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Barriers and facilitators to clinical trial participation among parents of children with pediatric neuromuscular disorders

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Abstract

Background/Aims—Pediatric rare disease presents a challenging situation of high unmet need and a limited pool of potential clinical trial participants. Understanding perspectives of parents of children who have not participated in trials may facilitate approaches to optimize participation rates. The objective of this study was to explore factors associated with parental interest in enrolling children with pediatric neuromuscular disorders in clinical trials.

Methods—Parents of individuals with Duchenne or Becker muscular dystrophy and spinal muscular atrophy were recruited through advocacy organizations, a registry, and clinics. These parents (N=203) completed a questionnaire including assessments of barriers and facilitators to clinical trial participation, parents' interest in trial participation, and their perceptions of others' views about participation in a clinical trial.

Results—Trial interest in participating parents was high (64% combined group). The most highly endorsed barrier to participation was the possibility of receiving placebo, followed by not having enough information on risks and trial procedures. Compared to parents of children with Duchenne or Becker muscular dystrophy, parents of children with spinal muscular atrophy endorsed significantly more information and knowledge barriers. The greatest facilitators of participation were (1) confidence in improving disease understanding, and (2) guarantee to receive the treatment after a successful trial. A logistic regression model, $\chi 2$ (4, n=188)=80.64, p<0.001, indicated that higher perceived barriers and more frequent trial communication by the provider were associated with lower interest, while positive trial perceptions by the child's providers and concordance in trial perceptions among those close to the decision-maker were associated with higher interest.

Conclusions—We found high parental interest in pediatric neuromuscular trials that was tempered by concerns about the potential for randomization to a placebo arm. Participants

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perceived that their trial participation would be facilitated by additional education and guidance from their clinicians. Yet intentions were negatively associated with frequency of provider communication, perhaps reflecting waning parental interest with a greater understanding of limitations in trial access, increased sophistication in their understanding of trial design, and appreciation of potential burden. To support parents' informed decisions it is important to educate them to evaluate the quality of research, as well as providing lay information explaining the use of placebo, trial processes, and potential barriers to long-term drug access. Our findings should inform the development of targeted educational content, clinician training, and decision support tools.

Keywords

Clinical trials; Duchenne muscular dystrophy; Becker muscular dystrophy; spinal muscular atrophy; recruitment; participation

Introduction

Pediatric rare disease presents a challenging situation of high unmet therapeutic need and a limited pool of potential participants. Trial discontinuation is a common problem in pediatric clinical trials, driven predominantly by failed participant accrual.[1] Thus, the success of trials ultimately depends on the ability of the research team to recruit sufficient numbers of eligible participants. There is little information on perceptions about trials among parents of children with rare diseases. Understanding the perspectives of parents of children who have not participated in trials may facilitate approaches to develop acceptable protocols, stimulate interest, and maximize participation.

Decision making in pediatric clinical trials

In a systematic review of sixty-seven studies, Wulf and colleagues reported on determinants of parental decision making in the context of pediatric clinical trials for common and rare disorders.[2] Parents' motivations included chance for individual benefit, altruism, hopefulness, a feeling of obligation, and the potential for better care. Frequently cited perceived harms were side effects, family burden, and randomization with placebo. The review also discussed common comprehension challenges such as distinguishing between trial participation and clinical treatment, as well as recall of the risks and study design concepts, especially randomization and placebo. The providers' communication approach was an important decision-making factor.[2]

Another recent review of qualitative studies described common themes related to enrollment of children in trials.[3] These included parents' perceptions of the child's ability to cope with trial participation, access to treatment not available outside of the research context, the appeal and risk of novel therapies, and social responsibility. One explanation for parental variation was the severity of the child's illness: parents of children with lifethreatening conditions perceived more pressured choice, and had a greater tolerance for risk. The authors concluded that parents facing life-threatening conditions in their children perceive that *to do something* is better than *to do nothing*.[3] Few studies were identified that included parents who chose not to enroll their children in research.

Subsequent survey studies conducted in the United States compared perceptions of actual or hypothetical research participation among parents/guardians who provided permission and those who declined participation for their child. Across studies, parental willingness to enroll the child and positive perceptions of trial participation were associated with factors such as the potential for individual benefit; altruism; low perceived risk of harm; positive perceptions of the research enterprise; trust in and perceived professionalism of the researcher; and comfort with/understanding of randomization and placebo.[4–7]

Overall, these studies conducted across a range of pediatric onset disorders identify common elements including anticipated individual and altruistic benefits, hopefulness and a feeling of community responsibility balanced with concerns about risks and randomization to placebo. The value of trust in and effective communication with healthcare providers and investigators is clear.

Clinical trials in neuromuscular disorders

Duchenne muscular dystrophy and spinal muscular atrophy are among the most common pediatric-onset neuromuscular disorders,[8,9] and both are subject of numerous clinical trials.[10,11] Duchenne muscular dystrophy is characterized by progressive muscle weakness, with onset in early childhood and death typically in the third decade.[8] Becker muscular dystrophy is a less severe manifestation.[8] Spinal muscular atrophy is characterized by degeneration of motor neurons of the anterior horn that results in atrophy and loss of muscle control.[9] There are four subtypes ranging from severe manifestations that are fatal in infancy/early childhood (type I) to much less severe manifestations with teen- to adult- onset (type IV).

There exists limited evidence about perceptions of experiences with trials among parents of children with pediatric neuromuscular disease. One qualitative study of trial experiences found that parents of children with Duchenne or Becker muscular dystrophy reported high expectations for child benefit and for ultimate trial success. Parents perceived themselves to have made informed choices, though the pressures of a progressive disease coupled with the psychological importance of maintaining hope impacted parents' decision making.[12] A focus group study about Duchenne muscular dystrophy trials described the importance of sufficient trial information and in-depth discussion with research teams to explore opportunities for participation. Parent participants reported concerns about making life-altering sacrifices to participate in research.[13] A survey of parents of children with spinal muscular atrophy found high levels of interest in participating in trials, though more than half reported no opportunity to participate. Most reported a willingness to participate in a placebo-controlled trial.[14]

Even with positive therapeutic progress in both disorders, therapeutic development continues. Recruitment challenges will arise as multiple studies recruit from a relatively small number of eligible participants. The primary objective of this study was to better understand the perceptions of parents of children with Duchenne or Becker muscular dystrophy and spinal muscular atrophy regarding participation in trials. Specific aims included exploration of perceptions regarding social norms and provider perspectives of trials, provider knowledge and communication, and barriers to and facilitators of trial

participation. Ultimately, these variables were assessed as predictors of parents' clinical trial interest.

Methods

Recruitment

Participants in the online survey were parents or guardians of children with Duchenne muscular dystrophy, Becker muscular dystrophy, or spinal muscular atrophy who had never been in a trial. For the muscular dystrophy group, recruitment occurred through an advocacy organization (Parent Project Muscular Dystrophy), a self-report registry (DuchenneConnect), neuromuscular clinics, and snowball recruitment. For the spinal muscular atrophy group, recruitment occurred through an advocacy organization (CureSMA) and snowball recruitment.

Parent participants were included in this analysis if they had children with Duchenne/Becker muscular dystrophy who were 4–12 years of age, or children with spinal muscular atrophy who were up to 12 years of age, and if they not previously consented to or attempted to enroll their child in a clinical trial. The spinal muscular atrophy group included parents of younger children due to the earlier initiation of trial participation in spinal muscular atrophy.

Survey

The survey comprises novel measures developed for this exploratory study. Items were chosen based on the diverse experience of the community-based participatory research study team as described previously,[12] prior qualitative interviews focused on trial decision making, and a review of the literature. While initially developed for use in a muscular dystrophy population, the survey items were later reviewed by a transdisciplinary group of experts in spinal muscular atrophy, including parents, an affected adult, advocacy leaders, and a clinical expert. The assessment of suitability for this population was also facilitated by prior interviews about trial decision making.

Participants in the online survey viewed an informed consent section prior to participation and chose "I agree to participate" prior to starting the survey; the study was approved with a waiver of written consent by the Western Institutional Review Board.

Demographic and clinical characteristics—Demographic information of the participant included age, marital status, highest level of education, and relationship to the affected child. Demographic information of the affected child included age, diagnosis, and whether care was received in the United States or Canada. For analyses based on diagnosis severity, individuals were categorized into "more severe" diagnoses (Duchenne muscular dystrophy; spinal muscular atrophy I and II) and "less severe" diagnoses (Becker muscular dystrophy; spinal muscular atrophy III).

Clinical trial interest—The outcome variable, clinical trial interest, was measured with a single item on a Likert-type response scale ranging from "very much do not want" (1) to "very much want" (5). For subsequent analysis, clinical trial interest was dichotomized into

positive (very much want, want) and ambivalent/negative (not sure, do not want, very much do not want).

Normative perceptions—Participants were asked whether family or friends close to them feel the same or differently about trial participation for the affected child. The response options were: (1) “They feel the same way I feel,” (2) “Some feel the same, and some feel different than me,” (3) “They feel different than I feel,” and (4) “I don’t know how they feel.” For the logistic regression, this item was dichotomized into incomplete or uncertain concordance (response options 2–4) and complete concordance (option 1).

Healthcare provider perceptions—Participants were also asked, based on their own opinion, whether their child’s doctor thinks that their child should be in a clinical trial. Response options were: (1) “I have no opinion about what my child’s doctor thinks,” (2) “Should not be in a clinical trial,” and (3) “Should be in a clinical trial.” For the logistic regression, this item was dichotomized into ambivalent/negative (options 1 and 2) versus positive (option 3).

Participants were also asked about the providers’ knowledge and expertise, and about frequency of communication about research. Knowledge was measured with a single item on a Likert-type response scale ranging from “very poor” (1) to “very good” (5), with an additional option stating “I have never asked questions about clinical trials.” Frequency of communication was measured with a single item offering response options ranging from “never” to “very often” on a four-point scale.

Barriers to and facilitators of participation—Twenty-four perceived barrier items and 13 perceived facilitator items comprise two novel measures used in this study. The items were assessed using seven-point, Likert-type items. Response options that ranged from “very untrue” (1) to “very true” (7) were scored so that higher values correspond with higher agreement. An exploratory factor analysis was conducted on the barrier items as an assessment of dimensionality and validity of underlying barrier domains.

Statistical analysis

Descriptive statistics were used across study variables. T-tests were used to test for differences in barrier item means between the Duchenne/Becker muscular dystrophy and spinal muscular atrophy groups; a Bonferroni correction was applied to compensate for multiple comparisons (i.e., significance was specified as $p<.002$).[15]

Exploratory factor analysis was used to evaluate the underlying structure of the barrier items and determine whether they could be adequately represented by a lesser number of composite factors, which facilitates the interpretation of the findings while also informing subsequent uses of the measure. Maximum likelihood was the extraction method, and the factors were rotated using a direct oblimin procedure.

Logistic regression was used to assess whether factor summed scores were significant predictors of clinical trial interest. All variables significantly correlated with trial interest at

$p<.25$ were entered into the regression, then removed using step-wise backward elimination until only those significant at $p<.05$ remained.

Results

Two hundred three parents are included in the analysis. Child's age in the muscular dystrophy group ranged from 4–12 years with a mean of 7.69 years (standard deviation=2.55). Age in the spinal muscular atrophy group ranged from less than 6 months to 12 years with a mean of 4.91 years (standard deviation=3.35). The majority (90%, $n=181$) of the children received their care in the United States, and the remainder in Canada. Demographics are presented in Table 1.

Clinical trial interest, normative perceptions, & healthcare provider perceptions

Responses to each of these items were similar across groups. There was high clinical trial interest with 64% in each group indicating a desire for their child to participate. Mean and standard deviation for each of these variables are shown for the aggregate sample in Tables 2 and 3.

Perceived barriers to clinical trial participation

Mean and standard deviation for each item assessing perceived barriers are shown in Table 4. Consistent with the descriptive nature of this study, exploratory factor analysis was used to evaluate the dimensionality of the 24 items assessing barriers to trial participation. The rotated solution yielded five interpretable factors that accounted for approximately 64.5% of variance: Anticipated Risk, Information Need, Anticipated Burden, Normative Beliefs, and Trial Attitudes. Appendix 1 provides additional detail about this analysis. Given the relatively small sample size, we included the summated average score rather than five individual domains in the regression model. When summed and averaged for analysis, the internal consistency of the 22 items comprising the measure of "perceived barriers" was high (Cronbach's alpha=0.92).

For the aggregate sample, the observed means for only three items were greater than four (a response indicating that these items were more "true" than "untrue" as trial barriers): the possibility of placebo, not having enough information about the potential risks, and not having enough information about day-to-day responsibilities. Table 4 shows item means for each group. T-tests were conducted *a posteriori* to evaluate differences between the groups for each of the barrier items. After applying a conservative Bonferroni correction to correct for multiple comparisons,[15] the only significant ($p<.002$) differences in observed means were for the five items that loaded highly onto the latent factor denoted as Information Need —"I don't know about any clinical trials" ($t=3.128$), "I don't have enough information about the day-to-day requirements" ($t=3.082$), "The goals of clinical trials are not clear to me" ($t=3.384$), "I don't have enough information about the potential risks" ($t=3.991$), and "I don't have enough information about the potential benefits" ($t=3.479$). In each case the information needs were higher in the spinal muscular atrophy group.

Perceived facilitators of clinical trial participation

Mean and standard deviation for each item assessing perceived facilitators are shown in Table 5. The observed mean for every item fell within the “true” range for parents of children with both conditions. The items with the highest means in the muscular dystrophy group were a guarantee to receive successful treatments after the trial and confidence in the potential for the trial to improve researchers’ understanding of the disease. These were also two of three items with the highest observed means in the spinal muscular atrophy group, with the third being absence of cost.

Predictors of clinical trial interest

A logistic regression was used to assess the impact of predictors (lower vs higher diagnostic severity, child age, normative perceptions, healthcare provider perceptions, frequency of doctor communication, average summed barriers) on the likelihood that respondents would report interest in trial participation. The final model contained four of the predictor variables: normative perceptions, healthcare provider perceptions, frequency of trial communication, and perceived barriers. The model was statistically significant, χ^2 (4, n=188)=80.64, p<0.001 and explained between 34.9% (Cox & Snell’s pseudo-R^2) and 48.1% (Nagelkerke’s pseudo-R^2) of the variance in trial interest. Ultimately, the model correctly classified 81.9% of cases. As shown in Table 6, the predictor most significantly associated with lower trial interest was higher perceived barriers, followed by perceived negative/ambivalent healthcare provider perceptions and incomplete/uncertain concordance of normative perceptions. Unexpectedly, higher interest was associated with lower frequency of trial communication.

Discussion

We found high parental trial interest that was tempered by perceived barriers, particularly concerns about the potential for randomization to a placebo arm. Our recruitment sources may have led to a sample favorably biased toward trial participation. Given the importance of advocacy groups and registries in educating about and recruitment for rare disease clinical trials, our participants may also comprise parents whose children are more likely to be recruited for trials. Parents’ receptivity was evidenced by their low endorsement of barriers and high endorsement of possible facilitators to participation. Many of the ‘non-participator’ families in this study may be seeking pathways to clinical trial participation through obtaining trial information, identifying feasible trials, and searching for trials that do not include a placebo arm.

The child’s age and illness severity were not significantly associated with interest in trial participation. This argues against the notion that with more serious child symptoms, parents experience increasing urge to participate as their risk-benefit analysis evolves. In a study of the effect of child’s health status on parents’ willingness to provide permission, Vanhelst and colleagues found higher participation rates for clinical research in ambulatory sick children than healthy or non-ambulant sick children.[16] They also found significantly different motivations for participating, with lower altruistic motivations in parents of non-ambulant

sick children.[16] Thus, additional exploration of the role of disease progression and severity in predicting neuromuscular clinical trial participation is warranted.

We found that the clinician's recommendation was a facilitator of participation. In addition, we found that normative beliefs are independently associated with intentions—that is, it was important that there was a "match" between participants' own intentions and their perceptions of the opinions of those close to them and of their children's healthcare providers. It was unexpected that a lower level of provider communication was associated with higher trial interest. Investigations among other pediatric populations have been inconclusive about whether knowledge increases parents' willingness to allow their children to participate.[17] It may be that more provider communication reduces interest for some participants as the reality of limited trial access or trial burden becomes increasingly apparent. It is also possible that parents feel that their information needs are not addressed during the provider communication or that they are seeking advice rather than information from their clinician encounters. These findings need to be considered in subsequent studies.

Perceived barriers to and facilitators of interest

The results presented reinforce the importance of identifying and separating motivators and barriers of trial participation, as previously recommended.[17] Perceived barriers were selected for the primary analysis because those items are more likely to have been experienced by these participants. In comparison, the facilitator items force the participants to hypothesize which factors may allow greater capacity for and interest in participation, which may not reflect actual experience. While a focus on barriers may connote a tone of negativity, it introduces the opportunity to isolate and address the diverse challenges encountered by individuals who may otherwise be willing and able to participate. This is especially important in groups of individuals who may be biased toward participation. Yet it will be interesting to further explore facilitators as a more active approach to allowing greater participation for those parents whose reasons for nonparticipation can be addressed.

This is especially true given that very few of the barrier statements were highly endorsed as a "true" reason why children were not involved in clinical trials. But despite relatively low aggregate salience, averaged barriers score was the strongest predictor of interest in trial participation among the constructs measured. It is also interesting to note that participants in the spinal muscular atrophy group endorsed the five barrier items that mapped onto Information Needs to a significantly greater degree than those in the muscular dystrophy group.

In contrast to barrier items, a large group of facilitators was highly endorsed as having the potential to increase interest in clinical trial participation. The three facilitator items with the highest observed means in the aggregate group were the possibility for enhancing researchers' understanding of the disease; a guarantee to receive a treatment after the conclusion of the trial; and the child's doctor suggesting a trial is a 'good fit.' These three items represent a range of challenges faced by trial sponsors, clinicians, and the advocacy community in attempting to empower parents to make informed trial decisions. The first item presents a specific educational opportunity to help families understand components of high-quality research that are most likely to lead to improved scientific knowledge. The

second represents the long-term objective of drug access—a challenging facilitator that can never be guaranteed, and that involves multiple policy- and decision-makers. The third suggests that tailoring physicians' communication about specific trials (rather than simply increasing the frequency of trial discussion) may be an effective strategy for augmenting trial participation—an outcome that clinicians must weigh against the potential for inappropriate persuasion and the many competing demands on the limited time in their clinical encounters.

Limitations

In a group of parents who were recruited predominantly through advocacy organizations, we were not surprised to find that most participants endorsed interest in clinical trials. Thus, our results are especially relevant to a group that is often targeted for recruitment into clinical research studies, but they may not represent the views of all families of children with these disorders. Future investigation could employ a similar procedure with a larger sample that is more representative. Recruitment through neuromuscular clinics could serve to minimize sampling bias. As this study was cross-sectional in design, inferences cannot be made regarding the direction of relationships or the extent to which these constructs evolve over time.

The social desirability bias may have also played a role; for example, parents may feel they 'should' highly rate altruistic facilitators rather than individual benefits. In prior qualitative studies, parents of children with Duchenne or Becker muscular dystrophy who participated in clinical trials reported that the potential for child benefit was a very high motivating factor while altruistic benefits were not nearly as important.[12] Further research may determine whether these discrepancies are true differences between the two populations or whether they reflect some degree of response bias.

Finally, during survey development our community-based participatory research group agreed that it may be challenging for families to determine whether they had previously been recruited for a trial. Families encounter trial information in a multitude of ways and there is often no clear differentiation between trial education and recruitment. Therefore for this exploratory study we did not collect data on whether our participants' children had ever been recruited or whether they had declined trial participation. Additional research could provide nuance about perceived barriers and facilitators across families with a range of trial exposure.

Implications

This assessment of parental perceptions of barriers and facilitators provides valuable evidence for the future of clinical trials in rare pediatric disorders. Though participants in this study demonstrated high trial interest, they reported preferences that challenge the research community, highlighted by their concern about participating in placebo-controlled trials. Though many sponsors and advocacy organizations share this concern, the use of a placebo group enhances empirical evidence on safety and efficacy. Similarly, parents' strong desire to maintain access to the study drug post-trial is understandable given the progressive disease course, but sponsors are generally unable to guarantee access even after a successful

trial. As the rare disease research community works toward more patient-centric protocols, adaptive trial designs, and ultimately permissive decisions about drug access, it is vital to educate parents about drug development, clinical trial design, the drug approval process, and drug access determinations so they can make informed choices.

Parents of children with spinal muscular atrophy reported specific needs surrounding education about clinical trials, including information about risks, benefits, and requirements of participation. This finding highlights a sincere but achievable challenge that resonates with many parents of children with neuromuscular disorders. The sheer number of outlets distributing information about opportunities can be difficult to navigate, and the information provided about participation may be fragmented.[13] Trusted sources that provide concise information may inform and empower patients and families; examples are resources provided by Cure SMA (www.curesma.org), DuchenneConnect (www.duchenneconnect.org), and Parent Project Muscular Dystrophy (www.parentprojectmd.org). The results from this study should inform the development of educational content and decision support tools related to trial participation.

Our findings suggest that clinicians play a key role and highlight the importance of the information exchanged during the clinical encounter on informed parental choice. Clinicians must also anticipate and prepare for discussions with families who desire trial participation, but for whom no trials are available or accessible. It was somewhat surprising that approximately one third of participants reported that their child's doctor never discusses research opportunities with them. However, overall the data suggest that the quality and tailoring of the communication regarding opportunities to participate in clinical trials is much more important than the frequency of communications. Additional tools for healthcare providers may provide useful support, such as decision aids and communication training. Further, efforts to improve the matching of individuals with trials of interest could serve to not only advance the research through larger, more representative samples, but also inspire in the participants and their families a confidence in high-quality research and the potential for progress in treatment development and implementation.

Similar research in other pediatric disorder communities would provide evidence of the degree to which our findings represent shared needs and opportunities. Interventions to address cross-cutting barriers and facilitators and to create more patient-centric protocols could have wide-ranging benefits to the conduct of pediatric clinical trials. Efforts that invite disorder foundations, patient advocates, and patient navigators to join with professional stakeholders in drug development may result in the most effective, family-centered outcomes.

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Appendix 1. Perceived Barriers to Clinical Trial Participation: Factor Analysis

EFA was used to evaluate the dimensionality of the 24 items assessing barriers to clinical trial participation. The rotated solution (Table A) yielded five interpretable factors that accounted for approximately 64.5% of item variance: Anticipated Risk, Information Need, Anticipated Burden, Normative Beliefs, and Trial Attitudes. The factor denoted as Risk accounting for approximately 37.7%. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was .879, and Bartlett's test of sphericity was significant (χ^2=3336.9, df=276, p<.001). Barriers 7 and 22 exhibited issues of cross-loading, which is likely due to participants having different interpretations of fairly general statements. Additionally, barriers 6 and 8 did not load highly onto a factor. Fitting the models without 22 and 6 improved the model fit such that the remaining five-factor solution exhibited no issues of cross-loading, and loadings for all but two items were greater than .5: barriers 7 and 8 had respective primary loadings of .462 and .368 on the factor we denote as Attitudes. Accordingly, barriers 22 and 6 were not included in the rest of the analyses.

Table A

Exploratory Factor Analysis: Perceived Barrier Items

	Factors				
Items	**Risk**	**Info**	**Burden**	**Norm Beliefs**	**Attitudes**
My child may not get any better in a clinical trial.	**.950**	−.045	.006	−.028	−.010
The clinical trial may not be successful.	**.946**	−.050	.030	−.030	−.012
My child could find the clinical trial too physically difficult.	**.683**	.092	−.019	.023	−.042
My child could receive placebo (which is inactive medication).	**.679**	−.053	.018	−.013	.012
My child could be hurt in a clinical trial.	**.656**	.166	−.057	.042	−.021
My child may not like being in a clinical trial.	**.566**	−.041	−.188	−.006	−.115
For my child, there may be more risks than benefits.	**.548**	.195	−.092	.185	.034
I don't have enough information about the potential risks of clinical trials.	.091	**.849**	−.021	−.106	−.063
The goals of clinical trials are not clear to me.	.028	**.844**	.061	.005	−.055
I don't have enough information about the potential benefits of clinical trials.	.123	**.833**	.004	−.024	−.011
I don't have enough information about the day-to-day requirements of clinical trials.	.001	**.775**	−.106	−.038	.097
I don't know about any clinical trials.	−.104	**.653**	.034	.066	−.026
I don't want my child to be a "guinea pig."	.124	**.339**	−.187	.107	−.161
Being in a clinical trial would interrupt my daily routine.	.007	−.028	**−.965**	−.033	.037
Being in a clinical trial would interrupt my child's daily routine.	.020	.001	**−.902**	−.074	−.041
Being in a clinical trial would take too much time.	−.045	−.008	**−.848**	.080	−.010

Items	Factors				
	Risk	Info	Burden	Norm Beliefs	Attitudes
A clinical trial would put a strain on my family.	.098	.026	**−.739**	−.033	.009
People I trust advised me not to put my child in a clinical trial.	−.042	−.007	.004	**.866**	.019
Other parents of kids with my child's disease advised me not to put my child in a clinical trial.	.067	−.045	.059	**.855**	.012
I have heard too many negative things about clinical trials.	.013	.003	**−.203**	**−.373**	**−.298**
I don't trust the medical teams involved in clinical trials.	−.028	.056	−.015	−.076	**−.917**
I don't trust health care services or medical science in general.	.115	−.117	.027	.010	**−.826**
It is wrong to conduct clinical trials on children.	−.008	**.258**	−.052	.135	**−.447**
I am not interested in the kinds of treatments provided in clinical trials.	.038	.138	−.101	.129	**−.350**

[a]Loadings greater than .2 are in boldface.

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Table 1

Participant Demographics

Characteristic	Response Option	*n*	%
Child's Diagnosis (*n*=203)	Duchenne muscular dystrophy	97	47.8
	Becker muscular dystrophy	3	1.5
	Intermediate muscular dystrophy	5	2.5
	Spinal muscular atrophy Type I	20	9.9
	Spinal muscular atrophy Type II	58	28.6
	Spinal muscular atrophy Type III	20	9.9
Relationship to Child (*n*=198)	Biological father	33	16.7
	Biological mother	153	75.4
	Adoptive father	1	0.5
	Adoptive mother	6	3.0
	Other	5	2.5
Parent's age (*n*=198)	30 years or younger	28	14.1
	Between 31 and 40 years	103	52.0
	Between 41 and 50 years	61	30.8
	51 years or older	6	3.0
Marital Status (*n*=198)	Married or in a Marriage-like Partnership	171	86.4
	Not Married or in a Marriage-like Partnership	27	13.6
Highest Level of Education (*n*=198)	High school diploma or less	25	12.6
	Some college	34	17.2
	Associate's degree or technical school	29	14.7
	Bachelor's degree	75	37.8
	Graduate or professional degree	35	17.7

Table 2

Interest in Trial Participation: *"Which is the most true for you? I _____ to put my child in a clinical trial."*

Response Option	*n* (%)		
	Combined *N*=203	**DBMD *n*=105**	**SMA *n*=98**
Very much do not want	1 (0.5)	0 (0)	1 (1)
Do not want	4 (2.0)	3 (2.9)	1 (1)
Am not sure whether I want	67 (33.0)	34 (32.4)	33 (33.7)
Want	67 (33.0)	37 (35.2)	30 (30.6)
Very much want	64 (31.5)	31 (29.5)	33 (33.7)

DBMD: Duchenne / Becker muscular dystrophy; SMA: spinal muscular atrophy

Table 3

Response Frequencies for Provider Knowledge, Provider Communication, and Provider Perceptions, and Normative Perceptions

Response Option	**Aggregate Sample *N*=203**
Provider Knowledge: "If you asked the healthcare providers at this clinic questions about clinical trials, how would you rate their knowledge?"	***n* (%)**
Very poor	12 (5.9)
Poor	22 (10.8)
Fair	33 (16.3)
Good	50 (24.6)
Very good	50 (24.6)
I have never asked questions about clinical trials.	36 (17.7)
Provider Communication: "How often does your child's doctor talk to you about research opportunities and advances?"	***n* (%)**
Never	68 (33.5)
Not very often	44 (21.7)
Sometimes	58 (28.6)
Very Often	33 (16.3)
Provider Perceptions: "In my opinion, my child's doctor thinks my child…"	***n* (%)**
Should be in a clinical trial	76 (37.4)
Should not be in a clinical trial	9 (4.5)
I have no opinion of what my doctor thinks	117 (57.9)
Normative Perceptions: "How do you think family / friends who are important to you feel about putting your child in a clinical trial?"	***n* (%)**
They feel the same way I feel	118 (58.1)
Some feel the same, and some feel different than me	47 (23.3)
They feel different than I feel	1 (0.5)
I do not know how they feel	37 (18.2)

Table 4

Perceived Barriers to Clinical Trial Participation

My child has not been enrolled in a clinical trial because…	**Combined**		**DBMD Only**		**SMA Only**	
	mean (*SD*)	***n***	**mean (*SD*)**	***n***	**mean (*SD*)**	***n***
My child could receive placebo (which is inactive medication).	4.52 (2.07)	195	4.66 (2.06)	102	4.38 (2.09)	93
I don't have enough information about the potential risks of clinical trials.	**4.21 (2.31)**	202	**3.61 (2.28)**	104	**4.86 (2.17)**	98
I don't have enough information about the day-to-day requirements of clinical trials.	**4.18 (2.31)**	202	**3.70 (2.21)**	104	**4.68 (2.31)**	98
The clinical trial may not be successful.	3.92 (1.95)	196	3.78 (1.98)	103	4.09 (1.92)	93
My child may not get any better in a clinical trial.	3.92 (1.96)	196	3.75 (2.02)	103	4.11 (1.89)	93
I don't have enough information about the potential benefits of clinical trials.	**3.80 (2.30)**	202	**3.27 (2.21)**	104	**4.37 (2.28)**	98
My child may not like being in a clinical trial.	3.71 (1.79)	195	3.72 (1.85)	103	3.70 (1.73)	92
My child could find the clinical trial too physically difficult.	3.53 (1.78)	196	3.47 (1.88)	103	3.59 (1.66)	93
For my child, there may be more risks than benefits.	3.51 (1.84)	196	3.23 (1.85)	103	3.82 (1.79)	93
My child could be hurt in a clinical trial.	3.50 (1.75)	196	3.24 (1.85)	103	3.78 (1.60)	93
I don't know about any clinical trials.	**3.34 (2.32)**	203	**2.86 (2.20)**	105	**3.86 (2.35)**	98
A clinical trial would put a strain on my family.	3.26 (1.80)	189	3.35 (1.81)	100	3.16 (1.78)	89
Being in a clinical trial would interrupt my child's daily routine.	3.26 (1.87)	189	3.18 (1.90)	100	3.35 (1.85)	89
The goals of clinical trials are not clear to me.	**3.12 (2.10)**	202	**2.64 (1.96)**	104	**3.62 (2.14)**	98
Being in a clinical trial would interrupt my daily routine.	2.93 (1.83)	189	2.81 (1.86)	100	3.06 (1.80)	89
Being in a clinical trial would take too much time.	2.86 (1.76)	189	2.72 (1.78)	100	3.01 (1.73)	89
I don't trust health care services or medical science in general.	1.97 (1.43)	195	1.84 (1.26)	102	2.12 (1.58)	93
I don't trust the medical teams involved in clinical trials.	1.93 (1.37)	189	1.81 (1.29)	100	2.06 (1.45)	89
I am not interested in the kinds of treatments provided in clinical trials.	1.82 (1.31)	203	1.79 (1.31)	105	1.85 (1.32)	98
It is wrong to conduct clinical trials on children.	1.80 (1.26)	203	1.64 (1.07)	105	1.97 (1.43)	98
Other parents of kids with my child's disease advised me not to put my child in a clinical trial.	1.33 (0.88)	189	1.23 (0.71)	100	1.45 (1.02)	89
People I trust advised me not to put my child in a clinical trial.	1.30 (0.79)	189	1.30 (0.82)	100	1.29 (0.76)	89

DBMD: Duchenne / Becker muscular dystrophy; SMA: spinal muscular atrophy; SD: standard deviation

Items for which the means are significantly (p<.002) different between groups are bolded.

Table 5

Perceived Facilitators to Clinical Trial Participation

I would be more interested in putting my child in a clinical trial if…	**Combined**		**DBMD Only**		**SMA Only**	
	mean (*SD*)	***n***	**mean (*SD*)**	***n***	**mean (*SD*)**	***n***
I was confident that the trial would improve researchers' understanding of the disease.	6.19 (1.27)	182	6.05 (1.38)	98	6.35 (1.11)	84
My child was guaranteed to get the treatment (if it worked) after the trial.	6.10 (1.67)	186	6.15 (1.71)	99	6.05 (1.63)	87
My child's doctor suggested that a clinical trial might be a good fit.	5.94 (1.58)	181	5.94 (1.56)	97	5.95 (1.62)	84
The clinical trial did not cost my family anything.	5.86 (1.74)	183	5.68 (1.79)	98	6.07 (1.66)	85
I felt that the researchers had a good reputation.	5.85 (1.73)	183	5.77 (1.76)	98	5.95 (1.49)	85
I agreed with the goal of the clinical trial.	5.81 (1.73)	186	5.76 (1.81)	99	5.87 (1.65)	87
There was a clinical trial available within a one-hour drive.	5.79 (1.80)	183	5.84 (1.70)	98	5.74 (1.93)	85
I knew that my child would receive the active drug and not the placebo (which is inactive medication).	5.66 (1.88)	185	5.77 (1.87)	98	5.55 (1.89)	87
I had a trusted source of information about clinical trials.	5.21 (2.05)	186	4.85 (2.07)	99	5.62 (1.97)	87
I had a better understanding of clinical trials, in general.	5.09 (2.01)	186	4.79 (2.07)	99	5.44 (1.90)	87
My child told me that he/she wanted to be in a clinical trial.	4.94 (2.11)	186	5.05 (1.91)	99	4.82 (2.31)	87
My child's doctor was part of the clinical trial team.	4.66 (2.16)	185	4.85 (2.04)	98	4.45 (2.28)	87
I knew another family enrolled in a clinical trial.	4.55 (2.06)	182	4.47 (2.05)	97	4.64 (2.08)	85

DBMD: Duchenne / Becker muscular dystrophy; SMA: spinal muscular atrophy; SD: standard deviation

Table 6

Binomial Logistic Regression

Model	B (SE)	Ratio [95% CI]
[Constant]	5.51 (1.12)	0.003
Perceived Barriers	−1.41*** (0.25)	0.25 [0.15, 0.40]
Healthcare Provider Perception	1.24* (0.50)	3.45 [1.30, 9.13]
Normative Perception	0.85* (0.40)	2.33 [1.07, 5.06]
Frequency of Physician Communication	−0.49* (0.22)	0.61 [0.40, 0.94]

SE: standard error; CI: confidence interval

Significance at $p<.05$ is denoted by * and at $p<.001$ by ***.