Enhancing the Incorporation of Patient Preferences and Perspectives into the Total Product Lifecycle

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Abstract

The Food and Drug Administration (FDA) and industry have shown interest in incorporating Patient Preference Information (PPI) and Patient Reported Outcomes (PRO) into the device, drug, and biologic regulatory decision-making process and total product lifecycle (TPLC). Engaging patients informs medical product development, clinical study design, and how the outcomes of each clinical study impact patient's lives and confirms patient concerns are addressed throughout. As the understanding of PPI and PRO in medical product development matures, it is critical to improve the methods of collection and use to maximize its utility in the regulatory review process. The need for such improvement was highlighted by the FDA during the Virtual ISPOR-FDA Summit 2020.

The current "Gold Standard" is a discrete choice experiment (DCE), but it is costly and time consuming. The goals of this poster are to propose additional methods beyond DCE in which PPI and PRO can be incorporated into the TPLC to enhance patient-focused medical product development while unburdening reviewers. Our focus is as follows:

- Guidance and framework development for industry and regulators
- Evaluation of best practices and suggestions for improvement in the Centers' programs
- Integration of patient data into regulatory decisions

Introduction

Patients are experts in their own chronic conditions. We aim to tap into this expertise to incorporate patient preferences into medical product development. Our goal is to provide thought leadership to regulators to aid in the treatment of conditions most important to patients in their daily lives. FDA seeks to incorporate PPI into the regulatory decision-making process across the TPLC, as illustrated in Figure 1:

- Device development
- Clinical study design
- How the outcomes of each clinical study impacts patients

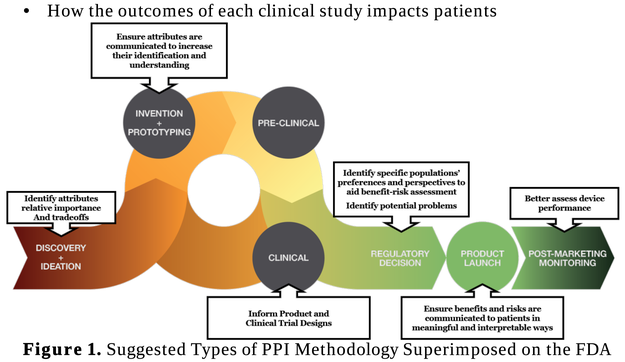

Figure 1. Suggested Types of PPI Methodology Superimposed on the FDA TPLC

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Materials and Methods

To advise FDA about the preference elicitation methods most appropriate for each phase of the TPLC, Booz Allen has conducted a literature review of the limitations and best practices of the most-used methodologies for eliciting PPI. These are Binomial Crossover Studies, DCEs, Best-Worst Scaling (BWS), Adapted Swing Weighting (ASW), Likert Scale Responses (LSR), and combination methods.

Results and Discussion

Limitations of each method can help address FDA's concerns about the inappropriate use of PPI methodologies. Conceptual limitations involve inefficiently informing and ineffectively engaging patients. Methodological limitations encompass incomplete data analysis or methodology validation. Logistical limitations incorporate incompletely facilitating patients' participation by underwriting costs, not accounting for the time necessary to perform a PPI study, and failing to effectively recruit and retain participants. A high-level summary is provided in Table 1.

Purpose/Method	Benefits/Risks	Best Practices
Identify Attributes/Tradeoffs • Literature Review • Patient Interview • Simple Direct Weighting • Swing Weighting • Best-Worst Scaling • Point Allocation • Direct-Assessment Questions • DCE	**Benefits**: Allows identification of attributes most relevant to patients for a direct comparison of attributes to determine those preferred by patients or the value patients place on a relevant attribute **Risks**: Poor question design (e.g., problems with wording, leading questions, scale formats) or questionnaire design (e.g., formatting problems, too long or complex questionnaire); the list of attributes provided by patients may not be sufficiently robust to capture attributes that can be addressed during TPLC and drug/biologic approval process	Standardize collection and interpretation of information on patient perspectives by the creation of valid, and reliable questionnaires
Ensure Patient's Understanding • Adapted Swing Weighting • Best-Worst Scaling	**Benefits**: Affords patients the opportunity to make informed decisions and to appropriately weigh pros and cons of options presented to them **Risks**: Patients may possess knowledge gaps and health literacy limitations	Ensure information is accessible; provide opportunities to collaborate with patients; educate patients; minimize cognitive burden
Inform Clinical Trial Design • Binomial Crossover • PROs o Simple Direct Weighting o Point Allocation	**Benefits**: Allows for the generation of quality data; provides an opportunity for patients to play an active role in the medical product development process **Risks**: Wide variation in the analytic techniques and data presentation methods used with few trials reporting clear PRO research objectives and analysis of results; limited sample size and representativeness	Promote equity in patient voices; promote patient diversity/representativeness; utilize a common framework and standardize study designs; analyze data appropriately and adequately validate methodologies; demonstrate the scientific validity and reproducibility of the study data used
Identify Preferences that Impact Patients' Benefit-Risk Assessment • Analytical Hierarchy Process • Binomial Crossover	**Benefits**: Account for biases patients may have that may affect their decisions or lead to poor adherence/negative outcomes **Risks**: Patients may possess bias or can become stressed/fatigued participating in studies; time constraints; lack of full collaboration between patient groups and trial sponsors; financial resource limitations; recruitment and retention issues	Utilize community-centered events to decrease the time burden and overall cost of study participation; emphasize the importance of understanding how patient preferences vary across patient populations
Ensure Risks are Communicated in Meaningful Ways by Patients • Discrete Choice Experiment • Focus Group Interviews • Concept Mapping	**Benefits**: Critical that patients understand risks to ensure clarity and allow patients to make meaningful decisions; provides clear information of the tradeoffs across product attributes that patients are willing to make **Risks**: Cross-level communication difficulties; confusion between patient engagement and patient activation; lack of email or other technological resources to access information; attributes may be elicited from a set of patients, and those responding in DCE may lack understanding of the terms and are unable to make meaningful decisions	Emphasize the importance of using patient-centered communication skills; empower patients; remind patients that all options confer some risk; avoid the use of technical terms and the use of solely descriptive language
Assess Device Performance • Discrete Choice Experiment • Best-Worst Scaling • Likert Scale Response	**Benefits**: Patients utilize performance information to inform decision making about using a device **Risks**: Methods require a skilled facilitator to ensure bias is not introduced by leading the patient	Implement robust assessments to ensure the safety, high quality, and efficacy of devices; utilize metrics, standards, and evaluation tools that will ensure medical product quality

Table 1. TPLC PPI elicitation method: Benefits/risks and best practices

Stage 1

Identify Attributes

- Elicitation methods qualify how patients value pros and cons of options
- Identify:
  - o Attributes
  - o Relative importance
  - o Tradeoffs
- Rigorous methodology

METHODS
- Value Tree
- Effects Table
- Small Group Elicitation
- Literature Review
- Patient Interview

OUTCOMES
- Quick and clear evaluation and communication of attributes involved in patient choice behavior
- Informs researchers and clinicians of patient needs

Stage 2

Elicit Preferences

- Mixed methodologies lend themselves to further analyses
- Structured weighting methods
- Ranking can be translated into weights if measured on the same scale

METHODS
- PPI Discrete Choice Experiment
- Simple Direct Weighting
- Ranking
- Swing Weighting
- Point Allocation

OUTCOMES
- Assigns points to attributes corresponding to the level of importance to the patient
- Weights allow attributes to be compared directly

Stage 3

Predict Decisions

- Benefit Risk Trade-off analyses quantify the value patients place on outcome measures/attributes

METHODS
- Multi-Criteria Decision Analysis
- Analytic Hierarchy Process

OUTCOMES
- Explicitly evaluates multiple conflicting criteria

Stage 4

Quantitative Analysis

- Use quantitative analysis to compare effects and bring the effects together to make an overall benefit-risk profile determination
- Assess the sensitivity of the quantitative analysis results to assumptions and uncertainties inherent to the decision problem

METHODS
- Simulation Models
- Bayesian Network Meta-analysis

OUTCOMES
- Quantitative comparisons of benefits and risks and sensitivity analyses

Figure 2. Stages of the determination of patient attributes, preferences, and their incorporation into a regulatory setting.

Conclusion

Incorporating data from PPI studies into the TPLC is beneficial to medical product development. Our literature search revealed best practices in applying these methodologies and that the utility of these practices vary across situations. Development of structured guidance and decision frameworks can support the systematic incorporation of PPI and PRO into the TPLC and aid the regulator decision support process (Figure 2). The benefit to developing these structured approaches can help generate consistent and effective results. In addition, the downstream effects could increase the quality of data to be used in regulatory decisions. As with the device pathways, the same basic principles can also be applied to the drug and device regulatory pathways to improve the wellbeing of patients.