



Are Patients at the Center of Your Trials?

Using Patient Engagement and Insights to Improve Clinical Research

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As the cost associated with developing and launching medical products rises, and the treatment landscape becomes increasingly competitive, companies are looking for innovative and effective ways to accelerate drug development. Leveraging patient involvement early and often in medical product design is one approach to facilitate the development of a program that will increase enrollment, decrease drop-out, and demonstrate value of the product in the context of patient unmet needs. Patients in today's health care market are more knowledgeable about treatment options and have an increased voice in decision-making, and product success is contingent on designing *patient-focused* medicines that demonstrate value in terms of what is important to patients.

*Patient-focused (also referred to as patient-centered): "ensuring that patients' experiences, perspectives, needs, and priorities are meaningfully incorporated into decisions and activities related to their health and well-being."*¹

Patient-Focused Drug Development: How Did We Get Here, and Where are We Now?

The journey to patient-focused drug development dates back to the AIDS crisis, when the lack of treatment options, limited public research funding, and the time intensive



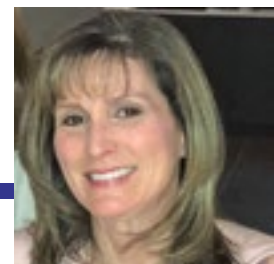
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regulatory review process drove patient activists to organize and demand improvements to facilitate access to treatments. The movement was highly successful in driving change from a funding, regulatory, and public health perspective.² Since 1990, billions of federal dollars have been allocated to HIV research, prevention, and treatment programs through the Ryan White CARE Act.³ Following significant lobbying and public demonstration efforts, the Parallel Track policy,⁴ which expands availability of investigational drugs to people with AIDS/HIV that were not eligible to participate in clinical trials but did not have satisfactory alternative therapies, was approved in 1992. Shortly after, the Accelerated Approval policy⁵ was implemented which allows approval of drugs based on surrogate endpoints that reasonably predict a drug provides clinical benefit. As a result of these and many other efforts of the collective movement, today there are over 30 products approved for the treatment of HIV/AIDS. In less than 30 years from the initial discovery of the virus, HIV/AIDS went from being a death sentence to a chronic disease where access to current treatments is available.

The efforts of the patient activists leading this movement laid the groundwork for patients and patient groups to engage in all aspects of medical product development – from early research and discovery, through market access and beyond. Today, efforts to facilitate **patient engagement** in medical product development are evident in a range of innovative programs across the spectrum.

There is increased funding for patient-centric research through organizations such as the Patient-Centered Outcomes Research Institute (PCORI)⁶; a myriad of efforts are available to educate patients on research, policy, and the life cycle of product development (e.g., European Patients' Academy on Therapeutic Innovation⁷); and a number of public/private partnerships have been established to further the patient engagement mission (e.g., Clinical Trials Transformation Initiative,⁸ Patient-Focused Medicines Initiative⁹). Patient advocacy groups and disease foundations are increasingly directly leading medical product development activities and engaging with regulatory bodies and payer groups in these efforts.

Direct patient involvement in regulatory review and decision-making has also increased in recent years. Between 2011 and 2016, there was an 82% increase in the number of patient stakeholders that were involved in various European Medicines Agency (EMA) activities, and in 2016 alone, there were at least two patients or caregivers represented at six different product review meetings.¹⁰ In the U.S., under the 2012 FDASIA reauthorization of the Prescription Drug User Fee Act (PDUFA),¹¹ the FDA pioneered the use of patient-focused drug development (PFDD) meetings to gather systematic input from patients and caregivers around unmet needs, experiences with existing treatments, and core impacts of the disease. Twenty-two meetings were hosted by the FDA between 2013 and 2017, the results of which may be

*Patient engagement (as defined in relation to the FDA's patient-focused drug development initiative): "activities that involve patient stakeholders sharing their experiences, perspectives, needs, and priorities that help inform FDA's public health mission. Such activities may include (but are not limited to): testimony at Advisory Committee meetings, submission to [regulations.gov](https://www.fda.gov/regulatory-information/search/fda-public-docket) public docket; meetings attended by patients, FDA, and other stakeholders; other correspondence with FDA; interactions through social media; and interactions with or information from patient representatives or patient advocates."*¹

leveraged in shaping a medical product program designed around patient needs. The 21st Century Cures Act of 2016 secured the opportunity for the FDA to expand the Patient-Focused Drug Development program, and has served as the impetus for many additional efforts to leverage the patient voice in the medical product review process. As of June 2017, all new drug approvals must include a brief statement summarizing any **patient experience** data that was submitted and reviewed as part of the application.¹²

Patient Experience Data: data that are collected by any persons and are intended to provide information about patients' experiences with a disease or condition. Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to (but not limited to):

- 1) the symptoms of their condition and its natural history;
- 2) the impact of the conditions on their functioning and quality of life;
- 3) their experience with treatments;
- 4) input on which outcomes are important to them;
- 5) patient preferences for outcomes and treatments; and,
- 6) the relative importance of any issue as defined by patients.¹²

With an expansion of the Patient Representative Program initiated under the FDA Safety and Innovation Act under Section 1137,¹³ the FDA has the opportunity to have the patient at the table in deliberations with industry, ensuring that the patient voice is part of its interactions, discussions, and dialogue on new medical products. The FDA and EMA have also formed a patient engagement cluster to facilitate the sharing of best practices involving patients in the regulatory review process and advancing the patient engagement effort globally.¹⁴

Patient Engagement and Insights across the Product Life Cycle

The key to designing a patient-focused product is to engage with patients early and often, using both qualitative and quantitative approaches for gathering patient insights. To the degree possible, patient input should be considered in the design and execution of all patient experience activities outlined in *Figure 1*.

This paper focuses specifically on strategies to build a patient-centric clinical trial design, including Phase II-III trials, real-world evidence, and post-market approval studies.

Patient-Centric Trial Design

Patient-centric trials consider patient needs, perspectives, and priorities together with the scientific objectives of the study, from design through dissemination. They are designed to maximize the convenience of participating; accurately project enrollment; keep patients engaged from screening through completion; and, answer questions that are important from the patients' perspective. Key components and potential approaches to facilitating patient-centric trial design are discussed below.

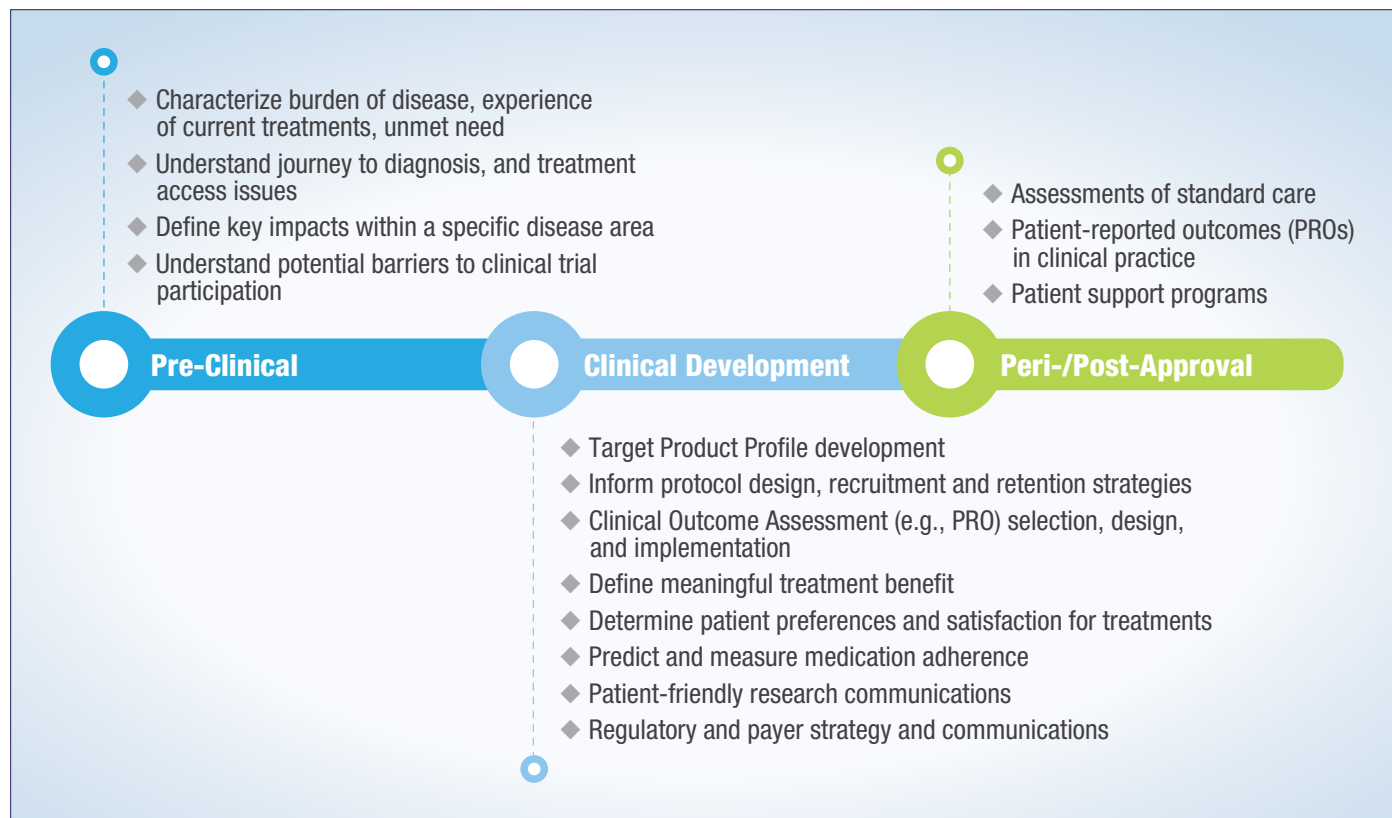
Building Patient Communities

Patient-centricity begins with education and awareness. According to the National Institute of Health, only 15%

of patients are aware that research is an option to them, with this percentage dropping in many therapeutic areas.¹⁵ Additionally, research from Tufts suggests that only 0.2% of patients are referred to clinical trials, citing time and lack of information as a reason for their lack of referral.¹⁶ These metrics paint a glaring picture of the industry-wide need to educate patients on clinical research as a treatment option and make the clinical trial process more patient-centric. This lack of awareness of clinical trials presents not only a chance to meet global unmet medical needs, but offers drug developers the opportunity to engage with research-naïve patient populations. This patient engagement begins with building patient communities by investing in global medical and social connection events. Establishing these communities and engaging with patients allows not only increased awareness, but the ability to harness the voice of the patient to understand how their needs can be better served.

The creation of patient communities happens when there is a commitment within research centers to engage with patients and by building established relationships with the medical community. With such a small percentage of patients being made aware of and participating in research, there is an obligation to ease the burden, improve the education, and increase the pathways for health care professionals to refer patients into studies. Social communities also need to be engaged to better understand other challenges of patient involvement, such as personal belief systems or economic drivers. Until communities are engaged, health checks are provided,

Figure 1. Patient Engagement and Insights across the Product Life Cycle



and advocacy groups are included as partners, the flow of patients into research centers will not be as successful. Ultimately, building patient communities takes time and perseverance, but if successful, a one-stop place for patients to access more research will be established.

Each patient community is different, and it is important to focus on the unique characteristics of that community. Through engagement, it is possible to discover what the local challenges might be, such as a prevalence of disease, a lack of transportation, economic challenges that affect time off for research needs, etc. With this knowledge, a place can be created for patients to come together and share experiences and resources. There is no more powerful voice in the research space than the patient who has been, or is currently, in a clinical trial. Through sharing their experiences with other potential trial participants, they can help other patients understand the research process and remove the myths and fear of the unknown. By creating these local community research centers and replicating that process across geographical locations, a system is constructed to increase patient awareness, ultimately leading to access to clinical trials and participation in the drug development process.

Protocol Design

To truly have a patient-centric approach to drug development, patients must have a seat at the table in protocol planning. Significant aspects of protocol design include determining whether the science is obtainable and the population exists in meaningful numbers. Including the patients' voice can help plan a protocol that has the widest acceptability among the target populations. There are a number of questions to be asked during the protocol design phase to ensure the focus on patient centrality is evident. Within the constraints of regulatory requirements, can the inclusion/exclusion criteria be tailored to increase the ease of enrollment? Can the logistics and visits be tailored to provide the best, most convenient patient experience? Both qualitative and quantitative research can help answer these questions. Access to a large sample set can provide statistically relevant input to guide the planning of a research program.

A key component in patient-centric studies is understanding the audience, including patients, clinicians, hospitals, etc. This is where a large, robust database of patients can be invaluable in understanding disease state and comorbidities. The addition of data from patients' online activities, purchasing patterns, interests, etc., can provide further understanding of the patient population and their experience. This additional information can ensure a rich assortment of patient types and insight into how to best tap into that population. When talking about big data, it is important to assess not only size but also appropriateness of the data to help find the patients needed.

Once Patients are Found, How Do You Keep Them?

Patient recruitment and enrollment is a huge goal, but only half the battle. Retaining patients in a trial is extremely important, and keeping them engaged throughout the process and ensuring they complete the trial procedures is what provides a clean and complete dataset for analysis.

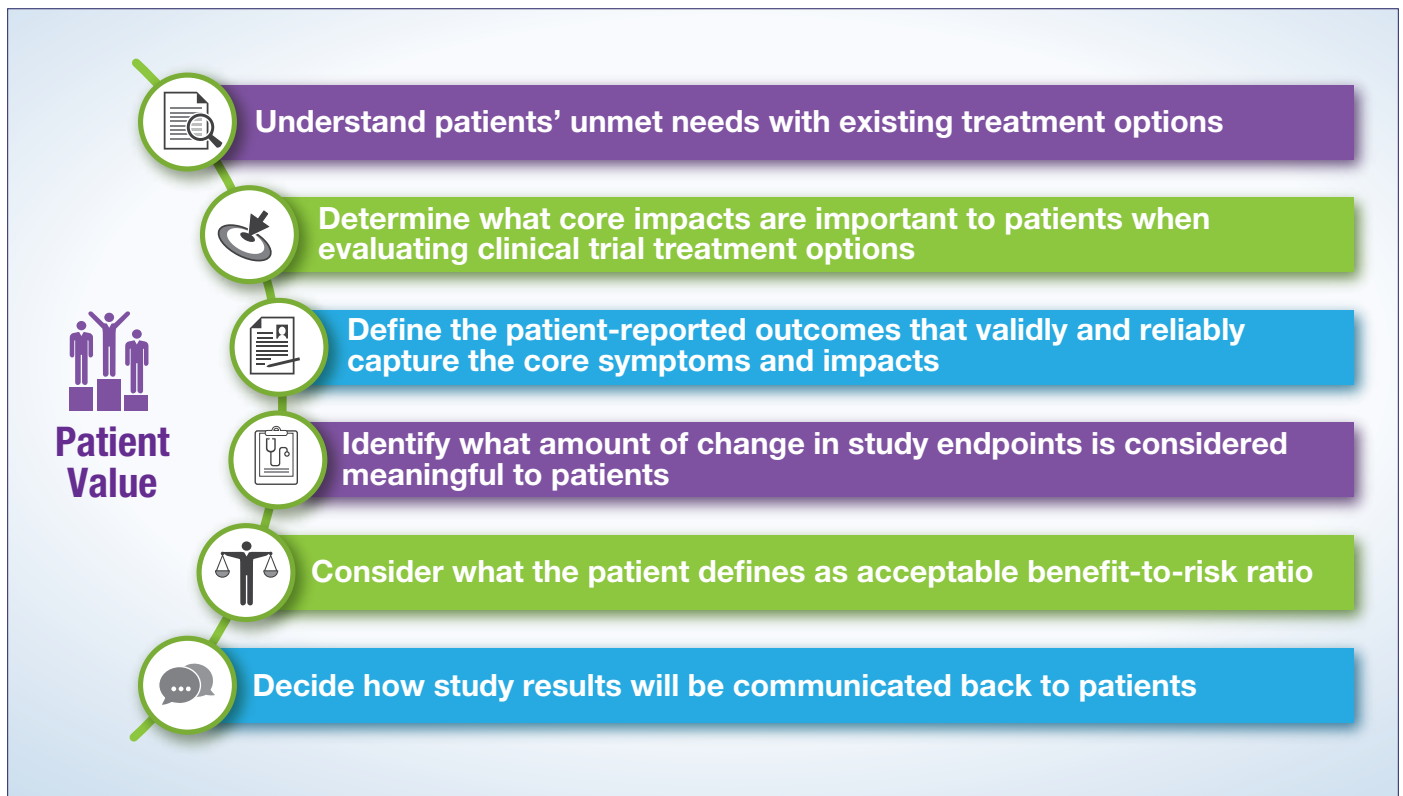
Every time a patient drops out of a study, it can cost up to \$36,000 to add a new patient,¹⁷ sometimes requiring the opening of new sites depending on dropout rates. The best way to ensure the engagement of patients is to support their experience, including understanding potential barriers (e.g., travel concerns, reimbursement, forgetting their appointments) and removing those barriers whenever possible. Patients want to feel valued and to know that sponsors understand that they are making a sacrifice to participate. Acknowledging and addressing those concerns can go a long way in keeping patients engaged in the trial by providing a patient-centric experience from protocol inception through to completion of the trial.

There are a number of ways to help engage and retain patients. Most importantly, listen to them. What do they need to keep them engaged? Providing transportation for patients who need it, sending reminders about upcoming appointments, providing rapid reimbursement of travel expenses demonstrate to patients that their concerns and needs are being heard, and their participation in the study is valued by the sponsor and community. Patients who truly feel that their participation will make a difference are much more likely to continue throughout the study. There are also unique and creative ways to engage and retain patients, such as study-specific apps that provide useful information easily (e.g., site and visit information, trial resources) and are often programmed to be fun and engaging to use. The use of an app gamifies the clinical trial experience by creating a virtual journey that softens a trial's clinical edge and creates a stronger bond between the patient and study. Ultimately, it is critical to always remember that the patients are the most important part of this process, and they should understand that this is acknowledged by everyone involved.

Building the Patient Value Story

In many countries and populations, patients now have more resources to learn about and engage in their own health care than ever before. Social media provides a means of social support and an opportunity to learn about patients' experiences with existing treatments. Patient advocacy organizations and medical associations have taken ownership of developing accurate, curated content so patients are more informed about their disease, the expectations as that disease progresses over time, and treatments options available to them. With increased access to health information, patients are more actively engaged in deciding when they want to start, stop, or

Figure 2. Developing a Patient-Focused Endpoint Strategy



change specific treatments. Research shows that actively participating in treatment decision-making results in a stronger likelihood of adherence to treatment.¹⁸

Informed Decisions Require INFORMATION

Patients need accurate, timely, and accessible information to make the best decision possible for them regarding their health care. This is where it is incumbent on those developing, regulating, and providing treatments to capture and deliver the information that demonstrates the value from the patient perspective. Building the patient value story involves designing an endpoint strategy that evaluates unmet needs, key impacts, and acceptable benefit-to-risk ratios as defined by patients (*Figure 2*).

To understand patient perspectives on these key questions, patient insights can be gathered through qualitative, quantitative, and mixed methods. One-on-one interviews, focus groups, and social media analyses are ideal for an in-depth characterization of the patient experience. These types of data are rich in quality, but small in sample size and ideally suited for hypothesis generation in trying to understand the core issues that are most important to patients. Quantitative approaches, including surveys and patient questionnaires, are ideal for characterizing the patient experience in a broader sample. These methods are ideal for confirming the results of the qualitative methods, and evaluating differences in key subgroups (e.g., countries).

Communicating Study Results Back to Patients

Patients take on risk, give their time, and are inconvenienced when they participate in research studies. Yet in over 50% of cases, they never hear anything about the trial results.¹⁹ They never know if they made a difference or what happened to the data that was collected. When results are available through clinicaltrials.gov, the content is not easy for patients to digest. For many published manuscripts, there are fees associated with obtaining the full-length articles. This does not foster transparency or encouragement for patients to participate in future trials. Developing and disseminating patient-friendly medical communications is a key unmet need in the field of medical product development.

The best way to communicate results to patients is to co-create study summaries with patients, physicians, and researchers so the message is both accurate, and communicated in a way that resonates with patients. In situations where results of clinical trials are not yet in the public domain, monthly or quarterly study summaries that provide information about the enrollment rates, educational information on the disease, or highlights of new studies can be very valuable to patients. Study protocols should ensure that the informed consent provides patients the opportunity to provide consent for the study investigators to share a study summary if they are interested in receiving this information.

Conclusion

By breaking down barriers and misconceptions about research, and educating patients and the public about clinical research, a community is created that is actively engaged in supporting medical product development. Working directly with this community to design protocols and solutions that make it convenient for patients to participate and stay engaged in the trial, recruitment and retention is facilitated. By designing endpoint strategies that measure patient-value and ensuring results are

disseminated to patients, patients will be provided with the information they need when making the decision whether or not to start a new treatment. Collectively, these efforts result in a patient-centric trial, and ultimately, a patient-focused medical product. ■

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