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Factors Influencing Parental Consent in Pediatric Clinical Research

Justin D. Rothmier, MD*; Mary V. Lasley, MD†§; and Gail G. Shapiro, MD†§

ABSTRACT. *Background.* Although previous studies have looked at the motivation behind enrollment in clinical trials of adults and healthy subjects, little is known about the factors influencing parental consent in pediatric clinical studies where the subjects themselves do not provide consent.

Objective. This study was conducted to define a group of factors that impact parental consent in the pediatric clinical trial. This may allow investigators to identify a subset of specific appealing aspects of clinical trials that will promote participation while also bringing ethical issues to light that may require further consideration.

Methods. Forty-four parents or guardians of children currently participating in clinical asthma research completed questionnaires from July 1999 to September 1999 pertaining to motives for allowing their child to participate in clinical trials. The responses were then rated on a Likert numerical scale.

Results. The most important motive for parents is learning more about their child's illness. Next important was the motive of helping medical knowledge. Availability of free medication was negatively correlated with family income.

Conclusions. Although altruistic motives are present in pediatric asthma research, most parents/guardians gave consent for their child to learn more about their child's asthma. Access to free medication was more important in families with lower incomes than in families with higher incomes. *Pediatrics* 2003;111:1037–1041; *motives, parents, guardians, participation, children, clinical trials.*

The clinical trial is ultimately dependent on the availability of subjects to conduct the research. The statistical power to discern differences between interventions depends on adequate sample size. This impels researchers to identify the most efficient and cost-effective recruitment strategies^{1,2} to increase their sample size. Each year, millions of people are enrolled into clinical trials worldwide, but researchers have yet to define exact parameters that enhance subject recruitment. Literature on recruitment strategies is scarce, with only a few studies actually commenting on improvement strategies and confounding factors, while most address the outcomes of the recruitment.^{3–5} Although there are scat-

tered studies that do address specific recruitment issues, such as subject payment or research location, there are no comprehensive evaluations of the multiple factors involved in recruitment.⁶ Review of the literature to date points to the conclusion that numerous reasons influence the participation of subjects in clinical studies, least of which is based on demographic variables.

The pediatric literature is even more deficient, with only a few studies done to date, mostly performed in other countries. Two Australian studies by Harth^{7,8} in the early 1990s examined characteristics of parents who enrolled their children in a randomized, controlled trial of a new asthma medication. This study found that nonparticipating parents had a higher socioeconomic status, more social support, and were less motivated to contribute to medical research. A French study in 1993 showed that 74% of parents when asked about hypothetical enrollment of their newborn into a clinical trial refused consent based on possible side effects and unproven efficacy.⁹ Most recently, a study from Nova Scotia in 1998 asked parents to enroll their 2-month-old children into a randomized, controlled pertussis vaccine trial revealed that altruistic reasons motivated the parents who enrolled their children, whereas nonparticipants expressed concern for painful procedures.¹⁰

Because of the overwhelming lack of literature supporting pediatric recruitment strategies for clinical studies, where the subjects themselves often do not provide the consent, we proposed a study to further explore this question. We assumed that there are several factors that influence parental consent when allowing their children to participate in clinical studies. We designed a questionnaire intended to determine these reasons. Once these factors are identified, they can then be applied to the design of new studies to enhance clinical subject recruitment in pediatric trials. Additionally, these factors can be brought to the attention of investigators and investigational review boards to ensure subjects are not being coerced into participating in clinical trials.

METHODS

A 2-page questionnaire was administered to 44 parents or guardians of children less than 18 years who were currently involved in clinical research asthma trials at Asthma, Inc (Seattle, WA), a nonprofit organization dedicated to clinical research through both National Institutes of Health and pharmaceutical-funded studies. The treatment protocols averaged between 2 and 3 blood draws per study duration, with the exception of 1 study with 23 total blood draws (over 28 weeks), accounting for only 1 child in our population. Study duration varied from 4 to 8 weeks, with a total of 4 to 8 visits per study, with the lone exception of 1 study that lasted 28 weeks and contained a total of 24 visits. Mean

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TABLE 1. Characteristics of Parent/Guardian Demographics

Age (Mean)	Mean Income	Sex	Ethnicity	Marital Status	Education	Employment Status
40	30 000–49 000	88.6% Female 11.4% Male	86.4% White 6.8% Black 2.2% Asian 2.2% Hispanic 2.2% Other	84.1% Married 6.8% Single 9.1% Other	13.6% High school 25% Some college 34.1% College 18.2% Graduate 9.1% Vocational	40.9% Full-time 25% Part-time 31.8% Unemployed 2.3% Other

compensation was around \$570 per study (\$230–\$1885) and was considered remuneration for time spent in clinic. All trials were targeted for patients with mild to moderate asthma, not severe disease. Studies containing more invasive procedures (lab draws) were for pharmacokinetic research, and the subjects were compensated for their time in clinic.

Each questionnaire contained an attached consent form and specific instructions for completion of the questionnaire, and was administered in person by the primary investigator (J.D.R.). The primary investigator was not a providing physician at Asthma, Inc. The consent form and instructions informed each subject that answers were confidential and would not be linked to their child in any way. The questionnaire was adapted from an instrument used to determine motivating factors for subjects participating in the Stroke Prevention in Atrial Fibrillation study.¹² The questionnaire contained 14 Likert-type questions¹³ using a 1 to 4 scale with 1 signifying the subject strongly disagrees with the statement, 2 signifying the subject somewhat disagrees with the statement, 3 signifying the subject somewhat agrees with the statement, and 4 signifying the subject strongly agrees with the statement. Listed as possible influential factors were financial benefit, free gifts, learning more about asthma, free office visits, free medications, receiving the newest drugs, influence of family/friends, type of treatment involved, location of study, duration of study, encouragement of physician, relationship with research staff, and social events associated with the study.

Items also included in the questionnaire relevant to this analysis, but not in Likert format, included demographic information of the parent/guardian filling out the information (ie, age, sex, marital status, education, income, and ethnicity), relationship to child in research study, age of child, and how the participant learned of the study. Answers to these questions were in multiple choice and fill-in-the-blank format.

Data Analysis

The responses to each questionnaire were entered into a computer spreadsheet using Microsoft Excel (Microsoft, Redmond, WA), then validated by the primary investigator. Demographic information regarding household income and level of education was entered. Mean values were obtained for each category using Microsoft Excel. Correlations were made between parental demographic information and their responses to each factor using a Spearman's ρ correlation on SPSS for Windows (SPSS, Chicago, IL) to identify specific demographic variables that possibly biased responses to certain factors.

RESULTS

All children involved in research at Asthma, Inc were between the ages of 4 and 17. Of the 44 persons given the questionnaires, 100% completed the questionnaire in full. All respondents to this questionnaire were from separate families. Only 2 individuals refused to complete the questionnaire, stating that they did not have time to spare for the survey. Table 1 summarizes the demographic information of the subjects filling out the questionnaires. Respondents ranged in age from 26 to 71 (mean 40 years) and the majority were female (88%). The subjects were also highly educated with 77% having attended at least some college. Eighty-six percent of the respondents considered themselves white, 7% black, and 2% responding as Asian, Hispanic, and other. Eighty-four

percent of the children come from 2-parent homes, whereas only 7% come from single parent homes. Twenty-five percent of the respondents¹¹ had let at least 1 of their children participate in prior research at Asthma, Inc. Forty-three percent¹⁹ were referred to Asthma, Inc by their primary care provider or another physician, 20%⁹ heard about the studies on a radio advertisement, and 9%⁴ cited other reasons for recruitment.

Table 2 shows the ranking of factors based on the mean Likert score from the questionnaire. Mean values >2.5 were considered to be a factor that positively influenced the participant's decision, whereas values <2.5 were considered to either negatively influence or not influence parental consent. This was arbitrarily determined since a value of 2 on our Likert scale correlated with an answer which did not influence parental decision, whereas a value of 3 positively correlated with influencing parental consent. In this population, the respondents favored the reason of allowing their child to learn more about his/her disease as the most influential factor for giving consent, with a mean value of 3.56. This was followed closely by helping improve medical knowledge at 3.52, and the ability of their son/daughter to receive the newest drugs at 3.2. Less convincing were a patient's relationship with the research staff (2.95), the financial benefit (2.68), availability of free medications (2.65), the encouragement of their physician (2.63), and opportunity to have free office visits (2.61). Respondents indicated the type of treatment in the research study (2.4), location of clinic (2.36), duration of study (2.31), influence of family/friends (1.75), social support gain from being a participant

TABLE 2. Factors Influencing Parental Consent Based on Mean Response (N = 44)

Rank	Factor	Mean Response	95% Confidence Interval
1	Learn more about disease	3.56	(*4.30–2.81)
2	Help medical knowledge	3.52	(*4.28–2.77)
3	Newest drugs	3.2	(3.97–2.45)
4	Relationship with staff	2.95	(3.70–2.20)
5	Financial benefit	2.68	(3.43–1.93)
6	Free medications	2.65	(3.40–1.90)
7	Encouraged by physician	2.63	(3.38–1.88)
8	Free visits	2.61	(3.36–1.86)
9	Type of treatment	2.4	(3.15–1.65)
10	Location of clinic	2.36	(3.10–1.61)
11	Duration of study	2.31	(3.06–1.56)
12	Influence of friends	1.75	(2.50–1.00)
13	Social support	1.72	(2.47–.97)
14	Gifts received	1.45	(2.20–.70)
15	Other	NA	

NA indicates not applicable.

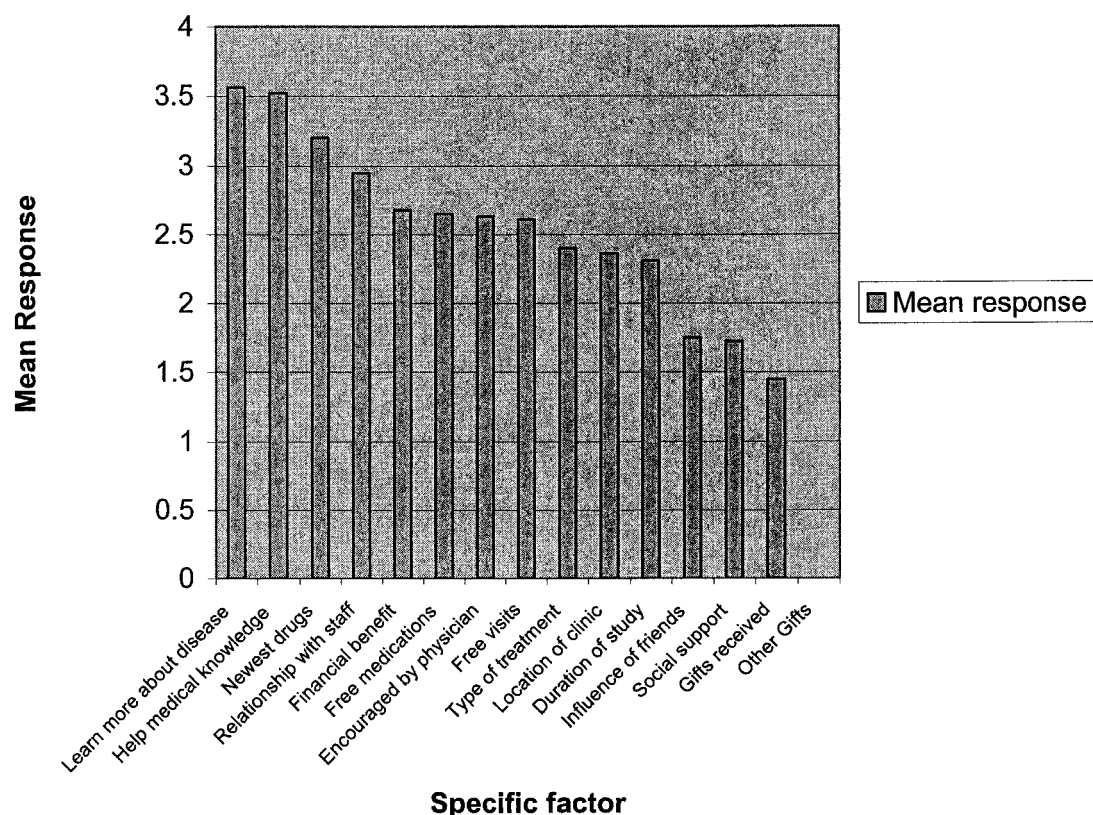


Fig 1. Subject responses. These depict the factors that influenced parental consent. Mean values >2.5 were considered to be a factor that positively influenced the participant's decision, whereas values <2.5 were considered to either negatively influence or not influence parental consent.

(1.72), and gifts received (1.45) were less important factors in their decision. Several participants indicated other reasons such as increasing their child's own awareness of their disease, or to better their child's health. Fig 1 shows the mean response for each factor.

To determine if the parent's/guardian's responses were associated with certain demographic variables, the annual household income and parent's education was correlated with each response, shown in Tables 3 and 4. As shown, many responses did not have statistically significant correlations with the parent's/guardian's demographic information. However, family income had a negative correlation with access to free medication ($P = .005$). Additionally, parent's education showed a negative correlation with helping medical knowledge, although it was not statistically significant ($P = .086$).

TABLE 3. Correlation Between Family Income and Influence of Different Factors on Consent

	Correlation Coefficient	Significance	N
Learn about disease	.009	.956	43
Help medical knowledge	-.023	.885	43
Obtain newest drugs	.031	.842	43
Relationship with staff	-.057	.715	43
Financial benefit	-.011	.942	43
Access to free medication	-.419	.005	43
Encouraged by physician	.204	.189	43
Access to free office visits	-.220	.157	43

DISCUSSION

Recruitment of the clinical research subject is an ever-daunting task. This is especially difficult in the pediatric population, in which another person is responsible for giving consent for the research subject.⁵ Previous studies looked at possible recruitment strategies to enhance participation, but all have failed to address specific factors that may influence parental consent.^{1-6,11-12} In recent years, a few articles have been published that address similar questions about motivation behind participation in clinical trials. Langley et al¹⁰ discovered most parents enroll their children in clinical trials for altruistic reasons such as the desire to contribute to medical knowledge and desire to help others, and that secondary gains such as free study materials was much less important in their decision. However, they do not comment on the socioeconomic status of their population, so it is difficult to conclude if their results are influenced by a selection bias. A study by Tait et al¹⁵ on factors that influence consent in pediatric anesthesia research also supports that altruistic motivations are important when obtaining parental consent, but they point out that the environment itself in which consent is obtained might influence their consent. They suggest the possibility that parents are more likely to give consent when approached in the inpatient setting, immediately before their child's surgical procedure than in an outpatient preoperative setting. Aby et al¹⁶ concluded that adult subjects enroll in clinical asthma, allergic rhinitis, and perennial nonallergic

TABLE 4. Correlation Between Parent's/Guardian's Education and Influence of Different Factors on Consent

	Correlation Coefficient	Significance	N
Learn about disease	.058	.710	44
Help medical knowledge	-.262	.086	44
Obtain newest drugs	-.107	.489	44
Relationship with staff	-.026	.869	44
Financial benefit	-.014	.928	44
Access to free medication	-.125	.420	44
Encouraged by physician	-.026	.869	44
Access to free office visits	-.156	.313	44

rhinitis trials for altruistic motives and illness-related health care, as compared with financial gain seen in previous studies with healthy volunteers.¹⁷⁻¹⁹ This study was designed to define a group of factors that impact parental consent in the pediatric clinical trial, which in turn will identify a subset of specific appealing aspects to clinical trials that will promote participation and lead to an increase in recruitment. In light of recent events including the death of an asthma research subject, the identification of possible coercive recruitment techniques might raise further ethical questions by investigational review boards when evaluating trial proposals. Researchers have a social responsibility to become aware of these techniques to avoid recruiting subjects under false pretenses, leading to possible safety compromises.

This study suggests that there are indeed specific factors that enhance parental/guardian consent when volunteering their children for a clinical research study. Based on the mean responses to each possible item, many parents indicated that several factors combined influenced the decision. Of the 15 possible factors, 8 had mean values >2.5 . Given that a mean value of 2.5 was a neutral value in our scoring system, all the mean scores >2.5 suggests these factors might have been positively considered in the decision-making process of the parent. As shown in other studies, our population stated the altruistic motivation of helping enhance medical knowledge as very important in their decision process. However, the most important motive in our population was to learn more about their child's disease.

We were concerned that socioeconomic status might affect the guardians' responses. Several demographic variables were correlated with each questionnaire response to look for relationships, which might bias the results of the data. After the annual household income was correlated with the responses to each possible influential factor, it was discovered that only the availability of free medications for the participant had a statistically significant negative correlation value ($-.419$; $P < .05$). This reveals that obtaining free medications for the child gains importance as the parent/guardians' socioeconomic status declines. This is supported by previous studies on participation showing the importance of controlling symptoms and/or receiving health care in populations not previously receiving medical care for their asthma/rhinitis symptoms.¹⁶ It is interesting to note that other possible factors which might influence

families with lower annual incomes, such as free visits and gifts, also had negative correlation values with family income, but were not statistically significant. Likewise, the financial stipend received for participation did not statistically influence the parent/guardians' decision when correlated with their income, unlike previous studies with adult subjects.^{14,17-19} Several possibilities could explain this discrepancy. First, many parents allow their child to keep the money for him/herself, as a reward to spend on miscellaneous items. This possibly becomes less important to their decision, thus explaining the lack of correlation to their income. The self-reported lack of importance placed on financial gain by our study sample may be artificially low because of the socially unacceptable value placed on admitting to such importance. The overall lack of statistical significance in this correlation might be accounted for by the relative lack of variation in incomes. A more complete distribution might have identified other influential factors not seen in this population.

Another possible source of bias is the education level of the parents. Extrapolating from previous studies showing a decrease in participation with a higher socioeconomic status,^{7,8} we were concerned there might be a negative association with education level. However, the parent/guardian's education level of our population did not significantly correlate with any factor. The most significant correlation in our population was the desire to help medical knowledge ($P = .086$), which had a negative correlation with parents education level. This is most likely explained by the poor distribution of education levels in our sample, since our population tended to be highly educated as a whole.

Our study is limited in several aspects. First, we did not have a control group for this study or a population of parents who denied consent, since our population currently had children enrolled in a clinical trial. We felt this was unnecessary since the objective was to quantitate those factors that influence consent and not those that deter a parent from giving consent. Additionally, several prior studies have already thoroughly described reasons parents have cited when denying consent for pediatric clinical trials.¹⁰ Often these reasons are specific to the type of studies, and often involve possible painful or uncomfortable procedures to the child, such as venipuncture or fingerpricks.¹⁰ The treatment protocols involved in this study included only minimal uncomfortable procedures. Most studies required only a pre- and posttrial blood draw, and the discomfort to the child was minimized by using a topical anesthetic cream before the venipuncture. This most likely explains why the type of treatment involved was not important to our population. Second, our data are compromised by failing to address several possible motives for participation. Specifically, we did not ask guardians about painful procedures (ie, venipuncture or fingerpricks), only about treatment protocols in general. In addition, we omitted questions pertaining to increasing their child's awareness of his/her asthma. Lastly, yet most significant, this study is limited by the small sample size, which then

decreases the power of the study. This can partially be accounted for by parents having multiple children in studies at our center, but mostly this is a result of the short time span of this study.

Although this study was conducted in the setting of clinical asthma research, its results can be extrapolated to other pediatric clinical studies. This study suggests that although altruistic motivations are present in pediatric asthma research, most parents are motivated by the opportunity for their child and themselves to actively learn more about the specific disease problem. It might be beneficial when recruiting participants for pediatric clinical trials to emphasize that participation can enhance their child's awareness of his/her disease, while improving medical knowledge. Furthermore, those populations with less resources or access to regular health care or medications are motivated to volunteer their children for clinical studies to provide them with improved health care.

This study has emphasized the relative nonimportance of financial and materialistic benefits of participation to parents in our population. Our population seems most influenced by the opportunities for their children and themselves to learn more about their child's disease, and the possibility of the clinical trial to facilitate disease education for their children. In the future, we will now try to explore disease education and awareness as possible new recruitment strategies for clinical trials.

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