Incorporating Patient Preferences into Product Development and Value Communication:
Why, When and How?

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Introduction

Should you be incorporating patient preferences into the assessment of the benefits and risks of your drugs and devices, and if so, when and how? As the importance of patient preferences is acknowledged by regulators and payers, we are often asked these questions by our clients. Responding to the demand for this type of work, Evidera has formed a dedicated Patient Preference team to help our clients implement and use appropriate patient preference elicitation techniques and associated decision analysis tools.

The focus of this new Patient Preference team differs from our established expertise in Patient-Reported Outcomes (PROs). While PROs are designed to measure a patient's perception of a health state, patient preference data is designed to assess the way patients make trade-offs between treatment attributes. Regulators' interest in PROs will continue, but they are also showing more and more interest in patient preference data.

This article summarizes recent developments in the use of patient preferences in decision making, the implications for evidence generation planning, and recent guidance on which patient preference methods are the most appropriate.

Patient preferences are increasingly required by decision makers

Most people would recognize that patient preferences have an important role to play in healthcare decision making, although it is only recently that decision makers have shown interest in quantitative methods for eliciting patient preferences. Previously, the patient's role in health policy development was mostly limited to representation on decision making committees.[1-3] Increasing recognition of the limitations of such an approach – focusing on the qualitative input of a small number of not necessarily representative patients, as only one voice in a large
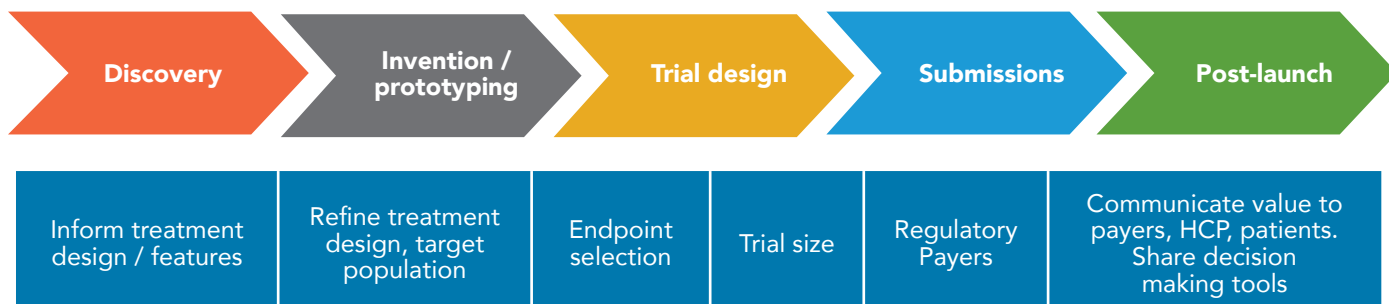
decision making group – has led to calls for the rigorous quantification of the patient voice.[4]

Regulators in the United States are responding to this call. This is illustrated by the United States Food and Drug Agency's (FDA) recent encouragement to device manufacturers to submit patient preference data as part of submissions, and their consultation on how best to collect this data.[5] This has coincided with the first regulatory approval by the FDA based on preference data.[6] In this instance, the Center for Devices and Radiological Health (CDRH) used patient preference data to determine whether the benefits of a weight-loss device (percent weight loss, weight loss duration) outweighed its risks (mortality). Partly on the basis of this analysis, they concluded that the device should be approved.

Similar developments are taking place in Europe with regulators and health technology assessment (HTA) agencies making use of patient preferences. Staff at the European Medicines Agency (EMA) recently published a manuscript outlining the piloting of methods to incorporate patient preferences into the assessment of oncology treatments.[7] They concluded that "our preference elicitation instrument was easy to implement and sufficiently precise to learn about the distribution of the participants' individual preferences." In Germany, the Institute for Quality and Efficiency in Healthcare (IQWiG) has successfully piloted techniques for eliciting and incorporating patient preferences into its economic evaluation methods and incorporated these methods into its methods guidance.[8]

These examples represent just the formal requirements of decision makers. But even where it is not yet formally required, patient preference data is being collected and submitted to decision makers. This research is being commissioned by several stakeholders, not the least of

Figure 1. Multiple uses of patient preference data in product development

Discovery	Invention / prototyping	Trial design	Submissions	Post-launch
Inform treatment design / features	Refine treatment design, target population	Endpoint selection	Trial size	Regulatory Payers	Communicate value to payers, HCP, patients. Share decision making tools

(Note: "Regulatory Payers" appears under Submissions; "Communicate value..." under Post-launch)

which are patient advocacy groups.[9] Further, it is hard not to see these developments as part of a broader trend to more systematically incorporate patient preference data into decision making. We watch with interest as, for instance, the FDA and industry negotiate the next round of the Prescription Drug User Free Act (PDUFA VI), which is expected to establish standards for conducting and analyzing patient preference research, and take steps to formally integrate patient preferences into regulatory decisions.[10,11]

Implications for evidence generation planning

The interest of decision makers in patient preferences has a number of important implications for how manufacturers should generate and use such data. Many of our health economics and outcomes research clients are familiar with collecting patient preference data using some form of a conjoint analysis as part of their marketing strategies. Given the expanded role of patient preference data, manufacturers will need to start planning for the collection of this data much earlier, with applications throughout the product lifecycle (see Figure 1).

For instance, combining patient preference data with data on the performance of treatments using decision modeling techniques, regulators are estimating the overall benefit-risk of a product. A similar analysis can be used to estimate patients' maximum acceptable risk (MAR) – the maximum likelihood of a certain risk a patient could tolerate in exchange for the benefits generated by a treatment. This data can be used to inform trial size calculations, ensuring a trial is powered sufficiently to demonstrate that the risk of a product is lower than the MAR.

Given the importance of these considerations to the chances that a treatment achieves authorization and reimbursement, it is natural to cascade these requirements back into the discovery and invention / prototyping stages of the product development cycle to ensure that treatments are designed in line with patient preferences to secure a positive regulatory response. As a consequence,

it is important to plan patient preference studies as early in the development process as possible.

For which products should patient preference data be collected? It is currently difficult to offer a definitive answer to this question, though it is possible to point to trends that will help determine the value of patient preference data on a case-by-case basis. First, is the product a device? The CDRH encourages manufacturers of medical devices to include patient preference data in their submissions, and, as we noted above, there is a precedence of such preference data informing the CDRH's decision. Second, is a decision likely to be preference-sensitive? Regardless of whether a product is a device or a drug, a benefit-risk assessment is more likely to be preference-sensitive if:

1 A product generates clear clinical benefits but has a greater risk of events that are likely to concern regulators, such as potentially fatal side effects.

2 A product generates similar benefits to standard of care, but with a different safety profile.

3 A product is in a crowded market, with no obvious preferred treatment.

Designing a credible and useable patient preference study

Designing and implementing patient preference studies, as well as the interpretation and application of the data, poses a number of challenges, including: the selection of a credible preference elicitation instrument; ensuring data is collected from a representative sample of patients; and generating outputs that are useful for decision makers. In this section we focus on just one of these, selecting a credible preference elicitation instrument. Recent reviews have identified many relevant methods (see Figure 2).

For those unfamiliar with the field of preference elicitation, the number of methods available can be overwhelming. Particularly given the lack of guidance as to the most appropriate method for a particular circumstance, and the use of different methods by

Figure 2. Methods for eliciting patient preferences[12]

Category		Method
Indirect	Choice based	Discrete choice experiment
		Best-worst scaling
	Matching	Time-trade-off
		Standard gamble
Direct	Ranking	Simple Multi-Attribute Rating Technique Exploiting Ranks (SMARTER)
	Rating	Visual analogue scales (VAS)
		Point allocation e.g., SMART
	Threshold analysis	
	Pairwise	Analytical Hierarchy Process (AHP)
		Measuring Attractiveness through a Categorical Based Evaluation (MACBETH)
	Swing weighting	Simple Multi-Attribute Rating Technique with Swings (SMARTS)
	Scoring rules	Bi-section method
		Difference method

different decision makers - with the FDA's first approval informed by preference data being based on the findings of a discrete choice experiment, the EMA piloted a variant of swing weighting, and the IQWiG explored both the analytical hierarchy process and discrete choice experiment.

The appropriate method is a function of:

1 The objective of the analysis, including whether it is intended to support internal decision making or regulatory submission;

2 The patient population, including whether they experience any cognitive impairments; disease prevalence; and likely diversity of preferences;

3 Lessons from previous experience of applying the method for a particular purpose;

4 Good practice guidelines.

Focusing briefly on the latter point, comprehensive good practice guidelines are not yet available, but guidance is starting to emerge. For instance, the

Medical Devices Innovation Consortium (MDIC) recently published a description of some of these methods[12], and the recent outputs from the International Society for Pharmacoeconomics and Outcomes Research's (ISPOR) Multi-criteria Decision Analysis Taskforce identified the differences between many of these methods and outlined both theoretical and practical principles that might be brought to bear on the choice of methods.[13,14]

More precise guidance is expected as the demand for patient preference data increases. A key source of such guidance could be the Innovative Medicine Initiative's call for research on eliciting the patients' perspective on the benefits and risk of medicinal products.[15] This project will not be completed for a number of years, but in the meantime, Evidera's Patient Preference team will be sharing expertise on this topic in upcoming webinars and publications.

Conclusion

A significant effort is committed to the quantification of clinical and safety endpoints to inform healthcare decision making. This is completely appropriate if we are to make decisions that benefit patients and society

more generally. Another important consideration, however, is that until recently, patients' preferences for these attributes have not received the same amount of attention. We are pleased to acknowledge changes in this attitude, and the increased quantification of patient preferences to inform decision making. While we have just started to determine precisely how patient preferences should be collected and incorporated into decision making, these are exciting developments, and we look forward to participating in a scientific discussion that will further advance these techniques.

In the meantime, given decision makers' interest in patient preference data, manufacturers should be systematically considering the collection of such data in their evidence generation planning and getting expert input into the design and implementation of these studies.

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