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Perceived Barriers to Clinical Trials Participation: A Survey of Pediatric Caregivers

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ABSTRACT

Introduction. Pediatric clinical trials are difficult to conduct, leading to off-label use of medication in children based on results of trials with adults. As a unique population, children deserve to have appropriately tested therapies. The purpose of this study was to evaluate pediatric caregivers' beliefs and perceived barriers to participation in clinical trials.

Methods. The study was completed within the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE), an affiliate of the IDeA States Pediatric Clinical Trials Network (ISPCTN). This was a cross-sectional survey, adapted from the Pediatric Research Participation Questionnaire. A convenience sample of pediatric caregivers was recruited in three areas of a highly rural Midwestern state between 2017 and 2018.

Results. A total of 159 caregivers completed surveys; the majority (72.3%) were previously familiar with clinical trials, but less than 20% had ever been invited to participate. Caregivers were willing to consider enrolling their child if a physician in whom they had high trust recommended the trials ($H = 10.1$, $p = 0.04$) and if there were perceived benefits, such as access to tests and medications not covered by insurance (correlation coefficient [CC] = 0.4, $p < 0.01$) and compensation for time and travel (CC = 0.3, $p = 0.04$).

Conclusions. Trust in their physician highly influences likelihood of a caregiver consenting to have their child participate in a clinical trial. Therefore, to facilitate opportunities for children to participate in clinical trials, physicians need to be trained so they can offer trials locally. In addition, trials need to offer benefits, such as increased access to tests and medications as well as appropriate compensation.

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INTRODUCTION

Clinical trial data are the gold standard for evaluating the safety, effectiveness, and feasibility of therapies and treatments.[1,2] However, such data rarely exist for pediatric populations.[3] As a result, treatments for pediatric patients often are prescribed "off label", meaning the use of these treatments is based on extrapolation from trials with adults.[4-6] Such practices are assumed to be safe and effective but are not optimal due to a variety of physiological, ethical, and practical concerns related specifically to children.[5,7-10] With little evidence supporting these treatments and in light of the potential risks, it is important that treatments be tested specifically in pediatric populations.

In the early 2000s, legislation requiring pediatric clinical trials for new pharmaceuticals was passed.[11] This legislation resulted in a considerable improvement in access to such trials for children.[12] Even with these mandates, however, pediatric clinical trials remain relatively uncommon. First, pediatric trials are difficult to conduct, posing a variety of logistical, ethical, and economic challenges.[12,13] Second, because children are defined as a vulnerable population, special procedures are required of the researchers, and disagreements can arise about a child's autonomy in choosing to participate.[14] Finally, participant engagement may be a challenge due to previously identified barriers among adults, including distrust of researchers, limited access to trials, and socioeconomic barriers such as need for travel and time off work.[15-17]

To address the limited access to pediatric clinical trials, the IDeA States Pediatric Clinical Trials Network (ISPCTN) was formed.[18] As part of this national collaborative, the Sunflower Pediatric Clinical Trials Research Extension (SPeCTRE) network was developed in Kansas. One of the initial goals of the ISPCTN network was to establish a means of assessing and creating opportunities for clinical trial research in children in the United States. Therefore, the purpose of the current study was to evaluate caregivers' (i.e., parents, foster parents, adoptive parents) perceived barriers to participation in clinical trials, and to assess whether barriers differed regarding self-participation versus child participation. Secondary aims were to assess whether perceived barriers of caregivers aligned with those identified in previous studies of caregivers, and whether specific barriers amenable to intervention could be identified. A second study was designed to evaluate perceived barriers of providers and healthcare staff to participation in clinical trials (Smith, under review); those data are reported elsewhere.

METHODS

The 48-item survey was adapted from the Pediatric Research Participation Questionnaire (PRPQ) by an expert panel of SPeCTRE network members. In addition to basic demographics and children's free/reduced lunch status, the survey consisted of closed-ended questions that measured perceptions and barriers of participants to clinical trials on a 5-point Likert-type scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree). Specifically, questions addressed beliefs about clinical trials in general (general beliefs), beliefs about the benefits of clinical trials to self (self-benefit beliefs), and trust in primary care providers (PCP). General belief questions addressed respondents' beliefs about the overall purpose and safety of clinical trials. Self-benefit questions were related to respondents' beliefs of personal value and benefits gained from participation in clinical trials. Questions related to trust in their PCP addressed respondents' trust that their PCP would make recommendations in the best interest of their patients. Reported child's free/reduced lunch status was used as a proxy for household income level.

A convenience sample of adult pediatric caregivers (at least 18 years of age) was recruited from outpatient clinics and back-to-school fairs

in two urban areas and a county fair in a rural area of Kansas. At time of invitation, caregivers were told about the study, informed the survey would take approximately 10 minutes to complete, and given the option to complete the survey on paper or electronically via a provided tablet.

Data were managed using REDCap® (Research Electronic Data Capture) hosted at the University of Kansas Medical Center. REDCap® is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry, 2) audit trails for tracking data manipulation and export procedures, 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for importing data from external sources.[19] The University of Kansas Medical Center Institutional Review Board (KUMC IRB) approved and monitored the study. Survey participation was voluntary and provided without incentive. Descriptive and statistical analyses were performed in IBM SPSS Statistics 23 using frequency, measures of central tendency, variance, t-test, and nonparametric statistical methods, including Spearman's Correlation Coefficient and Kruskal-Wallis H-Test.

RESULTS

A total of 161 individuals responded to the survey and 159 met criteria for inclusion. The majority of respondents (77.0%) were surveyed in urban regions; 5.7% were surveyed in rural regions, and 17.6% had missing location information.

Respondent Characteristics. The largest proportion of respondents were female (67.9%), non-Hispanic White (43.4%), college-educated (31.4%), and had private or employer-provided insurance (42.8%; Table 1). Respondents' age ranged from 19 to 65 years, with a median age of 34 years. The average household size was four individuals, with an average of two children. Approximately 11.9% of respondents were living in households with income at or below $45,510 (the household income level to meet federal qualification for reduced lunch).

History with Clinical Trials. The majority of survey respondents (72.3%) were familiar with clinical trials, but only 19.5% had been invited to participate. Of those invited, 48.4% of respondents (11.2% of the total), and 29.0% of their children (6.8% of the total), had participated in a clinical trial. Of those caregivers who had participated in a clinical trial, 77.8% had at least some college education. No significant correlations were found between respondents ever participating in a clinical trial and their insurance status (r_s = 0.111, p = 0.224) or type of health coverage (r_s = -0.110, p = 0.225).

Factors Influencing Likeliness to Participate and Allow Child to Participate in Clinical Trials. No significant correlations were observed between age or sex and participant general beliefs, self-benefit beliefs, or trust in their PCP (Table 2). A significant positive correlation was observed between respondents' education levels and self-benefit beliefs (H = 7.355, p = 0.025), but not with general beliefs (H = 1.496, p = 0.473) or trust in their PCP (H = 4.328, p = 0.115). A significant positive correlation was observed between respondents' employment status and trust in their PCP (H = 1154.0, p = 0.011), but not with general beliefs (H = 1647.0, p = 0.860) or self-benefit beliefs (H = 1472.0, p = 0.264).

Table 1. Respondent characteristics.

	N	%
Total Respondents	**159**	
Gender		
Female	105	67.9
Male	23	14.5
Missing	28	17.6
Race & Ethnicity		
Non-Hispanic White	69	43.4
Non-Hispanic Black	23	14.5
Hispanic white	14	8.8
Other	16	10.1
Missing	37	23.3
Education		
HS or less	44	27.7
Some college	34	21.4
College grad or higher	50	31.4
Missing	31	19.5
Employment status		
Employed	85	53.5
Unemployed/other	41	25.8
Missing	33	20.8
Health Coverage		
Private/employer	68	42.8
State	29	18.2
None	29	18.2
Missing	33	20.8

Table 2. Demographics and the degree of positive beliefs related to clinical trials.

Respondent Characteristics	General Beliefs	Self-Benefit Beliefs	Trust in PCP
Age t (p value)	-0.776 (0.440)	-0.463 (0.645)	-1.115 (0.267)
Sex H (p value)	1210.5 (0.834)	1232.0 (0.730)	1131.0 (0.932)
Level of education H (p value)	1.496 (0.473)	7.355 (0.025)*	4.328 (0.115)
Employment status H (p value)	1647.0 (0.860)	1472.0 (0.264)	1154.0 (0.011)*

*Indicates statistical significance.

No significant correlations were observed between respondents' demographics (age, gender, education level, employment status, and type of health coverage) or self-benefit beliefs and their likeliness to participate or allow their child to participate in a clinical trial (Table 3). Participants with more positive general beliefs about clinical trials were more likely to consider enrolling themselves (H = 13.284, p = 0.010) or their child (H = 13.623, p = 0.009) in fitness-related trials, but not clinical trials in general (H = 6.364, p = 0.174; H = 9.172, p = 0.057). Participants also were willing to consider enrolling their child in broader clinical trial opportunities if the trial was recommended by a trusted physician (p = 0.04).

Significant positive correlations were observed between respondents' likeliness to participate in clinical trials and certain benefits offered (Table 4), including gaining access to tests and medications not covered by insurance (r_s = 0.357, p = 0.010), free transportation (r_s = 0.300, p = 0.032), compensation for time and travel (r_s = 0.513, p < 0.01), and having alternative participation options, such as telehealth (r_s = 0.325, p = 0.020). Similarly, the likelihood of respondents' allowing their child to participate in clinical trials was correlated significantly with the benefits of having access to tests and medications not covered by insurance (r_s = 0.407, p = 0.003) and receiving compensation for time and travel (r_s = 0.296, p = 0.035).

Respondents' likelihood of participating in clinical trials increased with an increase in the number of benefits provided from the study (H = 10.596, p = 0.031). However, no statistically significant relationship was observed between respondents' likelihood of allowing their child to participate in clinical trials and an increased number of benefits provided from the study (H = 1.867, p = 0.760).

Offering trials through telehealth (r_s = 0.354, p = 0.011), on-site (r_s = 0.410, p = 0.003), or at a local practice or clinic (r_s = 0.374, p = 0.007) were correlated significantly with respondents' increased likelihood of participating (Table 5). However, these alternative modes of participation were not correlated significantly with respondents' likelihood of allowing their child to participate in clinical trial studies, unless the trial was on-site and recommended by their doctor (r_s = 0.318, p = 0.023) or was at a local practice or clinic and related to fitness (r_s = 0.279, p = 0.047).

Respondent Preferences for Learning about Clinical Trials. The majority of respondents reported they would prefer receiving information about clinical trial research studies from their health care provider (73.0%). Moreover, 69.8% of those selected only their health care provider and no other sources (e.g., webinar, telemedicine, educational brochure). Less than a quarter of respondents (23.9%) would prefer this information from more than one source.

DISCUSSION

The purpose of this study was to evaluate caregivers' perceived barriers regarding their child's participation in clinical trials and to determine if these barriers were consistent with those identified in previous studies. A major barrier appears to be that most respondents (80.5%) had never been invited to participate in a clinical trial. Less than one-fifth of survey respondents in this study had ever been invited, a finding consistent with a previous study of adolescent and young adult cancer patients in which only 13% of respondents were offered the opportunity to participate in a trial.[20] Of those in our study who had ever been invited to participate in a clinical trial, nearly half of adults and a third of children ended up participating.

Respondents to our survey who had participated in a clinical trial were likely to have at least some college education. This finding could reflect that trials were more likely to be offered to those with higher education or could reflect higher perceived self-benefit from clinical trials by those with more years of education, as our respondents reported. Patients with higher socioeconomic status were shown to be more likely to enroll in clinical trials.[21] In addition, having positive general beliefs about clinical trials significantly increased respondents' willingness to have their child participate in physical fitness research, and willingness to participate in physical fitness research themselves. Respondents also were more inclined to allow their child to participate if a trial was recommended by a physician and if they reported high physician trust. Our results suggested physical fitness trials may be an optimal entrée to engage caregivers and children in clinical trials. Future studies should evaluate whether engagement in low-risk fitness trials can increase perceived benefits and enhance willingness to engage in broader clinical trials, such as those for medications.

Further, our results suggested participants preferred hearing about clinical trials from their personal physician. These results are similar to findings from previous studies.[16,22] The preferred location for participation was at a local office. This finding emphasized the importance of having clinical trial sites in various geographic areas. Training local physicians and focusing on capacity-building related to their participation in clinical trials should be a focus of future interventions to enhance clinical trials access/conduct in underserved areas.

Finally, specific benefits of the trial to provide access to tests or medications not covered by insurance, free transportation, compensation for time and travel, and some options for alternative participation such as telehealth also increased willingness to participate in clinical trials as reported by caregivers for both themselves and their children. These findings contrasted with the findings of a previous study of asthma patients in which compensation was not a factor in parents' discussion of risks and benefits and was mentioned in only 10% of adolescents' responses.[23] However, results of a sister survey of physicians and healthcare staff by our team found providers also identified the importance of incentives for participants as a key factor in participation (Smith, under review).

This study had several limitations. First, due to the convenience sampling methodology of survey distribution, responses were not generalizable to non-urban regions. We were unable to demonstrate differences between rural and urban, as the majority of participants were recruited from two urban areas of the state. Second, complete demographic data were missing for about 20% of participants, so drawing conclusions about any demographic variables was difficult. The data that were reported indicated income levels that were generally higher than those reported in state level data. Third, the PRPQ

Table 3. Respondent characteristics correlated with likeliness to participate and allow their child to participate in clinical trials.

Respondent Characteristics	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Age t (p value)	-1.716 (0.094)	1.226 (0.228)	1.161 (0.253)	-1.415 (0.165)	-0.712 (0.481)	1.141 (0.261)
Gender CC (p value)	0.054 (0.712)	0.039 (0.788)	0.084 (0.568)	0.125 (0.393)	0.007 (0.963)	0.195 (0.180)
Level of education CC (p value)	-0.160 (0.274)	0.017 (0.907)	0.210 (0.148)	0.160 (0.273)	0.135 (0.357)	-0.053 (0.716)
Employment status CC (p value)	-0.233 (0.110)	0.016 (0.913)	-0.282 (0.052)	-0.200 (0.173)	-0.074 (0.618)	-0.165 (0.264)
Health insurance carrier CC (p value)	0.048 (0.751)	-0.21 (0.890)	-0.128 (0.395)	-0.058 (0.703)	-0.191 (0.204)	-0.141 (0.352)
General beliefs H (p value)	6.364 (0.174)	13.623 (0.009)*	4.708 (0.319)	8.596 (0.072)	13.284 (0.010)*	13.623 (0.009)*
Self-benefit beliefs H (p value)	3.325 (0.505)	2.853 (0.583)	6.008 (0.199)	3.8886 (0.422)	5.980 (0.201)	2.853 (0.583)
Trust in PCP H (p value)	9.202 (0.056)	7.358 (0.118)	7.259 (0.123)	10.082 (0.039)*	9.315 (0.054)	7.358 (0.118)

*Indicates statistical significance

Table 4. Likeliness of participating in a clinical trial given certain benefits.

Benefits Offered	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Tests/medications not covered by insurance CC (p value)	0.357 (0.010)*	0.407 (0.003)*	0.430 (0.002)*	0.329 (0.018)*	0.277 (0.049)*	0.177 (0.214)
Free transportation CC (p value)	0.300 (0.032)*	0.253 (0.073)	0.430 (0.002)*	0.360 (0.009)*	0.375 (0.007)*	0.361 (0.009)*
Compensation for time and travel CC (p value)	0.513 (0.000)*	0.296 (0.035)*	0.541 (0.000)*	0.294 (0.036)*	0.472 (0.000)*	0.306 (0.029)*
Alternative participation options CC (p value)	0.325 (0.020)*	0.204 (0.151)	0.342 (0.014)*	0.230 (0.104)	0.391 (0.005)*	0.335 (0.016)*

*Indicates statistical significance

Table 5. Comparison of likeliness of participating in a clinical trial given alternative options for participation.

Options for Participation	Any Clinical Trials		If Recommended by Doctor		If Related to Improving Fitness	
	Self	Child	Self	Child	Self	Child
Telephone participation CC (p value)	0.193 (0.175)	0.150 (0.294)	0.207 (0.145)	0.165 (0.247)	0.129 (0.365)	0.129 (0.367)
Internet participation CC (p value)	0.177 (0.213)	0.193 (0.175)	0.151 (0.290)	0.169 (0.235)	0.177 (0.215)	0.183 (0.198)
Telehealth CC (p value)	0.354 (0.011)*	0.222 (0.118)	0.339 (0.015)*	0.239 (0.091)	0.203 (0.154)	0.155 (0.279)
Local practice/clinic CC (p value)	0.374 (0.007)*	0.177 (0.214)	0.202 (0.156)	0.089 (0.533)	0.284 (0.044)*	0.279 (0.047)*
On-site CC (p value)	0.410 (0.003)*	0.271 (0.055)	0.460 (0.001)*	0.318 (0.023)*	0.347 (0.013)*	0.235 (0.097)

*Indicates statistical significance

was developed originally for use with caregivers of children with sickle cell disease or asthma and has been used among caregivers of children with cancer.[23] This study differed from those in that it did not focus on a particular disease state or on patients or families with documented health conditions. The modified tool has not been validated yet. Finally, the nature of this self-report data allowed us to assess only reported likelihood of participation in clinical trials, not actual participation. In spite of these limitations, this study provided insight into areas that may increase clinical trial participation of caregivers and their children.

CONCLUSIONS

In conclusion, the findings of this study suggested that caregivers were more likely to allow their child to participate in clinical trials when invited by a trusted physician. Less than a fifth of study respondents had ever been invited. To facilitate increased clinical trial participation for pediatric patients, local primary care physicians should be recruited to offer opportunities for trials to their patients. Physical fitness trials should be considered as an initial strategy for enhancing pediatric participation as willingness to participate in these trials was higher than willingness to participate in general clinical trials. Additional research is needed to investigate perceived barriers that physicians may have in offering clinical trials as a treatment option to their patients, more specifically, pediatric patients. In addition, the trials should offer benefits, such as access to tests and medications, transportation, or compensation that make participation attractive to caregivers.

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