

Report of the PARADIGM WP1 HTA Workshop on Early Dialogues held in London on 19th October 2018

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1: Executive summary

HTAi and PARADIGM convened a workshop on the 19th October 2018 with HTA Agencies to discuss patient involvement in Early Dialogues. Early Dialogues (also called Scientific Advice) is a multi-stakeholder discussion about confidential plans for key research studies planned to demonstrate the value of a health technology. They may be led by HTA and/or regulatory agencies. The rationale for involving patients was articulated, along with some of the common objections against involving patients. Attendees described the current processes of patient involvement, the challenges with implementing these processes, and the desired tools and resources that could make patient involvement in Early Dialogues more consistent, predictable and with baseline standards.

The rationale for patients to be involved in early dialogue was defined as:

- It ultimately improves the dialogue and the advice given
- Early dialogues are the right point in time for the patient input to have most impact because it will affect future clinical programmes and future investments
- It increases transparency of HTA processes and represents good governance
- As the stakeholder most affected by the therapies available, patients need to have a voice in these dialogues

Common objections heard against patient involvement in early dialogues:

- Patients will not be able to make objective inputs into early dialogues (too subjective / emotional)
- The details will be too complex for patients to understand
- Concerns over conflicts of interest

Common challenges with implementing patient involvement processes in Early Dialogues:

- Difficult to find a patient with the right profile for Early Dialogues and the capacity to participate due to the effects of the illness they are suffering from
- Involving patients takes a lot of internal resources within HTA Agencies
- Lack of clarity on exactly 'how' to involve patients (methods, guidance, tools missing)

After reviewing current process and sharing experiences of these among the attendees of the workshop, a clear set of challenges and needed tools was developed and prioritized. There were four broad areas identified where additional tools, resources and guidance is needed.

1. **Patient recruitment processes** – including developing criteria and guidance to help HTA Agencies find, select and enrol patients into the Early Dialogue processes
2. **Patient Interview Guidance** – including interview guides, standard questionnaires and guidance on adapting them to particular Early Dialogue topics
3. **Minimum standards framework** – including a framework of methods with guidance on their use, guidance for meeting chairs and patients and adaptation to meeting formats to accommodate patient needs
4. **Rationale for patient involvement in Early Dialogues** – including metrics that show the impact of patient involvement, case studies, definitions of early dialogues, and articulated rationale for patient involvement

As next steps, the group agreed to work together with HTAi under the PARADIGM consortium to further define and develop the tools and resources needed.

2: Attendees of the meeting

HTA Agencies Represented

Maria José Vicente Edo	Aragon (Spain)
Michelle Mujoomdar	CADTH (Canada)
Margaret Galbraith	HAS / EUnetHTA (France / Europe)
Chantal Guilhaume	HAS / EUnetHTA (France / Europe)
Heidi Livingstone	NICE (England)
Deborah Morrison	NICE (England)
Anette Grøvan	NOMA (Norway)
Bjørn Oddvar Strøm	NOMA (Norway)
Giulio Formoso	RER (Italy)
Sophia Brodin	TLV (Sweden)
Elin Thyr	TLV (Sweden)
Apology from: Jane Moseley	EMA

PARADIGM Observers

Mathieu Boudes	European Patients Forum and lead on PARADIGM
Nicholas Brooke	Synergist and lead on WP1
Callum Gunn	Athena Institute and representative of WP2 and WP3
Suzanne li	CASMI and representative from WP1

Facilitators

Neil Bertelsen	HTAi Patient & Citizen Involvement in HTA Interest Group
Karen Facey	HTAi Patient & Citizen Involvement in HTA Interest Group

3: Agenda and objectives

Objectives of the workshop

The workshop aimed to provide perspectives from HTA organisations on the potential to develop patient involvement in Early Dialogue/Scientific Advice processes¹. In detail, the workshop was designed to explore:

- 1. The rationale for involving patients and/or advocates in an early dialogue process**
 - a. For those agencies that already involve patients, what was their rationale for including them?
 - i. What kinds of insights do patients/patient representatives provide?
 - ii. What types of insights that patients/advocates provide are most useful?
 - b. For those agencies that do not currently involve patients, what is the rationale for not doing so?
- 2. The current challenges of initiating a patient involvement process in ED (for those agencies that do not currently involve patients)**
 - a. What are the specific concerns / perceptions that need to be addressed?
 - b. What are the practical barriers that need to be overcome?
 - c. Are there any systemic reasons for not involving patients/patient representatives (e.g. legal / regulatory / ...)
- 3. The current experience of involving patients and the challenges that have been identified so far (for those agencies that do involve patients in the ED process)**
 - a. How are patients involved?
 - b. What have been the positive experiences so far?
 - c. Specifically, what kind of insights are sought in the process?
 - d. What are the operational challenges?
 - e. What are the organisational challenges (e.g. What skills have been needed? What capacity is needed from the HTA agency? What capacity/skills are needed from the patient/advocate?)
 - f. What has been the patient feedback?
 - g. What has been the feedback (in general) from the industry?
- 4. What resources or tools would be useful in solving the identified challenges?**
 - a. Tools and resources that highlight the rationale for involving patients?
 - b. Tools and resources that could overcome particular challenges?
 - c. Tools and resources that may help the patient/advocate representative in this role?

¹ Early Dialogues are defined by EUnetHTA as intending to:

- Support developers of medical technologies by providing a collaborative approach between a wide range of European HTA agencies to provide advice on their product development plans.
- Supply prospective and timely advice, before the start of pivotal clinical trials, in order to improve the quality and appropriateness of the data produced by the developers that may ultimately lead to well-informed regulatory and HTA and reimbursement decisions in a timely manner.
- Present the common position on how the drug could be developed in order to fulfill the HTA requirements. EDs also aim to provide the individual views of the different HTA agencies to the applicant.
- All advice provided by HTABs is based on the documentation provided by the Applicant, reflects state-of-the-art of medical science and national/regional requirements at the time of advice and is not legally binding.
- Incorporate patient viewpoint systematically.

Agenda

Time	Session title	Who	Objective
10:00	Welcome and introductions	Neil Bertelsen & Karen Facey	To ensure that all attendees understand each other's perspectives and the desired outcomes of the workshop
10:20	Introduction to PARADIGM and Work Package 1 Overview of survey findings	Mathieu Boudes Nicholas Brooke	Attendees understand the scope of PARADIGM and why HTA perspectives are important to its success
10:30	Questions on PARADIGM	All	To give an opportunity to answer clarification questions
10:35	Short exercise: Write on Post-It notes the rationale for and against patient involvement in early dialogues Plenary: Why patient involvement in early dialogues – three agencies give the rationale for why they involve patients in ED	All NICE (10') CADTH (10') HAS (10')	Sets the scene on the rationale for ensuring patient insights are part of ED
11:05	Q&A	All	To give other agencies a chance to clarify processes and rationale with the presenting agencies
11:20	BREAK		
11:30	Breakout session (2 groups)		
	15 minutes: Why do we have patient involvement in early dialogues – what does it give us? 15 minutes: What are some of the objections you hear (the reasons why not to involve patients)? 60 minutes: How do we conduct this involvement and how does it differ between agencies? How have you had to adapt your ED processes to make patient involvement work?	Facilitated by Neil Bertelsen and Karen Facey	Each group articulates the rationale from the individual agency perspectives – drawing common themes where possible Each group looks at the objections to patient involvement in ED Each group considers the methods for conducting ED with patient involvement
13:00	LUNCH		
13:30	40 minutes: What challenges exist in implementing patient involvement in ED (put challenges onto post-it notes) – <i>consider also people with specific needs such as dementia or young people</i> 40 minutes: What would help address these – one idea on one post-it note: <ul style="list-style-type: none"> • Resources • Guidance • Tools • Processes 	Facilitated by Neil Bertelsen and Karen Facey	Understand the specific challenges in as much detail as possible Identify critical tools and resources that could be applied to address these challenges Identify what already exists and what would need to be created

14:50	BREAK		
15:05	Group Feedback – Rationale, challenges and solutions	All	Both groups feedback on the rationale for patient involvement, the identified challenges and the suggested tools or resources that could help
15:45	<p>Prioritization and identification of resources and tools</p> <p>1: Highlighting the most critical tools and resources that will help</p> <p>2: Highlighting where these tools and resources already exist and can be shared</p> <p>3: Prioritizing where there are no existing tools and how they might be created</p>	Room discussion and work on flip-charts	PARADIGM has a prioritized list of tools and resources that will help, as well as an identified list of existing resources that can already be shared and/or adapted
16:20	Wrap up	Neil Bertelsen and Karen Facey	Summarize findings and confirm meeting report content
16:30	Meeting closes		

4: Meeting report

4.1: Plenary sessions and discussions

4.1.1: Agreement on the process of developing this meeting report

At the start of the meeting the HTA Agency attendees were asked to confirm how they wanted the contents of the meeting recorded and reported. It was agreed that there would be no audio recording of the meeting and that the Chatham House Rule² would apply throughout the meeting, meaning that specific comments are not attributable to individuals or organisations.

In particular the agencies were clear that the confidentiality clauses that they sign as part of early dialogue processes mean that it is impossible to share specific examples from particular early dialogues, but that it is possible to discuss processes, challenges, and experiences in general.

4.1.2: Introduction to PARADIGM and Work Package 1

Mathieu Boudes, the lead of the PARADIGM project, thanked the attendees for making the time to give their point of view on Early Dialogues. Mathieu explained the concepts behind PARADIGM, an Innovative Medicines Initiative project to contribute to a sustainable framework that enables meaningful patient engagement in the three areas of:

- research and priority setting
- design of clinical trials
- Early Dialogues with regulators and HTA bodies

PARADIGM is a public-private partnership and is co-led by the European Patients' Forum and EFPIA. Its mission is to provide a unique framework that enables structured, effective, meaningful, ethical, innovative, and sustainable patient engagement (PE) and demonstrates the 'return on the engagement' for all stakeholders.

- Strengthen understanding of stakeholders' needs, expectations for engagement
- Ensure maximum synergies with similar initiatives
- Develop a workable suite of tools, sustainability roadmap with metrics
- Strengthen systems-readiness

Nicholas Brooke, the lead of Work Package 1 (WP1), described WP1 aims as identifying stakeholders' needs and aspirations for patient engagement in each of the three timepoints over the medicine's life cycle. This workshop with HTA agencies is a key deliverable of WP1. Nicholas outlined the use of online surveys as well as focus groups and workshops to understand the expectations and needs of other stakeholder groups. In particular, Nicholas highlighted the focus on vulnerable patient groups within the work package, including those with dementia, young patients and those with rare diseases.

Maria Jose Vicente Edo presented an overview of a Delphi survey that will take place between December 2018 and February 2019 to all stakeholders to determine their views on patient

² <https://www.chathamhouse.org/chatham-house-rule>

involvement at the three points in the medicine's life cycle. She expressed a need for more representatives from HTA bodies to join the survey and invited interested participants of this workshop to contact her directly to find out more details.

Discussion

The choice of patient groups within the project: The HTA Agency attendees were interested to find the rationale for choosing the vulnerable patient populations within the work package. This led to a discussion on some of the most challenging patients to find for early dialogues, which are often for more common diseases such as COPD or asthma. The agencies highlighted that in these more common disease areas, agencies often need to find patients with very specific experiences and although there are more patients with these common diseases, it has proved very difficult to identify patients with these specific experiences. Another area, highlighted by the EUnetHTA experience is the difficulty finding patients for some oncology indications, especially at the end-of-life stages of disease

The role of industry in PARADIGM: The HTA Agency representatives highlighted that they often have difficulty engaging in IMI projects because of the role of industry within these projects. They have to be wary of the perception that they are using tools and resources that could be perceived as being created with a lot of industry input. They flagged that because this workshop had been organised by HTAi, they were comfortable attending, and requested that any outputs from PARADIGM designed for HTA use, be created by the HTAi team with input from the HTA Agencies.

Perceived conflicts of interest: The HTA Agency representatives flagged that there are still concerns about the funding of patient organisations by the industry and that this can act as a barrier to increased patient involvement in HTA processes.

Delphi process to understand stakeholders' needs: Given the range of other work that has been undertaken it was questioned why the Delphi process was needed and how it would be assimilated with the other work if differences occurred, given there could be different inputs.

4.1.3: Scientific Advice at NICE (England) (see appendix A for slides presented)

Deborah Morrison of NICE outlined the process for Early Dialogues (Scientific Advice) at NICE as well as the rationale for patient involvement. Deborah explained that we first must understand the rationale for Early Dialogues. From the industry perspective, she explained that early dialogues are provided to increase the likelihood that a company's clinical development studies and other plans meet the evidence requirements of NICE. Including patients in this process is important because it increases the likelihood that these studies and plans meet the needs of patients too. She also noted that the face-to-face ED meetings, at NICE Scientific Advice, are very different to appraisal meetings as they are more interactive, and patients are able to ask the company questions and vice versa.

Early Dialogues have existed at NICE since 2009 and take a variety of forms, including:

- The standard Scientific Advice process
- Combined scientific advice with the UK regulator (MHRA)
- Combined scientific advice with the European regulator (EMA)
- Early dialogues as part of the EUnetHTA joint HTA processes and pilots
- Scientific Advice for small and medium enterprises (MedTech, Biotech...)

Scientific Advice face to face meetings at NICE generally consist of the following representatives:

- Industry: Health economics representative; Clinical lead; Regulatory lead
- NICE: Scientific Advice Chair; Member of the Scientific Advice team; Senior Technical Advisor
- External: Patient expert; Clinical expert; Health economics expert, NICE Senior (usually a former NICE Committee chair)

In terms of the rationale for involving patients in the Scientific Advice process, Deborah highlighted the fact that patients bring a unique set of insights to the dialogue. They can highlight the realities of living with a disease, pointing to specific attributes of the disease that most affect their daily life and long-term quality of life. It is for this reason that NICE look for specific patients with experience of aspects of the disease relevant to the ED, rather than a patient group representative that will have more general knowledge of the disease. Involving patients also gives patients a chance to influence how clinical trials are set up in order to provide the best evidence that the proposed outcomes can meet patients' needs.

In terms of finding the patient expert to be involved, NICE works through patient organisations to find suitable patients, or if that is not possible, tries to find patients using a variety of other means such as through physician contacts, or more general searches.

Patient insights have been useful in addressing a range of issues that come up in early dialogues, including:

- The proposed study population and subgroups
- The position of a new treatment in the treatment pathway
- The appropriateness of comparators as experienced by patients within the NHS
- The meaningfulness and acceptability of the proposed outcomes
- Measures of quality of life including when to measure these
- The appropriateness of the product formulation and delivery

IDENTIFIED RESOURCES: NICE is publishing guidance to help patients contribute to the NICE Scientific Advice process, including:

- [Hints and tips to help patient experts with NICE Scientific Advice meetings](#)
- [Brief guide to being a patient expert for NICE Scientific Advice meetings](#)

4.1.4: Including the Patient Perspective in CADTH's Scientific Advice Program (Canada) (see appendix A for slides presented)

Michelle Mujoomdar, Director of Scientific Affairs at CADTH explained the process of Early Dialogues at CADTH and the rationale for involving patient experts. Similar to the NICE approach, the CADTH Scientific Advice program has been developed to offer advice on early drug development plans from an HTA perspective, with particular emphasis on the Canadian setting. This advice is offered to input into decisions by companies around their pivotal clinical trial plans.

In this process, the patient is engaged as an expert, similar to the other experts who form the scientific advice team. This process was developed in consultation with members of the CADTH Patient Community Liaison Forum and is based around a patient interview.

A patient participating in the process signs a non-disclosure agreement and receives an honorarium for their time. In finding the right patient to interview, CADTH reaches out to patient groups to find an individual with:

- Long-term experience of the disease
- Experience with multiple therapies
- Aware of other's experiences (for example has moderated a chat group, answered help lines, led a patient group, etc.)

However, recruitment of a patient expert is challenging as the process is confidential and a public call is not made on a website, like that made for patient group submissions in an appraisal. So there is a need to draw on existing relationships to identify suitable patients and this is difficult when CADTH do not have an existing relationship with a relevant patient group.

CADTH have developed a process for the ethical recruitment of patients or carers that involves a multi-step process. A plain language consent form which can be given in written format or verbally has been developed that highlights the risks and benefits of being involved.

Individuals are reminded at multiple timepoints that they are in control of the information that will be shared and can redact information or withdraw from the process.

A conflicts of interest disclosure and confidentiality agreement are also signed before the interview.

IDENTIFIED RESOURCES: CADTH consent process for interviews including; plain language consent form, conflict of interest disclosure, confidentiality agreement

The interview is one-hour long and consists of semi-structured questions tailored for the relevant disease area and the specific advice being sought by the company. The interviewee is paid an honorarium. The accuracy of the interview summary is confirmed by the individual before becoming part of the report. This written summary is included in the record of the scientific advice provided to the company and insights are incorporated throughout the advice given.

Furthermore, individual insights contained within this interview summary are supported or contrasted with relevant sections of patient input from past CADTH drug reviews.

The types of insights that are useful to gain from patients during these interviews include:

- Experience of the patient journey from diagnosis
- Symptoms and their progression over time
- Treatment experiences and challenges with current treatments
- The most significant health issues related to the condition that impact daily life
- What is hoped for in a new treatment

From the scientific advices so far given, patient perspectives have been most important in the development of advice regarding outcomes and quality of life measures. The involvement has also been valuable to bring to life the condition and treatment experiences to CADTH researchers.

To highlight the need for patient involvement in Early Dialogues, Michelle shared some insights from an internal CADTH analysis of attributes that matter to patients. This review looked at the patient inputs into CADTH's Common Drug Review (when treatments are assessed by CADTH under its HTA process). This review identified 119 separate issues, or attributes that matter to patients, from a selection of patient group submissions, but found that only 50% of these were being captured in clinical trials. To close this gap, patient involvement in Early Dialogues will be essential.

4.1.5: Patient involvement at HAS (France) and EUnetHTA (Europe) (see appendix A for slides presented)

Maggie Galbraith of HAS explained that HAS leads the work package on Evidence Generation and is the coordinator of the Early Dialogues Secretariat within EUnetHTA and so presented on the early dialogue process of both organisations.

Within HAS, early dialogues are provided free to industry upon the application meeting certain eligibility criteria, and are principally used to provide recommendations on pivotal trial designs. The process takes approximately three months and there have been approximately 22 early dialogues conducted in 2018. However, the patient role in early dialogues remains to be defined at HAS, and a significant challenge is a lack of resources to devote time to this.

Within WP5A of EUnetHTA, there has been a concerted effort to test various approaches to patient involvement in Early Dialogues ranging from processes based solely around patient interviews to full involvement in the overall Early Dialogue process. Patient perspectives are recognised as being essential to forming advice by providing experiential knowledge of living with the condition and experiencing the available treatments. Patients can also advise on the signs and symptoms that have the greatest impact on their functional and psychological well-being.

The three main approaches that EUnetHTA has been testing include:

Approach 1 – Individual patient/patient’s representative - interviewed regarding the disease and their experience with no access to the briefing book (the dossier of information provided by the company)

- Collecting general insights on the disease
- Answering specific questions related to this specific Early Dialogue

Approach 2 – Approach 1 + discussion with local HTAB (only) regarding submission file (if applicant agrees)

- Collecting general insights on the disease
- Patient representative position on the application dossier
- *Note that this approach is particularly relevant for German patient representatives involved in any Early Dialogue in which the G-BA (the German agency) participates*

Approach 3 – Patient expert; Approach 1 + discussion with all participating HTABs regarding the submission file and participation in the F2F meeting with the Applicant

- Interview with the coordinator of the ED
- Face to face meeting
- Final review of the recommendation

Interviews are based on the HTAi patient group submission template, as this contains generalised questions that are still useful for the Early Dialogue timepoint. 10 out of 14 EUnetHTA Early Dialogues carried out through September 2019 have included contributions from patients following the above approaches. Patients involved in the process are given a clear understanding of the confidentiality agreement that they must sign as well as the EUnetHTA conflicts of interest form.

The feedback has been that patients appreciate the open question in an interview so that they can say what they want. Being able to see the summary of the interview is also important to them.

In a survey looking at the experience of seven patients who took part, some clear needs were identified:

- While most were happy with the information on the objectives of the Early Dialogue and what was expected from them, more training would be useful.
- Questionnaires need to have a glossary of definitions at the beginning so that the questions themselves are understandable
- Translation is important, and questionnaires (including any feedback questionnaires) need to be in the native language, and translators need to be provided for face to face meetings
- Access to the briefing book needs to be provided in more cases
- The final recommendations should be shared with patients

Other issues that have been highlighted during these EUnetHTA Early Dialogues is the amount of time taken to administer the patient involvement processes. Processing contracts, explaining the process, and translation of materials, questionnaires and summaries have all taken up scarce resources.

Another issue is that not all HTA agencies have the same conflict of interest rules, which can be challenging when looking for patients to take part across multiple countries, all governed by different conflict of interest rules.

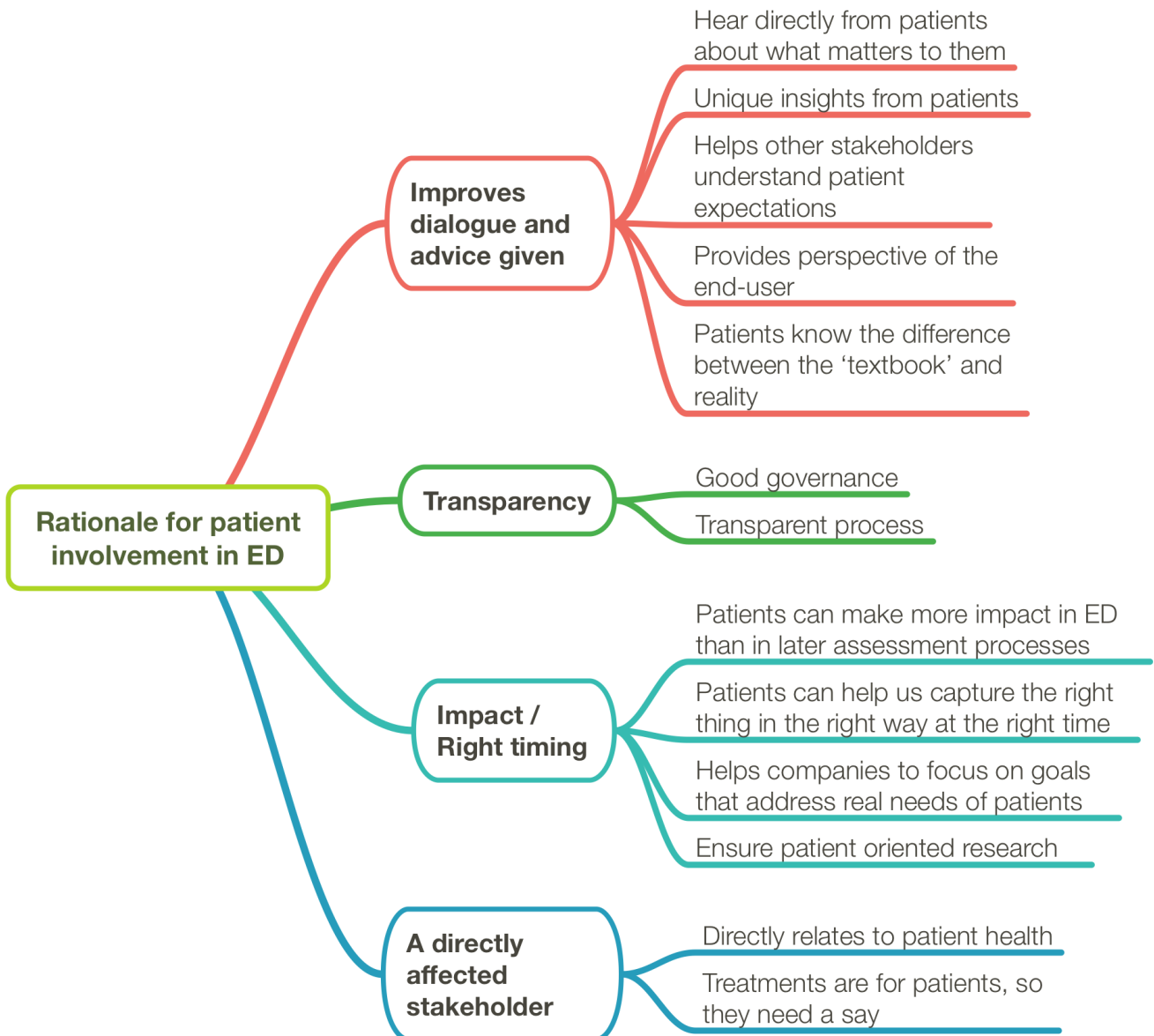
Finally, it would be useful if all companies taking part would be happy to share the briefing book with patients, but this is not always the case, meaning that in some processes the patients have less information than other stakeholders involved in the process.

4.2: Rationale for patient involvement and objections / challenges

4.2.1: Rationale for involving patients in Early Dialogues

HTA Agency attendees were asked to list all the advantages of patient involvement in Early Dialogues, the table below has been grouped into themes. Ultimately, the attendees agreed that the inclusion of patients in Early Dialogues improves the advice that is given to companies and thereby aids the decisions the company will make as they develop their program.

It was also highlighted that Early Dialogues is the right time for patients to input and to help shape the future development programs of companies, as well as creating a process that includes those directly affected by the potential therapies under consideration in the dialogue.



4.2.2: Objections and challenges to involving patients in early dialogues

When thinking about the reasons why patient involvement in Early Dialogues does not always happen, the attendees were asked to list objections they hear from others as well as the challenges that they see in implementing patient involvement in ED.



4.3: How patient involvement in Early Dialogues is currently achieved

In two breakout groups, the attendees were asked to consider the processes and methodologies currently used to gain the patient input into Early Dialogue processes.

4.3.1: Methodologies currently used, being tested or explored

The current methodologies that groups explored were:

- Interviews with individual patients / carers or patient representatives (1 or more interviewees)
- Involvement in Face to Face multi-stakeholder early dialogue meeting (a NICE process)
- Exploratory Research by HTA Agencies to Identify Patients' Insights

Interviews with individual patients / carers or patient representatives (1 or more interviewees)	
Why	<p>Provides specific feedback from affected patients and allows for open discussions in a semi-structured approach that highlight the experience, needs and expectations of patients around the issues outlined in the Briefing Book.</p> <p>The Early Dialogue team can pull out the relevant issues from the interview summaries to ensure they are incorporated at the right point within the advice given</p> <p>Allows for a flexible, semi-structured conversation that can be managed to ensure that key issues for input to the ED are obtained from the interviewee</p>
Recruitment	<p><u>Need a patient with relevant experience of the disease, not a patient advocate</u></p> <p>Need to identify very specific patient with the appropriate stage of disease and past treatment experience</p> <p>Can identify via patient groups, lay (public) members, social media, clinicians, patient portals</p> <p>Pre-screening of the individual to assess suitability and capabilities to be involved</p>
How	<p>Address confidentiality issues and ensure all consent forms, conflict of interest forms and contracts are understood</p> <p>Administer contracting process and provide guidance on expenses / honoraria process</p> <p>Directional interview to gain the perspectives and insights needed</p> <p>Patient Involvement team and Scientific Advice team work together to pull key items identified into a summary and identify areas that need to be discussed in the ED meeting</p> <p>Share summary with patients to amend or add new details</p> <p>Translate into English for use in the ED meeting</p> <p>(Ideally) Patients can review the draft report</p>

	<p>(Ideally) Document the impact of the patient involvement in this specific Early Dialogue</p> <p>Post- meeting (i.e. post F2F meeting with industry) interview to update on meeting discussions and to obtain feedback</p>
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Involvement in Face to Face multi-stakeholder (including industry) early dialogue meeting (a NICE process)	
Why	<p>Dynamic of the meeting changes when patients are included</p> <p>Allows to probe questions about what are the most important outcomes for patients, how, when and why to measure Quality of Life, sub-groups that have special needs</p> <p>Can clarify questions about the symptoms and treatment effects</p> <p>Allows emerging issues to be discussed and patient can emphasise the issues and aspects of the disease and its treatment that they feel are most important for others to understand</p> <p>Enhances transparency and legitimacy of the process where the patient insights can be further interrogated in the meeting</p>
Recruitment	<p>Only an individual who has been interviewed and signed all necessary contracts, conflict of interest forms, consent forms and confidentiality agreements may participate</p> <p>Explanation to the patient of any risks in taking part (for example, may not then be able to be involved in future engagements at the time of an assessment for this therapy)</p>
How	<p>Collaboration across the patient involvement and early dialogue teams within the agencies</p> <p>Pre-meeting interview conducted with patient is shared with all HTA partners in the ED process</p> <p>A clear process specified for timings on presentations for patient input</p> <p>Before the meeting, the chair speaks with patient and agrees where it will be most important that the patient contributes in the discussion</p> <p>A post-meeting evaluation conducted to assess the impact of the patient input</p>

Engagements with patients often happen prior to any meetings with the company.

At EUnetHTA for example, if the stakeholder is involved with the entire process, they not only have the phone interview, but they also participate in an e-meeting with participating HTA

bodies at the 'list of issues stage', approximately a month and a half prior to the F2F meeting with the company.

At NICE, a meeting is organised with the clinician and patient experts prior to the meeting with company.

At CADTH, the interview with the patient happens early in the process, ideally at the start of the project. CADTH also organises multiple calls with its clinical experts before CADTH meets with the company. The Face to Face meeting with the company happens later in the CADTH process than for some other agencies as CADTH use this meeting to present the draft advice.

Exploratory Research by HTA Agencies to Identify Patients' Insights	
Why	<p>Utilises systematic approaches used in other parts of HTA to understand patient issues</p> <p>Builds on the wealth of knowledge held in past patient group submissions to HTA bodies</p> <p>Does not require technical insights from the patients and reduces the burden on them</p>
How	<p>Using a variety of methods such as Rapid Qualitative Evidence Synthesis (QES), social media analysis, review of core outcome sets etc., HTA researchers could search for patient experiences and perspectives within a disease that answer questions raised in the ED Briefing Book</p> <p>Review previous patient group submissions on this disease, that have been provided by patients during the Health Technology Assessment of other treatments in this area</p> <p>Workshop convened with patients and patient group representatives to present the findings of above research to patients to find out what has changed, what is missing and discuss any issues not available in the literature</p>

4.3.2: An overview of the early dialogue process at NICE



4.3.3: An overview of the early dialogue process at EUnetHTA



4.4: Implementation challenges and resources needed to overcome them

Each breakout group were asked to consider the methods and approaches currently used or being piloted and highlight the critical challenges that have arisen in implementing these. After mapping out these challenges, each group were asked to identify tools or resources that could be applied to help overcome these challenges. Overall the group expressed the need to:

1. **Create consistency and predictability across patient involvement in ED processes**
2. **Have a menu of methodologies and approaches that could be applied**
3. **Set a minimum standard of patient involvement in Early Dialogues**

The challenges and resources needed are outlined below, along with any existing resources or tools that could be considered as a starting point for developing the future tools needed. A prioritisation exercise with all attendees was used to identify the themes and tools that should be prioritised for development within the PARADIGM project. The tables below are in the order of priority as defined during this exercise, with the priority areas being identified as:

- **PRIORITY 1:** Patient recruitment process (note: not patient advocates)
- **PRIORITY 2:** Patient interviews
- **JOINT PRIORITY 3:** Minimum standards framework
- **JOINT PRIORITY 3:** The rationale for patient involvement in Early Dialogues

Other resource needs were identified and are captured in the final table of this section.

Theme	Challenge	Tools/resources that are required	Identified existing tools to consider/adapt
Priority 1: Patient recruitment process	Difficulty finding a patient with the right profile and capabilities to take part (<i>not a patient advocate</i>)	Patient recruitment case studies for HTA showing how agencies have found the patients for their processes	GIN Public Toolkit
		Patient capability criteria guidance	NICE Hints & Tips Guidance
		Clear guidance for patients on what is expected of them	NICE brief guide for patients
		Pre-selection interview guidance and questionnaire	
	No clear guidance on vulnerable groups or on sensitive issues (such as end of life care)	Guidance on patient recruitment process and issues to consider	Liaise with the PARADIGM to identify tools that exist or are being created
	The administration process of recruitment, including the relevant forms, need to be clearly defined and standardised	Ethics guidance on the involvement of patients in Early Dialogues	HTAi Ethics Guidance /GDPR
Process to ensure confidentiality is maintained and conflicts of interest are transparent		NICE / CADTH consent process for interviews	

		Clear and transparent payment processes for honoraria and expenses (same as for HCPs)	NICE / CADTH / EUnetHTA processes
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Theme	Challenge	Needed tools/resources	Identified existing tools to consider/adapt
Priority 2: Patient interviews	No standard interview guidance exists across HTA agencies	Interview guide with prompts on how to conduct the interview as well as guidance on skills needed for interviewer	
		Standard questionnaires for patients with guidance on how to adapt for particular Early Dialogue topics and questions	CADTH / EUnetHTA questionnaires
	Interviews may have to be conducted in multiple languages	(Ideally) Translation services in the case of a European Early Dialogue (e.g. a EUnetHTA-type ED)	

Theme	Challenge	Needed tools/resources	Identified existing tools to consider/adapt
Joint Priority 3: Minimum standards framework	Many different approaches and methodologies are in use, but no framework exists to help determine which approach to use in particular circumstances	Framework of methods with guidance on the use of each method and the resource implications of each	
	No clear guidance exists across HTA bodies for the stakeholders involved in the Early Dialogues on patient involvement	Guidance for chairs of face to face meetings	GIN Public Toolkit
		Guidance for patients involved in the process	NICE Hints and Tips NICE brief guide for patients
	Face to face meetings may need adaptation to accommodate patients	What to consider for involving patients in face to face meetings guidance	NICE brief guide for patients
	Agencies not currently involving patients in Early Dialogues don't know where and how to start	How to start guidance as part of the overall minimum standards framework guidance	

Theme	Challenge	Needed tools/resources	Identified existing tools to consider/adapt
Joint Priority 3: The rationale for patient involvement in Early Dialogues	Not all stakeholders understand the rationale for why patients should be involved in Early Dialogues	Metrics to show that patient involvement improved the quality of the dialogue	
		Case studies that show the impact of patient involvement in Early Dialogues	
		Definition of Early Dialogues and the rationale for including patients	NICE brief guide for patients
	Not always clear what the purpose of Early Dialogues are at different points in the development pathway	A map of the development pathway with the purpose of Early Dialogues explained at each of the main timepoints	EUPATI diagram (Geissler et al.) Paradigm??

Theme	Needed tools/resources	Identified existing tools to consider/adapt
Other useful tools and resources identified	Development of an industry plain language summary of the Briefing Book	CADTH plain language template
	Training for HTA staff and committees on involving patients within Early Dialogue processes	
	Support for patients to participate in the process – general guidance, video interviews from all stakeholders involved on the experience and value of patient involvement in Early Dialogues, buddying etc.	

5: Next steps

At the end of the workshop, the attendees were asked to agree a series of next steps that would enable the creation of the prioritised resources and tools.

The attendees once again flagged that they would feel most comfortable if HTAi were to take the lead in developing these tools in partnership with them.

ACTION: PARADIGM to reallocate time for HTAi to work on Work Package 4, so there are sufficient resources for this to happen

The steps agreed at the workshop:

1. Summarise all tools needed in the meeting report (Done, see section 4.4)
2. Develop summaries of key themes prioritised to make clear the challenge that is being addressed and the goals of any resource or tool developed (Done, see section 4.4)
3. Establish a process and platform to confidentially share documentation among HTA agencies and those within HTAi working with them
4. Via a call to networks across HTAi and PARADIGM as well as any other relevant networks, collect example resources that could be considered as starting points for the tools that need to be developed
5. HTAi to work with HTA Agencies who attended the workshop to develop draft set of generic tools based on adapting what exists already, or creating new generic resources where needed
6. Host a face to face working meeting with the HTA Agencies at this workshop to refine, adapt and rewrite where necessary the generic tools created
7. Send the tools and resources out for consultation across stakeholder networks including HTAi and PARADIGM networks along with a call across PARADIGM to see if there exist methods for identification of patients with rare diseases across jurisdictions

Appendix A – Slides presented

Scientific Advice at NICE; rationale for patient involvement

Deborah Morrison, Senior Technical Advice, Scientific Advice

Heidi Livingstone, Senior Public Involvement Adviser

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Why we need the patient voice

MailOnline

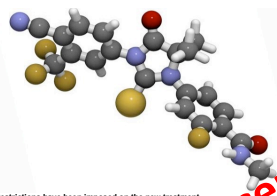
Another betrayal by the NHS watchdog
“betrayal”
 How can the NHS have come to this? What a breathtaking decision, callous even by its own standards, the Government's rationing watchdog NICE has said patients should be denied sight-saving drugs until they are blind in one eye...

NICE

THE ~~NEWS~~ TIMES

Health News

Prostate pill cuts death risk by a third



Restrictions have been imposed on the new treatment

Last updated at 12:01 AM, February 3 2014

A once-a-day pill for men with advanced prostate cancer cuts the risk of death by a third, "exciting" research has shown.

Experts said that, in a study of 1,500 men, enzalutamide allowed an average of 17 extra healthy months before the need for chemotherapy. It could soon become the standard choice for thousands of men with Britain's most common male cancer, if hormone treatments are approved.

The drug is available in Britain, but last week the NHS treatments adviser provoked anger from charities when it imposed unexpected restrictions.....

Prostate cancer drug decision a 'ouel twist'

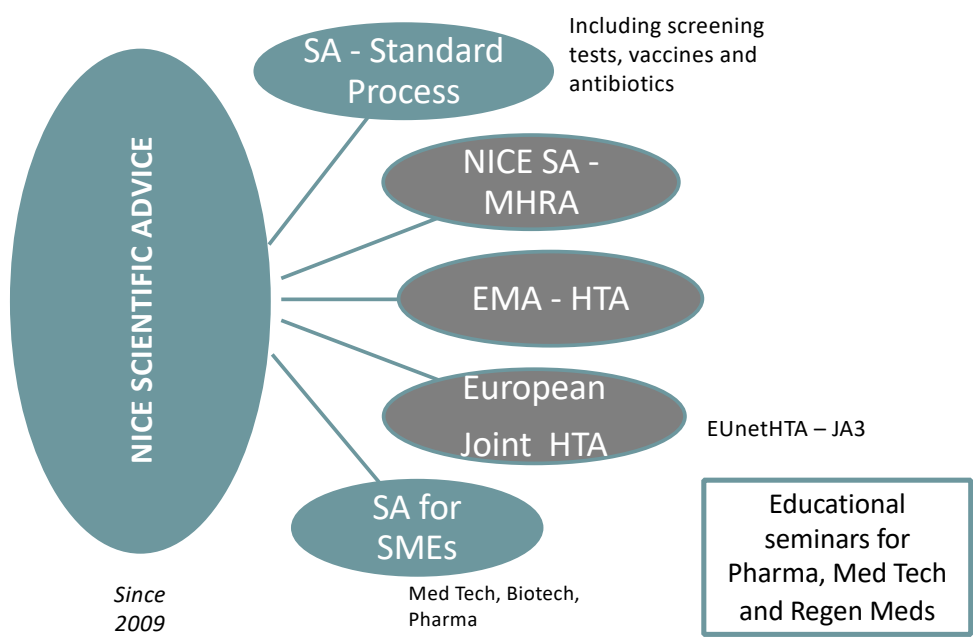
Why do companies seek NICE Scientific Advice?

A: to increase: the likelihood that the company's clinical development studies and other plans meet NICE evidence requirements

How does it help if patients participate in NICE Scientific Advice projects?

A: because it increases: the likelihood that the company's clinical development studies and other plans meet the needs of patients

NICE



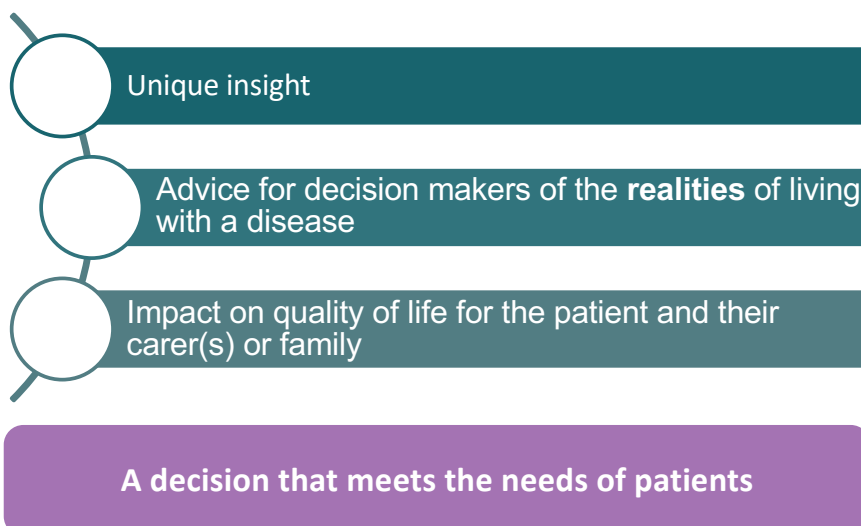
NICE

Scientific Advice Face to Face Meetings



NICE

What benefits do we all get from involving patients in the HTA Process?



NICE

Why do we involve patients in NICE Scientific Advice?

- They are the people for whom the advice that NICE Scientific advice provides will ultimately be most relevant
- So they have the chance to influence how clinical trials are set up in order to provide the best evidence that the proposed outcomes can meet patient's needs

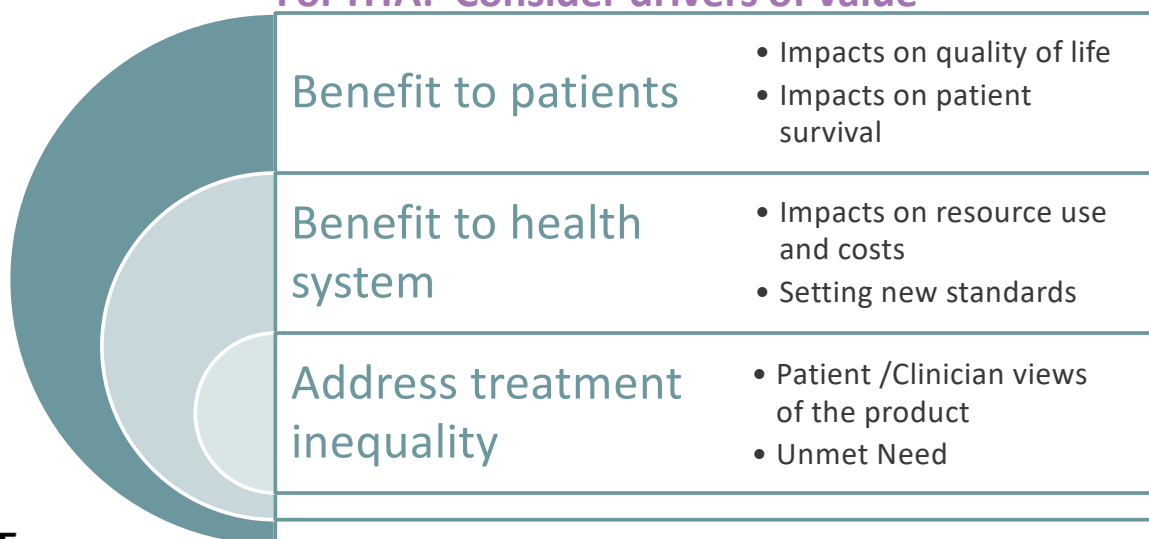
Companies get powerful feedback as to the relevance of their decisions early in a product's development

We have had very positive feedback from companies

NICE

What impact can patients have in HTA processes?

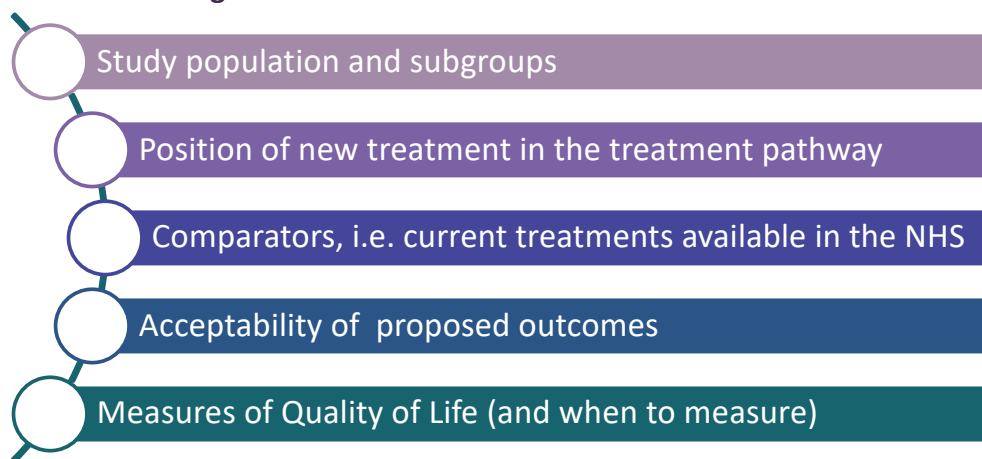
For HTA: Consider drivers of value



NICE

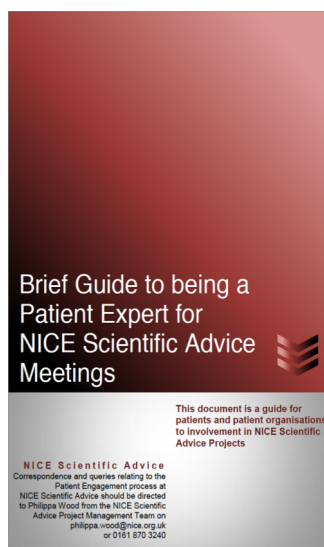
Typical Issues Raised for NICE Scientific Advice where patients can help.

Value Proposition Clinical Trial Programme



NICE

Guidance to help patients contribute to the NICE SA experience:



NICE

Including the Patient Perspective in CADTH's Scientific Advice Program

Michelle Mujoomdar – Director, Scientific Affairs

IMI PARADIGM Early Dialogues Workshop
19 Oct 2018

CADTH

Scientific Advice at CADTH

- Advice on early drug development plans from an HTA perspective, with emphasis on the Canadian setting
- Eligibility:
 - Prior to pivotal trials (Phase II or Phase III)
 - Excludes biosimilars, preventative vaccines, generic drugs
- Voluntary, non-binding, fee for service, cost-recovery program

CADTH Scientific Advice Team



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CADTH

Engaged as Experts

- Process developed with members CADTH Patient Community Liaison Forum
- Non-disclosure agreement & paid honoraria
- Use patient groups to find individual with:
 - Long-term experience with disease
 - Experience with multiple therapies
 - Aware of other's experiences - moderated a chat group, answered help lines, led patient group, etc.
- Recruitment is most challenging if we don't have an existing relationship with a relevant patient group

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CADTH

Ethical recruitment

- Recruitment and consent a multi-part process
- Plain language consent form (verbal or written), with risks and benefits developed
- Individuals reminded multiple times, they are in control of information shared and can stop or redact information
- Conflict of interest disclosure and confidentiality agreement also signed before interview

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CADTH

Including the Patient Perspective in Scientific Advice

- 1 hour interview
- Semi-structured questions tailored for disease area and advice sought by company
- Written summary of interview included in the record of scientific advice; accuracy confirmed by individual
- Individual insights supported or contrasted with relevant sections of patient input from past CADTH drug reviews

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CADTH

Including the Patient Perspective in Scientific Advice

- Individual patients (or carers) with the condition are invited to an interview:
 - *Patient journey from diagnosis, symptoms over time*
 - *Treatment experiences, challenges*
 - *Most significant health issues related to the condition that impact daily life*
 - *What is hoped for in a new treatment*
- Patient interview summary provided to the company and incorporated throughout the advice

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CADTH

Experience to Date

- Patient perspectives have been most important in the development of advice regarding outcomes and quality of life measures
- Valuable to illustrate the condition and treatment experiences to CADTH researchers, who have extensive expertise in trial methodology, but do not routinely interact with patients

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CADTH

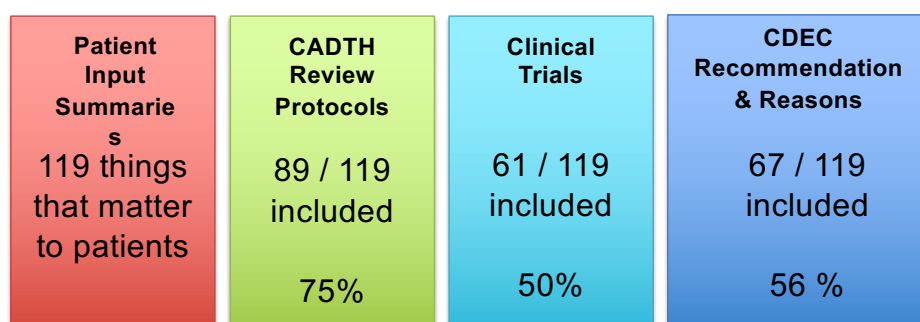
Why Does CADTH Include the Patient Perspective?

- HTA recommendations will ultimately affect patients for whom the technology is intended
- Only patients and their family/caregivers have
 - day-to-day lived experience with the disease or condition
 - direct experience with currently available treatments (if applicable) and possibly experience with the technology being reviewed
- Patients and their caregivers can provide **their perspectives** on the most important considerations and outcomes for a new technology

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CADTH

Use of Patient Input in CADTH CDR



CADTH

CADTH Evidence
Driven.

ACMTS Preuves
à l'appui.

22

HAS

HAUTE AUTORITÉ DE SANTÉ

Patient Involvement at HAS

Early Dialogues at HAS

- **Early scientific advice, not pre-submission advice**
- **Free for industry**
- **Access based on eligibility criteria**
- **Provide recommendations on pivotal trial (Phase 2B/3)**
- **3 month process**
- **Testing a « light » version**
- **~22 National EDs in 2018**

Early Dialogues at HAS

- **Patient role in *assessment* process is clear**
- **Contribution in *EDs* remains to be defined**
- **Lack of resources a significant barrier**

EUnetHTA WP5 – Principles on patient engagement



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- **Patient perspective essential for WP5:**
 - At the time forming the advice
 - Respect Conflict of Interest and Confidentiality rules

- Providing experiential knowledge of living with the condition and (available) treatment
 - Consider quality of life

- Advising on the signs and symptoms that have the greatest impact on their functional and psychological aspects of living

- Acceptability to participate in the proposed trial



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WP5

Patient engagement in Early Dialogues (ED)



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Testing 3 possible approaches

Approach	Patient contribution deliverables	Patient investment	Conflict of Interest and Confidentiality issues
Interview with Patient(s) (living with the condition) in local language collecting general feedback on the disease + answer to specific questions related to the dossier (Min: 2 countries)	<ul style="list-style-type: none"> - Minutes of the interview - Mention of patient contribution in final EUnetHTA recommendations - Feedback questionnaire 	~2 days of work	Low
Interview national Patient representative (living with the condition/carer) in local language collecting general feedback on the disease + patient representative position on applicant dossier	<ul style="list-style-type: none"> - Minutes of the interview - Mention of patient contribution in final EUnetHTA recommendations - Feedback questionnaire 	~5 days of work	High
Participation of EU patient representative (living with the condition/carer) to the overall ED process including interview with coordinator, F2F meeting, review final recommendation	<ul style="list-style-type: none"> - Minutes of the interview - Review final EUnetHTA recommendations - Feedback questionnaire 	~7 days of work	High



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Experience so far...

10/14 EUnetHTA EDs with patient contribution following the 3 approaches:

1. **6 interviews with patients**(France, UK, Spain)
2. **8 interviews with a national patient representative** (German patients' representative involved in any ED in which G-BA participates)
3. **4 EU patient representatives participating to overall ED process**

Method

An analysis based on feedback collected from 7 patients:

1. 5 patients (3 French, 1 Spanish and one English) (approach 1)
2. 1 German representative patient (approach 2)
3. 1 EU representative (approach 3)

Approach 1: Individual patient sharing its own disease experience with no access to Briefing Book (BB)

Approach 2: National Representative patient with access to BB

Approach 3: EU Representative patient with access to BB and participation to all the process (TC /F2F meetings and review final recommendation)

Preparation for the ED

Feedback	Proposal for improvement
<p>While 5/7 patients never received training</p> <ul style="list-style-type: none"> - Quite clear information in ED general objectives <ul style="list-style-type: none"> • 4/7 very satisfied • 2/7 mostly not; 1/7 not informed at all - Quite clear understanding of what is expected from them <ul style="list-style-type: none"> • 5/7 yes completely • 1/7 mostly not 	<ul style="list-style-type: none"> • Training: using different tools (EUPATI, national training tool...) and supports • A list of definitions at the beginning of the questionnaire

As a reminder, all patients have been contacted by a patients' organisation



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Interviews

Feedback	Proposal for improvement
<ul style="list-style-type: none"> - Positive feedback on the phone interview, and their overall interaction with EUnetHTA - Large use of the questionnaire to prepare the interview (5/7 used it) - Appreciate open questions with opportunity to develop topics at their convenience 	<p>Translation of the questionnaire in native language for HTAi questionnaire and feedback questionnaire</p>
<ul style="list-style-type: none"> - Patient had enough opportunities to express their opinion - Quite confident of the impact of their contribution 	
<p>Further access to Briefing Book and final recommendations requested</p>	<ul style="list-style-type: none"> • Briefing Book at disposal of interested individual patient? • List of Issue and Final recommendations to be shared Systematically with patients representatives



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Face-to-face meeting

Feedback	Proposal for improvement
<ul style="list-style-type: none"> • Interest in participating in F2F (because of the psychological impact of their physical presence) • Appreciate the opportunities for reactive statement 	<ul style="list-style-type: none"> • Participation to F2F meeting proposed to individual/national representative with simultaneous translation

Time investment and administrative tasks

Feedback	Proposal for improvement
Clear understanding of the confidentiality agreement	
No difficulties to complete the DOICU and contract documents	
Investment: minimum of half day to review the Briefing Book and only few hours to prepare the interview	
No major burden of administrative task but still possibilities for improvement	Clarify payment and exchanges via IT system