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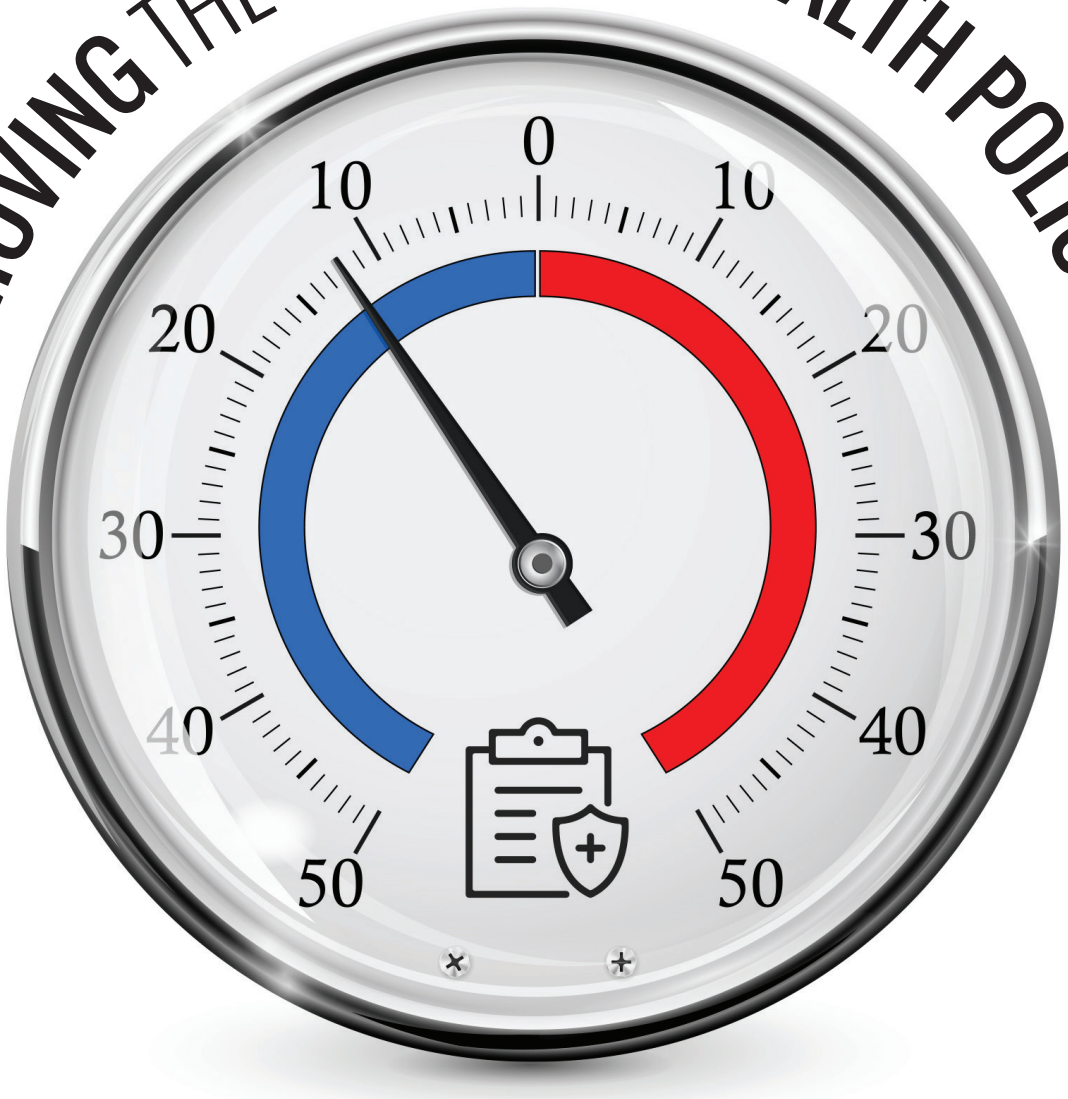

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Tips of the Trade: Delivering Patient-Centricity With Digital Real-World Evidence

Giles Monnickendam, MSc; Casey Quinn, PhD; Fatemeh Amini, MScR; Mark Larkin, PhD, Vitaccess Limited, Oxford, United Kingdom; **Diane Cannon**, Melanoma UK, Oldham, England, United Kingdom

There are potential obstacles to engaging patients in this research, including uncertainty surrounding when and how patients should be brought into the process.

The authors describe a number of tried-and-tested approaches to involving the patient community.

Introduction

When it comes to drug discovery there is a wealth of insight to be gained from the patient community. Involving patients in the design and development of real-world evidence studies, which in turn complement traditional clinical trials by demonstrating patients' lived experience of the condition and its treatments, can be a powerful means of emphasizing patient-centricity in drug development. In this article, the authors explore the technicalities of engaging patients in real-world evidence studies.

Acknowledging Patients as Experts

Until recently, a culture has prevailed in the development of new medicines whereby research has been conducted "on," "about," or "for" patients.[1] In contrast, patient-focused drug development ensures that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into the development and evaluation process.[2] This involves a shift from relying solely on clinician expertise to assess disease burden and treatment impact to acknowledging patients as "experts by experience" and involving them alongside clinicians.[3] The patient's perspective is actively sought to understand their experience of the disease and to design research around what matters most to them. For example, if a study demonstrates that a treatment generates improvement in a particular clinical metric while separately patients do not report any improvement in how they feel or function, then the value of the research is questionable. Understanding the patient perspective and involving patients early in research design can help avoid such misalignments.[4]

Real-world evidence has an important role to play in generating the patient insights needed to deliver truly patient-centric clinical programs.[5] Real-world evidence is derived from observational data obtained outside of randomized controlled trials. Within randomized controlled trials, selection, treatment, and assessment are tightly defined and controlled to maximize internal validity. In contrast, real-world evidence tends to select study subjects and assess outcomes much as they are, providing a more representative picture of the average patient's experience of the condition in their everyday life, and the value of treatments as they are provided in routine clinical practice.[6]

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The Patient Perspective in Real-World Evidence

Incorporating the patient perspective into the design and development of real-world evidence studies can improve the quality of data collected as well as its relevance to patients. Engaging with patient groups can also support faster, more cost-effective and representative recruitment into real-world evidence studies. However, there are potential obstacles to involving patients and patient organizations in the design and delivery of this type of research.[7] These include:

- Uncertainty surrounding when and how patients should be brought into the process
- Resistance or friction from other stakeholders
- Challenges catering to variable levels of health literacy
- Tight timelines for projects, which may discourage investigators from setting aside the time needed to engage properly with patients
- Lack of access to patients, especially within rare diseases
- Patient concerns that researchers' requests for their involvement are not "genuine"

When the objective is to facilitate patient-centric solutions for the pharmaceutical industry, it follows that potential participants in real-world evidence

studies should have the opportunity to shape the way in which this evidence is produced, so that it is of the greatest value. With this in mind, there are means of circumventing the possible obstacles to patient engagement in order to respect and make the best use of this potential.

Case Studies in Collaborating With Patient Advocacy Groups in Real-World Evidence Studies

Digital methods are increasingly being used to conduct real-world evidence studies on behalf of the pharmaceutical industry. The case studies referenced here involve the use of bring-your-own-device technology to gather patient-reported data in real-world settings, a methodology that can be developed and implemented across different conditions. Bespoke questionnaires are combined with validated patient-reported outcome instruments and delivered to study participants on mobile devices, typically via an app, to gather data on the characteristics of the patient population, treatment patterns, burden of disease, and impact to health-related quality of life. The insights and evidence generated by these studies have been used to improve understanding of real-world populations and treatment practices, enhance clinical trial design, and support regulatory and health technology assessment submissions. Patient advocacy groups and potential participants have been important collaborators in the design, development, and delivery of these real-world evidence studies.

Overall Study Design

Face-to-face interactive onboarding workshops are held with patient advocacy groups, representatives, and patients from target countries to provide insights for the design and implementation of the study. This includes input on:

- The components of burden of disease that should be addressed
- The relevance of different custom-made survey questions and patient-reported outcomes instruments and the acceptable frequency of administration
- The potential usefulness of importing patient-generated health data into the app
- The recruitment plan
- Communication methods

In one study exploring the real-world impact of a rare, chronic neuromuscular disease, the Scientific Advisory Board included at least one patient advocacy group representative from each target country (spanning the United Kingdom, the United States, and several European countries). Patient advocacy group members of the Scientific Advisory Board were consulted during the initial conceptualization of the study to ensure that the proposed design and outcomes were relevant to patients and were involved in reviewing and providing input on key study materials, including the protocol and patient-facing elements of the smartphone app. Importantly, consulting the Scientific Advisory Board from the outset has enabled the study's adaptation to meet country-specific requirements and cultural standards.

In another study, patient representatives were consulted extensively to understand the potential burden of completing surveys and patient-reported outcomes instruments, especially the real-world practical obstacles to completion for participants. This allowed for the content and format of the surveys to be optimized, providing sufficient detail for robust and meaningful insights while ensuring that completion rates and response quality remained high.

Recruitment

Patient organizations have played an important role in recruitment and retention of study participants, by providing guidance and communicating and advocating the study with the patient community. Patient advocacy group networks have also been an important route for acquiring validated and reliable study participants.

Remote recruitment models can be particularly valuable for rare disease studies, enabling sufficient participants to be acquired from small and geographically dispersed populations in a cost-effective manner. However, in studies where participants are recruited remotely, rather than physically at clinical sites, the risk of acquiring false participants must be addressed. Participants acquired via patient advocacy group networks are much more likely to be genuine, are self-selected as more engaged, and are usually knowledgeable about their conditions. Consequently, the likelihood of either falsified or inaccurate responses is much reduced. Self-confirmed validation of participants from patient advocacy group networks can be more effective compared with individuals recruited by other routes, where the process for validating identity and diagnosis can be challenging.

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Maintaining Engagement

Feedback can be sought from users as the studies progress in order to improve the user experience of the apps and promote ongoing engagement. Participant preference and satisfaction with the app is recorded interactively through online polls or focus groups. One advantage of digital technology is that it can be harnessed for large-scale feedback from study participants to adapt patient-reported outcomes instruments.

In a study exploring the real-world burden experienced by patients with melanoma in the United Kingdom (My Melanoma, developed in partnership with the charity Melanoma UK), the research team implemented the patient-reported outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE™), a measurement system developed by the National Cancer Institute to capture symptomatic adverse events in patients on cancer trials. The initial version of the bespoke study app contained 11 items from the PRO-CTCAE instrument item bank, selected by oncologists and as a result of a literature review. To ensure that the adverse events of greatest relevance to patients were included in the app, Melanoma UK study participants with any type or stage of melanoma were invited to participate in an online survey, where they were asked to rate the relevance of each of

the 78 adverse events in the item bank. Eight of the adverse events identified by online survey respondents and further corroborated by a focus group were not included in the original study app; the version of the PRO-CTCAE implemented in the study was subsequently updated to reflect the findings. This demonstrates the importance of including patients in the design of patient-reported studies, in order to ensure that the most relevant data is captured.

Concluding Remarks

Study sponsors and investigators should recognize that patients and patient organizations can provide invaluable input into the design, development, and implementation of patient-reported real-world evidence studies. While there are potential obstacles to successful collaboration, these can usually be overcome. By engaging patients and patient advocacy groups as early as possible in the design process and seeking their input throughout the various stages of research, researchers can ensure that the studies are tailored to their target population, measure what matters, and have the support and engagement of the patient community that is needed to collect rich, consistent, and representative data over time.

Developing relationships and communicating and consulting with patients (eg, through webinars, workshops, and focus groups) requires an investment of time and resource. Securing the input and engagement of the patient community to shape and deliver real-world evidence studies can, however, increase the quality and relevance of study outputs, and may even reduce the total time to complete a study in some circumstances, for instance by accelerating recruitment.

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This is particularly relevant for rare diseases, where patients can be both hard to reach and the obstacles to their involvement and engagement in studies poorly understood. Should this approach be implemented in real-world evidence studies as standard practice, collaboration with patients and patient advocacy groups could soon become the rule rather than the exception.

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