Giving patients' preferences a voice in the medical product lifecycle: why, when and how?

The public-private PREFER project: Work package 2

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Medical products are developed for patients. Taking the patient perspective into consideration and the need to provide more avenues for patient engagement have not only become increasingly important for the companies that develop new medical products, but also for the authorities that assess, regulate and decide which medical products are effective, safe, well tolerated and cost-effective [1-4]. One of the most important components of the patient perspective are patient preferences, qualitative or quantitative assessments of the relative desirability or acceptability to patients of treatment alternatives or the benefits, harms and other properties that differ among health interventions [5]. As such, there is an emerging consensus among industry, regulatory authorities, academia, health technology assessment (HTA) bodies, reimbursement agencies, clinicians and patient organizations, that patients' preferences should be taken into account in the medical product lifecycle (MPLC) [6].

Currently, however, the lack of standards and regulatory requirements on when and how to consider patients' preferences in the MPLC hampers patients' preferences taking a key position in MPLC decisions. More specifically, there is currently limited understanding or agreement of (i) the key needs and concerns relevant stakeholders (industry, regulatory authorities, HTA bodies, reimbursement agencies, clinicians and patient organizations) have on the collection and use of patient preferences in the MPLC; and (ii) which patient preference methods are most promising to inform benefit-risk decision making for industry, Regulatory Authorities, HTA bodies, and reimbursement agencies at different decision points in the MPLC [5, 7]. The PREFER project - a public-private research initiative – has recently been launched to address these and related research questions.

PREFER is a five-year project funded equally by the Innovative Medicines Initiative (IMI; Europe's largest public-private initiative aiming to speed the development of better and safer

medicines for patients) and by industry as in-kind contribution. IMI is a partnership between the European Union's Horizon 2020 program and the European pharmaceutical industry represented by EFPIA (the European Federation of Pharmaceutical Industries and Associations) (see de Bekker-Grob et al. [6] for more details). The results of PREFER will be disseminated broadly, including at the annual international and European ISPOR meetings, its health preference Special Interest Group, and publications in Value in Health.

PREFER work packages and their significance

PREFER contains four work packages, including a management work package (WP1) (Figure 1). Work package two (WP2) is the starting point of PREFER and aims to answer the main research question: 'when and how to consider patients' preferences in the MPLC?'. To provide more trust and evidence, PREFER work package three (WP3) will empirically test the findings and detected research questions from WP2 in different clinical case studies. Finally, to develop guidelines for the design, conduct, analysis and reporting of patient-preference studies, work package 4 (WP4) will generate recommendations on patient-preference elicitation to inform decision making during the MPLC using the results from WP2 and WP3. Obviously, we cannot create valuable guidelines at the end without taking relevant stakeholder views (industry, regulatory authorities, HTA bodies, reimbursement agencies, clinicians and patient organizations) into account at the beginning and during PREFER. As a result, we will organize several discussion and dissemination activities (e.g. a PREFER workshop in Berlin, May 2018, and a PREFER symposium in Basel, July 2019). See the PREFER website http://www.imi-prefer.eu/ for all upcoming events, background information, news, and more.

As PREFER is currently in its second year, this article will focus on the tasks of WP2 only; the exact approach for WP3 and WP4 is still work in progress. WP2 consists of eight distinct tasks (Figure 2). Each task is crucial to be able to answer the main research question: 'when and how to consider patients' preferences in the MPLC?' For each task at least one peer-review publication has been planned, including Value in Health, and abstracts will already be submitted to the European ISPOR meeting in Barcelona, November 2018.

Task 1: What do stakeholders want and need?

Nothing about them, without them. Task 1 aims to determine stakeholders' desires, expectations, concerns, and requirements on the assessment and use of patient preferences throughout the MPLC. Hereto, we will conduct (i) a literature review to identify English white literature as well as grey literature, (ii) about 150 semi-structured interviews with six different stakeholder groups (patients and patient representatives, physicians, academics, industry representatives, regulators, and HTA representatives) from France, Germany, Italy, Netherlands, Romania, Sweden, UK and USA; and (iii) several focus group discussions with patients from Italy, Romania, Sweden, and UK as well as with European industry representatives, European HTA representatives, European regulators and USA regulators.

Task 2: Which processes, conditions and contextual factors influence the utility and role of preference studies in MPLC?

To determine when preference studies are most beneficial in MPLC, Task 2 aims to identify the existing processes, conditions, and contextual factors that have meaningful influence on patient

preference assessment and application in decision making along the MPLC by different stakeholders. To address this research question the same approach as in Task 1 will be used.

Task 3: Where to include patient preference information in decision-making?

To ascertain that preference studies provide added value to decision-making, Task 3 aims to (i) identify the decision-making processes and decision points throughout the MPLC for pharmaceutical industry, regulatory authorities, and HTA bodies and payers, and (ii) determine critical decision points that have potential to include Patient Preference Information (PPI). Hereto, we will conduct a scoping literature review and will interview about 70 representatives of three stakeholder groups (pharmaceutical industry, regulatory authorities, HTA bodies and payers) from France, Germany, Italy, Netherlands, Romania, Sweden, UK and USA.

Task 4: What methods exist to explore or elicit patient preferences?

To determine which methods are most promising to explore or elicit patient preferences in the MPLC, a first important step is to identify existing preference methods. The aim of Task 4 is to provide a compendium of patient preference methods (that might have potential) in MPLC. We will conduct a systematic literature review and include at least 20 international experts from different continents in the field of health preference and/or medical decision making to confirm our results and to overcome any publication lag.

Task 5: How to communicate risk, educate patients and profile psychological variables?

In order to simplify the selection process of educational components in a preference study, it is crucial to develop a catalogue of available psychological instruments and an educational feature-

identifier tool. Therefore, the objective of Task 5 is to identify, describe and assess different approaches to communicate risk, educate patients and profile psychological variables that can affect the construction, elicitation, and interpretation of patient preferences. Hereto, three scoping reviews for presentation of risk, psychological instruments, and educational tools will be conducted.

Task 6: How to characterize patient preference elicitation and exploration methods?

Before we can determine which methods are most promising to explore or elicit patient preferences in the MPLC, we should first identify important criteria by which to characterize and appraise the patient preference elicitation and exploration methods, and determine numerical weights for these criteria for different stages in the MPLC. This is exactly what Task 6 aims to do. In Task 6 we will develop criteria by which to characterize and appraise the methods through incorporating existing criteria from ISPOR guidelines, MDIC's patient-centric benefit-risk framework, and expert stakeholder opinion. Additionally, we will ask health preference experts (including ISPOR members) to complete a Q-methodology exercise, to rank all the criteria by importance for several hypothetical scenarios in the MPLC. Finally, an analytical hierarchy process (AHP) will be applied among PREFER and non-PREFER members to determine numerical weights in order to ascertain the relative importance of the criteria.

Task 7: Which patient preference elicitation and exploration methods are most promising?

The objective of Task 7 is to appraise preference exploration and elicitation methods for different stages in the MPLC. First, each preference method identified in Task 4 will be characterized using the criteria determined in Task 6; i.e., a table of preference methods by criteria will be prepared.

Interviews with health preference experts will be conducted to assess the performance of the methods on these criteria (e.g., determine whether a certain criteria is met or not for a specific preference method). Second, the numerical weights of the criteria for different stages in the MPLC based on Task 6 will be linked to the data in this table. The AHP will give a score for the utility of each method for each hypothetical scenario, giving rough information on which preference methods are most promising at different stages in the MPLC.

Task 8: When and how to consider patients' preferences in the MPLC?

Last but not least, Task 8 aims to generate a report on 'when and how to consider patients' preferences in the MPLC' based on the outcomes of Tasks 1-7. Additionally, Task 8 aims to provide requirements and both methodological and clinical research questions for the candidate preference methods for testing in WP3's empirical case and simulation studies. While empirical case studies can be used to evaluate how actual patient groups may produce different results for different methods, different stages of the illness, etc., only a handful empirical case studies can be performed. The empirical case studies will provide information on the methodological research questions, and as such will generally provide additional evidence. Simulation studies, on the other hand, offer a broad range of possibilities, including the ability to run variations of parameters for different methods thousands of times. Example questions that may be addressed include: How do the preference methods perform when the attributes have very disparate utilities versus very similar utilities? How do the preference methods perform when there is considerable uncertainty on utility or considerable population heterogeneity in utility? How similar are the results from different methods as a function of properties of the simulated patient utilities and as a function of changing parameters in the methods?

Conclusions

The eight tasks of WP2 will be an important starting point to develop a systematic approach for considering the use of patient preferences across the MPLC. It will contribute substantially to the ideal achievement of PREFER: a global, harmonized approach to the use of patient preference studies by industry, regulatory authorities, HTA bodies, and reimbursement agencies, and, as such, will give patients' preferences a voice in the MPLC.

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Figure 1: PREFER Work Packages (WP) focusing on when and how to consider patients' preferences in the medical product lifecycle (MPLC)

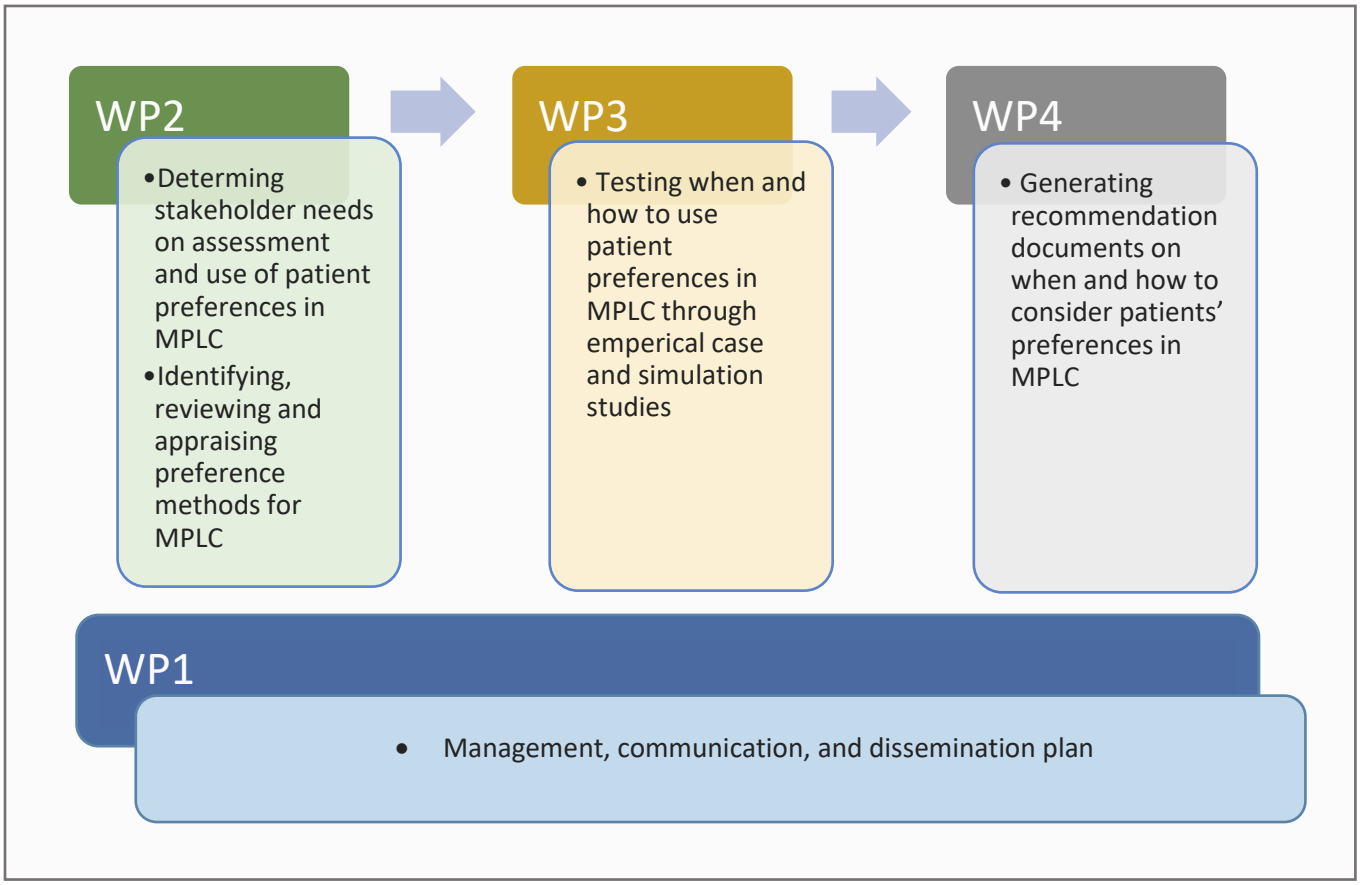

Figure 2: Conceptual model of PREFER Work Package #2 (WP2)