VALUE IN HEALTH 19 (2016) 746–750

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

A Framework for Incorporating Patient Preferences Regarding Benefits and Risks into Regulatory Assessment of Medical Technologies

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ABSTRACT

Background: In response to 2012 guidance in which the US Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) stated the importance of patient-centric measures in regulatory benefit-risk assessments, the Medical Device Innovation Consortium (MDIC) initiated a project. The project was used to develop a framework to help the Food and Drug Administration (FDA) and industry sponsors understand how patient preferences regarding benefit and risk might be integrated into the review of innovative medical devices. **Methods:** A public-private partnership of experts from medical device industry, government, academia and non-profits collaborated on development of the MDIC patient centered benefit-risk framework. **Results:** The MDIC Framework examines what patient preference information is and the potential use and value of patient preference information in the regulatory process and across the product development life cycle. The MDIC Framework also includes a catalog of patient preference assessment methods and an agenda for future research to advance the field. **Conclusions:** This article discusses key concepts in patient preference assessment of particular importance for regulators and researchers that are addressed in the MDIC Framework for patient centered benefit-risk assessment as well as the unique public-private collaboration that led its development.

Keywords: patient-derived preferences, preference-based measures, preferences, regulatory.

Introduction

Patient preferences or patient preference information can be used in a narrow sense to simply refer to the expression of preferences about the choice that patients face regarding which treatment option to use, for example, the preference of therapy with a device versus therapy with a drug, and has been used by drug and device companies as part of product development. Patient preference information, however, has a similar role in the regulatory process as it does during product development: defining how to frame benefit-risk issues so they are most germane for patient decision making, identifying preference subgroups for whom preferred decisions would be different, and supporting benefit-risk modeling to guide patient-centered decision making [1].

The Food and Drug Administration's (FDA's) Center for Devices and Radiological Health (CDRH) launched the Patient Preference Initiative [2] in September 2013 to examine ways in which it could broaden patient input in medical device regulation. This initiative stemmed from recognition in a landmark 2012 guidance [3] issued by CDRH that patients' perspectives on benefit-risk trade-offs will vary according to individual expectations and tolerance and should be considered by regulators for both premarket-approval applications and de novo petitions. A 2013 public workshop [4] convened experts in health economics, social sciences, patient advocacy, and the medical device industry for a robust discussion of methods and tools for measuring treatment preference as well as of gaps in the evidence base and tool set.

The learnings from this workshop helped shape the Medical Device Innovation Consortium's (MDIC's) Patient Centered Benefit-Risk (PCBR) project, which built a first-of-its-kind framework and catalog of patient preference methods on the basis of limited experience with regulatory patient preference studies. CDRH's pioneering study on patient preferences in obesity [5] as well as other experiences with patient preference assessment

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1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2016.02.019

methods outside the regulatory context, such as health economics research, has fostered a vision for how the patient perspective can be integrated into medical device benefit-risk assessment [1].

Advancing the Science of Patient Preference Assessment through Collaboration

In September 2013, CDRH launched the Patient Preference Initiative to gather patient and stakeholder views on the best way to measure patient risk tolerance and benefit preference. The Patient Preference Initiative emerged from FDA's 2012 Benefit-Risk Guidance in which FDA stated the factors to consider in making a benefit-risk assessment [3], including collecting patient-centric metrics to measure benefit and ways of measuring a patient's tolerance for risks. The comments generated by the guidance, workshop, and dockets were clear—there needed to be a scientific way to study patient preferences and have FDA staff consider such data when making benefit-risk assessments for medical products. The medical device community, including FDA, determined that the development of the field would require a multistakeholder approach through public-private partnerships (PPPs) that include patients and researchers. In May 2015, CDRH released a draft guidance on including patient perspectives in regulatory submissions [6].

The growing interest in patient perspectives and the more active role of patients in health care decision making led to the development of MDIC's PCBR project. MDIC is the first PPP created with the intention and objective of advancing regulatory science around the development and approval of medical devices. MDIC was formed in 2012 to improve the understanding of medical device regulation and helps develop the tools, methods, and approaches used in medical device development. MDIC membership is open to organizations that are substantially involved in medical device research, development, treatment, or education or in the promotion of public health and have an interest in regulatory science [7]. MDIC is a nonprofit 501(c)3 organization, governed by a board of directors representing industry, FDA, the National Institute for Health, and the Centers for Medicare & Medicaid Services. MDIC member dues fund the MDIC infrastructure and provide seed funding for projects. Additional funding for projects comes from grants, contracts, and directed donations. The goal of the PCBR project is to establish a credible framework for assessing patient preferences regarding the probable benefits and risks of a proposed medical device and for incorporating this patient preference information into premarket and postmarket regulatory submissions and decisions. The PCBR project began in May 2013, starting with assembling an expert steering committee to flesh out the project. The MDIC PCBR group submitted a proposal to develop the Framework and Catalog to the FDA Broad Agency Announcement and was funded in April 2014 (BAA HHSF223201400011C, "Patient-Centeredness: Integrating Patient Preference into Regulatory Submission"). A working group was formed to develop the Catalog and the development of both the Framework and the Catalog was overseen by the PCBR Steering Committee.

MDIC's PCBR Framework

The MDIC PCBR Framework is intended to provide insight and suggestions for how the patient's perspective on benefits and harms might be incorporated into the regulatory approval process [8]. It reflects commonalities that were identified across the disparate missions and perspectives of industry, FDA staff, patient advocacy groups, and others. As such, the Framework covers a wide range of topics, including background concepts on benefit-risk assessment and preferences, conditions when patient preferences may be especially valuable to collect data, potential uses for preference information throughout the product development life cycle, practical considerations when conducting a preference study, roles for preference information in the regulatory process and postapproval, and a research agenda to improve approaches for collecting and using preference data. These sections of the Framework build on one another, although they can also be read independently. Although the Framework depends on quantitative measures of patient preference and clinical trial data, the Framework itself is qualitative and conceptual—requiring of the reader only familiarity with the product development cycle and clinical judgment.

The terminology that at present describes patient-centered benefit-risk is rife with ambiguity because of its simultaneous evolution in distinct professional settings. To reduce this ambiguity, the Framework defines *benefit* as a favorable effect or desirable outcome of a diagnostic or therapeutic strategy and a *harm* as an unfavorable effect or undesirable outcome [1]. *Risk* is defined as the qualitative notion of the probability and/or severity of a harm. These definitions align with both scientific literature on benefit-risk assessment and regulatory precedence, in particular CDRH usage [1]. *Preferences* are defined as qualitative or quantitative statements of the relative desirability or acceptability of attributes that differ among alternative health interventions, whereas *attributes* of a medical device are features such as effectiveness, safety, tolerability, means of implantation/use, duration of the effect, duration of use, frequency of use, lifestyle aspects of use, and other device characteristics that impact benefit-risk considerations [1].

A key concept in the MDIC Framework is the intuitive and scientifically supported notion that patients vary greatly in the degree to which they will accept risk for a given benefit. For a given device with well-characterized benefits and risks, even when these properties are uniform over a population, some patients may consider the benefits to outweigh the risks, whereas others may not. A patient preference study can assess preferences for a population overall as well as heterogeneity in preference and whether there are distinct subgroups whose preferences would lead them to make different decisions. A major role for preference information in development and regulatory decisions is to provide information for whether to consider approving a device for an entire population or only for those patients whose preferences are such that they regard benefits as exceeding risks.

It can be challenging to know whether and when resources, budget, and time should be allocated to a patient preference study. This is especially the case at present because patient preference information is not a requirement for approval of medical devices, and its inclusion in a regulatory submission is optional at the election of the sponsor. The MDIC Framework identifies a set of factors that suggest patient preference information could be valuable in supporting development or regulatory review (Table 1). These factors relate to the unique perspective of patients with the condition, benefit-risk trade-offs inherent in the device (Fig. 1), and novelty of the indication or technology.

The MDIC Framework describes many roles for patient preference information in device development and review. These roles fall into three categories: 1) framing benefit-risk issues, 2) identifying subgroups of patients with decision-relevant differences in preferences, and 3) providing information for quantitative benefit-risk modeling. Framing benefit-risk issues includes helping characterize medical devices on the basis of benefit-risk assessments of existing treatments, determining which issues and end points are most important to patients (and most relevant