Mapping Tool to Understand Patient Engagement in HTA Submissions across Selected Neurological Conditions in Europe – Phase 1: Desk Research

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# 1 Background

Health technology assessment (HTA) is the “systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences”.

This is accomplished by evaluating health technologies for their clinical effectiveness, cost-effectiveness, safety, social and economic characteristics. The aim of HTA is to make evidence-based decisions about public funding of health technologies, for example, whether to place health technologies on national formularies. Health technologies include pharmaceuticals, diagnostic tests, medical devices and procedures.

When HTA was developed, 40 years ago, it was intended to assess all the implications of using a health technology, and explicit questions were developed for patients and families. These forms of HTA that study a range of impacts of a health technology (i.e., clinical and cost-effectiveness, safety, patient and social, legal and ethical aspects) are often called ‘full HTA’ or ‘comprehensive HTA’.

As HTA has evolved and been used to inform reimbursement and coverage decisions, comprehensive assessments are less common. In many jurisdictions, focus has been placed on clinical effectiveness and cost-effectiveness, allowing for HTAs to be conducted more efficiently and in larger numbers than comprehensive HTA allows.

Systematic research on patients’ perspectives and experiences has sometimes been replaced by processes to help patients participate in HTA. Research into patient perspectives and patient participation are complementary, and both serve as the basis for how patient involvement in HTA could be defined. Patient involvement is important because it allows for the identification of medical needs from the unique patient perspectives. Doing so supports the interpretation of the clinical evidence base and informs the value judgements that are inherent throughout the HTA process.

By “patient”, we refer to anyone who has direct experience of living with the condition being studied in the HTA or who may be eligible to receive the technology (e.g., specific members of the public who might be invited for vaccination or to undertake a diagnostic intervention). This can include individuals who have had or have the condition, informal caregivers (sometimes called “carers”) and voluntary groups that advocate for patients. The term “involvement”, although widely used, may be understood in different ways in different countries and alternative terms such as engagement,

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participation and empowerment may be used. According to the definition given by the HTAi Interest Group for Patient and Citizen Involvement in HTA, patient involvement in HTA encompasses 2 distinct, but complementary ways, in which HTAs could be strengthened by taking account of patients’ perspectives. That is, research into patient aspects (patients’ experiences, preferences, perspectives) and patient participation in the HTA process. This is also the definition we will use throughout this report.

There are 2 main sets of reasons for involving patients in HTA. The first set of reasons focuses on transparency, legitimacy and fairness in decision making. Patient participation is viewed as a means of enhancing trust in the HTA decision-making process and acceptance of the resulting decisions. As it is impossible to please everyone when making difficult reimbursement decisions, building trust and respect in the decision-making process is essential. A fair process for resource allocation requires transparency about the reasons underlying the decisions. Finally, the involvement in the decision-making process of those who are affected by the decision, is a basic democratic principle.

The second set of reasons relates to the patients’ evidentiary contributions. Patients are seen as contributors of valuable first-hand experiential knowledge of living with a particular health condition; they have experience with the health technology under assessment, or currently available technologies, the use of associated health services, and associated benefits, risks and side effects; and finally they have a clear view on what are their unmet needs. This is where the distinction between patients and the general public becomes clear, as it is only the patients and possibly their carers who have this personal knowledge and are able to provide this kind of information. Studies from the United Kingdom indicate that people with a chronic illness spend around 10 hours per year with health professionals; whereas, they spend 6,000 hours self-managing their condition. Illness, especially chronic illness, is one part of that person’s life and their families’ lives. In the real world,
the illness, as lived, may differ from the disease as described in the evidence-based guidelines and the outcomes measured in clinical trials.\textsuperscript{15}

The variation in HTA submission and evaluation processes between countries makes it complex to navigate for patients and/or patient groups. This may limit and discourage initiatives to engage in the HTA process and potentially impact their ability to have a meaningful impact on drug reimbursement decisions. Therefore, historically, patient involvement in HTA process and decision-making has not been extensive. However, such involvement is growing internationally with initiatives and projects providing insights both to patients and industry on how this could possibly be done effectively. Such initiatives include the PREFER (Patient PREFERences) project which aims to establish recommendations to support development of guidelines for industry, regulatory authorities, and HTA bodies on how and when to include patient perspectives on benefits and risks of medicinal products;\textsuperscript{16} the Patients Involved in National Institute of Clinical Excellence’s (PIN) (NICE) coalition of over 80 patient organisations, which is committed to enabling patient groups to engage productively with NICE;\textsuperscript{17} the European Patient’s Academy on Therapeutic Innovation (EUPATI) – project which aimed to develop educational material, training courses, and a public Internet library to educate patient representatives and the lay public about all processes involved in medicines development.\textsuperscript{18} In the year 2016, EUPATI published a guidance covering the patient involvement in HTA.\textsuperscript{19} Figure 1 and Figure 2 depict the suggested patient involvement activities for general HTA processes and for individual HTAs, respective, by EUPATI.\textsuperscript{19}

Figure 1 Suggested patient involvement activities for general HTA processes, according to the EUPATI\textsuperscript{19}
Figure 2 Suggested patient involvement activities for individual HTAs, by EUPATI19

1. Identifying & prioritizing
   - Allow patients to nominate health technologies for assessment.

2. Scoping
   - Invite patient organizations to comment on draft scope: via templates & at consultation meetings.

3. Assessing
   - Invite patients to nominate patient & clinical experts to attend HTA meetings.
   - Invite written submissions & personal (oral) testimony from patients.
   - Provide patients with easy-to-read document summaries, templates, written guidance, and telephone support.
   - Issue exit questionnaires to review patient involvement.

4. Reviewing & disseminating
   - Summarise how patient input was used in assessment, as part of HTA outcome report.
   - Provide easy-to-read versions of HTA outcome & invite patients to comment.
   - Establish system for patients to appeal HTA decisions.
In addition, the Patient Focused Medicines Development (PFMD) group, established in the year 2015, is an open, independent multinational coalition, based on expertise and commitment to develop and drive implementation of patient engagement (PE). PFMD’s overarching goal is to work with patients and other stakeholders to co-create and drive implementation of an integrated, efficient, measurable and robust meta-framework to deliver a consistent approach to patient involvement. In light of this goal, a mapping tool, i.e. a dynamic user-populated platform, has been developed that categorizes and ‘maps’ existing initiatives and frameworks to provide snapshot views of the patient engagement landscape through different stakeholder perspectives.

Lastly, on September 2016 the European Commission launched a new initiative that addresses the question whether and how to continue HTA cooperation at the European Union (EU) level beyond the year 2020. In this context, the Commission launched an open public consultation which ran from 21 October 2016 until 13 January 2017, aiming to gather detailed views and opinions regarding the future of the EU cooperation on HTA. The results of this HTA consultation confirmed the need for a sustainable EU collaboration on HTA beyond the year 2020, echoing the European Patients’ Forum’s (EPF) recommendations on stronger and deeper cooperation between European Member States.

Involving patients and patient organisations in the HTA process can prove to be challenging due to diverse and conflicting stakeholder interests. However, these challenges provide a window of opportunities for the patient community across Europe to rethink patient involvement in HTA. Some Member States already do involve patients in their HTA processes, while many others limit involvement to specific cases, or others do not do it at all, resulting in the absence of patients’ views when it comes to reimbursement decisions.

EPF suggests that EU-wide collaboration in HTA might look like opening the Pandora box because of this scattered landscape, but it could also lead to a much improved and efficient approach: local and national good practices exist and can be replicated, and tools are available to rethink and standardize principles of patient involvement across Europe.

**Neurological Disorders**

Neurological disorders are diseases of the brain, the spinal cord, the cranial nerves, the peripheral nerves, the nerve roots, the autonomous nervous system, the neuromuscular junction, and the muscles. They can be categorized according to either the primary location affected, the primary

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type of dysfunction involved, or the primary type of cause. The broadest division is between central nervous system (CNS) disorders and peripheral nervous system (PNS) disorders.

Neurological disorders result in several quality of life impacts for patients, their families, and healthcare systems. Fatigue is one of the most debilitating symptoms of several neurological disorders.25 Some conditions, such as multiple sclerosis, are associated with a number of other symptoms like depression, bowel and bladder dysfunction, weakness, impaired mobility, cognitive problems, and sexual dysfunction.26,27,28 These symptoms and others, such as pain and discomfort, have pronounced effects on a patient’s ability to take care of themselves, remain active, and stay employed29,30 and be productive at work.31 For patients with Alzheimer’s disease, memory loss and cognitive impairment are prominent symptoms that can lead to difficulty making decisions, alterations in behaviors, irritability, apathy, verbal and physical aggression, delusions and hallucinations. Oftentimes, Alzheimer’s disease is associated with family distress and financial losses.32 In many respects, the quality of life of caregivers is also a concern.33 Unlike cancer or cardiovascular diseases, neurological and pain conditions are not widely recognized and understood by the general population. This can lead to stigma that may prevent people from seeking help quickly, because of the possible negative social consequences.34

As a group, neurological disorders cause a much higher burden than digestive diseases, respiratory disease and malignant neoplasms.35 In Europe, disorders of the brain and mental disorders contribute to 26.6% of the total all-cause burden, corresponding to a greater proportion compared to other regions of the world. A report published in the year 2010 revealed, that the 4 most disabling single conditions were depression, dementias, alcohol use disorders, and stroke.36 Neurological disorders are the biggest economic challenge for European healthcare, costing €800 billion each

References

year, -6% of gross domestic product (GDP). Chronic pain may cost an additional 3% of GDP. The World Health Organisation (WHO) has calculated that the disability-adjusted life years (DALYs), from neurological diseases, will rise from a projected 95 million in the year 2015 to 103 million in the year 2030. The number of people living with dementia worldwide is estimated to reach 135.46 million in the year 2050. Despite significant advances in brain research in recent decades, many functions of the brain are still not fully understood. There is a high failure rate; only 8% of CNS drug candidates succeed compared to 15% in other disease areas. Moreover, clinical development time is one third longer than for other clinical areas and many companies specializing in drug development for neurological disorders are currently downsizing or closing their operations.

Research and funding for neurological research faces unique challenges that need to be addressed through integrated, coordinated, and co-operative efforts at the European and national levels. For example, the most impactful symptoms and markers of disease progression cannot be directly measured. Instead, they must be investigated by providing patients and their caregivers with opportunities to describe everyday life experiences with symptoms, everyday life impacts, the effectiveness of treatment, the management of side effects of treatment, the journey through treatment changes and the progression of their disease. Through qualitative interviews patients can provide invaluable insight on the frequency, the severity and the duration of symptoms and how they impact ability to work, to interact with friends and family, to care for themselves and their children, and to perform activities of daily living (e.g., household chores, bathing, dressing, and grooming). In addition, patients can inform researchers and medical professionals of the relative importance of certain symptoms and impacts compared to others, and the degree to which they are burdensome to cope with on a day-to-day basis.

37 EFNA. Book of Evidence. Available from: [link]
42 Lyles JS, Dwamena FC, Lein C, and Smith, RC. Evidence-based patient-centered interviewing. JCOM 2001; 8(7). Available at: [link] [Last accessed: August 2017].
Patient-reported outcome (PRO) measures, developed on the basis of patient input, can provide useful tools to measure patient experiences with disease and with treatment.\(^{46,47}\) However, for patients with neurological conditions such as dementia, the person caring for the patient during the day and during the night can provide additional essential testimonies about the difficulties experienced by patients. In this case, PROs cannot be used. Instead, observer-reported outcome (OBS-RO) measures can be useful but valid and reliable instruments are not always available.

Furthermore, many neurological disorders lead to long-term disabilities.\(^{34}\) For instance, in stroke patients, half of the patients surviving for 3 months after their stroke, will be alive 5 years later, and one third will survive for 10 years. Approximately 60% of survivors are expected to recover independence with self-care, and 75% are expected to walk independently. However, it is estimated that 20% of stroke patients will require institutional care. Many patients will at some point need assistance either by family, a close friend, or paid attendant. Long-term care and assistance for physical and psychosocial adjustment are also needed for other neurological disorders.

The European Federation of Neurological Associations (EFNA), a non-profit organisation which brings together several neurological patient advocacy groups, aims to help patients engage in HTA submissions and evaluations. In the year 2016, EFNA launched its Training Initiatives for Neurological Advocates (TINA). In an effort to meet its member organisations’ demand to equip patients with the knowledge and know-how to effectively participate in the generation of patient evidence and participate in HTA decision-making, EFNA has an interest in documenting current patient engagement systems and procedures, which are currently organised in European countries. The landscape assessment presented in this report focuses on patient engagement in 6 European countries: UK, France, Germany, Poland, Sweden, and Spain.

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2 Objectives

The objective of this report is to describe how HTA processes in Sweden, the United Kingdom, France, Germany, Poland and Spain currently take into account the patient perspective in the context of neurological disorders. More specifically, this research focuses on identifying the interactions of patients and groups advocating for neurological disorders with HTA agencies and the specificities of the submission and decision-making process that characterizes these interactions in each country.

2.1 Research Questions

To empower patient advocacy groups (PAGS), EFNA would like to conduct research that will help gain a better understanding of:

1. How are patients and PAGs allowed to interact with HTAs and what characterizes these interactions?
2. How do these interactions currently influence/impact HTA decisions?
3. How are PAG involvement perceived by HTA experts/PAGs? What could influence these perceptions?
4. How do interactions between PAGS and HTAs, the decision-making process, and perceptions regarding PAG/HTA interactions apply to neurological disorders?
3 Methodology

A targeted literature search was performed to identify sources of information on the involvement of patients in the HTA process in Sweden, UK, France, Germany, Poland and Spain. We reviewed bibliographic databases of life sciences and biomedical information and grey literature. The accessed sources are presented in Table 1.

Table 1 Sources

<table>
<thead>
<tr>
<th>Bibliographic databases</th>
<th>HTA websites</th>
</tr>
</thead>
<tbody>
<tr>
<td>ProQuest®</td>
<td>Sweden</td>
</tr>
<tr>
<td>MEDLINE®</td>
<td>Governmental HTA body: Tandvårds- och läkemedelsförmånsverket, (TLV) (non-governmental: Statens beredning för medicinsk och social utvärdering, SBU) Economic evaluations based on general guidelines issued by the TLV Center for Medical Technology Assessment (CMT)</td>
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<tr>
<td>Embase®</td>
<td>UK</td>
</tr>
<tr>
<td></td>
<td>Governmental HTA bodies: NICE (and National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre [NETSCC]) Economic evaluation requirements for medicinal products can be found on the website of the National Coordinating Centre for Health Technology Assessment (NCCHTA) as well as NETSCC</td>
</tr>
<tr>
<td></td>
<td>France</td>
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<tr>
<td></td>
<td>Governmental HTA body: Haute Autorité de Santé (HAS) No official HTA guidelines available; however, health economic evaluation methodologies were published by the HAS which are updated regularly</td>
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<tr>
<td></td>
<td>Germany</td>
</tr>
<tr>
<td></td>
<td>Governmental HTA agency: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, (IQWiG) Economic evaluations based on methods issued by the IQWiG (German only)</td>
</tr>
<tr>
<td></td>
<td>Poland</td>
</tr>
<tr>
<td></td>
<td>Governmental HTA body: Agency for Health Technology Assessment and Tariff System (Agencja Oceny Technologii Medycznych I Taryfikacji, AOTMiT) Economic evaluations based on guidelines issued by the AOTMiT</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
</tr>
<tr>
<td></td>
<td>Governmental HTA bodies: Instituto de Salud Carlos III (ISCIII) (national level) and various regional HTA agencies No official health economic guidelines available but recommendations on economic evaluation The Spanish Network for HTA: Agencias y Unidades de Evaluación de Tecnologías Sanitarias (AUnETS)</td>
</tr>
<tr>
<td></td>
<td>Regional HTA bodies in Spain</td>
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</tbody>
</table>
All the studies resulted from the search in the databases, were screened first based on their title and abstract. All studies identified as eligible during title/abstract screening were then screened at a full-text stage for their relevance to the research questions. The full-text studies identified at this stage were included for a top-line data extraction including citation details, study objective, country, and indication of which of the 4 research questions the information provided in the article can answer.

4 Results

This chapter describes the results of this review, by answering the research questions in 4 structured subchapters per country. When no information was found on specific topics, this is clearly stated. A summary of the findings per research topic and country is presented in the Table 2.
### Table 2 Overview of Responses to Research Questions

<table>
<thead>
<tr>
<th>Countries/ research topics</th>
<th>PAG/HTA interactions</th>
<th>Influence/impact on decisions</th>
<th>Perceptions</th>
<th>Specificities of neurological disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sweden</strong></td>
<td>Patient organisations participate in reference groups, working groups, consultants, reviewers, and through collaborations with government agency representatives. They are asked about their experience with disease and can submit qualitative reports. Dialogue forum with TLV. Role and ways of interacting with TLV is less clear.</td>
<td>Limited engagement due to company concerns for confidentiality prior to a decision being made. But more and more companies see added value. Only SBU allows patient-based evidence.</td>
<td>SBU is slow. 2-3 years for one project. No remuneration for working on projects. Laborious review process involves several new and old technologies. Questionable influence on the adoption of new policies.</td>
<td>Some projects have focused on neurological disorders but it is not clear to what extent specificities of these conditions are taken into account.</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td>Patient involvement is possible in all stages of NICE’s HTA. NICE’s Public Involvement Programme (PIP) (run by dedicated public involvement staff) provides direct support, resources and training to the patients and patient organisations who participate in NICE’s work. Patient participation across all HTA guidance types includes: submissions from patient organisations, participation in scoping, individuals attending committee meetings as patient experts, public consultation and an appeal process. NICE has at least two lay members as part of each decision-making committee, who bring a broad patient perspective to the committee’s decisions.</td>
<td>Patient experts impact on decisions by: Actively participating in the discussions for a specific health problem at the NICE Committee meeting and consideration of evidence; Contribution of evidence based on individual testimonies and experience; Providing clarifications and further insights; Consulting on draft recommendations; Commenting on factual inaccuracies in the final recommendations and lodging a formal legal appeal (if the appeal is upheld, then the appraisal will return to the relevant stage in the development process)</td>
<td>Patients: proper delineation of chairs’ and patient experts’ role in NICE approach is needed NICE: patient experts are invited to provide feedback on their experience being involved in NICE’s processes, for further improvement.</td>
<td>Case of Alzheimer Society’s engagement with HTA – Challenging outcomes commonly used in clinical trials but not meaningful for patients. NHS invite dementia patients for consultation about outcomes, which patients believe are core and any difficulties in completing these outcomes in disease-modification trials.</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>Since 2015, new initiative to include patients in review process with improved patient engagement through questionnaires and working groups.</td>
<td>Pilot initiative showed that patients do get involved and that patients’ contributions influence decisions. However, more time is needed to provide patient feedback.</td>
<td>Positive perceptions from the HAS and positive perceptions from patient groups.</td>
<td>There have been neurological projects but the process seems to apply to all conditions, regardless of neurological involvement.</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>4 appointed patient groups participate in committees, discussions, submit petitions,</td>
<td>G-BA is interested and there are resources to support patient engagement. However, volunteer work only. In addition,</td>
<td>Well-established system for patient engagement. However, lack of funding to patient</td>
<td>No information</td>
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<tr>
<th>Countries/ research topics</th>
<th>PAG/HTA interactions</th>
<th>Influence/impact on decisions</th>
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<th>Specificities of neurological disorders</th>
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<tr>
<td></td>
<td>complete questionnaires, and submit comments (IQWIG)</td>
<td>patients take part in discussions but can’t vote. Not all discussions are recorded.</td>
<td>advocacy groups makes it difficult to engage. G-BA decisions are increasingly scrutinized for evidence of patient involvement and consideration.</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>Patients interact with AOTMiT through patients’ organisations by completing relevant form/questionnaire provided by AOTMiT or providing orally their opinion at Transparency Council meetings. Public consultations in the process of assessment of reimbursement submissions are in place. Every citizen may pass her/his opinion, provided that she/he fills Declaration of Conflict of Interest, by completing the relevant template provided by AOTMiT. Under the process of analytical assessment, patients’ organisations that are relevant to the subject of assessment, are sought and asked for their opinions.</td>
<td>AOTMiT encourages the submission of any comments, suggestions and opinions regarding the performance/benefits of the product in question. AOTMiT highlights that they value the voice of the day-to-day patient care environment, expert setting of standards and new trends and the patient organisations in the process of assessment. However, there is no mechanism in place for measuring the impact of patient involvement on the decisions.</td>
<td>No information</td>
<td>Health policy program by Warsaw municipality: Activation of patients with neurological diseases</td>
</tr>
<tr>
<td>Spain</td>
<td>Even though the importance of patient involvement in HTA process has been acknowledged for years, patients have not been involved in any HTA process. Patient are currently involved in the in the development of Clinical Practice Guidelines (CPGs) and Shared Decision-Making tools (SDMTs). A methodological manual for patient involvement in the HTA is under development by AUnETS. It will be published end 2017- early 2018</td>
<td>No information found regarding patient engagement in actual reimbursement decision processes.</td>
<td>HTA agencies: lack of willingness and commitment to include users in the process; participation of users who are not sufficiently representative of the affected population. Patients: difficulty to accept/understand the scientific evidence; predominance of healthcare professionals in the composition of the working groups; All parties involved: lack of time; absence of effective strategies in the methods used. Spanish network of HTA (AUnETS): There is a short,</td>
<td>No information</td>
</tr>
<tr>
<td>Countries/ research topics</td>
<td>PAG/HTA interactions</td>
<td>Influence/impact on decisions</td>
<td>Perceptions</td>
<td>Specificities of neurological disorders</td>
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<td>mid- and long-term strategy plan for future action of patient involvement in HTA processes</td>
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**Abbreviations:** AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; AUnETS Agencias y Unidades de Evaluación de Tecnologías Sanitarias; CPGs: Clinical Practice Guidelines; G-BA: Gemeinsamer Bundesausschuss; HAS: Haute Autorité de Santé; HTA: Health Technology Assessment; IQWIG: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; NICE: National Institute of Health and Clinical Excellence; PIP: Public Involvement Programme; SBU: Statens beredning för medicinsk och social utvärdering; TLV: Tandvårds- och läkemedelsföröverk.
4.1 Sweden

Sweden’s history of using data to evaluate healthcare dates back to the 17th century. Throughout history, agencies and institutions in healthcare naturally included some forms of assessment of health practices, procedures, programs, and technologies. In the year 1955, the national health insurance program was put in effect. In the year 1958, specialized services, including hospitals with special units, were set in place in 7 regions of the country. However, the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) was founded in the year 1987.

![Diagram of Decision Makers and Decision-Making Processes in Sweden](https://www.ispor.org/HTARoadMaps/Sweden.asp)

Figure 3. Decision Makers and Decision-Making Processes Diagram in Sweden

The SBU is responsible for assessing healthcare interventions from the medical, economic, ethical and social perspectives. It now employs more than 40 full-time staff members and engages several hundred researchers, clinicians, managers, and policymakers throughout Sweden who are active in different aspects of its work. From the outset, the Government’s mandate for SBU included a concern about effective allocation and utilization of resources. Several projects question the value

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of certain technologies and aim to reevaluate the benefits of certain clinical practices. Overall, SBU can have a considerable impact on healthcare and its reports are disseminated worldwide.

One example of the SBU’s impact can be illustrated with research that showed that neuroleptics do not have a greater effect than placebo in patients with dementia and that instead, they may produce serious side effects. As a result, the prescription of neuroleptics in higher doses decreased almost immediately after the SBU report was published. This helped to improve the quality of care for elderly patients.\textsuperscript{52}

The Dental and Pharmaceutical Benefits Agency (TLV) determines whether a pharmaceutical product, medical device or dental care procedure will be subsidized by the state. It determines retail margins for pharmacies in Sweden, regulates the substitution of medicines at pharmacies and supervises certain areas of the pharmaceutical market. TLV has 2 decision-making boards that decide on pricing and reimbursement in the Swedish healthcare system, the Board for Pharmaceutical Benefits and the Board for Dental Benefits. The SBU is an independent national authority whereas the TLV is a central government agency.\textsuperscript{52} (Figure 3)

4.1.1 Interactions between PAGs and HTAs

\textit{Patient Perspectives in SBU}

There are many ways in which patients and patient organisations have contributed to SBU assessments. More specifically, patients can act as project members of reference groups and working groups, as consultants and reviewers, and through collaborations with government agency representatives.\textsuperscript{52}

Reference groups are made up of representatives from patient organisations and their families. In some instances, reference groups include other stakeholders as well. When an HTA project is initiated, a reference group is formed and all members meet regularly during all phases of the project. During these meetings, SBU representatives record the views of reference group members who are asked to evaluate the relevance and comprehensiveness of HTA project protocols. In follow-up meetings, patients are asked to share their experiences about the disease, review results and conclusions, and determine how they will be disseminated. Reference group processes are also evaluated. Patient representatives can also help develop report findings (e.g., literature reviews, qualitative research studies) and participate in media events. Patient perspectives are also valued on projects involving health professionals and specialists by describing their personal disease experience and interpreting the relevance and appropriateness of measurement scales.\textsuperscript{52}

On some projects, patient representatives are asked to participate as consultants only. In these instances, patients are asked to provide comments on protocols and draft findings, without necessarily contributing to the dissemination activities throughout the lifecycle of a project.\textsuperscript{52}

In the year 2012, discussions that took place during a conference led to a need for greater patient involvement. As a result, a patient representative has now been appointed to the SBU board of directors.

Moreover, SBU provides opportunities for patients to submit patient-driven evidence in the form of qualitative reports. These reports focus on how people perceive and experience a condition, their health, their quality of life and/or their care or support. Reports are evaluated for the quality of the evidence and methods based on SBU guidelines provided in the SBU Handbook on the Assessment of Methods in Healthcare (SBU \textit{2014}; Chap. 8). Included in this evaluation is scrutiny of how the patient/client or their relatives perceive various aspects of care, such as experiences of undergoing treatment or diagnosis, experiences of receiving different interventions, or of living with different conditions. Therefore, the focus here is on qualitative research, with special reference to perceptions of patient/clients.\textsuperscript{53}

\textit{Patient Perspectives in TLV}

Since its creation in the year 2002, TLV has undertaken initiatives to support patient participation. Both the Board for Pharmaceutical Benefits and the Board for Dental Benefits have government-appointed representatives from patient and consumer organisations. Patient and consumer organisation representatives are also asked to contribute to the TLV advisory council. In all cases, patient and consumer representatives are appointed by the government. Finally, patients and consumers can be members of a reference group that the TLV has designated for consultation on multi-year long-term development projects.\textsuperscript{52}

Patients and consumers can also take part in informal discussions that occur several times a year through a dialogue forum. Each forum follows a pre-established program that addresses ongoing strategic development projects at TLV and current trends and challenges in healthcare. Patient organisations that participate in the forum must meet certain criteria such as being a formally established organisation, being of a certain size, being active in several areas of society, being democratically structured, and being politically and religiously independent.\textsuperscript{52} It is important to note, however, that the TLV website does not include descriptions nor does it include examples of the role(s) that patients play in TLV discussions.\textsuperscript{54}

4.1.2 Influence of PAGs on HTA Decisions

The TLV makes important decisions about the cost-effectiveness and budget impact of medicines. For this reason, consultations with patient representatives help ascertain that the patient voice is taken into consideration throughout the decision-making process. Nevertheless, dialogue with

\textsuperscript{53} SBU. Evaluation and synthesis of studies using qualitative methods of analysis. Stockholm: Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU); 2016.

patients about ongoing reimbursement decisions has been limited by companies’ right for information to remain confidential, before a TLV decision is reached. More recently, increasing interest in gaining patient perspectives to provide added value that supports products during submissions, has pushed some companies to waive their rights to confidentiality, allowing TLV to share information with patient representatives. Furthermore, when TLV initiates reviews of medicines that are already in the reimbursement system, patients can be consulted to provide their perspectives about their experiences with treatment and have an impact on TLV decisions. Patients can also share their views on hospital medicines and medical devices, and have an impact on TLV decisions.

Despite opportunities for TLV to consult with patients, only SBU allows patient-based evidence to be part of an HTA. Farley reports that the increased involvement of patients is needed to improve the quality of HTAs and the quality of guidelines. One way to improve patient engagement would be to provide compensation to patients since currently, only clinical experts are being compensated for their involvement in TLV HTAs.

4.1.3 Perceptions of PAG/HTA Interactions

Werko and Andersson describe that TLV believes that patient participation during HTA of medicines and consumables, as well as hospital medicines and medical devices, will help mutual information sharing and increase the quality of decisions or recommendations. TLV aims to obtain information from patients about, for example, the need for several medicines of a certain type or why a certain product or formulation is preferred by a specific patient group. Such information can be considered in the HTA and the final decision or recommendation.

However, SBU has paid relatively little attention to issues that are of great concern to the general public, namely waiting times, and to issues of access to care. More specifically, certain projects take up to 2-3 years to complete and SBU does not remunerate people for working on its projects. In addition, processes are viewed as inefficient since several HTAs on new and old technologies are assessed at the same time and all aspects are considered (prevention, diagnosis, and treatment) during the assessment process. Some have also criticized that SBU is not as impactful as it used to be and that research findings are slow to influence the adoption of new policies.

4.1.4 Particularities of Neurological Disorders

Werko and Anderson describes several SBU and TLV initiatives that appear to be specific to neurological disorders. Examples are given of patients contributing to reference groups and projects on attention deficit hyperactivity disorder, autism spectrum disorders, assessments in psychiatry that occurred between the years 2009 and 2013, the investigation of methods to prevent mental health problems in children, psychosis and schizophrenia, and the prevention of self-injurious behaviors. This initiative was named the PRIO project. The National Board of Health and Welfare (NBHW) developed and tested a model for patient and relative engagement in mental health which has been pilot tested in the year 2015. More recently, the Government Healthcare Agencies Collaboration has been focusing on mental health in elderly patients. Currently, an ongoing project focuses on an evaluation of the sensitivity and specificity of the Patient Health Questionnaire-9 used
for depression screening in adults. This and other projects are posted on the SBU website (http://www.sbu.se/en/ongoing-projects/).

Based on Werko and Andersson’s\textsuperscript{52} descriptions, patient representatives and consumers have genuine opportunities to provide patient insight on disease experiences, to formulate questions and evaluate protocols, to assess outcomes, and to participate in the preparation of reports and other means of disseminating results. They report that these HTA/patient representative interactions are leading to changes in the implementation of services (e.g., mental health services for the elderly) and have an impact on decisions. However, it is not clear to what extent interactions with patients and other stakeholders are informed by the specificities of neurological disorders. Criticism regarding the lengthy SBU review process and the current tendency to perform broad and multifaceted assessments of health concerns\textsuperscript{50} does not favor a specialized approach to any disease area, including neurological disorders.

4.2 United Kingdom

The United Kingdom of Great Britain and Northern Ireland (UK) is comprised of 4 countries: England, Scotland, Wales, and Northern Ireland.

NICE is the HTA and advisory body in the healthcare system of UK. Key activities of NICE include the provision of pharmacoeconomic guidance, the set of quality standards and management of a national medicinal products database. NICE carries out cost-effectiveness evaluations for new pharmaceuticals and medical devices that are submitted for inclusion in the national formulary. For the execution of assessments, NICE collaborates with the National Institute for Health Research (NIHR).

NICE has a policy defining its approach for involving patients and carers in its decision-making.\textsuperscript{55} NICE’s Public Involvement Programme\textsuperscript{56} provides support, resources, and training to the patients and patient organisations who take part in NICE’s procedures.

The following sections present NICE’s approach to patient engagement in the development of HTA guidance. This includes participation in the scoping process, submission of evidence from the patient organisations, attendance of committee meetings by individuals as patient experts, public consultation and a process of appeal. Each decision-making committee within NICE includes at least 2 lay members (roles described below). Additionally, the resources provided by NICE to support patient engagement including public involvement staff, training, templates, and written support resources are also presented in this section.


4.2.1 Interactions between PAGs and HTAs

NICE provides support and advises on patient and public involvement across all its work programmes, through a dedicated team, the Public Involvement Programme (PIP). The PIP consists of 4 members working on HTAs. The PIP’s responsibilities include identification, training, and support of the lay people and organisations involved in each part of guidance. Their work is supported by NICE’s public involvement policy\(^{57}\) and its core principles as defined in its Charter.\(^{58}\)

The PIP provides written materials to support patient organisations and individuals to participate.\(^{59}\) In addition, the team assesses NICE’s engagement approaches aiming to improve their quality.

Independent advisory committees develop all NICE HTA guidance. Patient involvement in these procedures aims to include people’s unique perspectives on living with and being treated for their condition or disability. The committees provide recommendations across a wide range of clinical topics, and 2 members of each committee are lay people. Lay people are not patients, but they contribute in patient involvement processes by bringing a broad patient perspective to the committee’s decision-making. All stages of NICE HTAs process have opportunities for participation:

- Scoping process
- Evidence collection
- Committee consideration
- Consultation
- Appeal or resolution
- Publication
- Review

Figure 3 The NICE technology appraisal process—stages of patient involvement

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presents the NICE process for medicines’ HTAs and the opportunities for patient participation at each stage. NICE makes a distinction between lay members, patient experts, and patient organisations and their role in HTA processes.
Figure 3 The NICE technology appraisal process—stages of patient involvement

**Identification of Patient Organisations**

The PIP contacts organisations that have not been involved in a NICE appraisal before and explains the role of NICE, how the patient organisation can participate and offers support as needed. The PIP team identifies relevant patient organisations through the Internet, the Charity Commission (which provides registry of non-profit organisations with charitable purposes), and internal databases. For the organisations who wish to participate, the PIP team provides support materials at the relevant stages of the process, an introductory meeting and training session.

**Scoping process**

The topic under consideration is scoped using the PICO framework. Patient organisations are invited to comment on a draft scope document and to follow a workshop. They are asked to provide insights on the following key aspects:

- Outcomes of importance to patients
- Quality of life issues which may not be captured by conventional measures
- Tolerability and acceptability of the new medicine compared to treatment currently available

Upon finalization of the scope, the Department of Health decides on the reference of the topic to NICE for appraisal.

**Input from Patient Organisations**

Patient organisations identified during scoping are invited to submit input for consideration by the committee as part of its decision-making. Each organisation may produce an individual submission, or they may collaborate on a joint submission.

A template structure supports patient organisations in submitting key information. The evidence submissions from all stakeholders are published as part of the evidence at the consultation stage of the process (see below).

**Input from Individual Patients**

Organisations are asked to nominate people to attend the committee meeting to give testimony and to answer questions from a patient or clinical perspective. These ‘experts’ are also invited to provide a personal written statement (using a template) but do not take part in the committee’s

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**Note 1** – PICO framework: Population (who should be treated), Intervention (technical specification of health technologies under study, how they will be given), Comparator (health technologies currently used in the health service), Outcome (what outcomes/impacts are important).
decision-making processes. These statements are published together with the other submitted evidence.

Experts attend the committee meeting as individuals rather than as representatives of any organisation. The committee chair selects 2 patient experts from the nominations received. Ideally 1 of the experts will be someone with the condition relevant to the treatment being appraised, preferably someone using the new treatment. They provide an in-depth perspective on their individual experience. The other expert usually works or volunteers for a patient organisation and is able to offer the perspectives of a broad range of patients with the condition and their carers.

The patient experts give the committee a unique insight into what it is like to live with a condition and its impact on their life, their family and their ability to work. In addition, they provide insight to the benefits, risks, tolerability, side effects and ease of use of the medicine. The outcomes patients consider to be important may also differ from the clinical outcomes measured in the clinical trials and those incorporated into the cost-effectiveness evidence.

Patient experts are offered a payment for their attendance, as well as reimbursement of their expenses.

The NICE’s PIP has written a guide for patient experts, which explains what happens before, during and after a committee meeting, and outlines the experts’ role. Patient experts can speak to someone from the PIP to ask any questions they may have and clarify what will happen at the meeting. A member of the PIP meets the patient experts before the meeting starts, and provides support as needed. The committee chair and the lay members play a key role in ensuring the patient experts feel relaxed and confident about participating in the meeting. To support this, 1 of the lay members will usually sit next to the patient experts during the meeting.

4.2.2 Influence of PAGs on HTA Decisions

Committee Considerations

There are 2 NICE committee meetings taking place sequentially: the public and the confidential meeting. The patient experts, clinical experts and the pharmaceutical company’s representatives are invited to attend the public meeting. This meeting is also open to public members. During this meeting, the clinical, cost-effectiveness and patient issues are discussed in detail. Following the public meeting, only the committee members and NICE staff remain in the meeting, confidential information (academic or commercial) is discussed, and the initial recommendations are drafted.

The Role of the Committee’s Lay Members

Two lay members participate in each committee and have equal status to the other members. The lay members bring a broad patient perspective to the decision-making of the committee. Their role

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is to ensure that patient’s issues are heard and reflected in the committee’s decision-making. One lay member is responsible for summarizing and presenting the relevant patient evidence. Likewise, the other committee members are responsible for the clinical and economic evidence.

**Assessment of the Evidence**

The committee discusses all the available evidence related to the medicine under consideration, including formal published research (both qualitative and quantitative), economic modelling, expert submissions and commentary, and individual testimony and experience. The committee requests from the clinical experts, the patient experts and the pharmaceutical company to provide their insights and clarifications on any issues of uncertainty. The experts can participate in the discussions and answer the committee’s questions, without being asked to give a presentation. The committee always asks the patient experts if they have anything further to share before the end of the meeting, to ensure that issues of importance to them are not overlooked.

**Consulting on Draft Recommendations**

The committee’s provisional recommendations are sent in confidence to stakeholders and patient experts, who have 4 weeks to comment. After a week, the draft recommendations are published on the NICE website for a 3-week public consultation period to seek views on whether the evidence considered have been properly interpreted. The patient organisations or patients who were not invited to the NICE committee meeting, have the opportunity to comment on the recommendations during this consultation period.

Patient organisations are encouraged to comment on the draft recommendations whether they agree or disagree with the content. They can comment on the extent to which the recommendations have taken into account the evidence related to patient’s perspectives. In the case of lack of evidence, patient organisations can conduct research during the consultation period to inform their response.

**Considering the Consultation Responses**

The committee meets after the consultation period to discuss the submitted comments. Patients and clinical experts are invited to this meeting, only if significant new evidence has been submitted or in case the committee has questions for the experts.

**Final Recommendations**

Following the second meeting, stakeholder and experts are sent the final recommendations in confidence. Additionally, the committee shares information on:

- How the committee considered information provided by patient organisations and the patient experts
- Any comments received during the consultation period
- NICE’s responses to these comments

The final recommendations are published on the NICE website 1 week later.
**Appeal**

In the case of factual inaccuracies in the final recommendations, the stakeholder organisations can provide comments and lodge a formal legal appeal\(^\text{65}\) on 1 or both of the following grounds:

- That whilst developing the recommendations, NICE has failed to act fairly or that NICE has exceeded its powers
- The recommendations are unreasonable in the light of the evidence submitted

The appeals are heard in public in front of a panel\(^\text{66}\) consisting of 5 members including a lay person. The appeal panel cannot modify the recommendations. However, if any of the appeal grounds are upheld, then the appraisal will return to the relevant phase of the development process.\(^\text{67}\)

**Publication**

If no appeal is received, or if the grounds for appeal are not valid, the recommendations are published on the NICE website as formal guidance to the NHS. The evidence and submissions obtained throughout the process are published alongside the guidance (HTA report).

Each appraisal is also published in a plain language version. This version includes information on:

- What the guidance means for the patients
- An explanation of why NICE made the recommendation
- A link to a website called NHS Choices\(^\text{68}\) providing more information about the condition
- Contact information for relevant patient organisations to provide more information and support

**Review**

In a period between 2 to 4 years after the guidance has been published, relevant clinical and cost-effectiveness evidence is reviewed.\(^\text{69}\) NICE consults with stakeholders and patient organisations on whether there are new evidence and the recommendations need to be updated.

4.2.3 Perceptions of PAG/HTA Interactions

In the year the year 2012, NICE conducted a formal evaluation of the patient expert’s experiences participating in NICE’s technology appraisals process. The evaluation seek to explore the impact

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patient experts believed they had made to NICE’s decision-making. This exercise resulted in useful practical suggestions for improvement of the approach followed by NICE. The suggestions include: chairs to formally introduce themselves to the experts; introduce the role of the experts for the benefit of the public gallery; and clarify the difference between the lay members and the patient experts. These suggestions have then been incorporated as part of the action plan. Furthermore, patient experts are currently routinely asked to record their experiences of working with NICE to support continuous quality improvement. This is part of a wider plan to systematically gather data on experience and impact from all lay people working with NICE. As part of this approach, all lay members leaving any of the HTA committees fill an exit questionnaire which provides input for three-monthly reports with recommendations for improvements.

4.2.4 Particularities of Neurological Disorders

In the case of the Alzheimer’s Society (AS) - the leading patient organisation for people living with dementia and their carers in England and Wales - their journey to engage in health policy making, as described by Moreira, is used here to illustrate the processes by which patients are involved in public issues around health technologies and the interactions between PAGs and HTA.

Moreira identified 3 phases in the history of the AS’s engagement with HTA:

- In the first period, the AS established its identity around ‘caring knowledge’ by drawing on its volunteer membership, links with clinical specialists and support from the State
- In a transition stage, the AS re-considered its identity as a combination of experiential, clinical and scientific knowledge to redraw its relationship with volunteers and to expand its field of activism into HTA
- In the most recent phase, the AS deepened and expanded its network of associations to secure its role in the production of evidence that is used in health policy making

Between the years 2005 and 2007, the AS was involved in a major public controversy over access to dementia drugs on the National Health Service (NHS). The controversy began when NICE suggested in the year 2005, that dementia drugs be taken off NHS prescription packages, based on their cost-effectiveness value. The AS raised concerns of the uncertainty of quality-of-life measurements in dementia, that underpinned that evaluation and criticized NICE’s focus on positive changes in cognitive scores as outcome measures.

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The AS designed and conducted its own ‘research in the wild’\textsuperscript{74} in the form of a survey of their members, based on which they argued that it was the maintenance of abilities and quality of life rather than cognitive improvement that patients and carers valued.

In parallel with their engagement with NICE, the AS mobilized to form a public campaign on the issue – The Action of Alzheimer’s Drugs Alliance – which comprised a set of variant institutions including Royal Colleges, universities, academic institutions, and clinical centers.

In October 2005, Members of Parliament (MPs) from all parties passed an early motion in the House of Commons in which they ‘agree[d] with the Action on Alzheimer’s Drugs Alliance that effective drug treatments for Alzheimer’s disease should be available on the NHS and that NICE has failed to consider the important concerns [. . .] about its draft guidance’.

In view of this, NICE ordered a recalculatation of the available data and on January 2006, published a new recommendation that cholinesterase inhibitors should be available for patients with moderate dementia only. Nevertheless, they had still not considered the issue of quality-of-life measurement, which motivated the AS to join clinicians, researchers, and manufacturers in appealing the decision. The appeals were rejected, and clinicians withdrew from the coalition of challengers, leaving the AS to join the judicial review put forward by manufacturers. It was publicly suggested that, by challenging NICE’s methodology through the courts, the AS undermined the regulator’s public legitimacy in favour of commercial agendas.

In response to these losses and charges, the AS aimed to redefine its public identity by setting the agenda on the national dementia strategy. This took the form of developing a series of expert reports on the current and future state of dementia care, through the ‘Putting Care Right’ campaign (Years 2007–12). The start of the campaign was marked by the publication of the Dementia UK 2007 Report, where the AS sponsored experts from the London School of Economics (LSE) and the University of Kent to perform an assessment of the prevalence and economic cost of several types of dementia, and of levels of care provision across the country. This exercise not only included AS in the scientific effort to produce accurate estimates of the prevalence of dementia, but also, and importantly, endorsed the organisation’s capacity to speak for a group with specific needs in health care.

Well-connected with institutions of political representation (i.e., Committees of the House of Commons and Lords), the AS combined this political capital with the scientific authority of the report to be included in the negotiations that led to the establishment of the National Dementia Strategy in 2009.\textsuperscript{75} Combining formal participation in these forums with public activism, the AS initiated an assessment and critique of the state of dementia care in the UK through a series of campaign and lobbying actions, focusing on care homes (in the year 2008), hospitals (in the year 2009) and community settings (in the year 2011).

All campaigns were supported by reports using in-house quantitative research and a collection of subjective experiences from patients and carers. The use of systematic reviewing and research

\textsuperscript{74} Callon M, Rabeharisoa V. Research, “in the wild” and the shaping of new social identities. Technology in Society, 2003; 25: 193–204.
methodologies aimed to support the AS to speak for ‘systemic issues’ in the organisation of dementia care, such as the lack of specialized dementia care training and time-based tasking in care homes. Equally important was AS’ use of patients’ experiences of the issues. This exemplifies how the quantification of factors leading to institutional failure gains relevance and depth when paired with examples of personal experience.

The AS attributed the weakness of their arguments against NICE to the lack of methodological sophistication with which they had depicted the views of their members. Therefore, from the year 2008 and onwards, the AS linked with social scientists and other charities to produce, first a report on the diagnosis and management of dementia from the perspective of patients and then, 2 pieces of research about the issue of measurement of quality of life in dementia. The first was a literature review conducted by experts at the University of Kent, which identified an undue focus on health-related quality of life indicators in dementia research, particularly on cognition, and advocated the development of hybrid quality of life indicators that combine ‘objective’ with ‘subjective’ domains of well-being.76

Such expert endorsement of the position of the AS, in relation to the use of quality-of-life measurement in HTA was complemented by mixed methods research used to gather the views of rarely heard groups in quality of life in dementia research.77 The AS suggested that the research showed that ‘people with dementia, even those with more severe dementia, do not automatically find their lives dominated by the condition itself and the impact that it has on their mental functioning’.77 This challenged the assumptions of standardized quality-of-life measurement and academic quality of life research in dementia.73 The AS’ strategy was to publicly disclose key uncertainties in research on quality of life in dementia78 and to the pursuit of a transformation of this field of research by aligning itself with a network of research and policy actors. This not only strengthened the AS’ place on the collective negotiation about research policy in dementia in the UK from the year 2010 and onwards (through its membership of the Ministerial Advisory Board Group on Dementia Research), but also enabled it to influence the attention given to ‘hybrid’ quality-of-life indicators within that forum and in the programme of dementia research sponsored by the NIHR.

The AS’ case suggests that it is possible for patient organisations to have an impact on the HTAs by challenging outcomes commonly used in clinical trials that are not meaningful for patients. The AS publicly exposed core uncertainties in the measurement of quality of life in dementia and actively shaped the HTA research agenda on this issue. By explicitly investigating, together with experts, through a variety of methodologies, the role of ‘experience’ in quality of life measurement, the AS transformed it into a matter of collective enquiry. In other words, experiential knowledge became a part of the question to be investigated, rather than simply the answer to the issue of patient involvement in HTA.

77 Williamson T. My Name is Not Dementia: People With Dementia Discuss Quality of Life. Alzheimer’s Society, Location: Alzheimer’s Society, 2010.
Another initiative of patient involvement in dementia research, maybe linked to the AS case, and related policy making was recently published by NHS.⁷⁹

People living with dementia can currently only be offered management to improve their symptoms as no disease-modifying treatments are available, that would stop or delay the progression of the underlying disease pathology.⁷⁹ The first G8 Dementia Summit⁸⁰ in the year 2013 committed to find a disease-modifying treatment by the year 2025.⁷⁹ If a treatment was found to slow disease progression of mild to moderate dementia, then this would reduce the number of people living with severe dementia in the future.

However, across both published and ongoing disease-modification trials there is large variation in the outcomes used as endpoints, making it difficult to compare and contrast results.⁷⁹ To improve future disease modification trials there is a need for harmonisation among the outcomes measured, as well as for outcomes to be appropriate, sensitive to change and clinically meaningful.⁸¹,⁸²,⁸³ An example is the case of AS seen previously, who argued that it was the maintenance of abilities and quality of life rather than cognitive improvement that patients and carers valued. An agreed-upon core set of the best-available outcomes would enhance interpretation of data across trials. There is, therefore, a need for consensus from NIHR dementia researchers in the UK on a core set of outcome measures to be used across future disease modification trials in mild to moderate dementia. This will ensure that new trials can be combined in systematic reviews and contrasted as to their effectiveness.

To that end, NHS sought the voice of people living with dementia to consult them about overlapping core outcome sets that had been, or were currently being, developed and the outcomes found in systematic review of the literature. Specifically, they conducted 3 focus groups in Cambridge, London, and Sheffield, in partnership with the AS’ volunteer research network; consulting with people living with dementia and family carers about the acceptability of outcomes, which they felt were core and any difficulties in completing outcomes.

They conducted an e-mail consultation with focus group participants afterwards on a report of the main recommendations from across the 3 groups, to allow participants to comment on domains they had not discussed and to make sure the recommendations to be presented at the conference represented what had been said across the groups.

After the consultation, a conference was held, where the synthesis of acquired information was debated by a wider body of NIHR dementia researchers to reach consensus on a core set of outcomes. Twenty-seven people attended the conference from a wide range of specialties within dementia research. The conference began with an overview of the project, the systematic review

results and recommendations from the focus group consultations. Experts within each of the domains were asked to synthesize the results of the systematic review and validation data, to present recommendations for that domain at the conference. The conference attendees discussed their opinions after each presentation. After this was finished the whole group agreed on overall recommendations.

It was decided that only cognition and biological markers are core measures of disease modification. Cognition should be measured by the Mini Mental State Examination (MMSE) or the Alzheimer’s Disease Assessment Scale – Cognitive subscale (ADAS-Cog), and brain changes through structural magnetic resonance imaging (MRI) in a subset of participants. All other domains are important, but not core measures of the disease. They recommend using the Neuropsychiatric Inventory (NPI) for neuropsychiatric symptoms: the Disability Assessment for Dementia for Activities of Daily Living (ADLs), the Dementia Quality of Life Measure (DEMQOL) for quality of life and the Clinical Dementia Rating (CDR) scale to measure dementia globally.

A second e-mail consultation was conducted after the consensus conference, with the wider AS research network, who had not attended the focus groups, to gain further feedback on a report of the main recommendations made at the conference.

4.3 France

The Haute Autorité de Santé 84 (or HAS, translated as the “High Authority on Healthcare”) is the main governing body that regulates the healthcare system in France. Its general mission is to improve the quality and the efficiency of the healthcare system. In the year 2005, new legislation (articles 161-37, based on social security laws) increased the HAS’ mission. It can be summarized into 2 groups of activities:

1) Evaluation and recommendations
2) Accreditation and certification

For the first activity, HAS evaluates products and devices and makes recommendations about reimbursement. It also conducts evaluations of healthcare practices to ensure that healthcare professionals are held to standards of quality and efficiency. For the second activity, HAS is responsible for the accreditation and certification of healthcare institutions and medical professionals.

HAS is also responsible for providing healthcare professionals with the tools, guides, and methods needed to facilitate the development and implementation of healthcare projects.

HAS is composed of a college involving 8 representatives, 6 commissions, 400 agents, and 2,800 external experts. These experts include physicians and other healthcare professionals, consumer representatives, and patient and consumer organisations. The HAS’ evaluation and

recommendations can be solicited by private industry, professional and scientific groups, patient and consumer groups, HAS’ own research, and the public. Individual patients cannot contribute to the evaluation process.85

Decisions on reimbursement of medications and devices are done in 2 phases. First, HAS evaluates whether a medication or a device is able to meet safety standards. For medications, these standards are established at the European level by the European Medicines Agency (EMA) and at the national level by the AMM (“Authorisation de Mise sur Marché”). The safety of devices is evaluated by designated professional experts. Once the medication or device has been determined safe to put on the market, HAS uses scientific criteria to evaluate its efficacy and its efficiency, which results in a report that includes cost-effectiveness data and recommendations from HAS. This report is then reviewed in court (i.e., “pouvoirs publics”) and a final decision is made regarding the percentage of reimbursement that will be covered by France’s social security system.

4.3.1 Interactions between PAGs and HTAs

From September to October 2015,86 a HAS commission reviewed examples of patient engagement in other countries (NICE in the UK, Scottish Medicines Consortium [SMC] in Scotland, and Canadian Agency for Drugs and Technologies in Health [CADTH] in Canada). They also reviewed documents from the Ontario Health Technology Advisory Committee Public Engagement Subcommittee (OHTAC) in Canada, and documents developed by HTAi. Procedures and outcomes were reviewed to gain a better understanding of how patient organisations have been asked to take part in the evaluation and decision-making process of new and existing products. They focused on questionnaires which are being used to gain a better understanding of patient perspectives and patient satisfaction with treatment.

From November 2015 to January 2016, HAS proceeded to the development of its own patient engagement project. Its purpose was to include patient and consumer perspectives in the evaluation process, while clarifying the relative contribution of experts versus patient and consumer representatives who hold diverse organisational, economical, and professional interests. A distinction is made between HAS’ data-driven assessment compared to the testimonies provided by patient and consumer associations.

HAS projects can be accomplished over the course of several months, making it easier for patient organisations to prepare documents to be submitted for evaluation. HAS offers tools, guides, and methods to help patients prepare projects.87 In the context of the year 2015/2016 initiative, HAS projects only lasted for 3 months, that is, a decision was to be made after 3 months following a request. To meet this deadline, patient organisations were instructed to submit evidence at the very beginning after the request was made.

Within the context of this initiative, in January 2016, HAS developed a questionnaire, a set of procedures, and follow-up measures which were intended to improve the patient engagement system and favor patient participation.

A working group was then formed and meetings were held in January and April 2016. Participating in the group were patients and consumers, and members of different HAS services.

The working group focused on the development of a questionnaire aimed at gathering patient perspectives based on the translated versions of the questionnaire developed by HTAi.\(^88,89\) Two versions were used: 1 for medications and 1 for interventions that exclude medications. The HAS also used the examples, provided by NICE, to define the guidelines leading to the evaluation of healthcare technologies.

In addition, the working group defined guidelines and procedures dictating the period during which patients and consumers contributing to the planning of commissions, the routine support given to associations, and the role of patients and consumer representatives of groups taking part in the commissions. The results of this project were presented to the CISS ("Collectif Interassociatif Sur la Sante"). This initiative led to the posting on the HAS website, of a schedule of evaluations, to give patient and consumer organisations the opportunity to contribute to these evaluations. The HAS website also lists the name of the product being reviewed and information about the targeted indications. The postings refer to products that have been evaluated in the past.

Moreover, representatives of private industry organisations (LEEM and SNITEM) discussed with HAS the need to protect commercial knowledge. Specific judicial analysis about these concerns was conducted and then discussed with an ethics committee. The results of these discussions were then presented to the evaluation commissions.

On 12 October, 2016, the HAS college validated the new patient engagement system and a plan was developed to monitor and evaluate its implementation with the help of the patient engagement working group.

In September 2017, a summary of preliminary outcomes of the HAS’ new patient engagement procedure was published on their website.\(^90\) In this report, a summary of the contribution of patients and consumer associations was provided. Contributions included the following steps:

1) HAS receives a request for reimbursement from private industry

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2) With the agreement of private industry, HAS publishes information about the request (name of product, indication (AMM for medications or CE for devices), goal of the evaluation, and date limit for contribution)

3) Patient and consumer groups provide their perspectives with the help of questionnaires, proposed by HAS, and a guide made at their disposition to support their contribution

4) Patient/consumer contributions are transmitted to the project leader

5) A meeting is held by the commission

6) Recommendations are developed and discussed during a hearing

7) The recommendations are posted online

8) Further discussions take place between the DEMESP91 (Direction de l'Evaluation médico-économique et de santé publique) project leader and patient/consumer association representatives

9) A final questionnaire is completed by the association and is transmitted to the HAS (taking into account contributions from the past 6 months)

The DEMESP project leader and the relevant evaluation services are responsible for overseeing the implementation of Steps 1 through 9, based on an internal HAS guidelines, that details expectations at each step of the process.

4.3.2 Influence of PAGs on HTA Decisions

The report published on September 201790 described that during their pilot initiative, 75 medications were posted online to cater to patient and consumer engagement.

As a result, HAS received a total of 25 contributions and focused on 22 medications. These included 3 medications for neurological conditions: pain (PALEXIA® or tapentadol), multiple sclerosis (LEMTRADA® or alemtuzumab), and attention deficit hyperactivity disorder (INTUNIV® or guanfacine). The following patient and consumer associations participated in the evaluation process:

1) Pain:
   • Association francophone pour vaincre les douleurs (AFVD)
   • Association française de lutte anti-rhumatismale (AFLAR)

2) Multiple Sclerosis:
   • Ligue française contre la sclérose en plaques (LFSP)

3) Attention Deficit Hyperactivity Disorders:
   • HyperSupers TDAH France

Each patient/consumer association was given a month, by HAS, to provide their contribution. This interval appeared sufficient for HAS to produce their recommendations after 3 months. Some associations were not able to respect this time limit and were, therefore, not able to contribute in time for HAS to take their perspectives into consideration. As a result, some associations

complained about the brief time period and some of them were subsequently given more time to contribute before the next commission meeting.

Examples of patient and consumer contributions (across several conditions) that were considered during the development of HAS recommendations are as follows:

1) Burden for patients with respiratory problems who are required to go to the hospital to get their medication, when they in fact are receiving injections at home. This led to a change in access to the medication
2) Patient descriptions of their treatment journey during the fourth line of cancer therapy were viewed as informative and aligned with the advice of experts
3) The perspective of patients with muscular dystrophy emphasized the value of evaluation criteria that pertain to certain treatment outcomes such as being able to walk, and the speed with which the ability to walk is lost. Other valued outcomes include the number of months and years a child and his/her family can remain autonomous and how this helps to delay other major complications and intrusive interventions
4) In psychiatry, patient and consumers stated their wish to have other products accessible when patients do not react well to existing treatments. Information was provided regarding countries that offer different treatment alternatives as well as provide more complete case management of children in terms of educational institutions
5) Some associations brought up the need to have access to home treatment as would be the case for patients who required dialysis for renal insufficiency
6) There was also an interest in associations receiving better training to administer intravenous medications at home in order to authorize greater access to medications at home, such as in the case of dialysis treatment
7) Furthermore, some patient and consumer contributions alerted HAS to the misuse of certain medications

It is important to mention that prior to the HAS initiative described above, it is unclear to what extent patients could contribute to HTA decisions.

4.3.3 Perceptions of PAG/HTA Interactions

In their summary of the preliminary results of this patient engagement initiative, HAS described that this first effort was successful. They reported that patient engagement is democratic and the participation of patients and consumers is now made possible for those who contribute to evaluations. Overall, associations have shown their interest and have provided useful contributions. Based on preliminary findings, HAS plans to make some adjustments to its patient engagement process:

1) Improve the information that is made accessible to patients and consumers
2) Improve time delays and periods of contribution
3) Improve the mechanisms that take into account patient contributions
4) Improve publication of contributions
For now, HAS will continue to monitor the implementation of the current patient engagement processes and review patient and consumer contributions that have been submitted within the past year. Collaborations between HAS and the French Healthcare Associations will be set in place to support the involvement of patient and consumer associations and foster more systematic patient engagement practices.

From the perspective of patient associations, in the case of multiple sclerosis, there are at least 4 influential associations that have promoted the patient’s voice in HTAs in France:

- The French Association of Multiple Sclerosis (AFSEP)
- The Foundation to Support Research on Multiple Sclerosis (ARSEP)
- The French League Against Multiple Sclerosis
- The Union for the Fight Against Multiple Sclerosis

The French League Against Multiple Sclerosis contributed to the evaluation of LEMTRADA® (or alemtuzumab) during the HAS’ patient engagement initiative (see above). However, no additional information to describe how this particular organisation contributed during the evaluation process was included in the September 2017 report, nor is it clear to what extent the HAS commission members were cognizant of the specificities of multiple sclerosis during the evaluation and final recommendations made by the HAS.

Furthermore, on their website, the HyperSupers TDAH France, the patient association that participated in the HAS patient engagement initiative by providing contributions regarding the use of INTUNIV® (or guanfacine) to treat attention deficit disorder (see above), posted a summary report92, a summary of recommendations,93 and a summary of TDAH arguments.94

On their website, the TDAH95 states that it is their hope that these HAS recommendations will facilitate the treatment of patients by making them easier to read, and more efficient. They also hope that the general practitioner will be able to contribute to the patient journey, along with families, by supporting the coordination of treatments, and by ensuring that families are provided with concrete answers that will help them better understand their children and be themselves active contributors to the management of their health. The TDAH considers the publication of these HAS recommendations to be an important moment in the history of the association.

Accessed October 31 2017


4.3.4 Particularities of Neurological Disorders

As described above this past year, the contributions of patient and consumer organisations under HAS’ new patient engagement initiative has focused on products to treat 3 neurological conditions: pain, multiple sclerosis, and attention deficit hyperactivity disorder. The evaluation and decision-making process described above was applied to all conditions regardless of the particulars of these conditions.

4.4 Germany

The HTA evaluation and decision-making process in Germany involves 2 institutions: the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) and the Institute for Quality and Efficiency in Healthcare (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG). IQWiG drafts HTA reports, which are commissioned by the G-BA. The G-BA is responsible for the assessment, the appraisal, and the decision-making that takes place regarding various technologies. This includes medical diagnostics, therapeutic methods, and therapeutics.96

4.4.1 Interactions between PAGs and HTAs

Since the year 2004, patients or their caregivers, patient group representatives, advocacy groups and consumer organisations have contributed to the G-BA and the IQWiG. Patient representatives (“knowledgeable persons”) are appointed by a select group of relevant organisations to join G-BA bodies. There are 250 patient representatives who are currently participating in G-BA committees.96

The following patient organisations have been selected to appoint a representative:

- The German Disability Council (Deutscher Behindertenrat 2016)
- the National Association of Patient Advisory Centres (Bundesarbeitsgemeinschaft der PatientInnenstellen 2016)
- the German Association of Self-Help Groups (Deutsche Arbeitsgemeinschaft Selbsthilfegruppen 2016)
- the Federation of German Consumer Organisations (Verbraucherzentrale Bundesverband 2016).

This select group of relevant patient organisations and their affiliates provide great diversity in terms of disease and disabilities, and the types of representatives who are called to join the G-BA; they range from chronically ill patients, to persons with disabilities, informal caregivers, and advisors-to-patients. Patient representatives are selected based on their competence, that is, their experience with a particular indication. The health insurance funds determine the number of appointed persons in the committees, subcommittees and working groups. This number can range between 1 to 12.

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Relevant patient organisations have been granted a consultative role by the G-BA. This can be exercised by submitting written statements throughout the HTA process, providing advice on how to formulate questions and helping to conduct assessments. They can attend G-BA decision-making meetings, participate in the hearings of other self-governing committees, and take part in assessment meetings of the IQWiG. Relevant patient organisations also have the right to submit a request to initiate a decision-making process in the G-BA. The appropriate HTA will then be required to describe the benefits in question, the target population, the medical necessity and cost-effectiveness of the method to be discussed, and the level of urgency of the request. The G-BA’s role is also to help the relevant organisation formulate the request which will lead to a formal proposal.

In sum, the steps involved in fulfilling a request for an HTA decision are as follows:

1) The G-BA asks IQWiG to develop a report (patients participate in the development of reports)
2) The G-BA forms subcommittees and working groups to draft proposals
3) A public session is held by the decision-making body

Relevant organisations and patient representatives are involved in each step. The GBA makes open requests for evidence on its website and stakeholders, including patient organisations, are allowed 1 month to submit written statements.96

Throughout their involvement in the assessment and decision-making process, the G-BA provides financial and organisational support to patient organisations and their representatives. More specifically, travel expenses are reimbursed, and the G-BA provides compensations for the loss of earnings ensued by participants. In addition, the G-BA provides organisational and content support (e.g., training on methods, legal advice, assistance in the preparation of consultative documents,
organizing meetings, and access to G-BA offices). In addition, by-laws exist to protect patient participation and procedural rights.

As for the IQWiG, there also is a clear focus on compiling comprehensible information for patients and a new internet platform has recently been issued, addressing patients’ needs with respect to a wide variety of diseases and treatment options (http://www.gesundheitsinformation.de/index.html). This also correlates with the Institute's frequently expressed claim to assess “patient relevant outcomes”.

4.4.2 Influence of PAGs on HTA Decisions

The G-BA’s interest in patient engagement is based on what it can bring to the evaluation and decision-making process and what it can do for patients’ associations in return. In particular, the G-BA views patient experiences and perspectives “relevant”, as indicated by the designation “relevant organisations.” Moreover, the G-BA is interested in giving patients the same rights as other stakeholders, although they are not necessarily considered equal partners by other parties, and have a consultative right without having the right to vote. Furthermore, through patient engagement in G-BA evaluations and decisions, there is an opportunity to gain more knowledge that may help limit the underuse, the overuse and the misuse of health services, and to promote higher quality and efficiency of services. In addition, involving patients who participate in discussions and the decision-making process helps to legitimize the final decisions made by the G-BA and provides greater transparency regarding the achievement of these decisions. Finally, granting patient representatives the possibility to initiate HTAs, to influence decisions, and to cooperate with other G-BA members, builds the capacities of patient organisations to improve their engagement over time.

However, to date, according to Haefner and Danner, no efforts have been made to monitor patient engagement and a realistic assessment of the quality and integrity of the patient engagement system. The G-BA remains influenced by the politics of the country. Furthermore, the actual implementation of an HTA can sometimes follow months and years after a request has been submitted by patient representatives. Finally, not all discussions are being recorded with meeting minutes, particularly when patients are being consulted. Non-public meetings also remain confidential.

4.4.3 Perceptions of PAG/HTA Interactions

In November of 2015, the Federal Constitutional Court stated that the constitutional legitimacy of the G-BA as a self-governing committee might be missing. This criticism comes as a result of the fact that patient organisations have not been receiving state funds to participate in HTA committees. In effect, the G-BA is a powerful entity which has profound influence on decisions related to healthcare. Care is taken to be transparent about G-BA decisions by publishing the results on their homepage. However, G-BA decisions are being scrutinized for evidence that patients have indeed been consulted and even considered during the decision-making process. The G-BA website (https://patientenvertretung.g-ba.de/en/) provides links to each of the of the G-BA appointed advocacy groups. For instance, as described on its webpage, the Federation of German Consumer Organisations (vzbv) represents 41 German consumer associations.
Patient engagement appears to be steered by 4 large nationwide advocacy groups, whose role is to contribute to HTA discussions on behalf of a multitude of smaller patient advocacy groups. Further research is needed to gain a better understanding of how these smaller advocacy groups are being represented. It is unclear how the interests of smaller organisations are being communicated to the G-BA appointed groups and what impact they may have on discussions that take place at meetings. As several groups focus on specific diseases of interest to their members, further inquiry is needed to gain a better understanding of how they can present testimonies, and research findings to the larger groups, and how this information is being used to influence HTA decisions.

4.4.4 Particularities of Neurological Disorders

No information has been found in the literature to describe how the particulars of neurological disorders are being taken into account in interactions between smaller advocacy groups and G-BA appointed advocacy groups, and interactions at meetings between G-BA appointed groups and G-BA government officials.

4.5 Poland

The Health Technology Assessment Agency in Poland (AOTMiT) was established as an advisory body to the Ministry of Health (MoH). The President of AOTMiT leads and oversees all AOTMiT activities. The other most important bodies within AOTMiT are (both appointed by Minister of Health):

- The Transparency Council of AOTMiT (TC): an advisory, independent body with 20 highly qualified members
- The Council for Tariffs Affairs of AOTMiT (CTA): an advisory, independent body with 10 highly qualified members

The role of AOTMiT in the decision-making process is connected with assessment and appraisal, which is consistent with international standards regarding HTA. Assessment is provided by the analytic team, using Polish HTA guidelines (April 2009 – in English) and is related to revision of industry submission. Appraisal is prepared by the TC and President of AOTMiT. That is, assessment with added context-specific judgments such as: impact of alternative options, social consequences, organisational implications, relative priorities, and wider social and ethical aspects.

AOTMiT’s opinion is said to be crucial for the ministry of health (MoH), but the decisions in practice are not always consistent (reimbursement granted by MoH with or without negative opinion of AOTMiT, reimbursement not granted by MoH when the opinion was positive). AOTMiT assesses both drug technologies (90%) and non-drug technologies (10%).

Health technology reports, prepared by manufacturers or consulting firms, according to guidelines, are submitted to AOTMiT and then assessed by this organisation. Reports can also be prepared

by independent institutions upon request of AOTMiT. According to the Directive 89/105/EEG, the pricing and reimbursement process should not take longer than 180 days. However, past experiences clearly indicate that it takes longer to make a reimbursement decision.  

4.5.1 Interactions between PAGs and HTAs

In the year 2015, HTAi published a document with good practice examples of patient and public involvement in HTA, shared by HTA agencies in different countries. The AOTMiT provided insights of the current approaches of patient engagement in Poland. The approaches are described in the following paragraphs.

The AOTMiT’s purpose of patient involvement in HTA process is to provide the patient’s perspective at the analytical assessment and appraisal level. Individual patients can communicate their opinions to AOTMiT through patients’ organisations. The patients’ organisations represent the views of patients and/or carers by:

- Completing a form/questionnaire provided by AOTMiT, following AOTMiT’s invitation
- Providing orally their opinion to Transparency Council, after having applied for hearing

In addition, public consultations in the process of assessment of reimbursement submissions are in place, when applicant HTA analysis as well as agency’s verification analysis are published on Agency’s website for 7 days. Every citizen may pass her/his opinion, if she/he submits a declaration of conflict of interest, by completing the relevant template provided on the website.

Under the process of analytical assessment, patients’ organisations that are relevant to the subject of assessment, are sought and asked for their opinions.

On 25 October 2017, AOTMiT announced on their website the first training for supporting patient organisations to engage in the HTA process. The training will be conducted by AOTMiT staff on 5 December 2017 and representatives of patient organisations are invited to attend.

The training will provide information on the refund process in Poland and the role of the AOTMiT. The training is a response to patients’ organisations’ expectations for raising awareness / knowledge about the AOTMiT decision-making process and the health system.

The objective of the training is to familiarize participants with how reimbursement decisions are made in the country and the specifics of elated activities in accordance with HTA principles.

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It is anticipated that after the training, the participants will know the basics of the agency's functioning, are able to place themselves in the process of reimbursement, know how to make decisions within the process and can find basic information about the ongoing reimbursement process.

4.5.2 Influence of PAGs on HTA Decisions

AOTMiT encourages the submission of any comments, suggestions and opinions regarding the performance/benefits of the product in question, by completing the relevant form provided in AOTMiT's website.101

AOTMiT highlights that they value the voice of the day-to-day patient care environment, the expert setting of standards and new trends, the patient organisations representing the beneficiaries of healthcare (i.e., patients), and many other healthcare market stakeholders.101 They emphasize that patients' attention and experience in the most diverse areas of the health sector allow them to consider specific benefits in the process of assessment, making the process more transparent, objective and reliable, while providing a basis for valuation meeting all stakeholders' expectations.

However, there is no mechanism in place for measuring the impact of patient involvement on the decisions. Identification of the main impact of involvement in HTA is difficult, given that there is no standardized methodology for patient involvement in the HTA assessments. Consequently, no feedback is provided to patient organisations on how their input is used and its value to HTA.

4.5.3 Perceptions of PAG/HTA Interactions

No information was found in the literature for perceptions of PAG/HTA Interactions in Poland.

4.5.4 Particularities of Neurological Disorders

Among the health policy programs of local government units listed in the AOTMiT website, the project "Activation of patients with neurological diseases of Stołeczne Centrum Opiekuńczo-Leczniczego Sp. z oo" has been initiated by the Warsaw municipality.102

No further information was found in the literature specific to Neurological disorders in Poland.

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4.6 Spain

A national HTA agency (Instituto de Salud Carlos ISCIII) and several HTA organisations in the autonomous regions (Comunidades Autonomas) coexist and cooperate in the country. The ISCIII was created under the Health Act of 1986 as an autonomous public institution attached to the Spanish Ministry of Health, which proposes and develops guidelines related to health care. The main objective of the ISCIII is the collaboration and support of research and technological development through its many centers and regional agencies, in health care. The ISCIII provides HTA reports to the Inter-territorial Council (Consejo Interterritorial del Servicio Nacional de Salud de España, CISNS), the ultimate decision-maker for reimbursement of health technologies.

The autonomous regions also can establish HTA organisations (agencies or services). The functions and processes of these HTA organisations are regulated at the level of the autonomous community, and there is no national standard. Typical functions of these organisations include HTA, improving rational use of health technologies, and supporting the decision-making process at various levels of the national health system. Currently, there are 7 regional HTA agencies/services in Spain. They are presented in Error! Reference source not found..

Figure 6 The Spanish HTA Network AUnETS

Additionally, other autonomous communities also have units for planning and advice on decision-making that could include some sort of HTA evaluation. Each regional HTA agency or service is responsible for producing information on the efficacy, effectiveness, safety and cost-effectiveness of new health technologies.\textsuperscript{103}

To coordinate the services of the national and regional HTA agencies, a platform of HTA agencies, the AUnETS (\textit{Agencias y Unidades de Evaluación de Tecnologías Sanitarias}) was established. The AUnETS is under auspices of the CISNS. Main objectives of the AUnETS are:

- Efficient sharing of existing resources in producing a variety of outputs and services
- Acting effectively as a valid point of contact for national and European health institutions
- Fostering common projects and joint lines of work among members

The HTA process for decision-making related to the national catalogue of services in Spain is presented in Error! Reference source not found..
Figure 7 HTA process for decision making related to the national catalogue of services in Spain

Steps 1a and b: The central and regional governments request HTA evaluations to the national and regional agencies.
Step 2: The ISCIII and regional agencies collaborate to produce the required HTA information.
Step 3: The ISCIII produces the HTA report and submit it to the Interterritorial Council.
Step 4: The Interterritorial council decides about the inclusion or exclusion of technologies in the national catalogue.
Step 5: The decision of the Interterritorial council is implemented by the central and regional governments.

4.6.1 Interactions between PAGs and HTAs

On the world day of patients in October 2017, the Spanish Patient Forum (Foro Español de pacientes, FEP) highlighted the importance of the patient in the National Health System. The president of FEP emphasized that patients are not yet at the centre of the system, but as any other stakeholder, patients deserve to have a say in the health strategies.106

Even though the importance of this issue has been acknowledged in Spain for years, patients have not been involved in any HTA process. However, a methodological manual for the involvement of

patients in HTA activities is under development and planned to be released at the end of the year 2017- beginning of 2018, by AUuETS.  

Currently AUuETS address the information and participation of patients in their assessment products differently using various strategies. Spanish AUuETS have used strategies to include patients in the development of clinical practice guidelines (CPGs), shared decision-making tools (SDMTs), and other assessment products. It is important to highlight that currently patients are not properly engaged in the development or evaluation of any HTA report.

A review of scientific evidence conducted by researchers of Agencies of Health Quality and Assessment of Catalonia (AQuAs) in the year 2014, showed that most of the 25 revised CPGs combine more than 1 strategy of including the patient perspective in their development and evaluation process. The most commonly used strategy was the review of the guide’s draft, either the full document or only the information for patients. On the other hand, in the development and assessment of 10 SDMTs, the patients’ perspective was included through a qualitative research study using focus groups and/or structured or semi-structured interviews. Finally, 4 studies were described on screening programs, 3 on developing systems for prioritising patients on the waiting list, 2 that assessed user satisfaction and 1 that defined health indicators. Different qualitative research techniques were used in all the studies, with patients/caregivers and/or the general population as a strategy for the inclusion of users, focus groups being the most often used technique.

In the year 2015, HTAi published a document with good practice examples of patient and public involvement in HTA shared by HTA agencies in different countries. The AQuAs and Basque Country (Osteba) provided insights of the current approaches of patient engagement in Spain. The approaches are described in the following paragraphs.

**AQuAS’s patient involvement approach**

AQuAS is a public entity of the Catalan Health Ministry with more than 20 years of history. AQuAS’s role is to generate scientific and relevant knowledge for all the agents of the Catalan Health System to inform decision-making processes to contribute to the improvement of its quality, safety and sustainability. The AQuAS strategic lines are observation, assessment and innovation, using information and communication technologies as tools.

AQuAS’s purpose for patient involvement is to complete and enrich the professionals’ perspective in the development of their products and services. Especially in CPG development, AQuAS takes patients’ expectations and relevant suggestions into account, to increase the usefulness and accuracy of the final guideline. AQuAS is already incorporating the perception, opinion and preferences of patients and carers (family and non-family) into the CPG it elaborates. The Spanish handbook about patients/careers in the development of CPG, can be found [here](http://www.redets.msssi.gob.es/informesEvaluacion/elaboracion/home.htm).

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In the development of CPGs, AQuAS uses different strategies to involve patients that are not mutually exclusive:

- Research focused on patient/carers' perspectives to be incorporated into the CPG. When there is little or no published literature, an original qualitative study based on the most appropriate techniques in each case (in-depth interviews, focus groups, etc.) should be carried out rigorously. Based on the results from such studies, patients’ and carers’ major concerns can be ascertained and further addressed in the CPG.

- Incorporating patients/carers as members of the drafting team developing the guideline. This is the most complex option entailing prior preparation and a certain knowledge level as well as communication skills both on the part of the professionals and the patients/carers involved throughout the entire process of CPG development.

- Participating in the initial review of the CPG first draft and/or external revision. The objective here is to ensure that patient/carer criteria and experiences are included in the CPG (e.g., in the clinical questions and measurements of relevant outcomes). This information might be very helpful for the preparation of the Annex “Information for patients” of the CPG. Moreover, and independently from the drafting team, patients/carers can participate in the external revision process of the CPG, both individually or through organised groups of people sharing a similar or the same health problem as the one covered in the CPG.

AQuAS collaborates with the Patient Advisory Council (Consell Consultiu del Pacient), which represents all Catalan patients' associations. While developing a CPG, patient and carers (family and non-family members) associations can be used as the initial point of contact to properly select the most adequate participant profiles.

When patients are members of the developing group working on a CPG, they can provide input using the same processes or tools as the health professionals of the team (e.g., e-mails, drop box, and verbal presentations). If patients are external reviewers, they fill out specific templates for communicating their insights/input.

There is no differential treatment for patients/carers than other stakeholders who are members of the developing group, when it comes to support of participation. AQuAS receives everyone’s input and explains how it was used and its value to the project.

**Osteba's patient involvement approach**

Osteba is a public entity of the Health Department of the Basque Government and its role is to inform decision making process for the Basque health system (public system) and the Spanish health system. Osteba assesses all types of health technologies and its purpose for patient involvement is to include the perspective of all stakeholders in those assessments.
Patients/carers can be involved in submissions, participate in committees or freely submit information when a new project starts. Patients can also be involved in CPG development. There is a preference by the agency to involve individual patients and/or caregivers than patients’ associations. The patients/carers can provide their input by completing an information template. Osteba provides explanations of the HTA process and its implications at individual, country, national and international level, to enable patients/carers to participate. Osteba provides them the report for consideration and review before it is published like the process followed for the other stakeholders.

4.6.2 Influence of PAGs on HTA Decisions

Neither AQuAs nor Osteba have a mechanism in place for measuring the impact of patient involvement on the decisions. They only try to assure that patients participate in all the project steps and agree with the final product (e.g., CPG, patient brochure).

The main impact of involvement witnessed by the agencies is the removal of barriers among all stakeholders (members of AQuAS, health professionals and patients, carers, citizens and organisations representing the views of patients and/or carers) and the most comprehensive definition of outcomes and measurements. Some patients/carers facilitators have great interest in participating in this kind of projects, ability to learn quickly how to develop a guide, and willingness to work in a group with people from other disciplines.

The information regarding patient involvement with the national HTA agency or the regional ones is limited. Patients seem to be involved through AQuAs or Osteba when it comes to guidelines or brochures, but there is no information found regarding patient engagement in actual reimbursement decision-making processes.

4.6.3 Perceptions of PAG/HTA Interactions

Including patients in the assessment process is complex and faces a number of factors that may prevent (barriers) or promote (facilitators) fully or partially its implementation into professional practice. According to the latest AQuAS’s publication on patient involvement in HTA, national experiences show that the major barriers include: lack of willingness and commitment on the part of HTA agencies to include users in the process, lack of time on the part of all parties involved, participation of users who are not sufficiently representative of the affected population, the difficulty to accept (or understand) the scientific evidence on the part of users, predominance of healthcare professionals in the composition of the working groups, and the absence of effective strategies in the methods used.

Facilitators include: the fact of considering patients in the authorship of the works and allowing them to participate by contributing with their own experiences. The process is also facilitated by a good attitude on the part of healthcare professionals towards the involvement of patients by providing them with quality, accessible, appropriate and scientific evidence-based information.

Challenges for the future include: deciding how to effectively include patients in the HTA process and the most opportune time to do so, the need to develop specific research studies and techniques that assess the real impact of HTA on patient’s lives, promoting the use of information technology
(websites, blogs, forums) in this process, conducting user training on the methodology to be used, and make the proportion of professionals/patients more equitable in the working groups. It is also challenging to decide what skills or competencies the patient should have to be part of the process. Finally deciding on the most useful information and training of patients, HTA developers and other stakeholders for patient involvement to be a success.\textsuperscript{108}

Short term patient involvement actions (strategy for remaining of 2017):\textsuperscript{104}

1. Public Declaration.
2. Establish procedures for patient invitation, selection and participation to AUnETS activities.
3. Pilot experiences: Most AUnETS HTA agencies will increasingly involve patients in HTA reports, starting in 2017, to test the procedures and learn from experience. Patients will be involved in:
   - Protocol development (helping to define objectives and scope of the report)
   - Reviewing the preliminary version of the HTA report
   - Contributing to the patient version of the summaries.
5. Declaration of interest document adapted for the patient participation.
6. Promoting synergies with other spaces for patient participation established by the Spanish Ministry of Health as the Network of Health Schools for Citizenship.

Mid-term patient involvement actions (strategy in the year 2018-2019):\textsuperscript{104}

1. Extend the scope of patient participation: reviewing literature and other resources to introduce patient related issues in HTA reports
2. Training for HTA technicians to improve capacity on patient involvement and on the incorporation of patient contribution to HTA reports
3. Dissemination activities targeting patients, carers and users and their associations
4. Active dissemination of the public calls to increase participation of patients’ associations.
5. Patient involvement evaluation: conduct a qualitative evaluation and create a checklist to facilitate patient involvement and transparency

Long-term patient involvement actions:\textsuperscript{104}

1. Extend patient participation to all HTA reports
2. Modify methodologies and procedures in relation to the results of the evaluation
3. Establish mechanisms to incorporate and document patient contributions and document them in a transparent manner
4. Conduct primary studies to introduce patient perspective in HTA when necessary
5. Ensure representatively and diversity in patient involvement
6. Consider patient participation in AUnETS structure
7. Adapt current selection and prioritization tools to allow patient involvement

4.6.4 Particularities of Neurological Disorders

No information has been found in the literature specific to Neurological disorders in Spain.
5 Discussion

The purpose of this research was to describe patient engagement in HTA decision-making processes in 6 European countries: Sweden, the UK, France, Germany, Poland and Spain. Our review of the literature focused on 4 key objectives: 1) describe interactions between patients/patient groups and HTA bodies, 2) describe their leverage and influence on the decision-making process, 3) describe how patient engagement is perceived by all parties involved, and 4) describe evidence that would suggest that the specificities of neurological disorders are being considered at different stages of the HTA process.

For each country, we first described governmental and non-governmental agencies that play a key role in gathering evidence and making decisions that impact reimbursement of drugs and medical devices, and influence the healthcare service delivery system. We described the ways in which patients and patient advocacy groups can prepare evidence and inform HTA agencies, take part in discussions and submit comments, and be involved in the dissemination of results. Our review suggests that more than at any other time in history, interactions with patients are not only discussed, but HTA bodies in several countries have implemented procedures to transform the HTA process, acknowledging the importance of listening to the patient’s voice. We found that UK has the most structured and transparent mechanisms in place for involving patients in the HTA process. NICE’s dedicated public involvement staff is responsible for providing support, training and resources to enable the engagement of patients in all stages of an assessment. Patients not only cooperate with NICE in the development of decisions (e.g., participate in meetings, provide evidence, comment on draft and final recommendations) but also have the power to lodge a formal legal appeal for changing them in case of factual inaccuracies.

In countries like Sweden, France and Germany, patient groups usually play a consultative role, which allows them to attend meetings. However, we found significant variations between countries and even between country-specific agencies. For example, in Sweden, the SBU provides guidelines and training that allows patient groups to submit qualitative descriptions of their disease experiences. In contrast, patients do not have the opportunity to submit patient-driven data to the TLV and overall, despite positive messages on their website that support patient engagement, the nature of patient participation in TLV meetings, aside from broad dialogue forums, is unclear. In Germany, a very structured system is in place to allow 4 G-BA-appointed patient advocacy groups to participate in meetings and submit written statements. At the request of the G-BA, the IQWiG prepares evidentiary reports in consultation with patient group representatives. In France, a new initiative being pilot tested which provides patient groups with the opportunity to complete questionnaires that HAS developed based on examples found in other countries.

Likewise, in Poland, patients interact with AOTMiT through patient organisations by completing relevant forms/ questionnaire provided by AOTMiT or providing orally their opinion at the transparency council meetings. Patients’ organisations that are relevant to the subject of assessment, are sought and asked for their opinions. Public consultations in the process of assessment of reimbursement submissions are also in place. Every citizen may pass her/his
opinion, provided that she/he submits a declaration of conflict of interest, by completing the relevant template provided by AOTMiT. Lastly, in Spain, even though the importance of patient involvement in HTA process has been acknowledged for years, patients have not been involved in any HTA process. They have been involved only in the development of CPGs. However, a methodological manual for systematically involving patients in HTAs is currently under development and will be published near the end of the year 2017 - early 2018 by AUnETS.

Our second objective was to describe the influence that patient advocacy groups may have on the HTA decision-making process. Our results showed that in Sweden, despite the many opportunities that patient group representatives have to get involved, concerns about information confidentiality from private sector industry has prevented TLV decisions from involving patients. However, recognition of the added value that patients can bring to support products has more recently inclined some companies to be more transparent. In addition, the time that spans between the request to make a decision and the date when a decision is made can be up to 2 to 3 years. Some have questioned the actual influence that the intense patient engagement in SBU activities has on the HTA decision-making process in Sweden.

In the UK, NICE takes into account patients’ input in every step of the HTA process. The patients are asked to review and comment on draft recommendations based on evidence of personal experience with a certain condition. They are even given the possibility to comment on factual inaccuracies in the final recommendations and to lodge a formal legal appeal which can lead to amendment of the recommendation if any of the appeal grounds is upheld. The case of AS in the UK exemplifies how patient organisations can impact HTAs by challenging outcomes commonly used in clinical trials that are not meaningful for patients and carers. In France, the new HAS initiative has been well received and despite criticisms from patient groups regarding the time they have to submit evidence, a number of consultations with patient groups, albeit without having the right to vote, have led to concrete changes in medical practices and therapies.

In Germany, however, our review did not allow us to discern any concrete instances where patient engagement influences G-BA decisions. In fact, the HTA process has been criticized for its lack of involvement and consideration of patient perspectives. More specifically, despite the existence of patient engagement materials and training, both the G-BA in Germany and the SBU in Sweden have been criticized for the lack of funding that is dispensed to patient groups who actively participate in HTA committees. Thus, in both countries, a major barrier to the patient influence on HTA decisions is the lack of financial support to patient groups, which ultimately could affect the quality of their involvement in projects. In Spain and Poland, no mechanism is in place for measuring the impact of patient involvement on the decisions. Furthermore, no example of having influence on the HTA decision-making process on the part of patients in these countries, has been identified through our review.

Our third objective was to gather perceptions from all parties, government and non-government HTA bodies, and patient advocacy groups regarding the systems that are currently in place to involve patients. Despite commentaries found in a few sources, it was difficult to truly reflect on the perceptions regarding the current systems in each country. There were perspectives shared on HTA websites and by some authors. However, we were not able to gather much information on the perspectives of patient groups themselves and this may be due to several reasons. One of them
may be a lack of involvement with HTAs due to limited awareness or training about the systems that are in place to become involved. Furthermore, patient groups may predominantly want to serve their members with information about treatments, opportunities to meet other members such as fundraising events, and do not foresee their involvement beyond these activities. Many questions about the needs of patient groups and perceptions regarding engagement activities with HTA bodies could best be answered through direct interviews and focus groups. Clearly, further research is needed to gain a better understanding of the patient voice by conducting survey research with patients’ groups and other key decision-makers in each country.

Our fourth objective was to evaluate the extent to which patient engagement specific to neurological disorders are taken into account during the HTA process. In the UK, NHS invited dementia patients for consultation about outcomes, which they believed are core for use in disease-modification trials. This initiative may be linked to the AS case, through which patients and carers expressed the outcomes that they value most (i.e., maintenance of abilities and quality of life), contrary to NICE’s cognition and biologic indicators. In France and Sweden, we have found examples where patient engagement specific to neurological disorders resulted in consideration of the patient perspectives that were formally shared with the HTA decision-makers, although this was not always the case. However, in many cases, it is not clear at all to what extent comprehensive knowledge about the chronic nature of some neurological disorders and the impact they have on patients’ ability to remain independent over time is shared with decision-makers. In addition, it is not clear whether HTA decision-makers are informed about the challenges associated with the design and ongoing involvement of patients in clinical studies on neurological disorders. Most of all, despite evidence of patient engagement, detailed accounts of the impact that treatments may have on the activities of daily living of patients with neurological disorders that are associated with dementia, mental illness, or disability, may not have been considered by HTA bodies when making final decisions about reimbursement for treatment, medical devices, or healthcare practices. In sum, patient perspectives on their experience with neurological diseases and available treatments are needed to provide intricate details about the everyday life difficulties that patients and their caregivers face during the years, and sometimes decades, after diagnosis. Greater transparency about the discussions that go on at HTA meetings is needed to answer these questions. Interviews with patients and decision-makers may provide insight regarding the specific dimensions of neurological disorders that could resonate with HTA decision-makers and influence the decisions that impact the lives of patients and their carers.
6 Conclusion

In this research, we aimed to elucidate the systems and practices that are currently in place to support patient engagement in HTA processes in France, the UK, Spain, Sweden, Germany, and Poland. Our review suggests that in many countries, patient organisations have several opportunities to take part in the development of written statements and reports to provide patient perspectives on treatments, medical devices and healthcare practices. However, the lack of voting rights, the lack of funding to support advocacy group efforts, confidentiality issues, and the lack of transparency regarding the content of discussions that take place at HTA meetings make it difficult for patients to influence HTA decisions in many countries. Further research involving patients and other stakeholders is needed to gain a better understanding of how patient groups representing patients with neurological disorders can improve the HTA decision-making process, and find tools to communicate the important dimensions of neurological disorders which can be impactful and beneficial to patients.
7 Next steps

To build on the results of this literature review and further document and review how HTA processes currently take into account the patient perspective in general and specifically in neurological conditions (e.g., what are the HTA processes in neurological conditions compared to other conditions), we propose the following 5-step approach:

1. **Conduct qualitative interviews with HTA experts/members, patients, caregivers and PAG representatives, and pharmaceutical industries** to understand their perspectives regarding patient engagement in the HTA process, the impact of patient engagement in the decisions and future trends. This step involves:
   a. Development of interview guides, including early key opinion leader (KOL)/PAG involvement
   b. Recruitment of HTA experts/members of HTA agencies, patients/caregivers/PAG representatives (we will target PAGs in the specific conditions of interest for this project; if not possible, we will target PAGs in neurology) and pharmaceutical industry representatives; contracting; scheduling interviews
   c. Conducting and analyzing the interviews
   d. Synthesizing and reporting the results

2. **Review of HTA submission cases (i.e., HTA reports) in selected countries and describe the impact of PAG engagement on HTA decisions (based on actual cases in neurological conditions).** Based on the outcomes of the interviews, we will know for each country the extent to which patients are involved in the HTA process, the global impact they have on HTA decisions and whether patient involvement is reported in HTA reports. If the patient engagement related information is included in the HTA reports, a next step could be to review 1 by 1 these HTA reports in order to have an in-depth overview of the impact patient involvement has on actual HTA decisions (e.g., Does the presence of a patient submission relate to the reimbursement decision?; What was the content of the patient submission?)

3. **Face-to-face workshop** to present results, promote direct discussion between patients/caregivers/PAGs and HTA experts and brainstorm about tools that could be developed to empower local PAGs

4. **Develop conclusions** about current and future trends and unmet needs, identify what works and what doesn’t work, determine what tools people would like to have, and make **recommendations** for future tools developments