

Working Together to Enhance Rare Disease Research – The Role of Patient Advocacy Organizations

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CHALLENGES OF RECRUITING FOR RARE DISEASE STUDIES

There are more than 6,800 conditions listed in the National Institutes of Health's Office of Rare Diseases Research, and approximately 8,000 rare diseases that affect millions of individuals worldwide. Rare disease research is currently the fastest growing area of drug-related research and development.^{1,2} Due to the low number of individuals with a specific rare condition, successful and cost-effective research designs and methodologies that are sensitive to the unique requirements of the disease are challenging.¹ In order to design studies that support the development of treatments for individuals with rare disease, it is important to carefully consider the following two key research elements:

1. The careful design and planning of research methods for patient recruitment and data collection

Rare diseases pose unique challenges to study planning and patient recruitment due to their inherent low patient numbers.

2. The selection of meaningful trial endpoints (including patient-reported outcomes) for the target population

Stakeholder groups (regulators, payers, policy makers, and patients) are calling for drug development programs to be increasingly patient-focused.² In order to adequately define

and select the target population, it is important for researchers to have a good grasp of what meaningful endpoints need to be measured.³

This article seeks to identify and focus on the challenges of study planning and recruitment and to provide potential solutions through strong collaborations with patient advocacy organizations (PAOs).

TRADITIONAL PATIENT RECRUITMENT METHODS AND CHALLENGES

Researchers in rare disease populations have traditionally followed the same patient recruitment methods used in more common disease areas, such as recruiting patients via hospitals or medical clinics, recruiting agencies, newspapers and websites or social media pages.⁴ When using these methods to develop, inform and/or validate endpoints or obtain key insights in a rare disease population, however, there can be several potential challenges to successful recruitment. These challenges stem from the limited pool of rare disease patients in any given area or location, making it difficult to enroll an adequate sample from only a few sites, hospitals or cities. In order to achieve the desired sample, data collection may need to be expanded to several times the number of sites, or even additional countries, compared to what is needed in more common disease areas.

This process can greatly increase both the time and the expense required for execution of the study.

Screening and properly identifying eligible rare disease patients pose challenges as well. A planned recruitment strategy can play a major role in the effort required for identifying eligible patients. For example, newspaper advertisements viewed by a general population often elicit responses from individuals who are not diagnosed with the target condition, which increases the screening burden. Additionally, if the perspective of a clinician or observer (including caregivers, parents, spouses, etc.) is required, recruiting clinicians and/or observers can also increase the screening burden by requiring the coordination and/or necessity of the participation of both parties.

With these challenges to recruitment and screening in rare disease populations for endpoint development/validation or obtaining key insights, it is important to explore innovative methods for recruiting within a rare disease population and capturing high-quality, informative data. One such method that has increasingly shown promise is a strong collaboration with patient advocacy organizations (PAOs) to recruit patients, observers and/or clinicians for these rare disease studies.



HOW CAN RARE DISEASE PATIENT ADVOCACY ORGANIZATIONS HELP?

The Impact of Rare Disease PAOs

Currently, there are more than 1,300 rare disease organizations in the United States alone that support the efforts of furthering an understanding of rare diseases in some way.⁵

Typically, rare disease PAOs focus their resources on either assisting patients and families or contributing funds/efforts to research that will further 1) understanding of the disease process, 2) development of diagnostic tools, 3) development of preventative interventions, and/or 4) development of treatments.¹

Due to the rarity of these life-altering diseases, patients and their families often feel isolated from others with the disease or become frustrated over the lack of information or support available.^{1,6} As a result, patients and their families typically turn to either rare disease PAOs or to rare disease umbrella organizations for support. Rare disease umbrella organizations include the National Organization for Rare Disorders (NORD), the European Organization for Rare Diseases (EURORDIS), Orphanet and the Genetic Alliance (*Table 1*). In particular, rare disease umbrella organizations play a huge role in furthering the objective of the rare disease PAOs by joining with PAOs to provide the assistance they need to develop and implement

research strategies.⁷ In addition, these umbrella organizations also advocate for policies that address the needs of the patient and their families, or focus their efforts on collecting information from expert centers, laboratories and ongoing research projects in order to make this information available within the rare disease community.^{6,8}

Most rare disease PAOs also support patients by focusing on their education and the education of their families, and/or the treating clinicians, and connecting patients with skilled physicians.⁸ With such assistance in navigating the rare disease landscape, it is easy to see how pivotal and central these organizations have become to the life and well-being of the patients, families and treating physicians.

WORKING WITH RARE DISEASE ADVOCACY ORGANIZATIONS TO FIND AND COLLECT DATA

Establishing a Successful Partnership

In order to establish relationships with PAOs, it is essential to identify the key contacts within the organization. Umbrella organizations typically offer listings and contact information for a majority of rare disease PAOs on their websites, making them a great source to identify the point of contacts at the PAOs that focus on the rare disease of interest. Typically, the points of

contact for these organizations are members who are serving as the organization president or a member of its board of directors. As geneticists, clinicians, researchers, public health officials and people who have been personally impacted by the disease (either through their own experiences or the experiences of someone they know), they can provide valuable insight to the design and planning of a research study for rare diseases.^{1,9}

Communicating Study Objectives and Understanding PAO Goals

Once a relationship with a PAO is established, the ability to effectively plan a recruitment strategy with the help of these organizations is dependent upon two factors: 1) transparent and effective communication of study objectives with the PAO, and 2) a sound understanding of the goals of the PAO. Including the PAO in the research planning process will help create a mutual partnership where both engaged parties have a vested interest in seeing the research move forward (*Figure 1*), and increase the informed patient-centeredness of the study to best reflect the needs, values and role of the patient with this rare condition.

Transparency with the organization at the onset is essential. Providing information on the goals of the endpoint study and recruitment needs will offer the PAO an overview of the study and allow it to determine

Table 1

LISTING OF RARE DISEASE UMBRELLA PATIENT ADVOCACY ORGANIZATIONS
Canadian Organization for Rare Disorders
European Organization for Rare Diseases (EURORDIS)
Genetic Alliance
Japan Patients Association (JPA)
Korean Organization for Rare Diseases
National Organization for Rare Disorders (NORD)
New Zealand Organization for Rare Disorders (NZORD)
Organization for Rare Diseases India
Orphanet
Taiwan Foundation for Rare Disorders

whether its goals are aligned with research study goals. Different PAOs have different areas of focus when it comes to furthering the progress of appropriate care and treatment development for a rare disease, and therefore, having a general understanding of the research study could help them see whether their resources will meet the needs of the study.

An early understanding of a PAO's organizational structure and function is important to the planning process for a several reasons. First, it is important to consider the PAO's focus and networking capabilities, as this will determine its ability to reach the target population. For example, PAOs that offer frequent opportunities for members to commune and interact, such as frequent in-person meetings and/or conferences, may be able to provide easy on-site recruitment access, thus increasing the possibility of collecting data in shorter time frames. A second consideration is the number of platforms the organization uses to connect with its patient population. Access to multiple platforms, such as email lists, websites, group venues or social media (e.g., Facebook, Twitter)

increases advertising opportunities to individuals with the rare condition and their families throughout the duration of a study.

Recruiting via PAO Community Networks

After learning about the goals and organization of the PAO and discussing the goals of the study with the PAO, researchers and the PAO contact person can collaborate to identify possible recruitment strategies. Many rare disease patients become motivated to get involved with community networks within a PAO, which makes the PAO an excellent source of identifying people with a specific rare disease. *Table 2* lists some of the resources that a PAO may have available to help researchers identify potential subjects. These existing sources of potential research subjects can be a great asset for study recruitment. Recruited subjects can be invited to participate in any study type (e.g., cross-sectional survey, qualitative interviewing, observational or interventional trial). Most importantly, due to the continued close-knit connections that these rare disease PAOs have with patients and their families, PAOs have the trust of the patients and families involved.

Mutual Respect and External Influences

When working with PAOs, it is important to note that these organizations can be protective of their members and may perceive outside interventions as conflicts of interest or invasions to the privacy of their members. People with rare diseases and their families trust these organizations; therefore, it is important to respect these boundaries and to fully cooperate with any requested procedures when communicating with the membership. For example, many PAOs work hard to host patient conferences that allow patients, their families and clinicians to come together and learn about the disease. Not surprisingly, many PAOs will request that researchers interested in enrolling, interviewing, surveying, etc., not approach the patients and families during patient conferences and not schedule any research activities during the conference proceedings. In this instance, a well-planned strategy and transparent communication will ensure that both the needs of the PAO and the needs of the research study are met.

Figure 1



Table 2


PATIENT ADVOCACY ORGANIZATION (PAO) RESOURCES FOR IDENTIFYING STUDY SUBJECTS
Rare disease websites and social media outlets
Patient databases
Community group and PAO electronic mailing lists (listservs)
Clinical sites and geographic areas with high patient concentrations
Listings of clinicians who treat patients with specific rare diseases
Rare disease conferences
Rare disease websites and social media outlets

Another significant consideration is that there may be external influences beyond the researcher's control. PAOs may be approached by multiple groups interested in conducting research studies among their membership. As a result, the PAO leadership must consider whether multiple research study requests will overwhelm their members, and the PAO may prioritize these requests. Additionally, the research objectives and strategies of a PAO may be influenced by financial resources, availability of effective treatments and the experiences and priorities of the group's founders.¹ Awareness

of potential road blocks early on in the research process can help mitigate any unexpected burden to the endpoint research budget and timeline.

CONCLUSION

The challenges presented in studying rare diseases require innovative methods and out-of-the box thinking that can be addressed through collaborations with rare disease PAOs and umbrella organizations. The solutions that come from these partnerships can serve to be both cost-effective and time-efficient when conducting research in rare

diseases. PAOs can help researchers identify the target population, conduct screening activities and involve patients, observers and/or clinicians in research. These organizations offer valuable resources and can provide expertise as lifetime partners in research efforts to better understand rare diseases and aid in the development of treatments to enhance and extend patients' lives. 

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References

- 1 Rare Diseases and Orphan Products: Accelerating Research and Development. Institute of Medicine (US) Committee on Accelerating Rare Diseases Research and Orphan Product Development; Edited by Marilyn J Field and Thomas F Boat. Washington (DC): National Academies Press (US); 2010. ISBN-13: 978-0-309-15806-0 ISBN-10: 0-309-15806-0.
- 2 U.S. Food and Drug Administration, Office of New Drugs, Center for Drug Evaluation and Research. FDA and Rare Diseases, Sept. 11, 2013. Available at: <http://www.pcori.org/assets/2013/09/PCORI-Rare-Diseases-Roundtable-Pariser-091113.pdf>. Accessed Aug. 21, 2014.
- 3 Vernon M, Wyrwich K. Methods for Selecting and Measuring Endpoints that are Meaningful to Patients in Rare Disease Clinical Development Programs. *The Evidence Forum*. 2014 March; pgs. 10-12.
- 4 Forsythe LP, Szydowski V, Murad MH, Ip S, Wang Z, Elraiyah TA, Fleurence R, Hickam DH. A Systematic Review of Approaches for Engaging Patients for Research on Rare Diseases. *J Gen Intern Med*. 2014 Aug; 29 Suppl 3:788-800.
- 5 National Institutes of Health, National Center for Advancing Translational Sciences, Office of Rare Diseases Research. Available at: <http://rarediseases.info.nih.gov/resources/5/support-for-patients-and-families>. Accessed Sept. 3, 2014.
- 6 U.S. Food and Drug Administration. Orphan Products: Hope for People with Rare Diseases. Available at: <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143563.htm>. Accessed Sept. 9, 2014.
- 7 Dunkle M. A 30-year Retrospective: National Organization for Rare Disorders, the Orphan Drug Act, and the Role of Rare Disease Patient Advocacy Groups. *Orphan Drugs: Research and Reviews*. 2014; 4:19-27.
- 8 Mavris M, Le Cam Y. Involvement of Patient Organisations in Research and Development of Orphan Drugs for Rare Diseases in Europe. *Mol Syndromol*. 2012 Nov; 3(5):237-243.
- 9 World Orphan Drug Congress USA 2014. Top 50 Orphan Drug Thought-Leaders. Available at: <http://www.parentprojectmd.org/site/DocServer/top50thoughtleaders.pdf?docID=14443>. Accessed Sept. 11, 2014.