Patient-focused Drug Development: Moving towards Better Outcomes

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The COVID-19 reset

The COVID-19 pandemic has exposed the fragility of healthcare systems and revealed racial, ethnic and cultural disparities across the world. Now is the chance to address the root causes of these inequities and build better, more resilient systems.

One area that is primed for improvement is addressing the lack of patient-focused drug development (PFDD). In almost every industry, end users are actively engaged in product development. But this is not the standard in drug development. Patients rarely play an integral part and have traditionally been left out for numerous reasons.

These include regulatory requirements on patient contact and data privacy, long-standing traditions of viewing the physician alone as the decision-maker on choosing a medication, and complexities in recruiting patients to engage in clinical trials.

This results in at least three pervasive issues: products that only partially meet patient defined needs; products approved with little evidence of therapeutic impact for populations not represented in trials; and low levels of trust in the drug and its use.

There is an opportunity to improve this.
The US Food & and Drug Administration (FDA) defines PFDD as a “systematic approach to help ensure that patients’ experiences, cultural traditions, perspectives, needs, concerns, and priorities are captured and meaningfully incorporated into drug development and evaluation.” The goal is to create better medicines that more fully meet the needs of patients and caregivers, and improve overall health outcomes for diverse groups.

Spurred by a deeper understanding of biologic and genetic differences among populations, many believe an empowered and involved patient group can help decisions on treatments, participation in research and access to new technologies.

Numerous frameworks and initiatives have emerged to support increased PFDD, but adoption is slow. The future of medicine should include treatments that patients want and need while addressing the lack of diversity in traditional clinical trials. To do so, drug developers are encouraged to actively engage with their end users – the patients.
Models to increase patient-focused design

Below are five models aimed to increase patient participation in therapeutic development. By embedding these practices into the drug development process, there is an opportunity to reset therapeutic innovation to better meet the needs of the end user.

3.1 Expanding clinical trial participation

Patient inclusion in drug development must be diverse, especially as genetic variation among patients can impact their response to a drug's efficacy and safety. Therefore, diverse representation is important to account for those differences in clinical trials. The benefits and risks a patient can expect from an intervention are evaluated during clinical trials.

In reality, this is not often assessed with a sample representative of the entire patient population for which the product is indicated.
In the US, 80-90% of clinical trial participants are white despite FDA efforts to expand recruitment. In oncology trials, only 4% of participants are minorities. This can lead to therapeutics being approved (and widely prescribed) without an understanding of the variability in response across patient populations.

A 2015 study found that roughly 20% of new drugs approved in the previous six years demonstrated different responses across different racial and ethnic groups. Furthermore, there are often varied responses to therapeutics based on sex, with women significantly more likely to suffer adverse reactions. Without intentional inclusion, the knowledge gained through clinical trials will yield limited insight and, could jeopardize patient care. 

A powerful example is provided by the HIV prevention Prep (pre-exposure prophylaxis), which is a medication that offers an efficacious way to prevent HIV transmission between partners. The Descovy Prep trial included no women and thus no conclusions could be drawn on its safety or efficacy in females. Appropriately, the FDA took a hard stance against this during regulatory review, limiting the product indication to males and requiring additional data on effectiveness in women. Failure to properly include women in this trial and more broadly can limit access and the understanding of drug variability.

Globally the need to increase diverse ethnic and racial patient participation in clinical trials is even more critical. Entire continents are being left out of clinical trials. Less than 5% of the clinical trials registered at clinicaltrials.gov, for example, are conducted in Africa. As of 22 July 2021, less than 2% of all clinical trials registered were being conducted in Africa. This data showcases the limited representation of certain communities or geographical regions in current trials, which limits the generalizability of the resulting data for decision-making.

3.2 Direct involvement

Patients are the true content matter experts of their disease. Their first-hand accounts of living with their disease and their disease management preferences should inform what a product looks like to serve their needs. Current drug development programmes take a more passive approach; pre-clinical efforts focus on designing a drug to interfere with a particular disease mechanism in the body, and clinical studies measure standard safety and efficacy endpoints. While this is critical in producing quality treatments, not expanding the focus may lead to missed opportunities to understand and incorporate assessments of additional elements patients’ value in a medication.

Recent efforts in oncology to be more inclusive of patients’ needs showcase the value of expanding endpoints. Traditionally, cancer patients were treated based on measurements of overall survival (OS), no matter what side effects accompanied the OS increase. Yet, cancer patients often seek to balance disease management with quality of life. This is especially true for advanced-stage cancer patients who may prefer a medication that offers quality of life benefits over those that offer the greatest quantity of life. Recognizing the need for increased PFDD, in 2018, numerous medical organizations came together to recommend the incorporation of quality-of-life measurements as part of clinical trial endpoints. These organizations are also working on methods to incorporate that information into shared decision-making with patients in the clinic setting.

Enhancement of patient engagement can be achieved by directly asking patients and caregivers for their opinions and their feedback on meaningful treatment benefits. Establishing frameworks, such as done by Patients Active in Research and Dialogues for an Improved Generation of Medicines (PARADIGM), for stakeholders that work on enhancing patient engagement and developing tools for monitoring and evaluating the initiatives will be important for understanding their impact and benefit (see image below).

Surveys, informal online feedback, interviews, or focus group discussions represent possible approaches to gain insight into patient needs and preferences with an ultimate goal to improve quality and safety of care. In a case study from Washington State in the US, patient surveys and monitoring clinical performance have been effective in improving patient education, post-acute care coordination and providing more durable medical equipment. Through direct communication, drug developers will be empowered with evidence of what patients really need and want. This has the potential to fuel innovation across multiple industries.
3.3 **Increased access for rare diseases**

Acquiring an accurate diagnosis is often the first and most challenging step in rare disease management. This is rooted in a lack of understanding of rare diseases and subsequent limited treatment options for patients.

The International Rare Disease Research Consortium (IRDiRC) launched in 2011 with an ambitious vision to: diagnose all patients suspected of having a rare disease within one year and to enroll undiagnosed individuals into a globally coordinated pipeline for diagnosis and research; approve 1,000 new therapies for rare diseases focusing on those with no approved therapies; and develop methods for evaluating the efficacy of diagnoses and therapies for rare disease patients.

Although hundreds of new associations between genes and diseases are discovered every year, their functional understanding is lacking, precluding these genetic discoveries from being used to develop new therapeutics. IRDiRC recognizes the powerful contribution of model experimental systems towards gaining insight into the biological roles of candidate rare disease genes. Thus, efforts to establish connections between clinicians that discover new disease genes and scientists that study them using model organisms, such as the Canadian Rare Diseases Models and Mechanisms Network, are important for significantly enhancing the understanding of disease etiology and identifying promising candidate therapies.16
3.4 Incorporating real world evidence

The landscape for clinical development has drastically changed in recent years, leading to more clinical trials, greater trial complexity and development of targeted therapeutics for use in specific patient populations. Randomized, double-blind controlled trials have been the gold standard for clinical research for decades and the data captured represents all aspects of the trial, including the precise measurement of endpoints and outcomes deemed critical for approval of the medication. However, the observation period and treatment courses are reflective of a small number of patients in a controlled environment. These trials do not mimic patient activity in the real world.

Real World Evidence (RWE) is emerging as not only a source of vital information from administrative billing, electronic medical records or patient-generated data, but also critical in advancing evidence generation to support efficacy or safety of a drug after it is approved and in use. RWE has been leveraged for decades by various organizations in biopharma, but now additional stakeholders have recognized the applications of the data. The FDA and European Medicines Authority (EMA) have accepted RWE to support additional therapeutic area approvals as part of post-market authorization across global markets. Biopharma has also expanded its use of RWE to better characterize patient populations, deploy post-approval safety and monitoring, generate synthetic control arms for new drug approval and expand the label of an existing medication.

The impact of a treatment on the patient experience is also more easily captured in RWE. Traditional methods of capturing patient-reported outcomes (PROs) have been plagued by inconsistency in data collection methods. However, with advances in wearables, sensors and other instruments behind capturing PROs, more consistency and clinical validation is now possible. For RWE and PROs to have broader impact on PFDD, it will be important to give greater attention to how outcomes are measured and captured, address technology accessibility and data standards, and regulatory organizations will need to harmonize privacy standards around biodata.

3.5 Building multistakeholder collaboration

Multistakeholder collaboration is another excellent way to increase patient participation and PFDD. For example, Innovative Medicines Initiative (IMI) is the world's largest public-private partnership facilitating collaborations between the European Commission and the European pharmaceutical industry for the purpose of delivering medical innovations. Collaboration between entities is critical. All major regulatory agencies (e.g. US FDA, EU EMA, Japan PMDA and China NMPA) have adopted various practices and implemented new incentive programmes that have played important roles in the advancements and approvals of many new drugs.

These practices include, but are not limited to:

- designation as special drug/review/access categories
- accelerated pathways/priority reviews
- incentives such as reduced/waived fees or vouchers
- fostering learnings and education
- improved accessibility and market exclusivity

In addition, there are strong efforts in social engagement via social media for pre- and post-marketing engagement, continued evidence collection in real world effectiveness and pharmacovigilance work. An example can be found with organizations such as the Chinese Organization for Rare Disorders (CORD), a patient-initiated non-profit organization that focuses on promoting communication and cooperation among patient groups, healthcare providers, pharmaceutical companies and government agencies.
The PFDD approach aims to focus drug development on patient needs. It emphasizes their input and builds channels for their voice to be heard. In healthcare, an alignment is needed between the value of a clinical solution as perceived by an individual and value perceived by society. To overcome this, institutional reform is critical.

There are clear examples where patient involvement has a direct positive impact on the processes and practices in the regulator annual reports. The EMA showed that patient involvement in scientific advice results in the following: 79% of patients agreed with the development plans, 53% of the patients’ comments resulted in further discussion, and 20% of the patients’ input resulted in a modification of the final advice. Inclusion leads to better access and outcomes. Engaging diverse patients directly in drug development is important to move towards more equitable outcomes.
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7. Ibid.


10. Ibid.


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