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The Value of Patient Engagement

Incorporating the patient voice from clinical development to commercialisation

Contents

Background

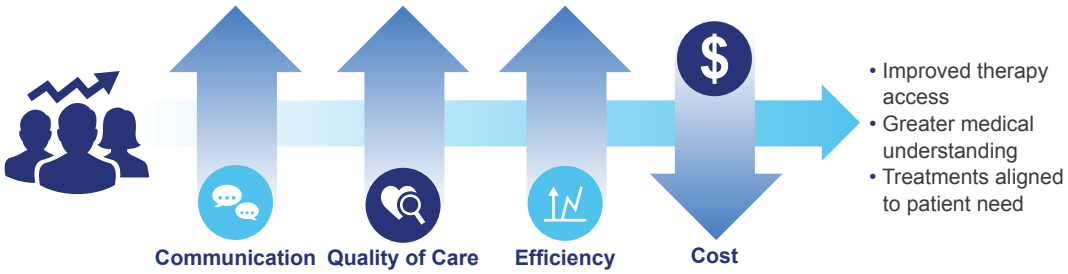
Patients increasingly want to be more involved in their healthcare, decisions about it and research towards its improvement, and there are some shining examples of patients moving front and centre to lead discussions. They can even be seen to push regulatory authorities and pharma and medical device companies into updating rules and practices.

In addition to the potential value of patients themselves being more involved in treatments that may ultimately be able to help them, patient engagement can provide vital benefits to the life sciences sector, e.g., by contributing to higher patient enrolment rates as well as patient retention. As a result, clinical trial samples are more likely to be representative of the general population and therefore more relevant to society.

Patients can be engaged in the drug development process by participating in clinical trials, assisting with evidence generation and advising as experts on the disease burden and treatment journey, both in Europe and the US. They can bring first-hand accounts of the symptoms and impact of a disease, their day-to-day experiences with therapies, the management of side effects and the life-changing accommodations that are required to receive treatment. As valued members of the research team, patients can also help define the treatment benefit of a new drug and orient the design of a trial by engaging with pharma and medical device companies and healthcare professionals throughout the lifetime of a study.

Recognising the benefits of greater patient engagement, regulatory authorities and payers alike have been working to integrate the patient voice into their processes. In the US, this can be seen within the clinical trials process, where the Food and Drug Administration (FDA) has been driving the conversation and reforming clinical trial and drug development rules to make them much more patient-focused. Alongside the FDA, the Institute for Clinical and Economic Review (ICER) has been making its presence felt stateside in matters of cost-effectiveness. Meanwhile, in Europe, much of the focus has been on bringing the patient voice into the health technology assessment (HTA) process, whether at a national level or, with the emergence of EUnetHTA and European Joint Clinical Assessments, at a central level.

Across both clinical trials and HTA, patient engagement activities including the development of patient-reported outcomes measures (PROMs), qualitative interviews and the inclusion of patients as thought leaders have created opportunities for the patient voice to be heard. For patients and their families and caregivers, engaging in drug development and HTA decisions could also lead to greater access to therapies.



From regulatory or HTA approval to post-marketing activities, patient engagement can help move scientists' understanding of a new medicine or an indication's benefits closer to how patients will respond to treatment in the real world. When applied correctly, patient engagement can produce better treatments that are more closely aligned to patient needs and then help improve access to them. There is, however, still more to do if stakeholders are to develop ways to truly integrate the patient perspective into the generation of evidence for new products.

This white paper will provide a perspective on where the industry is now, what challenges it faces, the benefits of engaging patients during the clinical trials process, how their needs within HTA can be different and how to make a success of patient engagement.

Patient engagement today

As a term, 'patient engagement' is used in many different ways. From a medical point of view, it is about engaging patients, their families or caregivers with treatment decision-making, whereas regulators and HTA bodies are more concerned with understanding patients' needs and eliciting their voice as part of the overall decision-making process.

What all these activities have in common is an acknowledgement that patient engagement is an important driving force for improving healthcare delivery systems.

Sophie Tsai is a physician by training and an Associate Scientist focused on patient-centred outcomes at Pharmerit International. Based in Bethesda, MD, she has seen a real change in approaches to patient engagement, beginning with shifts in the dynamics of patient-doctor relationships.

"In the past, physicians made all the decisions, they held all the cards, they dictated how it was going to be. But, over time, patients started to become more actively involved and we see patient advocacy organisations being more energised, leading to patients who are more educated and more informed," Tsai says. "Now, patients are taking the reins of decision-making, they want to know more and to be more involved."

There have been systematic efforts in the US to facilitate patient engagement, starting with the Prescription Drug User Fee Act (PDUFA) V in 2012 and PDUFA VI in 2017, as well as the patient-focused drug development meetings organised by the FDA. To date, the US regulator has organised 25 of these meetings, which seek better disease understanding from a patient point of view.

Similar efforts can be seen in Europe, notes Krystallia Pantiri, a Rotterdam-based Research Consultant who covers patient-centred outcomes with a specific interest in patient engagement at Pharmerit International.

"We can see diversity in both the patient engagement activities and the HTA landscape in countries like the UK, France or Germany, where patients sit on the committees assessing health technologies and have voting rights like other stakeholders present. However, in other countries like Poland or Spain that is not the case yet."

"Patients are taking the reins of decision-making, they want to know more and to be more involved."

Looking at Europe's three big markets - the UK, Germany and France - provides a number of opportunities for patients to interact with their national HTA bodies, including drafting reports on certain evidence or participating in the scoping and guidance development processes. However, there are a number of differences between these markets.

Outlining one of them, Pantiri says: "When there are disagreements about a decision, patients can lodge an appeal, but only in France do they have voting rights, though it is up to patient associations to proactively check what assessments are ongoing."

The environmental changes that have facilitated the spread of patient engagement ideas are underpinned by multiple factors, including the internet, either directly in terms of increasing access to medical information or indirectly by strengthening communication between patients and their caregivers, particularly in the rare disease field.

Pharma's patient engagement challenges

Patients and their families and caregivers are increasingly being recognised as therapeutic area experts given their day-to-day hands-on experience with their respective conditions. The rise of patient engagement in the US and Europe presents a number of challenges for pharma and medical device companies and the way they work, if they are to successfully incorporate the patient voice into drug development.

In Europe, the region's scattered HTA landscape presents an immediate potential obstacle for new products and indications and, once authorised, companies face a country-by-country campaign to win reimbursement. The way value can be demonstrated to payers is changing[1], but there remain administrative challenges for approaching patients and working with them across multiple countries.

"This geographical variation automatically means pharma and medical device companies are called to employ many different approaches when they want to engage patients in a research project," Pantiri explains. "Regulations as to how they can approach patient associations are all different and come with strict rules. It's important pharma and medical device companies are transparent about any financial relationships they have with patient associations, otherwise it's highly possible that patient associations' credibility would be damaged."

But Europe's diverse HTA landscape is just one of the challenges the pharma and medical device industry faces if it is to improve the way in which it incorporates the patient voice into clinical trials and the industry's regulatory and value discussions.

In the US, pharma and medical device companies must also come to terms with the 21st Century Cures Act and the changes it makes with respect to patient-focused drug development. The systematic approach aims to help ensure patients' experiences,

perspectives, needs and priorities are captured and then meaningfully incorporated into drug development and evaluation[2].

Kelly McCarrier, Director and Qualitative Research Lead at Pharmerit International, explains: "This clearly shows the FDA's ability to drive the conversation and it has been especially helpful in making patient engagement more of a focus for the industry. Really, the FDA is now in a position where they are essentially funding the development of PROMs, putting in place a top-to-bottom approach to try and get things moved to a place where trial operations and drug development are much more patient-focused."

As this patient engagement trend continues, it will require pharma and medical device companies to be aware of, and manage, patients' expectations of this process as patients make use of their new-found voice. Whether in HTA or regulatory discussions, it is important for there to be clarity about how the system works, what procedures mean and what the roles of different stakeholders are.

The creation of roles such as chief patient officer and patient engagement director are a welcome step in the right direction, but the holders of those titles still have to convince people within their company of the need for better patient engagement, and need support to do so. The location of a patient engagement department, as part of Medical Affairs or in other parts of the organisation, may also affect how receptive a company may be to these particular initiatives.

Top 5 challenges

1. *Understanding regulations/ policies in a dynamic and evolving landscape*
2. *Differing market needs*
3. *Building an internal culture for patient-focused research*
4. *Lack of infrastructure and limited cross-functional collaboration*
5. *Senior leadership scepticism, which often means education and communication of KPIs and ROI*

Tsai says: "Patient engagement is on companies' minds and it's definitely something that they see as important. But within companies, the concept still seems to be that it's going to be more time-consuming or add more cost to their operations. This is not true, but it's making decision-makers within the pharma and medical device industries hesitant, because they have significant time constraints and maybe they have to jump through a lot of hoops to make this happen."

Meeting these challenges head-on is the only way to change patient engagement from being a nice-to-have for pharma and medical device companies to the must-have it has become.

Benefits of patient engagement

Engaging patients early in the process has powerful benefits that can improve the quality of evidence.

It starts from the study design stage, where incorporating the patient voice through qualitative interviews can produce more pragmatic clinical trial designs that take into account what matters to patients, work to reduce patient burden and in doing so increase patient participation and retention. That leads to greater availability of patient-relevant outcomes, which can cascade into more patient-centred trials that then produce more meaningful and applicable outcomes.

One of the ways to incorporate the patient voice into a clinical trial is to develop and include PROM tools that help pharma and medical device companies to understand the degree of disease severity from a patient's perspective.

McCarrier explains: "The PROM field has been a big part of this movement towards getting more patient-centred measurements incorporated within clinical trials and we've been involved with making sure the measurement of clinical trial outcomes is relevant to patients. In many ways this rose organically from patients initially and has then been systematised and codified in some of the FDA's guidance documents around PROMs[3]."

PROMs allow for an assessment of factors that are relevant to patients and their everyday life, from understanding disease severity to gaining an appreciation of how an intervention alleviates or worsens symptoms or side effects. It's a step-change from traditional endpoint approaches.

From study design to PROMs, partnership with patient groups can be a powerful way to improve the dissemination of results and accelerate the uptake of the findings.

Case study

A ground-breaking treatment for cystic fibrosis

One of the most striking recent examples of patient engagement in the drug development process is Vertex's triple-combination treatment for cystic fibrosis (CF) Trikafta.

The drug shows clear signs of targeting the genetic root of the disease, instead of just alleviating symptoms, providing a much-needed breakthrough for patients with this hard-to-treat disease.

Vertex's research that produced Trikafta[4] was partially funded by patient advocates through an unusual 'venture philanthropy' model. This saw the CF Foundation make an initial $40 million investment to discover compounds that might correct the core genetic defect in people with CF.

The resulting clinical programme produced such compelling clinical evidence that Trikafta was approved five months earlier than expected, offering new hope to patients in an area of unmet medical need.

The collaboration between the CF Foundation and Vertex was honoured[5] by US President Barack Obama during his 2015 State of the Union address. He cited the story of CF research as an example of how non-profits, pharma, researchers, patients and their families can work together to produce more targeted and effective treatments for diseases.

Involving patients in HTA

There are benefits to patients, and therefore pharma and medical device companies, to greater involvement within the European HTA process, but resources are often an issue.

Pantiri says: “Unlike other stakeholders, many patient associations are facing problems of sustainability. Their volunteers engage in HTA work without financial support and doing so takes time away from personal, work or family engagements, on top of the disease or treatment burden that motivated their engagement in the first place.

“Without funding, patients are left with few opportunities to mobilise resources and organise information in a way that will reach the levels provided by other stakeholders.”

In addition to funding assistance, she also cites training as another area where support may be required to help patients navigate HTA systems.

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If companies do provide training, there is a further need for transparency around industry finance agreements and communications with patient groups. Without this, companies may put their credibility and reputation at risk. To avoid misalignment, it should be clear where the common ground lays between a pharma or medical device company and a patient association.

With expectations set, patient representation needs to be supported so that, wherever possible, they can sit in the meetings where decisions are made. It is also important for patients to understand what regulators and HTA bodies expect from them and to be given feedback about the evidence they provide.

How to successfully engage patients

Timing is everything when it comes to successful patient engagement and pharma and medical device companies should be wary of delaying patient involvement.

"Start the planning process early," counsels Tsai. "Don't think of it as something that's very difficult or hard to achieve - there are various degrees of involvement that you can pursue, and some may be quite simple. One way is to have a patient advocate sitting on the decision-making or review panels for research documents, processes, protocols or designs."

In addition to bringing patients onboard, McCarrier notes: "From my perspective in working in health economics and outcomes research (HEOR) and on endpoint construction, companies who are doing very well in this area are those that have invested in infrastructure resources to maintain communities of engaged patients throughout the drug development process."

Involving patients, and having the resources to keep them engaged, is an approach that makes it easier for clinical trial sponsors to have direct patient involvement at multiple time points throughout their processes, allowing a continuous feedback loop between the company, researchers and patients.

Patient journey studies[6] offer one way of uncovering patient insights in a variety of areas, such as unmet needs, barriers to efficacy and adherence, treatment preferences and quality of life impact, with clear utility within regulatory and HTA decision-making processes.

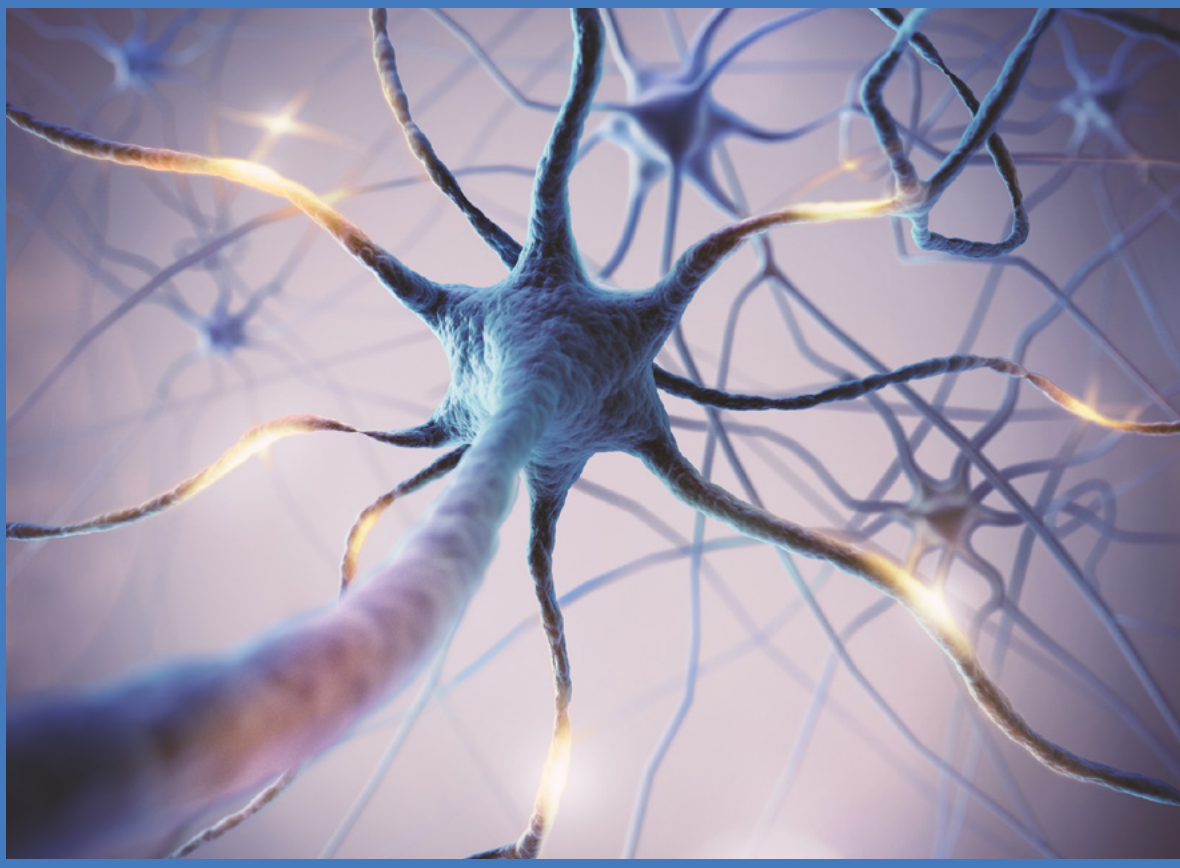
Patient journey studies offer one way of uncovering patient insights in a variety of areas.

With relationships grounded in mutual trust, pharma and medical device companies will be able to present product value arguments that are rooted in patients' reality. Information such as how patients feel emotionally or physically while receiving medical care can also assist with the development of future treatments to be tailored towards those elements that are actually important to patients.

Case study

Neurology patient understanding

In 2017, Pharmerit International was asked by the European Federation of Neurological Associations (EFNA) to assess the European landscape for patient engagement in HTA, with a focus on neurological disorders[7].



We conducted a literature review and a series of qualitative telephone interviews across six European countries (Sweden, UK, Germany, France, Poland and Spain) to find out how patients interact with HTA agencies, what impact patients had on HTA decisions, how patient engagement is perceived and how it can be improved.

The project used the Patient Engagement Quality Guidance (PEQG) tool to assess patient engagement practices in a robust and structured manner and to drill down to what demonstrated quality, what was missing and what could be improved.

This project unearthed insights into how to best bring the patient perspective into HTA committee discussions and showed where patients might take part. It also enabled Pharmerit International to produce a landscape assessment for each country within the project and demonstrate how interactions between patient and HTA experts could be aligned.

Conclusion

Patient engagement has emerged as a driving force for improving healthcare delivery systems.

All stakeholders broadly agree on the need to truly integrate the patient perspective throughout a product's generation, development and approval. However, the precise methods for how to implement patient engagement remain a challenge.

Patient-centred studies engage patients and uncover what matters to them, in the process building a body of evidence to prove patient priorities to payers and regulators. Patient-centred studies can identify actionable levers that can be pulled to affect a treatment or accessed during additional research, and can be implemented throughout the drug development and approval process.

The ultimate goal is patient access to medical care and this can be done in a more informed way by consulting a treatment's end-users. It all starts with finding out what elements are most relevant to the patient's day-to-day experience.

Pharma and medical device companies need to arrive at the point where building trusted partnerships with patients and caregivers in approval and HTA practices is not questioned, but simply a routine part of standard practice. It is equally important to ensure that there is mindfulness regarding the resources it takes for patients, and their caregivers and families to be involved with the drug development and approval processes and that there is transparency in these collaborations.

Patients and their caregivers are experts in their own experiences and deserve the recognition of other subject matter experts within the drug development and approval processes. Engaging patients in the drug and medical device development process should not only be recommended, but expected by industry, regulatory bodies and HTAs worldwide in order to improve patient outcomes.

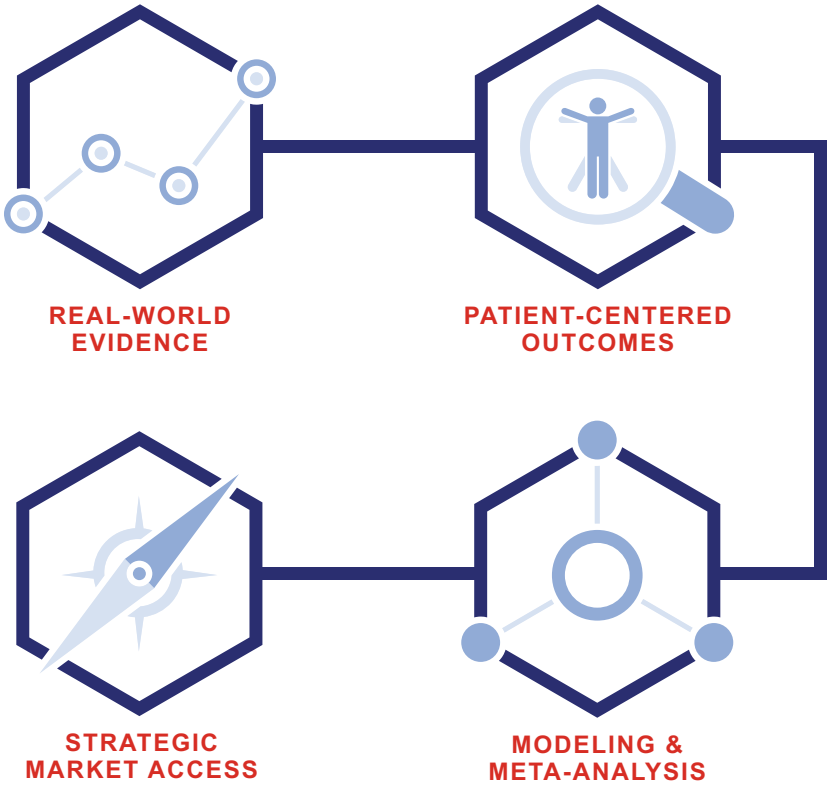
About Pharmerit International

Pharmerit International is a global, premier health economics and outcomes research (HEOR) consultancy with 20 years of experience supporting pharma, biotechnology, and medical device organizations in health economics and outcomes research (HEOR) and market access worldwide.

Pharmerit delivers quality research across four multi-disciplinary Centres of Excellence, Modelling & Meta-Analysis, Patient-Centred Outcomes, Real-World Evidence, and Strategic Market Access.

Pharmerit recently announced that it will be merging with the OPEN Health Group (www.openhealthgroup.com). The combined entity will have approximately 700 people, 15 offices, and representation across three continents.

The consolidation of publications, medical communications, HEOR, RWE, and market access creates a unique entity equipped to be a leading global HEOR and Medical Affairs Consultancy.



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Contributors

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Sophie (Jui-Hua) Tsai is an Associate Scientist in Patient-Centered Outcomes and Real-World Evidence & Data Analytics, located in Pharmerit's Bethesda, MD office. She has experience in patient and stakeholder engagement, patient advocacy group (PAG) engagement, patient/caregiver/physician preference studies, (including discrete-choice experiment, best-worst scaling, time-trade-off), strategic evaluation of patient-reported outcomes (PRO) instruments for use in a clinical trial, and PRO instrument development, spanning over a variety of therapeutic areas, including oncology, rare diseases, infectious diseases, paediatric diseases, and neurodevelopmental diseases.

Prior to joining Pharmerit, Sophie completed her post-doctoral fellowship with the Center for Health Services and Outcomes Research (CHSOR) at the Johns Hopkins University. During this time, she partnered with the US Food and Drug Administration (FDA) and patient advocacy groups (such as Parent Project Muscular Dystrophy and the Foundation for Prader-Willi Research) to engage stakeholders and the disease community in preference research. She led focus groups at an FDA public workshop to determine patient and FDA reviewer priorities and preferences in prosthetic devices.

Her research focuses on applying stated-preference methods to prioritize clinical outcomes associated with the disease and preferences for the benefits and risks of treatments. In her manuscript titled, "Research as an Event: a Novel Approach to Promote Patient-focused Drug Development," she introduced a novel and resource-efficient method to partner with patient groups and engage patients in research. She holds a Medical Doctor degree from Taipei Medical University and a Master of Health Science degree at Johns Hopkins University, and she is a Master of Business Administration (MBA) candidate at the Johns Hopkins University.

Krystallia Pantiri

Krystallia Pantiri is a Research Consultant in Strategic Market Access and Patient-Centered Outcomes, located in the Rotterdam office, the Netherlands. Her all-round experience includes (systematic) literature reviews to inform network meta-analyses, global value dossiers and HTA/reimbursement dossiers, patient/stakeholder engagement, preference studies and qualitative patient reported outcomes (PRO) research. Disease areas she has worked in include vaccines, inflammatory disease, respiratory diseases, oncology, hematology, neurological disorders and orphan diseases.

Krystallia has extensive experience with reviews of epidemiology, disease burden and treatment patterns, using the results as input for landscape analyses, strategic advice and value story development. She has been working on international projects involving development and validation of PRO instruments and analysis of quantitative and qualitative data. In this context, she performs literature reviews, coordinates patient and clinician research and writes corresponding protocols, reports and publications for peer-reviewed journals. She has presented work at international conferences including ISPOR and ISOQOL. Krystallia joined Pharmerit in 2013 with a Master's degree in Health Economics, Policy and Law (Erasmus University Rotterdam, the Netherlands).

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