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WHITE PAPER

The Patient Voice: Engaging Rare Disease Patients Improves Clinical Trial Enrollment & Retention

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EXECUTIVE SUMMARY

Clinical researchers struggle to understand why most clinical trials lag in enrollment or why patients withdraw early. Clinical trials in rare diseases are very complex and present unique challenges. However, rare disease trials have one distinct advantage: rare disease patients are very vocal, well-informed, and altruistic, and—along with caretakers, family members, and advocates—are eager to share their experiences.

By listening to individual patients, researchers can understand the disease from their perspective: What are their barriers and daily challenges? What is their experience and what would make a difference for them? Engaging patients, families, and advocates, and incorporating their perspective into the design of a new clinical trial can make the study more appealing to patients. Patients may be more willing to participate if their input is sought and applied. This can result in shorter enrollment timelines, reduce overall development costs, and bring new therapies to market sooner.

By using actionable strategies to find, listen to, and learn from patients themselves, we can include this important perspective in the study design, making studies more patient-friendly.

RARE DISEASES DRUG DEVELOPMENT OVERVIEW

Clinical drug development in rare diseases is complex because there are more than 7000 indications across dozens of therapeutic areas, and involves small numbers of diverse patient populations. For most rare diseases, the natural history and progression are variable and poorly understood.¹

The definition of “rare disease” varies internationally.² A condition is considered rare in the US if it affects fewer than 200,000 people, in Japan fewer than 50,000, and in the European Union less than 1 in 20,000 people.²

For most rare diseases, there is no cure. Only a few hundred rare diseases have treatment options; the US Food and Drug Administration (FDA) has approved approximately 326 new drugs since the passing of the Orphan Drug Act in 1983.¹ There is an opportunity to develop and advance therapies for thousands of indications for which no standard treatment exists.

Figure 1: Rare Disease Prevalence²

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| 7,000+ types |
| 80% caused by faulty genes |
| 350 million people globally |
| 30 million in the US |
| 30 million in the UK |
| 50% appear in childhood and 30% of those children don't live to age 5 |

WHAT ARE THE BARRIERS FOR POSITIONING NEW CLINICAL TRIALS IN THE RARE DISEASES SPACE?

Because rare disease trials present such unique challenges, they require a special approach based on the specifics of the disease, the patient ecosystem, and study goals. Finding enough suitable patients and retaining them throughout the course of the study is a major challenge for drug developers. Poor enrollment and retention contribute to study delays and result in longer development timelines and higher drug development costs.³

¹ Everyday Life Foundation for Rare Diseases. White Paper on Development of Rare Disease Drugs Submitted for Publication. <http://everylifefoundation.org/orphanet-to-publish-white-paper-on-development-of-rare-disease-drugs-using-the-accelerated-approval-pathway/>. Accessed April 25, 2017.

² Global Genes®. Rare Diseases: Facts and Statistics. <https://globalgenes.org/rare-diseases-facts-statistics/>. Accessed April 25, 2017.

³ Gray, Scott. Putting patients' and families' needs first can increase trial enrollment, reduce delays. CenterWatch News Online. <http://www.centerwatch.com/news-online/2016/02/01/26783/>. February 1, 2016. Accessed April 25, 2017.



Rare disease trials typically accrue fewer patients over a wider geographical area than standard studies and often require patients and families to travel long distances to sites.³ As many of these patients have a debilitating disease and/or are children, they need assistance from a family member or caregiver to accompany them to site visits. Depending on the study requirements, travel time and out-of-pocket travel costs can make participation impossible.⁴ Support for travel to the clinical site—including things such as transportation, translators, child care, medical visas for cross-border travel, and temporary housing—is part of a patient-centric solution. While financial hurdles can be overcome with pre-paid debit cards and comprehensive travel programs, there are other non-financial considerations that patients and families must address before they can participate. Understanding their needs is critical to ensuring they become engaged, remain involved, and complete the study.

Researchers have historically assessed patients' needs after the study protocol is finalized. Investigative site staff are often asked to assess a new study and develop a recruitment plan based on their perspectives alone. However, patients with rare diseases, their loved ones, and the larger advocate community are eager to contribute to making sure new clinical trials are designed with patients in mind. From the schedule of assessments, to the selection of endpoints, to eligibility criteria and visit windows, incorporating the patient perspective into protocol development increases the likelihood that a trial is relevant to the actual patients.

To engage these patients and ensure compliance and limit drop-out, drug developers must listen to their experience, include them in the initial stages of protocol and study design, and ultimately make the study requirements less disruptive.³ It is extremely challenging to incorporate this input after the study protocol is finalized or once a study is underway.

THE VALUE OF PATIENT & CAREGIVER INSIGHT

Patient advocacy groups are critical stakeholders in any clinical development program. Some advocacy groups are vocal and mature, and may possess significant resources and knowledge. They play a significant role in helping drug developers understand the disease and patient pathways and provide insights into the needs of patients and their families. Advocacy groups provide several benefits:

- Raise study awareness
- Encourage patient enrollment and retention

⁴ Danielle Stevenson. Clinical trials for rare diseases - finding and keeping patients. BHD Foundation. <https://www.bhdsyndrome.org/forum/bhd-research-blog/clinical-trials-for-rare-diseases-finding-and-keeping-patients/>. May 22, 2015. Accessed April 25, 2017.



- Guide study design
- Motivate researchers
- Connect industry with patients

Advocacy groups are open to relationships with industry; they want transparent and honest relationships with drug developers and they want them to remain involved in the disease community over the long term as a resource, not just to enroll their clinical trials. Engage with them by asking them to describe the ideal partner. By being supportive, drug developers create trust and reinforce study branding. Study timelines may benefit from endorsements from patient advocacy groups. The opposite is also true; there are instances in which industry has not partnered well with disease-specific groups, and trials and development programs have almost been halted.

Locating advocacy groups is easy because they are so visible. Try to align selected sites and investigators with the advocacy group's location to facilitate partnerships. This creates a multi-faceted partnership between investigators, advocacy groups, and patients.

Strategy 1: Find the Patient Voice

Patients with rare diseases are a unique, vocal group. Their communities are often highly motivated and closely connected, and they are actively searching for new potential treatments and clinical trial opportunities. However, for less prevalent rare diseases, the communities are not well established, and patients themselves can be difficult to identify. When finding the patient voice, look for:

- Where are the patients?
- Who are the treating physicians and where are they?
- Who are the key opinion leaders, scientists, and medical professionals who are leading research, advancing diagnostic tools, and furthering treatments?
- Who are the advocacy groups?
- Whom do they listen to? Who influences them?
- Where are the research centers, hospitals, and clinics that treat these patients?

Insight on these factors allows us to identify and find the right patients.



Strategy 2: Know the Patients & Speak Their Language

What are we listening for and trying to find? Look at bloggers, individuals, parents, and advocacy websites to understand how they communicate:

- What adjectives do they use?
- What makes them happy, sad, scared, or intimidated?
- What are their daily challenges?

Find commonalities in their responses and speak their language:

- Do they all hate public transportation?
- Do they all hate traveling in cars at certain times of the day?
- Do they have strong opinions on their physician or local hospital?
- Do they discuss pharmaceutical and biotech companies? How do they speak about them?
- Whom do they trust?

When designing the trial, assess common barriers and make the trial as convenient and easy as possible for patients to participate. The more accessible the study is, the more likely patients will participate.

Strategy 3: Learn From Patient Advocacy Groups

Listening to advocacy or support groups is very effective. Drug developers can learn a lot in a quick, 15- to 20-minute telephone conversation. These groups are eager to share their experience and to educate others. Listen to trends, commonalities, and terms in the conversation and incorporate them into the study design and patient- and caregiver-facing materials.

Strategy 4: Incorporate the Patient Voice, Perspective & Experience Into the Study Design

An extremely important first step in engaging patients is listening to their voices and understanding the condition from their perspective. The challenge is translating their input into the study plans from a clinical perspective.

The best approach to incorporating the patient voice into the study process is by including patients on planning committees and involving them in the protocol and study design, in the same way that we involve key opinion leaders and other stakeholders.



Strategy 5: Create & Build Rare Disease Communities

When drug developers have identified rare disease groups, they should turn their focus to building relationships with relevant organizations, patient communities, key influencers, and leading investigators. Through these early efforts, drug developers will build strong, trusting relationships and bring stakeholders into the planning process. This is the time to link the stakeholders: sponsors, biotech and pharmaceutical drug developers, leading researchers, patients, and their caregivers.

SUMMARY & RECOMMENDATIONS

The words that patients, caregivers, advocacy groups, and stakeholders use tell a powerful story. The success of rare disease trials is based on our ability to understand their voices and incorporate their motivations and concerns into the planning process.

Too often, drug developers do not consider the patient's perspective until the study is underway. Instead, sites and CROs develop recruitment plans that are not informed by patient input. We are learning that rare disease trials require a different approach; one that considers the special needs of patients, caregivers, and families and makes trial participation as easy as possible.

The first step in accelerating clinical trial enrollment is to engage patients. Listen to how they talk about their disease. Understand their language, speak it, and incorporate it into the clinical strategy when positioning the trial. Bring patients into the initial stages of protocol development and study design by developing patient committees and including them as stakeholders. Then, find relevant advocacy groups and physicians and build trusting relationships—trust is a big component when trying to advance a new therapy in a rare disease. Finally, bring the stakeholders together: sponsors, biotech and pharmaceutical drug developers, leading researchers, patients, and caregivers.

By including patients as stakeholders and involving them early in the planning process, drug developers will see tremendous benefits in overall efficiencies: selecting capable sites, retaining patients, and collecting data. Study teams will be well prepared to mitigate potential enrollment and retention barriers and to develop patient-specific recruitment and contingency plans that will facilitate study completion.



CONTACT INFORMATION

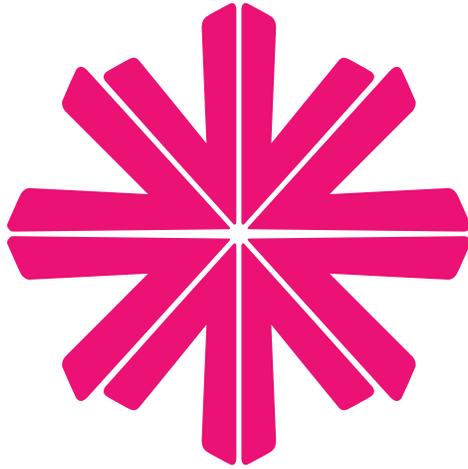
Can you meet your enrollment targets and mitigate the risk of drop-out? If not, it may be time to look for a trusted partner with experience and expertise managing studies in rare diseases.

For further information about PRA's service offerings or to schedule a complimentary consult with our rare disease expert, please contact Scott Schliebner, Vice President, Scientific Affairs—Rare Diseases.

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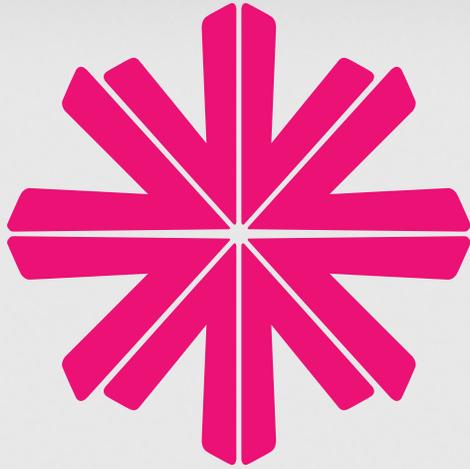
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