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Perceived Barriers to Pediatric Clinical Trials Implementation: A Survey of Health Care Staff

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ABSTRACT

Introduction. Clinical trials are the gold standard for assessing the effectiveness and safety of treatments. The objective of this study was to assess provider opinions regarding implementing pediatric clinical trials in various practice settings across Kansas.

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). A cross-sectional, 36-item survey was administered to a state-wide convenience sample targeting health care providers and clinic staff.

Results. A total of 115 health care providers and clinic staff completed surveys; 31% were physicians. Physicians were more likely than other clinic staff to have experience with clinical trials (correlation coefficient [CC] = 0.270, p = 0.004). When compared to urban respondents, rural providers were less supportive of recruitment for clinical trials in their practices (CC = -0.251, p = 0.008) and more likely to feel comfortable referring patients for clinical trials involving treatments that their insurance did not cover (CC = 0.302, p = 0.001).

Conclusions. A range of rural and urban health care professionals supported conducting pediatric clinical trials but identified several barriers as well. These results will support future pediatric clinical trials across the country including Kansas. ***Kans J Med 2022;15:189-193***

INTRODUCTION

Clinical trials are the gold standard for assessing the effectiveness and safety of treatments in health care.[1] Dramatic improvements in health care outcomes have resulted from clinical trials, such as reduced mortality in childhood leukemia.[2] Despite the benefits of pediatric clinical trials to health outcomes, children routinely receive medical therapies that have not been studied in clinical trials involving pediatric subjects.[3] For example, over 75% of hospitalized children may receive a medication "off-label", in a manner not explicitly approved in children.

Numerous factors may restrict broader implementation of clinical trials in pediatric settings. Prior studies have reported patient and provider time constraints, lack of trained staff, and scarcity of appropriate facilities for clinical trials procedures as potential barriers.[4,5] These barriers point to a lack of dedicated resources for pediatric clinical trials.[6] In an attempt to increase the availability of pediatric clinical trials resources, the National Institutes of Health funded the IDeA States Pediatric Clinical Trials Network (ISPCTN).[7] The ISPCTN's primary objectives are to: 1) extend clinical trials opportunities to children and communities, and 2) increase the capacity of participating states to conduct pediatric clinical trials.

Participating sites within the ISPCTN are located in states that are part of the Institutional Development Award (IDeA) Program. The IDeA Program, which was established by congressional mandate in 1993, seeks to broaden the geographic distribution of NIH funding through faculty development and institutional research infrastructure enhancements in states with historically low NIH funding.[7] As the program for the ISPCTN in the state of Kansas, the Sunflower Pediatric Clinical Trials Network (SPeCTRE) deployed targeted surveys to assess barriers and facilitators to clinical trials participation faced by parents/caregivers and health care providers residing in rural and urban communities across one rural IDeA state, Kansas. The objective of the current study was to identify and determine the relative importance of specific factors relating to implementation of pediatric clinical trials in various practice settings across the state.

METHODS

The study team administered a 36-item survey online and in person to a convenience sample of health clinic providers, nurses, and non-clinical administrative staff (administrative assistants and schedulers). Clinic managers were excluded from the survey. Subjects were recruited into the study in person by research staff who visited clinical sites or community events or via targeted email. Participants were surveyed over a two-year period (2017-2018).

Sampling strategy focused on ensuring that health care providers and staff working in a variety of settings were included. Participating subjects were recruited from one of three settings: 1) community-based outpatient clinics, 2) county health departments, and 3) academic medical centers and affiliated clinics. Emails were distributed to health care providers and staff who had signed up for education and outreach activities through the University of Kansas Medical Center Area Health Education Centers (AHECs). The AHECs' mission is to enhance the quality and accessibility of health care services in Kansas through partnerships with communities, health care professionals, and organizations across the state.

The study team used distinct procedures for in-person and online enrollment. For in-person enrollment, written documentation of risks and benefits was provided to respondents with questions answered by the study team. Recruitment occurred at clinical sites as noted above or at community events such as health fairs and county fairs. Following verbal informed consent, respondents completed surveys by paper or on an electronic tablet based on participant preference. Online enrollment was completed via email with initial content including an informed consent statement. Affiliated clinical sites invited their staff to participate and the individuals with recent participation in education

activities at the AHEC.

Survey items were adapted from established tools[4,8] and beta tested for understandability with five research and clinical staff at clinical sites affiliated with project. Beta testing suggested small wording changes, primarily grammatical, that would be helpful to aid health care provider understanding of items. Content and themes were retained from items in previous published surveys[4,8] as well as the 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree) although verbiage varied slightly on some survey items. Additional items addressing basic demographic information, practice type, experience with clinical trials, and preferences for learning more about clinical trials also were included. Survey responses were recorded in REDCap®[9] either directly from participants or entered from paper surveys.

The University of Kansas Medical Center Institutional Review Board approved and monitored the study. Survey participation was voluntary and provided without incentive. Data analyses were completed in IBM SPSS Statistics 23 (Armonk, NY) using t-test or non-parametric statistical methods, including Spearman's correlation coefficient (CC) and Kruskal-Wallis H test, as appropriate.

RESULTS

A total of 145 participants completed at least one survey item and 115 completed all survey items, for a completion rate of 79%. Response rate from site visits was 100%; response rate from email could not be determined due to changes in the listserv membership during the study period. Demographics of participants are detailed in Table 1. Physicians and nurses represented the most frequent professional roles for participants (31% and 32%, respectively). The largest proportion of respondents was recruited from clinic-based practice (39%), with a smaller number of respondents engaged in hospital-based practice (14%). The majority of respondents (68%) served urban and suburban communities while 32% of respondents were from areas considered rural. The majority of surveys were completed online (53.4%).

Only 23% of respondents had ever enrolled a patient into a clinical trial; 43% had referred a patient to participate in a clinical trial. Clinical experience by years of practice was associated significantly with respondents' level of experience with clinical trials (no experience, experience referring, and experience enrolling; H = 17.233 (Kruskal-Wallis Test), $p < 0.05$). Physicians were significantly more likely than other clinic providers to have experience with clinical trials (CC = 0.270, p = 0.004).

Most respondents (55%), regardless of clinic role, were interested in learning more about clinical trials. Respondents most often reported interest in learning about available clinical trials in their area (35%). A comparable number of respondents preferred receiving information on clinical trials through in-person (68%, 99/145) and online (96%, 139/145, e.g., Skype, webinar, telemedicine) educational activities. Roughly one third of respondents (64%, 93/145) requested continuing medical education (CME) credit for such sessions. Physicians (CC = 0.210, p = 0.23) were significantly more likely to prefer CME learning opportunities than were other clinic roles. Of note, no learning modalities neared 50% preference from respondents.

Table 2 describes beliefs regarding clinical trials according to the 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree). Because responses were distributed non-normally, data were reported as medians (interquartile range [IQR]). Respondents considered clinical trials safe and effective (Med 4 [IQR 3-5]) and agreed that clinical trials help discover new treatments (Med 5 [IQR 4-5]). Participants differed on the impact of available time on implementation of clinical trials (Med 3 [IQR 3-4]). Respondents agreed that limiting costs incurred by patients (Med 4 [IQR 4-5]) and the clinic (Med 4 [IQR 3-5]) would increase their desire to offer and/or participate in clinical trials. Respondents endorsed that reducing the burden of paperwork would be important for their practice to participate in clinical trials (Med 4 [IQR 4-5]) but were equivocal that their practices were not ready for a clinical trial (Med 3 [IQR 2-4]). An understandable and accessible protocol was attractive to practices considering clinical trials (Med 4 [IQR 4-5]). Respondents expressed disagreement with statements that they would not offer a clinical trial to participants if it involved use of a placebo in a study arm or randomization (Med 3 [IQR 2-3]).

Table 1. Participant demographics (n = 145).*

	N (%)
Gender (n= 116)	
Male	22 (19%)
Female	94 (81%)
Ethnicity (n= 115)	
White	95 (83%)
Black	13 (11%)
Other	7 (6%)
Age (years) (n=117)	
18-34	44 (38%)
35-44	27 (23%)
45-54	21 (18%)
55+	25 (21%)
Professional Role (n = 118)	
Physician	37 (31%)
Advanced Practice Provider	16 (14%)
Nurse	38 (32%)
Other	27 (23%)
Practice Location (n = 117)	
Urban/Suburban	79 (68%)
Rural	38 (32%)

*Efforts attempted to reflect the health care workforce in the state of Kansas with the largest proportion (30.3%) of respondents being under 35 years of age and most respondents (52.4%) identified as White and Female. Other for ethnicity and professional role was not defined by respondents although professional was presumed to include administrative assistant and clinic schedulers.

Table 2. Respondent beliefs rearding clinical trials.

	N	Median[1]	Question 1	Question 3
I consider clinical trials a safe and effective treatment option for my patients.	119	4.00	3.00	5.00
I feel comfortable offering a clinical trial as a treatment option to my patient.	118	4.00	3.00	5.00
I would not feel comfortable if my patients were not assigned to receive a treatment in a clinical trial (i.e., is assigned to receive a placebo, sugar pill).	118	3.00	2.00	3.00
I would offer a clinical trial treatment option to my patients if I had more time.	119	3.00	3.00	4.00
I would offer a clinical trial as a treatment option to my patients even if the standard treatment has not failed.	119	3.00	2.00	4.00
I would recruit my patients into a clinical trial if the protocol was easy to understand.	122	4.00	4.00	5.00
I would recruit my patients into a clinical trial if it didn't cost my practice/clinic.	124	4.00	3.00	5.00
I would offer a clinical trial treatment option to my patients if their insurance could cover tests/medications for them related to the trial.	123	4.00	4.00	5.00
I support clinical trial recruitment and enrollment at my practice/clinic.	124	4.00	3.00	5.00
I do not feel comfortable offering a clinical trial as a treatment option to my patients.	119	2.00	1.00	3.00
I would recruit my patients into a clinical trial if I had a training to complete the necessary paperwork.	120	4.00	3.00	4.00
I would recruit my patients into a clinical trial if I had trained staff to complete the necessary paperwork.	120	4.00	4.00	5.00
I would only offer a clinical trial as a treatment option to my patients if the standard treatment has failed.	119	3.00	2.00	4.00
I feel my practice/clinic is not ready to conduct a clinical trial.	119	3.00	2.00	4.00
I would not feel comfortable offering a clinical trial to my patients if the research involves randomization (where they receive one of two treatments).	119	2.00	2.00	3.00
I would recruit my patients into a clinical trial if the informed consent was easy to understand.	118	4.00	4.00	5.00
I believe clinical trials help us discover new treatment options to improve patient care.	121	5.00	4.00	5.00

[1]Median and interquartile (Question 1= 25% and Question 3= 75%) range on 5-point Likert scale (1 = Strongly Disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly Agree.) Respondents endorsed an interest in clinical trials although preparedness remains a challenge for participating practices.

There were no significant differences in providers' perceived barriers to referring patients to clinical trials based on their years in practice (Table 3), except the perceived cost to their practice ($H = 11.283$, $p = 0.024$.) A significant positive correlation was observed between perceived cost to their own practice and providers' age ($CC = 0.247$, $p = 0.007$), years in practice ($H = 11.283$, $p = 0.024$), and level of experience with clinical trials ($H = 0.192$, $p = 0.038$). Negative correlations were observed between providers' perception that their practice is "not ready", their age ($CC = -0.230$, $p = 0.013$), and level of experience with clinical trials ($CC = -0.347$, $p < 0.05$). Additionally, providers' level of experience with clinical trials was correlated positively with perceived barriers, including time ($CC = 0.243$, $p=0.008$,) complexity of the protocol ($CC = 0.194$, $p=0.036$,) lack of trained staff ($CC = 0.337$, $p< 0.001$,) and complexity of informed consent ($CC = 0.259$, $p = 0.006$.)

Table 3. Correlation between provider perceived barriers to recruiting based on their years in practice, age group, and level of experience with clinical trials.

	Years in Practice		Provider's Age Group		Level of Experience with Clinical Trials	
	H#	p value	CC#	p value	CC#	p value
Lack of provider time	2.459	0.652	0.115	0.223	0.243*	0.008
Complexity of the protocol	3.483	0.480	0.107	0.252	0.194*	0.036
Cost to the practice/clinic	11.283*	0.024	0.247*	0.007	0.192*	0.038
Lack of trained staff	4.374	0.358	-0.031	0.739	0.337*	0.000
Complexity of informed consent	2.964	0.564	0.141	0.134	0.259*	0.006
Overall, practice is not ready	8.712	0.069	-0.230*	0.013	-0.347*	0.000
Patients' medical insurance coverage	8.850	0.065	0.179	0.055	0.064	0.491
Lack of access to standard treatment	3.448	0.486	0.16	0.09	0.122	0.189
Lack of training	2.453	0.653	-0.043	0.642	0.043	0.652

*Denotes values with p value less than 0.05.
#CC = correlation coefficient, H = Kruskal-Wallis H test.

The three benefits most cited as potential incentives for pediatric clinical trials participation included compensation for time and travel (72%), providing tests and medications not covered by insurance (64%), and providing the opportunity at a local practice or clinic rather than traveling to the research site (64%). Additional logistical considerations such as option for telephone participation (63%) or telehealth visit (40%) as well as childcare support (68%) were noted by many respondents.

DISCUSSION

Consistent with past studies,[4,10] this survey of health care providers and non-clinical office staff found that a majority of respondents were interested in participating in clinical trials, but only a small fraction had enrolled patients in such studies. The findings additionally supported previous studies[6,8] that identified an interest in clinical trials among providers and staff but also found a lack of familiarity with their availability and conduct. The present study provided new insights into the perceived barriers to clinical trials participation reported by non-physician health care staff including advanced practice providers, nurses, and non-clinical office staff. While prior literature supported the assertion that primary care physicians are the preferred person of contact for clinical trials participants,[11-13] successful implementation of clinical trials requires engagement and, at least, basic knowledge/skills for non-clinical and support staff to identify potentially eligible subjects in an efficient manner and otherwise carry out a trial.

Respondents reported agreement with survey items that addressed resource constraints and clinic preparedness as barriers to clinical trials participation. Particularly, the need to have clinical trials protocols that were easy to understand, the desire to minimize expense to the clinic for participation, and the need to have adequate training in the protocol before participation were supported strongly by respondents. Previous studies also have reported that knowledge, logistical, and financial constraints prevent participation.[12] Training and financial support of on-site research staff at all locations could address these concerns.

Time constraints were less often reported as a barrier to clinical trials participation in contrast to prior studies.[6,10] In particular, preparedness presented an obstacle to clinical trial implementation with a minority of health care staff ready to engage in such research. Compared to caregiver perceptions, health care staff reported less concern regarding the structural components of experimental design such as randomization to placebo.[5,10] Health care staff were supportive of enrollment in clinical trials when effective alternative treatment existed but expressed more reservation to offer higher-risk studies. This reservation was like what parents report related to risk-benefit.[5,14]

To address knowledge gaps, results from the survey suggested that multi-modal educational interventions that include in-person and online options with offered CME were preferred methods for disseminating information on clinical trials. Health care staff drawn from rural, urban, academic, and community practices showed interest in online and in-person education. Additional qualitative evaluation of staff perspectives on educational activities could identify preferred modalities better. Surveying a greater number of participants from provider, nursing, and clinical roles also could better characterize knowledge gaps in each group. Closing such gaps is critical to expanding clinical research in lower resource regions.[15] Few health care staff believed that remote options via telephone or telehealth would encourage patient participation in clinical trials. With the increasing use of telehealth across Kansas, such attitudes may change.[16]

The study provided specific insight into the most common and most important perceived barriers to pediatric clinical trials participation faced by health care providers and staff in Kansas. Strategies could provide an evidentiary basis for their use in other rural and/or underserved settings nationally. Expansion of this study to other IDeA States Pediatric Clinical Trials Network (ISPCTN) member states could generalize barriers and perceptions better in states with more limited research infrastructure and guide future policy. Future qualitative research may include the addition of technological options for sharing information that was absent in the current study, such as text messaging and smartphone applications.

Several limitations affected this study. Convenience sampling from a limited number of sites could result in selection bias. The sample size precluded conducting some important sub-analyses, particularly comparisons between rural and urban settings. Broader engagement of rural practices throughout the state could allow such comparisons in the future. Respondents from Kansas may not be representative of other ISPCTN communities; future studies are planned that will engage other sites. Adjustments to the wording of survey items may reduce their comparability to the source tools. However, beta testing for item comprehension was deemed necessary to maximize internal validity. Finally, non-clinical staff roles were not specified; further characterization of these roles could identify targeted concerns that need to be addressed to enhance clinical trials participation.

CONCLUSIONS

Physicians and other healthcare providers and staff across a broad range of disciplines and geography in Kansas support the performance of pediatric clinical trials but identify logistical barriers that reduce their willingness to refer potential subjects to or participate in such studies. Poor self-efficacy, cost, logistics, insufficient time, and administrative challenges were potential targets for intervention to increase pediatric clinical trials participation. These results will help to inform future, larger-scale assessments of barriers and facilitators to clinical trials participation planned for the ISPCTN and will aid the introduction and successful implementation of pediatric clinical trials in Kansas and similar regions.

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