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Perceived barriers to pediatrician and family practitioner participation in pediatric clinical trials: Findings from the Clinical Trials Transformation Initiative

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ABSTRACT

Despite legislation to stimulate pediatric drug development through clinical trials, enrolling children in trials continues to be challenging. Non-investigator (those who have never served as a clinical trial investigator) providers are essential to recruitment of pediatric patients, but little is known regarding the specific barriers that limit pediatric providers from participating in and referring their patients to clinical trials. We conducted an online survey of pediatric providers from a wide variety of practice types across the United States to evaluate their attitudes and awareness of pediatric clinical trials. Using a 4-point Likert scale, providers described their perception of potential barriers to their practice serving as a site for pediatric clinical trials.

Of the 136 providers surveyed, 52/136 (38%) had previously referred a pediatric patient to a trial, and only 17/136 (12%) had ever been an investigator for a pediatric trial. Lack of awareness of existing pediatric trials was a major barrier to patient referral by providers, in addition to consideration of trial risks, distance to the site, and time needed to discuss trial participation with parents. Overall, providers perceived greater challenges related to parental concerns and parent or child logistical barriers than study implementation and ethics or regulatory barriers as barriers to their practice serving as a trial site. Providers who had previously been an investigator for a pediatric trial were less likely to be concerned with potential barriers than non-investigators. Understanding the barriers that limit pediatric providers from collaboration or inhibit their participation is key to designing effective interventions to optimize pediatric trial participation.

1. Introduction

In the United States, the number of registered clinical trials for adults exceeds the number for children by a factor of 10 [1]. While clinical trials have long been recognized as the gold standard source of evidence for medical decision-making, a number of factors have contributed to difficulty in performing clinical trials in children, including: 1) a relatively small population of available participants; 2) the high cost and lack of incentives for pharmaceutical companies to perform drug trials; 3) potential legal risk to the pharmaceutical sponsor; 4) ethical concerns regarding participation of children in trials; and 5) a lack of adequately trained pediatric investigators [2–4]. Since 1997, multiple federal policies have attempted to stimulate pediatric drug development through encouragement of pediatric-specific studies [5–9]. Despite these incentives, relatively few pediatric trials have been performed, and many trials have enrolled < 100 participants [1].

Abbreviations: AAP, American Academy of Pediatrics; ABDD, antibacterial drug development; CTTI, Clinical Trials Transformation Initiative; FDA, Food and Drug Administration; NIH, National Institutes of Health; Peds ABDD, Clinical Trials Transformation Initiative Pediatric Trials in Antibacterial Drug Development; US, United States

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Even if sponsors and investigators can overcome the above factors to launch a pediatric clinical trial, low enrollment can cause even the best-designed trial to be unable to meet its stated objectives [10]. The obstacles that prevent recruitment and enrollment of children into clinical trials are complex and can include a combination of factors related to the participants, their parents, and their doctors [11,12]. The role of the non-investigator primary pediatrician or pediatric specialist is substantial. Families are more likely to participate in trials if approached by the child's primary physician [13,14]. However, primary providers may be reluctant to enroll or refer children to trials, which leads to poor recruitment rates and decreases trial success [15]. Therefore, the design and execution of future pediatric clinical trials relies heavily on understanding the attitudes of non-investigator primary providers toward trials. However, little is known regarding the specific barriers that limit non-investigator pediatric and family practice providers from participating in and referring their patients to clinical trials. The purpose of this study was to describe factors influencing providers' awareness and willingness to refer their patients for pediatric clinical trials and the perceived barriers to their practice serving as a pediatric clinical trial site.

2. Methods

2.1. Participants

We administered a voluntary online survey in August and September of 2015 to a convenience sample of medical providers who provide care and treatment to children. We identified potential participants through 2 mechanisms: 1) we partnered with a recruitment firm to identify family practice physicians and general pediatricians from their database of United States (US)-based physicians who are interested and willing to participate in surveys; and 2) we identified physicians of 6 sections of the American Academy of Pediatrics (AAP), including Section on Clinical Pharmacology & Therapeutics, Section on Infectious Diseases, Section on Critical Care, Section on Hospital Medicine, Section on Advances in Therapeutics and Technology, and Section on Neonatal-Perinatal Medicine. These sections included providers who are primarily US-based, although some sections included a small number of international members. An emailed invitation to participate in the survey was sent to potential participants identified by these 2 mechanisms. Participants were also asked to forward the invitation email and survey link to either other pediatric practitioners. Any surveys received from providers who did not provide care for children were excluded. This study received a determination of exempt status by the Duke University Health System Institutional Review Board. Participants provided their agreement to participate in the survey by activating the survey link sent in the invitation email and initiating the online survey.

2.2. Data collection

When completing the survey, providers were asked to share their experiences with and perspectives in referring pediatric patients to clinical trials. Providers were asked to rate the importance of multiple factors to consider when referring pediatric patients to clinical trials using a 4-point Likert scale (very important, somewhat important, somewhat unimportant, unimportant). Participants could also choose "unsure" if they were not certain of the importance of a factor. Providers reported whether they had previously served as an investigator for a pediatric clinical trial. Providers were then asked to reflect upon the severity of 30 potential barriers to pediatric trial implementation, considering what they anticipated would be barriers at their site. The specific barriers were identified by the Clinical Trials Transformation Initiative (CTTI) Antibacterial Drug Development (ABDD) team members, who include experts in pediatric clinical trials from the pharmaceutical industry, academia, and the Food and Drug Administration (FDA). Identified barriers were classified into 4 categories: study implementation, ethics and regulatory, parental concerns, and parental and child logistics. Providers used a 4-point Likert scale (major barrier, moderate barrier, somewhat of a barrier, not a barrier) to indicate the severity of each barrier. Participants could also choose "not applicable" if they believed the barrier would not apply to their site, or "unsure" if they were uncertain of severity of the barrier.

2.3. Data analysis

Descriptive statistics were used to describe the quantitative data and thematic analysis was used to analyze the open-ended responses. The providers were divided into 2 groups: those with previous experience as an investigator for a pediatric clinical trial and those without this experience. We compared the probability of providers answering "not a barrier" among these 2 groups using Fisher's exact test. P values < 0.05 were considered to be significant. Analyses were conducted using SAS 9.4 (SAS Institute Inc. Cary, NC).

3. Results

3.1. Study population

A total of 168 providers participated in the survey. Of these, 32 were excluded because they were not pediatric providers. Therefore, the final sample size was 136. Most of the providers practiced either family medicine (55/136; 40%) or general pediatrics (45/136; 33%). The majority (110/136; 83%) had practiced medicine for more than 10 years (Table 1).

3.1.1. Experience with referring pediatric patients to clinical trials

Thirty-eight percent (52/136) of providers had previously referred a pediatric patient to a clinical trial. Of those who had not previously referred a patient, almost all (76/84; 92%) were not aware of any drug trials to which they could refer their patients. However, most (65/84; 77%) were interested in learning more about referral to drug trials. When asked to consider the importance of different factors when referring their pediatric patients to a clinical trial, providers were in agreement that it is very important to consider the potential benefits (120/136; 88%) and potential risks (127/136; 93%). Most providers also reported that it was either very important (29/136; 21%) or somewhat important (89/136; 65%) to consider the distance to the study site, and most believed it was very important (49/136; 36%) or somewhat important (72/136; 53%) to consider the time needed to discuss the clinical trials with the parents of their pediatric patients.

Table 1
Pediatric provider characteristics.

Pediatric Provider Characteristics (N = 136)	No. (%)
Specialty	
Family Medicine	55 (40)
General Pediatrics	45 (33)
Pediatric Hospitalist	21 (15)
Pediatric Infectious Disease	15 (11)
Years practicing medicine[a]	
< 5 years	9 (7)
5-10 years	14 (11)
> 10 years	110 (83)
Approximate distance from practice/institution to the nearest academic medical center or children's hospital	
Practice is located in an academic medical center or children's hospital	23 (17)
< 30 min	70 (52)
30 min to 2 h	39 (29)
> 2 h	4 (3)
Previous investigator for a pediatric clinical trial[a]	17 (12)

[a] 3 participants did not answer these questions.