Decision making Barriers and Facilitators for Pediatric Neuromuscular Clinical Trials

Barbara Bowles Biesecker, PhD, MS

April 1, 2016

Clinical Trials in Rare Genetic Conditions

- Clinical trials more often an option for rare disease as novel drugs emerge to repair/compensate for genetic variants
- Studies on parental decisions to enroll their sons with DMD in clinical trials suggest high expectations of benefit and a personal drive to offset the progressive nature of the condition
- Evidence is needed to guide consent protocols to support informed choice for clinical trials

Peay et al., Genet Med 2015 Peay et al. Cont Clinical Trials 2016

DBMD and SMA

- DBMD and SMA are progressive neuromuscular disorders that often result in death by late 20's
- DBMD and SMA provide a useful model to evaluate factors contributing to interest
- There are no FDA approved therapies, but a number of therapeutic agents are in clinical trial

Research Question

What are the factors associated with clinical trial interest among parents of children with Duchenne or Becker muscular dystrophy (DBMD) and spinal muscular atrophy (SMA)? Specifically, what are the perceived barriers and facilitators?

Target population: parents who have not enrolled their child(ren) in trials

Study Aims

- To describe parents' clinical trial interest, their perceived attitudes of those close to them ("normative attitudes") and those of the child's healthcare providers ("provider attitudes")
- To describe perceived barriers and facilitators to participation–differences in DBMD vs SMA
- To assess factors influencing clinical trial interest: child's age, diagnostic severity, normative attitudes, provider attitudes, frequency of provider communication, average perceived barriers and facilitators

Target Population

- Parents of children with DBMD or SMA whose care is provided in US & Canada
- DBMD children 4–12 years old
- SMA children birth–12 years old
- No prior enrollment in a clinical trial
- Response limited to one parent per child

Research Team

- Led by Parent Project Muscular Dystrophy and guided by a Research Advisory Group using a community-based participatory research (CBPR) approach, a process by which stakeholders act as equal partners to identify and explore a phenomenon of importance to a community
- Results from a qualitative interview study of 15 parents of boys with DMD enrolled in 6 clinical trials informed development of this survey study

Funded by NINDS R21NS077286

Study Design

- Cross-sectional online survey
- Assessment of variables using novel scales: normative perceptions, provider attitudes, perceived barriers & facilitators
- Dependent variable: Clinical trial interest
- Surveys distributed via advocacy groups: Parent Project MD, cureSMA; a registry: Duchenne connect; neurology clinics & snowball recruitment

Variable Assessment

- Clinical trial interest: 5-pt scale from very much do not want to enroll child to very much do want to
- Normative perceptions: Family/friends close to them feel the same or differently about trials (1–4)
- Provider attitudes: Providers knowledge/expertise about clinical trials (1–5) + I have never asked
- Degree of provider communication: How often does your provider talk about research? (1–4)
- Perceived barriers: 24 items (1–7)
- Perceived facilitators: 13 items (1–7)

Results: Participants (*N*=203)

Participant Demographics

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

Table 1. The mean age of children with DMD or BMD was 7.7 ± 2.6 years, while the mean age for children with spinal muscular atrophy was 4.9 ± 3.4 years.

Results: Outcome

Interest in enrolling child(ren) in a clinical trial:

- 64% in each group very much want or want their child to participate in a clinical trial
- 32% unsure in the DBMD group
- 34% unsure in the SMA group

For analysis data was dichotomized into:

- 64.5% Positive interest in a trial
- 35.5% Ambivalent or negative about a trial

Descriptives

Descriptive Statistics for Key Variables

Construct	possible scores	mean	*SD*	*n*	95% CI
Perceived Barriers	1–7	4.98	1.11	189	4.82–5.14
Perceived Facilitators	1–7	2.44	1.06	181	2.29–2.60
Clinical Trial Interest	1–5	2.07	0.88	203	1.95–2.19

Table 2. Lower scores on perceived barriers and facilitators indicate greater endorsement of items as more “true for you.” Lower scores on the dependent variable indicate greater clinical trial interest.

Normative & Provider Perceptions

Important Family/Friends perceptions about a trial

- Feel same as you do: 118 (58.1%)
- Some feel the same: 47 (23.2%)
- Some feel differently: 1 (0.5%)
- Unsure how important others feel: 37 (18.2%)

Provider perceptions about enrolling child in a trial

- No opinion about trial participation: 117 (57.9%)
- Feels child should be in a trial: 76 (37.6%)
- Feels child should not be in a trial: 9 (4.5%)

Provider Knowledge & Communication

Provider knowledge about clinical trials

- Very good: 50 (24.6%)
- Good: 50 (24.6%)
- Fair: 33 (16.3%)
- Poor: 22 (10.8%)
- Very poor: 12 (5.9%)
- Never asked provider about trials: 36 (17.7%)

Provider talks about research opportunities

- Very often: 33 (16.3%)
- Often: 0 (0%)
- Sometimes: 58 (28.6%)
- Not very often: 44 (21.7%)
- Never: 68 (33.5%)

Perceived Barriers

No significant differences between DBMD & SMA

For the combined data, 3/54 items scored below the mean (most true for the parent)

- …my child could receive placebo 3.48 (*SD* 2.07)
- …I don't have enough information about the risks of clinical trials 3.79 (*SD* 2.31)
- …I don't have enough information about the day-to-day requirements 3.82 (*SD* 2.31)

Perceived Facilitators

No significant differences between DBMD & SMA

For the combined data, 13 scored in the ranges of most true for the parent

- …I was confident the trial would improve researchers' understanding of the disease 1.81 (*SD* 1.27)
- …my child was guaranteed the treatment [if it worked] after the trial 1.90 (*SD* 1.67)

Regression Model

Logistic Regression

MODEL (R^2=0.350)	B (SE)	Ratio (95% CI)
[Constant]	-5.83 (1.10)	0.003
Perceived Barriers	1.40** (0.25)	4.07 (2.51–6.60)
Normative Agreement	0.84* (0.40)	2.33 (1.07–5.06)
Provider Attitudes	1.22* (0.50)	3.37 (1.27–8.95)
Frequency of Physician Communication	-0.47* (0.22)	0.63 (0.41–0.96)

Table 3. Significance at $p<.05$ is denoted by *, and at $p<.01$ by **.

Discussion

- Consent to enroll in a clinical trial should aim to achieve realistic expectations of benefit
- Parents should be encouraged to speak frankly with their child's doctor about her opinion about trials but work toward making the best decision for their child and family
- Information on potential risks and burden should be emphasized and placebo-controls studies should be thoughtfully discussed.

Collaborators

- Holly Peay, PhD, MS-RTI North Carolina & Parent Project Muscular Dystrophy
- Diana Escolar, MD-Chief Medical Officer of Akashi Therapeutics
- Jill Jarecki, PhD-Families of Spinal Muscular Atrophy
- Ben Wilfond, MD-University of Washington
- Aad Tibben, PhD-University of Leiden, Netherlands