The Increasing Role of the Patient in PHASE IV STUDIES AND REGISTRIES

Even though Phase IV studies and patient registries have been increasingly required by regulatory agencies for several years now and a wide range of technologies exist to design and manage them in an efficient manner, life-science organizations are still struggling to effectively implement large real-world observational studies. Key challenges such as study design, study implementation, site motivation, and patient retention are being increasingly discussed between all parties involved, leading to more successful study outcomes.

On a related track, comparative effectiveness research (CER), a US-focused initiative, and health technology assessments (HTA), its European counterpart, have introduced new paradigms in drug development since the established predominance of randomized clinical trials (RCTs). It is fair to say that CER and HTA are now changing significantly how products are developed, approved, and commercialized.

Obtaining Patients Insights in Assessing Health Care Options

An example of the increasing role of the patient is the creation of the US-based Patient-Centered Outcomes Research Institute (PCORI). As an independent, non-profit organization, PCORI conducts research to assist health care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options for patients. This research recognizes that the patient's voice should be heard, and that patient experiences should be taken into consideration as part of the health care decision process.

With more than $3 billion to spend between now and the end of the decade[1], PCORI will support many studies encompassing a broad range of study designs that are relevant to patients and their families.

To facilitate efficient use of the funding, Congress directed PCORI to collaborate with existing federal agencies that already engage in health outcomes research, particularly the Agency for Healthcare Research and Quality (AHRQ) and the National Institute of Health (NIH).

One of the principle duties of PCORI is to identify priorities for research. This work is guided by the following four questions asked from a patient's perspective:

- Given my personal characteristics, conditions and preferences, what should I expect will happen to me?
- What are my options and what are the benefits and harms of these options?
- What can I do to improve the outcomes that are most important to me?
- How can the health care system improve my chances of achieving the outcomes I prefer?

To provide answers to these questions, PCORI will conduct outcomes research studies that will collect patients' experiences as well as other important factors affecting their health. Considering the significant momentum behind this new initiative, it is expected that — on a broader basis — Phase IV observational studies and patients registries will become increasingly important, not only in the United States but in all major countries in Europe and Asia.

The Growing Importance of Phase IV Studies and Registries

While pre-approval randomized clinical trials (RCTs) remain the gold standard for collecting efficacy and safety data, biopharmaceutical companies recognize the fact that collecting a large amount of real-world data complements RCT-based information by providing additional information about the long-term safety and side effects of new products as well as about effectiveness and product utilization in a variety of subpopulations.

In addition, health care providers and payers are demanding clinical evidence that new medicines provide better patient outcomes or greater value than current standard of care. When designed properly, Phase IV studies and registries can also provide data to support clinical effectiveness as well as cost effectiveness to health authorities, pricing commissions, insurance payers, and regulatory agencies.

Gaining insight in product effectiveness is important for supporting product reimbursement within each country where the product is marketed — especially when innovation and differentiation are key business drivers.

Biopharmaceutical companies are also keenly aware that patients feel more and more empowered. Patients want to improve their quality of life, are motivated to know more about their particular disease, and want to be proactive about managing their health.

This represents a new paradigm for drug manufacturers and medical device companies since they need to design Phase IV studies and registries to reach a much broader and diverse population by enrolling patients either directly through recruitment campaigns or via the assistance of research-naïve community-based physicians across the globe.

Collecting Patient Reported Outcomes (PROs) via the Web

Due to the need to know how products are impacting patients in their own environment, there is an increasing demand for capturing patient reported outcomes (PROs) as part of Phase IV studies and registries.

Documenting quality of life, adverse events and real-time patient health status directly from the patient, caregiver, parent, spouse, or observer — without direct interaction from a health care provider, is a critical

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component of these types of real-world studies.

In addition to providing basic health assessment data, the patient may offer information that can help the drug or device manufacturer better understand product utilization, medication compliance and treatment satisfaction. The patient can also identify any occurrence of major symptoms, any events linked to disease progression and any potential safety concerns or adverse events issues.

Through Web-based systems such as electronic patient reported outcomes (ePROs) systems and interactive patient portals, life-science companies are able to keep patients fully engaged in the study in a variety of ways — from Quality of Life questionnaires to symptom assessments to email alerts reminding them to provide feedback in a timely manner.

Gaining Efficiencies by Using Clinical Technology

There are many advantages of collecting PROs via the web, including lower cost implementation since there are no significant expenses related to collection devices or telecommunications.

In addition, the data supplied by the patient can be integrated seamlessly into an electronic data capture (EDC) database for near real-time review and analysis. Patient questionnaires or surveys can be taken in the comfort of the patient's home or during a routine visit to their health care provider, if appropriate.

To maximize compliance and ensure highest possible quality of PRO data, the solution needs to be user-friendly and intuitive. The patient or caregiver needs to be able to use any familiar device such as a home computer or a mobile phone and enter data via an Internet browser of their choice.

In most cases, the interaction with the patient needs to be in the local language for ease of use and to keep the patient interested in continuing with the study.

From an implementation point of view, it is important to have some flexibility in the patient enrollment configuration. Depending on the scope of the study, a health care provider or a pharmacist may invite the patient to answer questionnaires or take part in a study.

It is also feasible to have an EDC system auto-enroll patients into a web-based patient reported outcomes solution following a certain set of predefined criteria.

As a third scenario, the patient may take the opportunity to enroll directly into a study following a recruitment campaign that provides all the necessary information such as the scope of the study, procedures regarding patient consent, benefits for participating in the study and the type of data requested to be entered by the patient.

Interactive disease management portals represent another key area to gain efficiencies in Phase IV studies and patient registries, especially if many sites are involved or if a well defined patient population is targeted by the study. Rare diseases registries are good examples of studies that can benefit from implementing a portal as part of the entire solution. Such platforms allow study investigators, patients and drug or device manufacturers to stay connected and share information quickly and easily. In this case, patients and investigators will have access to the portal and be able to use any appropriate applications, such as EDC to collect data, to run reports in order to analyze the data, and to be trained in specific areas via on-demand eLearning modules. While contributing data to the study, patients can also retrieve up-to-date information on their disease, communicate with other patients, and feel part of a community.

The Future

With 78% of the population in North America, 58% of the population in Europe, and 24% of the population in Asia[2] (which has the fastest growing rate) having access to the Internet, the global use of clinical technology to capture PROs or participate in a disease management portal can lead to a better experience and increased convenience for the patient.

This translates to higher patient retention and improved data collection and quality for Phase IV studies and registries.

Equally important, social media platforms are increasingly being utilized for a variety of functions, from patient recruitment and retention to data collection and reporting.

Patients are also using blogs and online discussion forums to connect and share information with other participants.

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{Editor's Note: (1) A. Eugene Washington, M.D. and Steven H. Lipstein M.H.A., The Patient-Centered Outcomes Research Institute – Promoting Better Information, Decisions and Health, New England Journal of Medicine, 2011; 365:e31
(2) Source: Internet World Stats – www.internetworldstst.com/stats.html}