Patient preferences in the medical product lifecycle

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Author contributions:

JW and EBG conceived the topic and framework for the symposium panel and paper, chaired the panel, and prepared a joint draft of the paper. NSC, FTP, MD, RF, HLH presented at the panel and contributed their academic ideas to the paper. All authors reviewed and revised the draft for academic content and approved the final version for publication.

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There is an emerging consensus that evidence on patients' perspectives provides crucial guidance for decision-making throughout the medical product lifecycle (MPLC). Considering the patient voice has become increasingly important for developers of new medical products and for authorities that assess, regulate and decide which products are effective, safe, well tolerated and cost-effective [1, 2]. However, as key stakeholders, we lack a shared understanding about *how* to consider patient preferences in the MPLC [3].

This commentary captures opinions of thought leaders presenting at the symposium on "Patient preferences in the medical product lifecycle" in Basel, Switzerland in July 2019. The symposium was jointly sponsored by the International Academy of Health Preference Research (IAHPR; www.iahpr.org) and the research project 'Patient Preferences in Benefit and Risk Assessments during the Treatment Life Cycle' (PREFER; www.imi-prefer.eu). This commentary is one of a series of papers reporting on health preference research symposiums held alongside IAHPR meetings [4-6].

At the symposium, a varied panel shared their experience as researchers, policy-makers, industry leaders and patients, on the use of patient preferences in the MPLC and spoke to the following six questions.

1. **Does patient preference information in reimbursement decision-making lead to higher quality decisions and increased public acceptance of decisions regarding allocation of healthcare resources?**

Although it is widely acknowledged that patient preferences contribute important evidence for reimbursement decisions, there are challenges in assessing its impact in decision-making. First, there have not been enough published examples where preference studies have been submitted as part of the reimbursement process, on which to judge on their impact. Secondly, even where examples are available, the complexity of decision-making means it is difficult to single out the impact of preference information from the impact of other decision 'inputs' such as clinical and economic evidence and societal factors. Thirdly, preference studies are mostly undertaken late in the product development process. When this occurs, there may be a tendency to retro-fit the attributes to those which the product in question addresses, or which have been measured in the trials. There is the risk that such attributes are not addressing those things that matter most to the patient. The health technology assessment (HTA) body may well recognize this discrepancy [7]. Likewise, the patient voice might be

dampened if what matters to them is not addressed by the new product, with or without a preference study to support it. Fourth, where a preference study is sponsored by a manufacturer, there may be a perceived conflict of interest resulting in a high level of scrutiny, but also a potentially high and possibly inappropriate level of scepticism in their findings.

Undertaking preference studies early in the development process is an opportunity to strengthen their impact on both the development process and reimbursement. There are examples where preference evidence has impacted decision-making and therefore potentially improved the 'quality' of decisions [8, 9]. As such, the panel were generally of the view that preference information will improve the quality of decisions, although less decided on whether the consideration of patient preference information increased public acceptance of decisions regarding allocation of healthcare resources. At least it has the potential to increase the transparency of the decision-making process, and there was general agreement that broader stakeholder involvement in the decision-making process was desirable.

2. **What should happen first to achieve successful integration of patient preference information into the MPLC?**

To date, successful integration of patient preference information into the medical product lifecycle has been slow, unsystematic, or very limited [10, 11]. To promote successful integration, it is necessary first to address the concerns of users of preference information. Publication of examples where preference information has been beneficial and creating projects that involve collaboration across stakeholders would also promote successful integration. For some conditions there are multiple companies with similar interests. Therefore collaboration between competing companies when undertaking studies would allow companies to pool resources and expertise, and reduce any perception of biased interests.

Who should fund preference studies presents a dilemma. Regulators look to industry to generate good quality preference studies to support their decision-making [12]. However, pharmaceutical and medical technology companies may be averse to spending research resources to undertake studies that are not seen to influence regulators decisions. The uptake of preference studies and examples of impact might be expected to break this deadlock, even if progress is gradual initially. Finally, industry standards, research standards and quality guidelines for undertaking preference studies are needed to support the use of patient preferences in regulatory and HTA decisions. Text books in the field (such as that currently being developed by IAHPR), consensus guidance, and a more consistent approach to

developing protocols before undertaking a preference study should all assist the perceived rigour and therefore integration of preference studies. Rigour can be improved by adhering to an *a priori* study protocol; for example, via the HPSTR database [13], and reporting according to appropriate peer-review standards such as those recommended by the ISPOR review task force [14] and through publication in a peer-reviewed journal.

3. Which preference methods are most promising or acceptable to be used in regulatory assessments or reimbursement decision-making?

As with any research area, the method needs to suit the research question. Currently, discrete choice experiments (DCEs) are perceived as the gold standard for evaluating preferences and are widely used. However, they are not suitable in all scenarios: when there are many attributes to consider (which may be the case in a new disease area in particular) or when patients might not be able to process a large amount of information being given to them. Also if the question relates to a rare disease, preference studies via DCEs may not reach a sufficient sample size to allow for valid statistical analyses and reliable preference data. In such circumstances, innovative approaches or other methods might be more suitable.

The importance of using appropriate qualitative methods in the early stages of undertaking a preference study is now well established [9, 15, 16]. The development of consensus guidance to aid the selection of appropriate methods for different research questions was encouraged by the panel.

4. At what point in the MPLC is patient preference information most useful, and for what purpose?

Whilst funding can be challenging to obtain for preference studies, it may be easiest to obtain funding to elicit patient preference information during product development to support marketing, or for reimbursement decisions. Typically funding availability is greatest in the 12-24 months approaching product approval and launch, and is likely to be quite restricted early in the MPLC. However, consideration of patient preference evidence early and if feasible continuously in the product lifecycle can provide strong benefits for stakeholders. The net present value of engaging patients in the MPLC is high in the early phases of development [17]. The challenge is to secure the funding at this early stage of development. Once again, good examples of the impact of such early preference initiatives are needed in the literature to foster this shift of attention to earlier investment. Moreover, patient preference data may play an important role in designing trials [18], to help understand what risks and benefits should be measured and what effect size is meaningful for patients. It has also been shown

that trials can achieve faster recruitment and completion when patient input had been solicited during the design [19].

Resources to undertake preference studies would be best directed to those products where preferences are most likely to influence the regulatory or reimbursement decisions. We need to understand the conditions and factors that make these decisions most sensitive to preferences [12], and should promote further research to help understand this. It is important for companies to have an early discussion with regulators and HTA bodies to both identify products for which patient preference information might be of particular benefit to decision-making, and to identify relevant effects for which risk-benefit trade-offs might be elicited, and to determine what constitutes patient value. Of note, the nuance between regulators and HTA agencies and the purpose for which they might use preference information also needs to be considered.

5. Is there a role for use of preference information elicited from people other than patients to inform the MPLC?

The decision problem and context are important considerations when deciding whose preferences are relevant. Where the general public are the payers for care, their preferences might be relevant for informing priorities about health and social care provision, and resource allocation at a population level (and this is typically done, for example through use of the EQ-5D and similar preference-based outcome measures).

Once resources are allocated to a specific area, patient preferences on how to develop or prioritise treatments or products within that area become most relevant. Where patients are able to provide preferences every effort should be made to obtain preferences from patients themselves, or in some cases their caregivers, and the use of a proxy might not be acceptable. It is important to also remember that the relevant individuals to seek preferences from may differ in different cultural or geographical settings. This also raises the question of who is the 'patient'? A patient preference study needs to clearly define the characteristics of the 'patient' of interest, using inclusion and exclusion criteria. Within a disease, people may have different characteristics, some of whom may be candidates for the drug based on the marketing authorisation or reimbursement criteria, others not. Further, participants within a clinical trial may be a very narrow subset of patients affected by the disease. For products targeting prevention, it may be service users or the general public rather than 'patients' that are most relevant. There is a continuum of 'patients', at one extreme is the general public, who are all potential service users, and at the other is an individual patient with a specific condition making an

individual decision about their treatment [20]. The patient population of interest will lie somewhere on this continuum.

6. How might patient preference information best be elicited from patients and when? For example, is it acceptable (or even preferable) to elicit information alongside clinical trials?

Eliciting preferences alongside a trial may be opportunistic. However, there are also arguments against eliciting preferences alongside a trial. Participants in a trial might be less risk-averse than other patients with the same condition. Whilst a trial may be helpful scientifically to accommodate randomisation and investigate comparative effects, it may not be the best setting for investigating preferences which would ideally be generalizable to the wider patient population. Preferences elicited alongside a clinical trial are also unlikely to give information on uptake by the broader patient population, which are useful particularly in the public health setting. If preferences are to be elicited alongside a trial, the timing of elicitation is important. Patients may be naïve to the product at the start of the trial, but some will be more familiar with the product by the end (though, they may be blinded to allocation). Product preferences may also be associated with trial drop-out, introducing a selection bias if preferences are elicited from participants later on in a trial.

Concluding remarks

To conclude, the symposium was unanimous about the important role of patient preference information and that collecting preference data from an early stage of product development has clear benefits. There is a role for qualitative approaches to gather evidence on patient experiences and to inform the development of preference instruments. Qualitative evidence complements the quantified weights and trade-offs that preference information provides. Finally, it is important to recognise patient heterogeneity, in terms not only of defining the characteristics of the patient group of interest, but also of considering when in the patients journey is the most relevant time point to elicit preferences.

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