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# How to Navigate Rare Disease Clinical Trial Recruitment

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In this discussion, we interview Sara Riordan, VP of Strategy at Genome Medical, on the complexities of recruiting for rare disease and gene therapy trials. Sara shares her insights on overcoming recruitment challenges, leveraging data for site selection, and the critical role of healthcare providers in facilitating trial access.


## Moe Alsumidaie: What are the main challenges in recruiting patients for rare disease trials?

Sara Riordan: Recruiting for rare disease trials is challenging due to the small pool of eligible participants, often as rare as one in 10,000 or even 100,000 people. This scarcity makes it difficult to meet diversity goals. Patients and families are usually overwhelmed by the complexities of managing a rare disease, making it unrealistic to expect them to self-advocate and seek out trials independently. Providers, too, may be overwhelmed by the complexity of symptoms and, if not specialists, may lack awareness of available trial opportunities. These

Sara Riordan, VP of Strategy at Genome Medical

familiar challenges—finding the right patients, achieving diversity goals, and managing patient and

provider overwhelm—are all escalated in the context of rare diseases. Addressing these issues requires a multifaceted approach that includes better education and support for patients and providers and innovative recruitment strategies that can reach these small, dispersed populations.

## Moe Alsumidaie: How do these challenges increase for gene therapy trials?

Sara Riordan: Gene therapy trials face compounded challenges, primarily due to identifying patients with specific gene variants. Many remain undiagnosed due to limited access to genetic testing, often because providers are unaware of available tests or concerned about costs and restricted access to genetic counselors. For instance, less than 2% of patients with cardiovascular conditions meeting genetic testing guidelines receive it. This lack of access is a significant barrier. Additionally, while gene therapies hold great promise, there is often fear and trepidation around these novel treatments, especially in communities with past harms in medical research. Educating patients in rare disease communities about gene therapy trials requires a thoughtful approach considering these sensitivities. Building trust through transparent communication and culturally sensitive education is crucial to overcoming these barriers and encouraging participation in gene therapy trials.

## Moe Alsumidaie: What data-informed approaches aid in site selection?

Sara Riordan: Sponsors should connect with clinical researchers at academic medical centers and multidisciplinary clinics, as these institutions have direct access to rare disease patients. This can inform trial site selection by setting up sites where patients are already being seen. However, this approach may exclude patients in rural areas or those far from specialized centers. Telehealth genetic

services can play a crucial role here, and we focus on delivering data that illustrates where patients with rare genetic diseases are located to inform site selection and travel feasibility. Decentralized or hybrid models are also being embraced, which lift barriers to enrollment, especially as many rare diseases present with disabilities or unique challenges that make travel difficult for patients and families. By leveraging technology and data, we can create more inclusive and accessible trial opportunities for patients regardless of location.

## Moe Alsumidaie: How can sponsors overcome delays in medical record transfers?

Sara Riordan: To address delays in transferring medical records, having access to disease registries and assimilated natural history data can significantly speed up the process. Engaging with rare disease advocacy organizations to encourage their communities to be research-ready can help create cohorts where data is already assimilated and accessible for natural history studies or synthetic control groups. This readiness can make the data trial-ready and facilitate quicker enrollment processes. By streamlining data collection and transfer, sponsors can reduce the time it takes to qualify patients for trials, ensuring that eligible participants remain engaged and interested in the study. This proactive approach enhances efficiency and improves the overall patient experience in the trial process.

## Moe Alsumidaie: How is real-world evidence used in eligibility criteria?

Sara Riordan: Real-world evidence (RWE) is crucial in informing eligibility criteria for rare disease trials. Given the small patient populations, it's important not to make inclusion and exclusion criteria so strict that recruitment becomes impossible. Genetic diseases often have variable phenotypes or clinical presentations, so data-informed choices about parameters are essential to maintain scientific rigor while maximizing enrollment potential. RWE from electronic health records, claims databases, and disease registries can provide

valuable insights into how patients with a particular rare disease express symptoms or use medications. This information helps build eligibility criteria that reflect real-world practices. For instance, the requirements might be adjusted if a significant portion of patients with a rare disease exhibit a comorbidity like mild liver dysfunction. By aligning trial criteria with real-world patient experiences, we can enhance the relevance and feasibility of clinical trials.

## Moe Alsumidaie: What role do genetic counselors play in trial access?

Sara Riordan: Genetic counselors are pivotal in facilitating trial access by ensuring accurate diagnoses. They meet with patients and families to identify and facilitate medically appropriate genetic tests, interpret and explain genetic testing results, and help get additional family members tested. This process not only speeds up the time to diagnosis but also provides much-needed counseling and support during times of uncertainty and grief. Once a diagnosis is made, genetic counselors are well-positioned to educate patients and families about clinical trials, particularly for gene therapy or genetically targeted therapies. Their patient-centered approach, which blends scientific explanation with consideration of the patient's values and experiences, builds trust and is vital to engaging patients in trial opportunities. Genetic counselors play a crucial role in expanding access to clinical trials by acting as a bridge between patients and research opportunities.

## Moe Alsumidaie: What policies and collaborations accelerate rare disease drug development?

Sara Riordan: The FDA has made strides in accelerating rare disease drug development through initiatives like the Orphan Drug Act of 1983, which provides incentives such as tax credits and market exclusivity to encourage pharmaceutical companies to develop treatments for rare diseases. Recent expedited programs, such as Fast Track designation and accelerated approval, have facilitated faster development and approval of rare disease drugs. Small disease populations make it challenging to recruit patients for randomized trials,

and many argue that it's unethical to place patients with rapidly degenerative conditions and no available treatment into a control arm. Greater adoption of alternatives, like using synthetic or natural history control arms, can make trials more feasible. It's also crucial to incorporate the patient and rare disease community voice early in the protocol development process, as they are the true experts and can provide vital feedback on trial design feasibility and meaningful endpoints. We can drive more effective and ethical drug development for rare diseases by fostering collaboration and patient engagement.