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Engaging Participants in Rare Disease Research: A Qualitative Study of Duchenne Muscular Dystrophy

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ABSTRACT

Purpose: Clinical trials in Duchenne muscular dystrophy (DMD) are increasing due to technical advances in genetics, muscle biology and muscle imaging, and translational science. Yet the ability to achieve and measure progress in clinical trials in DMD is severely constrained by recruitment difficulties and low levels of patient and family participation. Clinical trials that do not have full inclusion of patients may affect how well new therapies perform in clinical practice.

Methods: This study qualitatively investigated family-centered and clinician-based knowledge, attitudes, and perceptions of engagement in clinical research in DMD. Thirteen focus-group sessions (8 parent based and 5 clinician based) were held at 5 demographically and geographically diverse sites (Houston, Texas; Minneapolis, Minnesota; Pittsburgh, Pennsylvania; Sacramento, California; and Washington, DC). Thematic analysis was used for identifying patterns of meaning across the dataset.

Findings: Totals of 28 parents and 33 clinicians participated in innovative and thoughtful discussions regarding clinical research in DMD and approaches to eliciting family engagement. Five overarching themes emerged from our qualitative data. The theme of Information discussed the lack of accessible and coherent information, as well as the overabundance of fragmented information. The theme of Conversation demonstrated the importance of having open and in-depth dialogue about research with families in eliciting trust and obligation toward the research process. The Barriers and Incentives themes presented the parents' and clinicians' views of the life-altering sacrifices that families make to participate in research and ways to reduce these burdens. Under the Solutions theme, parents and clinicians also suggested innovative ways to incentivize families and clinics and thoughtful solutions to increase family engagement in research.

Implications: Effective recruitment for clinical studies in rare diseases requires a truly committed and engaged study team, as well as the necessary resources to overcome the multitude of barriers that families face. A clearly delineated recruitment plan, developed together with families, should be the standard operating procedure during clinical trial development. Protocols utilizing direct family-centered strategies for providing information and for recruiting research participants in studies in rare diseases are essential. (*Clin Ther.* 2016;▮:▮▮▮–▮▮▮) © 2016 Elsevier HS Journals, Inc. All rights reserved.

Key words: clinical trials, Duchenne muscular dystrophy, family engagement, recruitment.

INTRODUCTION

A global issue and a serious concern for most research studies in rare diseases is the successful and rapid recruitment of study participants.[1] Our ability to achieve and measure progress in clinical trials in rare diseases is severely constrained by recruitment difficulties and low levels of patient and family participation.[2–6] Successful completion of clinical trials fully depends on efficacious engagement with the intended beneficiaries. Clinical trials that do not have full

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inclusion of patients may affect how well new therapies perform in clinical practice. Specifically, substantial barriers exist to recruiting and conducting clinical trials in pediatric patients with rare neuromuscular diseases, such as Duchenne muscular dystrophy (DMD). DMD is the most common form of muscular dystrophy and affects 1 in 3500 to 6000 males in the United States.[7–11]

In the United States alone, there are currently >20 active clinical trials in DMD requiring >2300 boys with DMD to enroll.[12] These figures may not include many investigator-initiated observational studies, sample collections, or quality-of-life surveys. Among the current studies that have met enrollment numbers, the inclusion of minority groups is also significantly low.[13–14] A representative population sample in clinical trials is essential both from an ethical perspective and for external validity of findings.[15–17]

There are a multitude of challenges regarding recruiting and engaging participants in research in DMD. Significant challenges include the heterogeneity of the condition, the small number of individuals with DMD, and the limited clinical sites with the expertise in recruiting for and performing clinical studies in DMD.[4,14] Moreover, many interventions in DMD are targeted to specific mutations (nonsense mutations or mutations that are amenable to certain exon-skipping therapies), leading to further challenges in identifying eligible patients. Logistical barriers to clinical trials may include the absence of an infrastructure for clinical trials; the absence of systematic, centralized databases; the potential lack of therapeutic equipoise; and the lack of resources to provide coordination of collaborative efforts at multiple study sites. Additional challenges of researchers include the ethical issues involved in performing research studies in children compared with adults, and the lack of suitable, clinically relevant, or so-called "hard," end points in pediatric patients with neuromuscular disease.[18]

Clinical trials in DMD are increasing due to technical advances in genetics, muscle biology and muscle imaging, and translational science.[19–24] Challenges exist in recruiting, and these challenges continue to undermine the research. Given the growing importance of patient engagement in clinical and translational research,[6,25] we sought to identify knowledge and attitudes on engagement in clinical research studies among parents of boys with DMD, as well as researchers and clinicians involved in research in DMD. From qualitative investigation of family-centered and clinician-based attitudes and perceptions, the insight gained may improve the design of future DMD clinical research protocols and improve participation in future clinical trials.

PATIENTS AND METHODS

In the present study, we targeted the recruitment efforts toward sites involved in the Cooperative International Neuromuscular Research Group, a clinical research academic consortium, and associated Muscular Dystrophy Association clinics. Five geographically and demographically diverse sites (Pittsburgh, Pennsylvania; Washington, DC; Houston, Texas; Minneapolis, Minnesota; and Sacramento, California) with varying levels of DMD research recruitment and participation were selected to maximize variability. For example, sites varied from being active and engaged in numerous clinical studies in DMD to having had limited research involvement. Recruitment was focused on parents (primary caregivers) of boys with DMD who were being served at the designated muscular dystrophy clinics and clinicians involved with research or recruitment efforts within the Cooperative International Neuromuscular Research Group sites. The inclusion criteria for parents were limited to having a child with DMD, the ability to understand and speak English, and a willingness to participate in a 1-time-only focus-group interview lasting up to 120 minutes. The criteria for the inclusion of clinicians were focused on their direct involvement with clinical trials and other studies in DMD. Before the initiation of the study, focus-group guidelines were developed with the assistance of a trained focus-group moderator. The focus-group guidelines began with a broad definition of *research*, inclusive of all types of studies (observational, interventional, and surveys). The recruitment plan, focus group study, and guidelines were approved by the institutional review board at the University of Pittsburgh (protocol 14010024). Written informed consent was obtained from all parents and clinicians before participation in the study.

Focus-group sessions were conducted between July 2014 and October 2014 at each local site in central locations convenient to the participants. Parents in the DMD focus groups received $25 remuneration for participation and reimbursement for transportation;