful, it has focussed a lot on procedures and there was still a need to focus on methods.

Conclusions

- Reliability of JA/CA is not reported as a major factor preventing or limiting use
- The implementation of the Companion Guide and submissions requirements documents give greater confidence in the JA/CA, but mostly have not impacted on whether agencies use them
- Agencies recommend:
    - There is a need to ensure that there is sufficient methodological expertise within authoring teams through internal capacity building and/or external methodological expertise
    - There needs to be alignment of the procedure followed and time allowed for authoring. Robustness of JA/CA is reduced if authors are not given sufficient time to follow the defined procedure
    - A factual accuracy process to correct errors in JA/CA before publication can help to give confidence in the findings.

14. Results: Evidence and Methodology

Fitness for purpose of procedures

Figure 24: Countries reporting evidence and methodology as a limiting or preventing factor

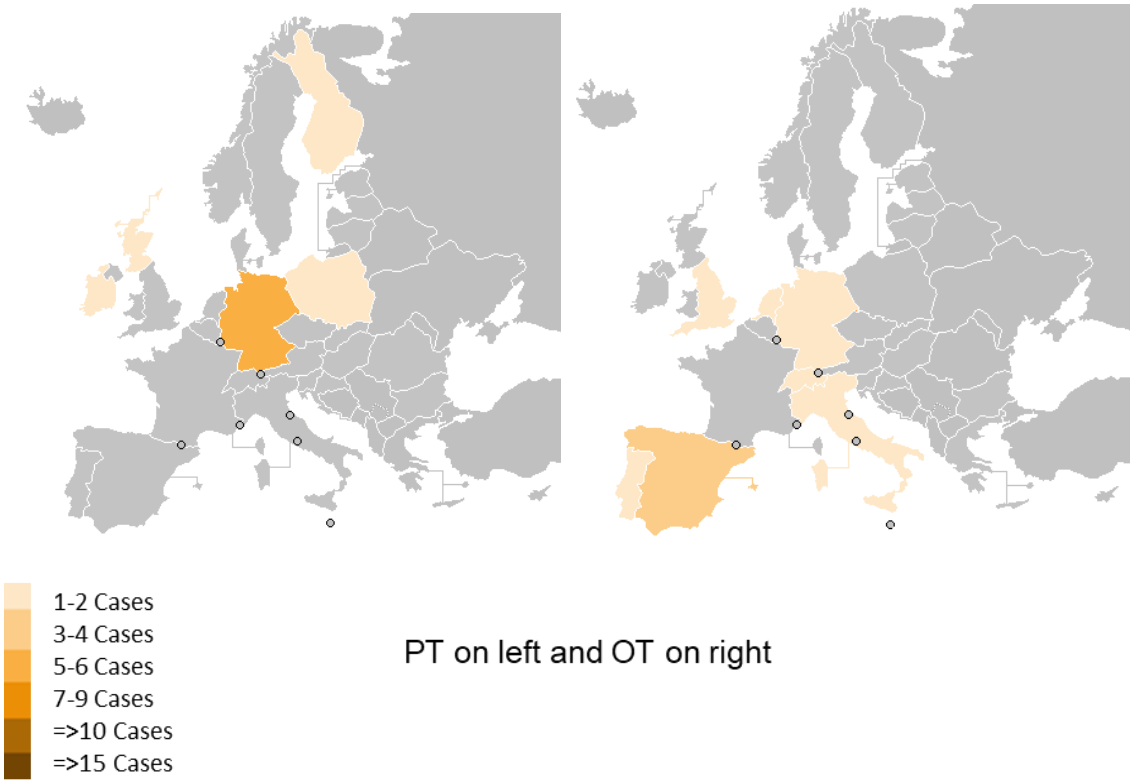


Table 11: Limiting and Preventing factors reported about evidence and methodology

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Evidence too restrictive	1	1	2	5	**9**
Evidence too wide	1	0	0	2	**3**
Out with agency approach	3	1	2	1	**7**
Total	**5**	**2**	**4**	**8**	**19**

Number of agencies reporting

Agencies are asked in the implementation feedback survey if the following factors either prevented or limited use of the JA/CA.

- Whether the type of evidence included in the JA/CA were too restrictive, for example inclusion of randomised data only
- Whether the type of evidence included in the JA/CA was too wide, for example inclusion of all available evidence

- Extent to which the evidence and methodology used aligned with that used by the agency.

The data (figure 24 and table 11) show that for OT in the majority of cases issues arose from the choice of evidence included in the assessment rather than that the approach to methodology was out with that adopted by the agency. For PT, more agencies comment on evidence and methodology being out with the agency approach than the choice of evidence inclusion. However, the numbers in all categories are small.

In regard to evidence inclusion, among OT users a number of interviewees noted that they or their decision makers had reviewed the JA/CA and decided that an agency assessment was not timely based on the evidence availability in the report.

> *"We shared the report with the relevant managed clinical network. They scanned it and considered that insufficient evidence to indicate action at this time".*

It is positive that agencies are using JA/CA to support topic identification and decisions about agency assessments. However, it may not be the best possible use of joint HTA resources if outputs of the process primarily inform a decision that an agency assessment is not timely because of evidence availability. At the stage of determining topics for joint assessment and scoping these, it may be appropriate to include consideration of evidence availability and the types of evidence to be included in the JA/CA. This might help target joint HTA resources on topics most likely to result in agency assessments.

Survey data shows that the methodology used for JA/CA is not a key limiting factor. This is consistent with the findings from the WP7 case study[4] that identified that the EUnetHTA guidelines do not hinder uptake.

Agency perceptions of changes introduced in JA3

In JA3 EUnetHTA developed recommendations and guidance for involving European patient organisations.

Most agencies were aware of the procedural changes and viewed this change as positive. The involvement of patients in JA/CA was seen most positively by agencies who engaged patients less in their agency process compared with agencies who already had methods of patient engagement. Several agencies are currently developing their own procedures for involving patients and learning from EUnetHTA on improving patient involvement was felt to be helpful. A number of agencies reported that whilst the improved patient involvement in JA/CA would not specifically

[4] https://eunethta.eu/wp-content/uploads/2019/06/Implementation-Report-May-2019-FINAL.pdf

impact on their ability to use the JA/CA, the involvement of patients does improve their confidence in the findings of the JA/CA.

> *"It doesn't impact the ability to use it but the ability to understand and trust its conclusions".*

One agency also felt that the evidence and methodology focus in JA3 had become more pragmatic with less focus on specific terminology which helped them engage better in the process.

> *"JA2 seemed to very focussed on the core model and all the terminology around this, and we struggled to get our heads round a lot of what was being discussed and proposed. We have felt much more engaged in JA3, and this has made it much easier to get a handle on what is going on and get involved"*

Agency recommendations for the future

Some agencies indicated that the role of patients in scoping needs to be extended. In addition, having developed the procedures for involvement, there is a need to ensure that there is follow through from the procedures to engagement.

> *"Development of procedures for patient involvement is a good step but often patient organisations do not engage and hence often it does not improve the assessment".*

In addition, patients are only one group of experts and there is a need for engagement of clinical experts and potentially also payers.

> *"Patient participation has improved a lot through changes. Contribution of clinical experts has not improved much in PT and needs to be improved".*

> *"Would be good to have more involvement from a payer perspective – particularly in terms of their input into the [OT] project plan".*

Considering other aspects of evidence and methodology, it was felt that there should be an increased focus on methodology, particularly in respect of updating existing EUnetHTA methodological guidelines and developing new methodological guidelines in emerging areas such as personalised health and precision medicine.

Partners underlined the ongoing need to develop mutual acceptance of certain methodologies (use of GRADE was highlighted by several agencies).

> *"It is important that EUnetHTA supported methods are accepted by the partner agencies and there is mutual agreement in the use of certain methodologies. The piece of work done by the Common phrases and*

GRADE task group, as well as the PICO subgroup, is very important in this matter".

Several agencies identified that once these methods and processes have been agreed by EUnetHTA, these then needed to be fed back to staff involved in agency assessment through training and knowledge transfer. One agency stated:

"It is very important that all agency staff involved in the national HTA is well trained in utilising the joint HTA tools and assessments. Also, it is essential that there is good communication and knowledge transfer between staff experienced in the European joint work and national HTA"

Conclusions

- The methodological approach adopted by EUnetHTA is not a key factor limiting or preventing use of JA/CA
- The decisions made about the study types to be included in an OT assessment is more frequently reported as a limiting factor than methodological approach. Consideration of evidence availability and evidence inclusion in OT assessments should be considered as part of topic identification and scoping.
- The recommendations and guidance for involving patients developed during JA3 has been positively welcomed.
- Agencies recommend:
    - Methodological guidance is regularly maintained and extended to cover new and complex issues arising in HTA
    - The methodological approach adopted by EUnetHTA needs to be consistently applied across all JA/CA
    - Agencies need to identify and resolve any methodological areas where agency adopted approaches actively hinders the use of JA/CA
    - Agencies need to ensure that methodologies and processes agreed through EUnetHTA are communicated to agency assessors through training and knowledge transfer
    - Principles of patient engagement need to be followed up and turned into actual engagement
    - Principles of engagement need to be developed for other expert groups e.g. clinical experts and payers

15. Results: Usability and Reporting Structure

Fitness for purpose of procedures

Figure 25: Countries reporting report structure as a limiting or preventing factor

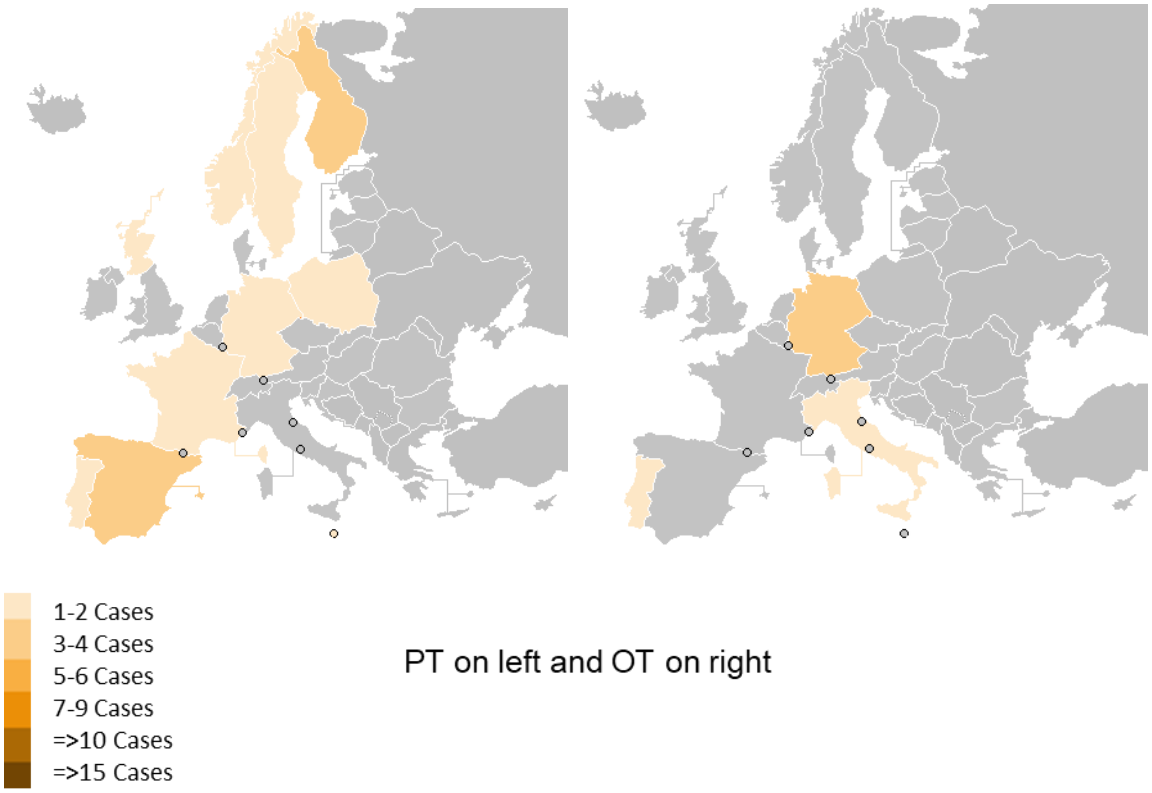


Table 12: Limiting and Preventing factors reported about report structure

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Agency must use a specified structure	1	4	18	2	**25**

Number of agencies reporting

For PT assessments many countries report having to use a specified report structure for their agency assessments. This acts as a factor that limits (but not prevents) their use of JA/CA (figure 25 and table 12). Specification of a report structure appears to be much less of a limiting factor for OT assessments.

Usability is related to familiarity with the JA/CA report structure. It is expected that at the beginning of the introduction of a new template, agencies will experience challenges because of a lack of familiarity with the reporting structure and experience of using it. These challenges should reduce over time as more reports are published and familiarity with the template increases.

Agency perceptions of changes introduced in JA3

In JA3 the PT assessment report template has been revised.

There was limited feedback available on changes to the PT template given the relatively small number of PT assessments published in the last 12 months. Those that have used the new template were largely positive reporting that it is easier to use, simpler and less repetitive. There were also favourable comments on the availability and use of medical editors.

> *"The new template is now more simplified and less repetitive".*

> *"Input of medical editor was very useful….and we suggest keeping this for future assessments".*

In JA3 the OT template has not yet been revised (a pilot for the revised template started after the implementation data cut-off), but improved standardisation of the process and a small number of changes to the presentation, summary and discussion have positively influenced the readability of the JA/CA.

> *"The assessments have become more standardised and the format more familiar and therefore it is easier for us to use the assessments in JA3".*

> *"More standardised structure of the assessments"*

Agency recommendations for the future

Some agencies felt that further instruction is still required for authors on how to use the new template

> *"We are currently an author of an assessment and would be helpful to have more information on the requirements / expectations of authors in each section".*

An outstanding issue for PT assessments is about the length of the assessments. From interviews, there is, however, no clear sense of the best way forward. Some agencies require detailed JA/CA and others want shorter more concise documents. Some agencies want specific headings included and covered in the JA/CA and others do not.

> *"The structure of the reports has improved, but they are still too excessive"*

For OT assessments one agency commented that there is still a need for further improvements in clarity and readability.

> *"In order to make OT assessments more useful, it is important that they have a clear conclusion on the value of the product in relation to the relevant comparator/s. Several conclusions of EUnetHTA reports do not*

help the reader to know the answer to the relative effectiveness question due to unclear language"

Conclusions

- The requirements for agencies to use a specific report structure acts as a limiting factor in use of JA/CA but rarely prevents use
- The new template for PT assessments has been positively received from those who have used it
- Changes to the OT process and influence of these on the report structure have also been positively received
- The heterogenous needs of agencies in their assessments means that defining a report structure that meets all agencies' needs completely is unlikely to ever be fully realised. A balance will be required between different agency needs and time and resources available for authors.
- To accurately capture usability issues, the introduction of new templates needs to allow sufficient follow-up time for agencies to become familiar with it, before it is further revised
- Agencies recommend:
    - Further guidance is provided for authors about using the template and information expectations
    - Active brokering of an agreement about the length of JA/CA to meet most needs of most agencies
    - Agreement on the conclusions that can be made in JA/CA
    - Editing of JA/CA to ensure language is clear

16. Results: Language

Fitness for purpose of procedures

Figure 26: Countries reporting language as a limiting or preventing factor

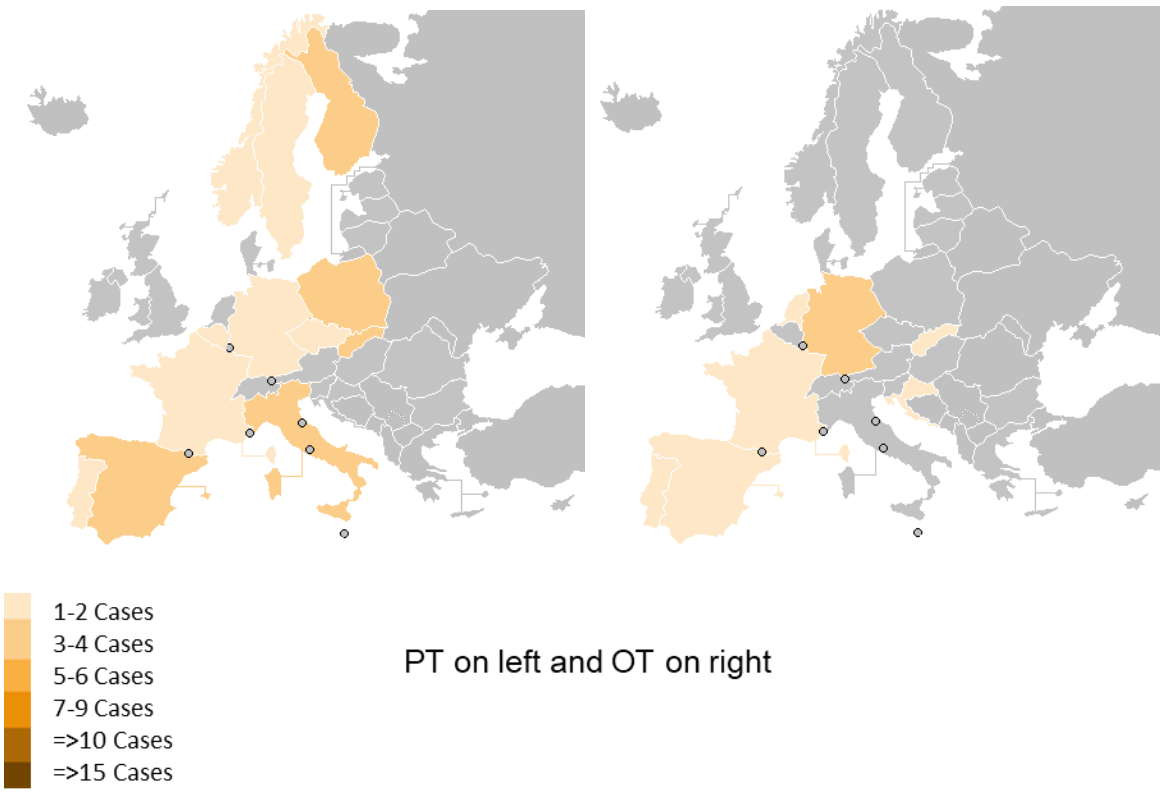


Table 13: Limiting and Preventing factors reported about language

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Agency assessments must be written in national language	1	3	22	7	**33**
Documents received must be in national language	0	0	1	1	**2**
Total	**1**	**3**	**23**	**8**	**35**

Number of agencies reporting

The implementation feedback survey collects data about whether the language that the agency must use is a factor that prevents, or limits use of JA/CA.

The data show (figure 26 and table 13) that agencies can be required to write their assessments in a national language and that this can act as a limiting factor particularly for PT assessment users. However, it does not prevent use.

Very few agencies report that the requirement to receive documents in a national language limits their use of JA/CA and none report that it prevents use of JA/CA.

Agency perceptions of changes introduced in JA3

Not applicable

Agency recommendations for the future

There was quite a strong view that language and specifically the use of English in agency assessments could be a tool to improve use of JA/CA. This was suggested as one of the few areas where potential legal changes could be made.

Agencies with the freedom to prepare reports in English commented on how this made use easier.

> *"Agency can publish reports in English or even partially in English which makes it more convenient to re-use the EUnetHTA report without the need to translate the information"*

Conclusions

- Many agencies must prepare their assessments in their national language. This acts as a factor that limits use, because text needs to be translated and cannot be directly used. However, it does not prevent use of JA/CA.

- There is a perception that a change to allow technical documents to be written in English is required to support implementation, this change is seen as possible by agencies but to make this change requires legal changes for some countries

17. Results: Transparency and Independence

Fitness for purpose of procedures

Figure 27: Countries reporting transparency as a limiting or preventing factor

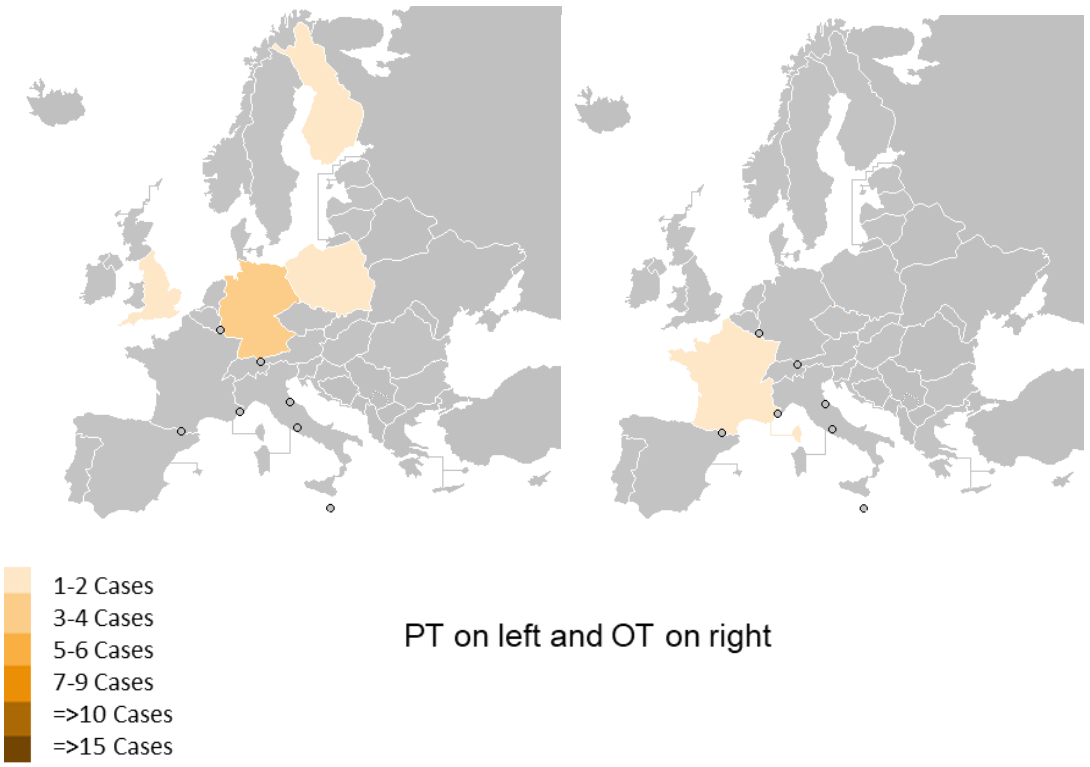


Table 14: Limiting and Preventing factors reported about transparency

	Prevented use		Limited use		**Total**
	PT	OT	PT	OT	
Transparency of process	2	0	1	1	**4**
Access to documents informing assessment	3	0	4	0	**7**
Total	**5**	**0**	**5**	**1**	**11**

Transparency of process and availability of documents are not reported to be a major factor limiting or preventing use (see figure 27 and table 14).

Where transparency is reported to be an issue it is mainly for PT assessments and relates to the availability of documents supporting the JA/CA procedure. Company submission documents are now published, and it is expected that this will be less of an issue for future PT assessments.

Agency perceptions of changes introduced in JA3

The main key change made to improve transparency has been the publication of submission dossiers for PT assessments. This change has also been implemented for OT submission dossiers but was not implemented at the time of data cut off.

The key procedural changes made to improve independence were common across PT and OT assessments and were:

- Publication and communication of DOI form and guidance
- Establishment of the EUnetHTA COI committee

Agencies either felt that publication of PT submission dossiers was a helpful change, or they viewed this as a neutral change. Some agencies did not need to see the submission dossier and others did not consider there was enough time in their agency process to review both the JA/CA and the submission dossier.

> *"A positive change and good that the REA actually cross-refers to the submission dossier. Really pleased as lack of submission dossier was a big issue in JA2".*
>
> *Not sure it is a big or particularly helpful change as would probably just use the EUnetHTA report rather than also check the submission dossier.*

All the agencies interviewed were aware of the changes made to declaring COI. There was a clear consensus from the interviewees that having these procedures in place give users more confidence and trust in JA/CA, though not necessarily changing how they will use the JA/CA.

> *"It increases trust in the assessment".*
>
> *"They are again positive changes. They create a more transparent process...but there are bigger issues that impact on our ability to use EUnetHTA REAs at a national level, in particular relevance"*

Agency recommendations for the future

Regarding publication of the data behind the assessments one agency commented that publication of company submission dossiers could be extended to also included clinical study reports.

In regard to COI, Some felt that the COI policy may need to be more flexible in some instances to ensure appropriate access to clinical expertise and that the length of the document put people off from participating in assessments.

> *"The COI procedure was actually too restrictive. Compared to the [national] COI procedure, an expert can declare an interest but normally*

this expert wouldn't be excluded as reviewer but flagged or skipped on those matters at which his interest might affect his judgement".

"we are told that the DOICU form can be quite long and some people drop out rather than complete it. So, a recommendation would be to simplify the DOICU".

Conclusions

- The principles of transparency and independence adopted by EUnetHTA are not key factors limiting or preventing use of JA/CA
- The publication of company submission files is viewed as having a positive impact on PT implementation
- Changes made to the COI policy adds confidence to use of JA/CA
- Agencies recommend:
    - Ongoing monitoring of the COI policy to ensure that the stringent measures in place are not acting as a barrier to getting the best possible expert involvement

18. Recommendations for implementation support in a future model of HTA cooperation

The fifth and final key question that we answer in this report is:

> *"What support for implementation should be built into a future model of HTA cooperation?"*

In JA3 implementation support has mainly focused on raising awareness of JA/CA, encouraging use, sharing implementation experiences, putting in place a reporting system to monitor use, feedback to EUnetHTA to support improvements in processes and reaching out to agencies who are not part of the network but are potential users of reports. Because the details and requirements of a future model of HTA cooperation are not yet known JA3 implementation has not worked towards a set of specific implementation requirements for using JA/CA.

Most agencies agreed that support for implementation should be built into a future model of HTA cooperation. However, there was a range of different views and opinions on what types of implementation support should be available.

Agencies considered that the level of implementation support required will differ by agency and country, and will be dependent on:

- how developed HTA systems are in individual countries
- the levels of HTA experience and expertise within these countries
- whether HTA cooperation has a legislative basis in the future.

Agencies with less developed systems or limited HTA experience will require more implementation support. Likewise, if there is a legislative basis more implementation support will be required to support the changes needed.

One respondent felt that to really strengthen HTA in Europe capacity building is required, specifically to support HTA in smaller and less developed countries. This was echoed by a respondent from a country where HTA is still establishing who felt that the HTA regulation would serve as a lever for capacity building and that capacity development should be built into the future model.

> *"The needs of member states for implementation support will give a broad spectrum of responses, depending on how developed their HTA systems are and how recently HTA activities have started….a key priority is capacity building and organisational development particularly for smaller countries…the potential that is not yet tapped for smaller agencies could be bigger if we do some capacity building to take these agencies forward".*

Another respondent felt that implementation support could best be provided centrally:

> *"A central support office would be helpful, providing a central contract point for different support…. for example, training, background information on assessments and procedures and translation support if needed by some partners".*

In terms of specific types of implementation support that could be offered in the future a range of options were discussed and proposed.

Monitoring, audit and indicators

Audit tools and indicators can help agencies measure whether they are implementing outputs appropriately. Some agencies considered the use of audit and indicators as important as they provide guidance on what is acceptable use. However, others noted that these can be intrusive and unpopular.

> *"For PT audit and implementation and workshops indicators most important".*

> *"monitoring and audit may be seen as intrusive".*

Training and workshops

It was noted that some training on how to update, adapt and adopt JA/CA might be needed.

> *"Some training and update on how to adapt/adopt HTA assessments might prove useful for implementation purposes"*

However, it was also noted that face-to-face approaches do not always work well because agencies use reports over different time periods. Having online resources enables agencies to use them when they need them and for more staff to take part.

Online resources and repositories

Sharing implementation experiences through webinars and case studies was viewed as being helpful because agencies can see the challenges other agencies face and how they overcame them.

> *"The sharing of implementation experiences and webinars and case studies are helpful as enables you to see the difficulties agencies went through and how they worked through them"*

It was also noted that assessment specific webinars where authors shared the key results and issues in assessments could be helpful for agencies to understand an assessment and its importance.

> *"Webinars are useful. Important that we are aware what is out there and available for use – so good mechanisms for sharing information on assessments"*

Outreach and field teams

In certain situations (such as where HTA systems were still establishing) dedicated advisers to support implementation, to engage agencies to discuss and to resolve issues and to promote outputs might be needed.

> *"For OT as still in early stages of development nationally workshops and implementation advisers would be most helpful"*

Conclusions

- Implementation support is required in the future model of HTA cooperation
- Support should be centralised and provided in a range of different formats to fully meet the needs of a range of different HTA agencies across Europe with different levels of HTA infrastructure, expertise and experience.
- A clear framework needs to be developed and agreed upon, so users of JA/CA understand the expectations of use.
- Acting alongside the framework there needs to be appropriate organisational development for agencies to ensure a sustainable model of HTA cooperation.
- In the first instance those agencies still establishing HTA systems require early facilitative support to put in place the capacity, expertise and processes to implement the framework.
- Suggested modalities for support:
    - Audit and indicators to support agencies to monitor acceptable implementation
    - Online webinars, case studies and training about JA/CA and implementation experiences
    - Outreach and field teams to support developing HTA systems

Appendix 1: Implementation feedback survey

The same set of questions are used for all JA/CA.

The Intranet survey function automatically records the person who completed the entry, the date of completion and if the survey was fully completed

Number	Question	Response options	Responses	Sharepoint branching logic[5]
1	Please provide your agency name	Free text	-	
2[6]	Have you used the EUnetHTA assessment? (*tick the most applicable, use the free text box at the end of the survey to provide further explanation if needed*)	Radio Buttons Choose 1	Yes, to support our usual assessment procedures	Directed to question 6
			Yes, as an alternative to our usual assessment procedures	Directed to question 6
Joint HTA			Yes, other	Directed to question 3
			No	Directed to question 4
3	Please describe	Free text	-	Directed to question 6
4	Please mark the response that best describes your situation	Radio Buttons Choose 1	This topic area is out of agency remit	Directed to question 17
			Work on this topic is not currently planned, but the topic area is in agency remit	Directed to question 5
			Work on this topic is planned but not yet started	Directed to question 5
			We carried out work on this topic but did not use the EUnetHTA Assessment	Directed to question 16
5	Might the topic be considered in the future? If so, what is the planned completion date?	Free text	-	Directed to question 17
6	When you used the EUnetHTA assessment, which parts did you use?	Radio Buttons Choose 1	Used methods and/or evidence from specific sections of the assessment in your report	Directed to question 7
			Used information from all sections of the assessment in your report	Directed to question 8

[5] If there is no branching logic given in this column, then the questionnaire proceeds to the next question in the numbered sequence
[6] Question amended part way through joint action, answers not available for all assessments

7	Which sections of the EUnetHTA assessment did you use?	Multiple selection	Health condition and use of the technology	
			Description of the technology	
			Clinical effectiveness	
			Safety	
			Checklist for ethical, social, organisational and legal implications	
8	When you used the EUnetHTA assessment, what did you do?	Multiple selection	01. Read the assessment for background information	
			02. Cited in your report as background or additional information	
			03. Used the EUnetHTA literature searches	
			04. Used the assessment to inform the evaluation or consideration of a company submission of evidence	
			05. Made significant changes to information used	
			06. Made minor changes to information used	
			07. Carried out translation only (please specify if translation was to the main text or the summary)	
			08. Made no changes to the information used	
			09. Updated evidence	
			10. Added local information	
			11. Added budget impact or cost effectiveness analysis	
			12. Added information about organisational, ethical and/or legal aspects	
		Free text	13. Other	
9	Was the main text of your report produced in your national language?	Radio Buttons Choose 1	Yes	
			No	

10	At which level was your report aimed?	Radio Buttons Choose 1	Local	
			Regional	
			National	
11[7]	What were the benefits of using the EUnetHTA assessment?	Multiple selection	01. Efficiency – Using the EUnetHTA assessment reduced the amount of time and / or resources required to carry out agency assessment work.	
			02. Quality – Using the EUnetHTA assessment improved the quality of the agency work	
			03. Knowledge – Using the EUnetHTA assessment provided access to expertise and/or data that the agency would not otherwise have had	
			04. Credibility - Using the EUnetHTA assessment gave additional credibility / validity to agency work.	
			05. Timeliness – Use of the EUnetHTA assessment improved the timeliness of decision making (e.g. led to an earlier decision about use of a health technology)	
		Free text	06. Other (please specify)	
12	Please provide additional detail on any of the benefits you have identified of using the EUnetHTA assessment (e.g. the amount of resource / cost saved in days, WTE or money)?	Free text	-	
13	Did your report directly inform a decision?	Choose 1	Yes, a reimbursement decision	

[7] Question amended part way through joint action, answers not available for all assessments

			Yes, another type of decision, please describe the type of decision	
			Yes, policy strategy or clinical guideline	
			No, please describe the aims and audience for the report	
14	What was the outcome of the reimbursement procedure?	Radio buttons Choose 1	Positive decision	
			Negative decision	
			Positive with restrictions	
15	Please provide a web link to any publicly available documents	Free text	-	
16	Which (if any) of the following factors prevented or affected your ability to use the EUnetHTA assessment?	Multiple selection	01. No limiting factors identified	
			02. Awareness: We did not know the EUnetHTA assessment was available	
			03. Timing: The EUnetHTA assessment was not available	
			04. Timing: Notice of an assessment was too short to adjust work planning to allow (best possible) use	
			05. Timing: The EUnetHTA assessment was not up to date	
		Free text	06. Timing: Other	
			07. Evidence and methodology: The range of evidence included was too restrictive	
			08. Evidence and methodology: The range of evidence included was too wide	
			09. Evidence and methodology: The methodology used was out with the approach adopted by the agency	
		Free text	10. Evidence and methodology: Other	

			11. Reliability: The EUnetHTA assessment was not of sufficient quality	
			12. Reliability: We disagreed with the findings	
			13. Reliability: We disagreed with the quality assessment.	
			14. Reliability: We needed more methodological information to assess the reliability	
		Free text	15. Reliability: Other	
			16. Relevance: The scope of the national assessment was different (e.g. in terms of comparator, population etc)	
			17. Relevance: We needed different content information (e.g. alternative presentation or other information such as economic information)	
		Free text	18. Relevance: Other	
			19. Transferability: We had difficulty transferring the information to our local context	
			20. Language: Reports we write must be in our national language	
			21. Language: Documents we use must be in our national language	
			22. Reporting structure: Reports we write must use a specified structure	
			23. Accountability: We need greater transparency of the process of producing the EUnetHTA assessment	
			24. Accountability: We need greater availability of documents used in the EUnetHTA assessment	
		Free text	25. Accountability: Other	
		Free text	26. Other limiting factors	

17	Have you undertaken any dissemination activities to promote awareness of the EUnetHTA assessment?	Radio Buttons Choose 1	Yes	
			No	
18	Please describe dissemination activities	Free text	-	
19	Are you happy for EUnetHTA to get in touch to follow up any of your responses?	Radio Buttons Choose 1	Yes	
			No	
20	Thank you for completing the survey. Please provide any other comments on this EUnetHTA assessment	Free text	-	

Appendix 2: Response rate

Table 1: Response rate by agency – JA3 assessments

Assessment	Publication Date	Responses from expected agencies[8]	
		Number (N)	Percentage (%)
OTCA01 (Wearable cardioverter-defibrillator)	Nov-16	36 of 42	86%
OTCA02 (Antibacterial-coated Sutures)	Apr-17	31 of 42	74%
OTCA03 (NIPT)	Feb-18	34 of 42	81%
OTCA04 (MammaPrint)	Jan-18	31 of 42	74%
OTCA05 (Magnetic stimulation)	Apr-17	33 of 42	79%
OTCA06 (TAVI)	Dec-18	25 of 42	60%
OTCA07 (FLACS)	Oct-18	22 of 42	52%
OTJA08 (Glucose monitoring)	Jul-18	29 of 42	69%
OTCA09 (HIFU ablation)	Apr-18	29 of 42	69%
OTCA10 (Stool DNA testing)	Jul-19	19 of 42	45%
OTCA11 (3D Implants)	Apr-19	20 of 42	48%
OTCA12 (CRP POCT)	Jan-19	27 of 42	64%
OTCA14 (Robot assisted surgery)	May-19	23 of 42	55%
OTCA15 (Irreversible electroporation)	Jul-19	22 of 42	52%
OTCA16 (Bioresorbable stents)	Jan-19	25 of 42	60%
OTCA17 (Lithium triborate)	Nov-19	13 of 42	31%
OTCA18 (Regional hyperthermia)	Oct-19	15 of 42	36%
OTCA19 (Screening for osteoporosis)	Sep-19	19 of 42	45%
OTCA20 (EVAR / TEVAR)	Nov-19	12 of 42	29%
OTCA22 (POCT: D Dimer and Troponin)	Dec-19	14 of 42	33%
PTJA01 (Midostaurin)	Nov-17	42 of 49	86%
PTJA02 (Regorafenib)	Oct-17	41 of 49	84%
PTJA03 (Alectinib)	Jan-18	40 of 49	82%
PTJA06 (Polotuzumab)	Mar-20	15 of 49	31%
PTJA07 (Ustekinumab)	Oct-19	21 of 49	43%
PTJA08 (Siponimod)	Feb-20	15 of 49	31%
PTJA09 (Brocilizumab)	Mar-20	10 of 49	20%

[8] Calculated based on 42 agencies currently using HTA to assess non-pharmaceutical technologies and 49 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 2: Response rate by country – JA3 assessments

Assessment	Responses from expected countries[9]	
	Number	Percentage (%)
OTCA01 (Wearable cardioverter-defibrillator)	24 of 25	96%
OTCA02 (Antibacterial-coated Sutures)	23 of 25	92%
OTCA03 (NIPT)	24 of 25	96%
OTCA04 (MammaPrint)	24 of 25	96%
OTCA05 (Magnetic stimulation)	23 of 25	92%
OTCA06 (TAVI)	20 of 25	80%
OTCA07 (FLACS)	18 of 25	72%
OTJA08 (Glucose Monitoring)	22 of 25	88%
OTCA09 (HIFU Ablation)	21 of 25	84%
OTCA10 (Stool DNA testing)	16 of 25	64%
OTCA11 (3D Implants)	18 of 25	72%
OTCA12 (CRP POCT)	22 of 25	88%
OTCA14 (Robot assisted surgery)	18 of 25	72%
OTCA15 (Irreversible electroporation)	17 of 25	68%
OTCA16 (Bioresorbable Stents)	21 of 25	84%
OTCA17 (Lithium triborate)	13 of 25	52%
OTCA18 (Regional hyperthermia)	15 of 25	60%
OTCA19 (Screening for osteoporosis)	17 of 25	68%
OTCA20 (EVAR / TEVAR)	13 of 25	52%
OTCA22 (POCT: D Dimer and Troponin)	14 of 25	56%
PTJA01 (Midostaurin)	28 of 30	93%
PTJA02 (Regorafenib)	28 of 30	93%
PTJA03 (Alectinib)	25 of 30	83%
PTJA06 (Polotuzumab)	12 of 30	40%
PTJA07 (Ustekinumab)	18 of 30	60%
PTJA08 (Siponimod)	13 of 30	43%
PTJA09 (Brocilizumab)	8 of 30	27%

[9] Calculated based on 25 countries currently using HTA to assess non-pharmaceutical technologies and 30 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.