



Patient Preferences in Health Technology Assessment in Europe

Recent Advances and Future Potential

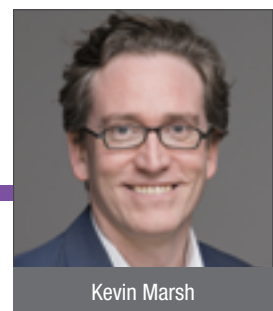
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Introduction

Healthcare decision making involves value judgements, such as whether the benefits of a treatment outweighs its risks, whether the benefits associated with a therapy are worth its cost, or which patient groups' outcomes should be prioritized for funding. Decision makers are increasingly interested in using quantitative preference data on how stakeholders make such trade-offs to support their decisions. For instance, the US Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) encourages manufacturers to submit patient preference information (PPI) to support its benefit-risk assessment.¹

Health technology assessment (HTA) often also involves the use of quantitative preference data, with general population preferences being the basis for the calculation of the tariffs used to estimate utility inputs for the cost-effectiveness analysis.² That is, a societal perspective is often adopted. While patient input is sought, often in the form of qualitative insights on the burden of the disease, submissions from patient advocacy groups, or patient representatives being members of decision-making committees,³ there has traditionally been little or no role in HTA for quantitative PPI.

Recently, however, this has started to change. Across Europe, HTA agencies are consulting on the use of PPI,



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Table 1. Overview of the Use of PPI in European HTA

PREFERENCE METHOD	USE OF PREFERENCE INFORMATION				
	Demonstrate unmet need	Valuing impacts on patients	Trial design	Unclear	Under consultation
Ranking (e.g., SMART exploiting rankings)				Belgium	
Pairwise (e.g., analytical hierarchy process)		Germany		Netherlands	
Choice based (e.g., discrete choice experiment [DCE] or best-worst scaling)	UK	Germany	UK	Hungary Denmark	UK Ireland
Matching (e.g., time trade-off or standard gamble)		Sweden		Czech Republic Netherlands	Ireland
Under consultation					Netherlands Denmark

setting precedents by considering it in their decision making, and providing advice on its use. In some instances, the role of PPI has been formalized in methods guidance. This article provides a snapshot on the use of PPI in Europe and reflects on how its use may change in the future.

The Use of PPI by HTA in Europe

An ongoing ISPOR working group has mapped the use of PPI by HTA agencies in Europe.⁴ The mapping involved a literature review; a review of agency websites; a survey of agency staff; and, a consultation with local experts. The results of this review, supplemented by more recent examples of the use of PPI by HTA agencies in Europe, are summarized in Table 1.

The table illustrates how agencies in key markets – in particular Germany, Sweden, and the UK – are leading the use of PPI. In Germany and Sweden, the goal of PPI use has been to base economic evaluation on a more accurate estimate of the value of impacts on patients than would be generated by the QALY. In Germany, the Institute for Quality and Efficiency in Healthcare (IQWiG) has recommended in its method guide that PPI be used to estimate the aggregate benefit in an economic evaluation.⁵ In Sweden, it is recommended that PPI be used where the QALY is thought to be inappropriate, such as when valuing changes in short-term pain.

In the UK, PPI has been used by the National Institute for Health and Care Excellence (NICE) in two other ways – in the unmet need section of the submission, demonstrating the value that patients place on finding alternative modes

of administration⁶; and to inform the selection of endpoints that are included in a trial. The latter use was the subject of a recent scientific advice offered by NICE on the design of a trial for a COPD treatment. In their press release advertising that they'd provided the scientific advice, NICE stated that it was their aim “to encourage more companies to seek its advice on the development of these studies ... so they can be used in the clinical development programs.”⁷

These examples represent the better documented use of PPI in HTA. But the use of PPI may be broader than examples suggest. The ISPOR review reported expert testimony that PPI has been used in reimbursement submissions in Belgium, the Czech Republic, Denmark, Hungary, and the Netherlands.⁴ The precise use of PPI wasn't clear from this data.

Ongoing consultations also point to a broadening use of PPI in the future. Pilots and consultation on the use of PPI by HTA agencies were identified by Denmark, Ireland, the Netherlands, and the UK. Exploration of the use of PPI in HTA is also being supported by the Innovative Medicines Initiative's Patient Preferences in Benefit-Risk Assessments during the Drug Life Cycle (PREFER) project. Its objective is to generate recommendations on when and how to collect and use PPI to support decision making by industry, regulatory authorities, and HTA bodies.⁸ PREFER has established a formal structure to incorporate input from reimbursement agencies into its activities, with representation from agencies from Austria, Belgium, and Germany on its Stakeholder Advisory Group.

Table 2. Challenges and Implications of Using PPI in Reimbursement Decision Making

CATEGORY	CHALLENGE	RESEARCH AGENDA
Conceptual	How are preferences defined?	<p>The need for further clarity on what constitutes PPI is illustrated by the different types of preference data identified in Table 1. Are all these types of data “preferences” or should we only be focusing on a subset of these data? For instance, are choice-based methods, such as DCE, the only source of valid PPI, or do other methods, such as rating the importance of treatment attributes, provide useful PPI?</p> <p>This will depend on how PPI is intended to be used in HTA. For instance, incorporating patient preferences into an economic analysis will require valid trade-off data, while selecting endpoints to include in a trial will only require ranking data. Initiatives such as IMI PREFER will help to define methods and their potential use. Some of the consultation work being undertaken by agencies, such as that in Denmark, will also consider how different types of preference data can contribute to HTA.</p>
Normative	1) Whose preferences should be elicited – treatment-experienced or treatment-naïve patients; patients or patient representatives?	<p>Most of the work currently being funded elicits the preferences directly from patients rather than their representatives, although patient representatives are often involved in the research project as advisors.</p> <p>There are arguments in favor of either treatment-naïve or treatment-experienced patients being the subject of preference research. Treatment-experienced patients have more insight into the attributes included in the design, although they will not necessarily have experienced all of them, as is the case with rare side effects. Furthermore, it is often not always possible to identify a treatment-experienced sample when a study is being undertaken pre-launch. This could be addressed by undertaking the preference study with trial participants, but this introduces a sample bias, as those who opt into trials tend to be more risk tolerant. When consulted, the FDA often recommends that preferences are elicited from both treatment-naïve and treatment-experienced patients.</p>
	2) Should preference focus on patient outcomes, or also process factors such as mode of administration?	<p>Agencies such as NICE explicitly exclude process utility from their reference case. There are, however, examples of process factors informing submissions to NICE, including PPI being used to demonstrate unmet need as a consequence of the mode of administration of current treatments, and general population preferences being used to estimate changes in process utility, which was subsequently included in the economic analysis.⁵ As agencies define how they will use PPI, it will be important that they explicitly address the role of process utility.</p>
Methodological	Which preference methods should be adopted?	<p>Initiatives such as IMI PREFER will help to answer this question, however, it is uncontroversial to predict that they will conclude that the appropriate method will depend on the way in which HTA agencies use PPI.</p>
Practical	How can budget, time, and expertise constraints associated with collecting PPI be overcome?	<p>Regulator-quality PPI can be expensive to collect, involving expertise that is currently in short supply. There are important roles for various stakeholders in addressing this challenge.</p> <ul style="list-style-type: none"> ● Academia has a role in providing the training required to boost the capacity to deliver rigorous PPI. ● Regulators can provide guidance on when PPI can add value and which methods are appropriate in different circumstances, which will ensure the efficient use of research budgets. ● CROs should innovate the way they provide preference research services to improve efficiency.
Procedural	How should PPI be considered alongside clinical or economic evidence?	<p>How can preference studies add to or replace the QALY paradigm? In what stage of HTA should preference studies be utilized?</p> <p>Considering PPI as supportive for HTA is relatively uncontroversial, including demonstrating unmet need, informing trial design, and identifying and quantifying the gaps and uncertainties in economic analyses.</p> <p>Incorporating PPI into economic analysis is more controversial, as most agencies adopt a societal or health service perspective, and thus use general population preferences to value the impacts of treatment. There are exceptions, such as IQWiG, whose use of therapy area-specific efficiency frontiers means that PPI has a clear role in generating aggregate benefit functions.⁵ However, for most agencies, incorporating PPI into economic analysis requires further normative work to reconcile patients’ preferences with their societal perspective.</p>

Challenges to Incorporating PPI into HTA

Despite the increased interest of HTA agencies, the use of PPI in reimbursement decisions raises a number of issues. Five categories of challenges were identified by a recent review by Huls et al.⁹ These are summarized in Table 2 with reflections on the implications for the use of PPI in HTA.

Conclusion

PPI is increasingly used to support regulatory decisions, and sponsors and HTA agencies are actively exploring how this data can also support reimbursement decisions. This latter effort is still in its exploratory phase. A small number of HTA agencies have specified the use of PPI in their methods guidance, but most agency use of PPI is less systematic, either being in the form of novel examples of the use of

PPI or at a pilot stage. These case studies and pilots point to the likely increase in the use of PPI for HTA. Where the existing methods fail to capture the value of technologies to patients – e.g., improvements in the mode of administration or health impacts that are not easily captured in the QALY, such as acute pain – PPI has a role to play in HTA. There are issues to be addressed, however, before this role becomes clear. Ongoing initiatives will help provide insight into some of these questions and concerns. In the meantime, sponsors considering the use of PPI are advised to consult agencies on a case-by-case basis to consider its acceptability and likely impact. ■

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