

What Parents Want: Pediatric Studies that Appeal to Parents and Meet Ethical Guidelines

By Robert M. Jacobson

There are substantial hurdles to pediatric clinical studies. The developmental immaturity of children creates logistical barriers to communication, transportation, administering medications, etc. Many pediatric diseases are relatively rare. This article will discuss the paramount challenge: ethically attracting children to participate with their parents' permission. We will review published studies on recruiting and retaining children as research subjects. We will consider what we know about parental attitudes toward clinical research, their reasons for enrolling their children, and their reasons for refusing to enroll their children. I will then offer recommendations based on these findings and my own experience to enhance the chance of study success. We will not discuss the ethical considerations, but they qualify every perspective.

Surveys

A 2006 survey conducted in the United States recruited parents from a major urban tertiary children's hospital, specifically in the emergency department, the outpatient areas, the pediatric intensive care unit, and the neonatal intensive care unit. Investigators approached 161 parents, of which 84% consented to an oral face-to-face survey.¹ The results were very encouraging. Sixty-four percent of the parents affirmed that research with children is beneficial and investigators should conduct such research. Only 5% disagreed categorically. Thirty-four percent answered, perhaps wisely, that it depends.

These investigators, as well as investigators who have conducted similar surveys, found that race, gender, past experience, and parental education do not affect these attitudes.^{2,3} It may come as a surprise that race is not associated with these attitudes, but as we will discuss below, racially dependent issues with research participation are generally not about research per se, but rather about trusting the investigator.

If the majority of parents, in general, support pediatric research, why then is it so difficult to engage parents and recruit children to pediatric studies? Studies done with focus groups of parents have demonstrated certain aspects that influence parents' decision-making.^{4,5} Parents consider the pluses and minuses of studies and weigh the potential benefits against the cost and risks of the study. Parents generally do not decline participation because they object to the study. Instead, refusal usually results from weighing the benefits, costs and risks for their child. Of course, various factors and perceptions influence this balancing.

Let us begin with the benefits that parents perceive. Parents recognize the altruistic benefits of participating in research in general, the benefit to other children, and the contribution to medical research. Over half of the parents participating in focus groups across a variety of investigations endorsed these concepts.⁶⁻¹² Parents recognize the personal benefits as well. These benefits include access to treatments not otherwise available, better care and monitoring of their child, and additional information about the health and condition of their child.

Parents only occasionally endorsed other benefits. These benefits include access to health care professionals, meeting others in similar circumstances, the offer of hope, intellectual interest, and the perquisites of being in research, such as free medication, free transportation, free medical care, and financial compensation.¹³⁻¹⁷ Notably, the parents

reported that the financial aspects were unimportant, although parents may be disinclined to admit, even to themselves, that they give any weight to such matters.

Similarly, focus groups identified perceived minuses of participating in research. These minuses include the potential risks and side effects of a new drug, as well as its unproven efficacy. They also include the inconveniences of participation, such as study visits and paperwork hassles; the discomfort for the child; the notion of being randomized, especially to an ineffective treatment; the loss of privacy; and additional costs, such as lost wages.¹⁸⁻²²

We can categorize these factors into four categories: parental, child, study design, and investigator.

Parental factors concern knowledge and trust.²³⁻²⁵ Parents who are more confident in their general decision-making abilities are more likely to participate in research. In addition, parents who are more trusting of the medical system are more likely to participate. Similarly, parents who feel less pressured into making a decision are more likely to participate. Finally, parents who feel well-informed both in general and specifically about the study are more likely to participate. Parents who find the consent form readable and who have actually read the consent form are more likely to participate.

Child factors influence parental decisions to participate in research as well.^{26,27} For example, if the child wants to participate, the parents are more inclined to participate. Surprisingly, the child's health status has equivocal effects. Severity of the disease is not a major factor, but a previous history of illness decreases the likelihood of participation, probably because previous treatments have been inadequate. However, if a long-term illness is serious but stable, parents tend to decline, expressing fear of upsetting a stable condition. If a parent perceives that the child has no other options than research, participation is more likely.

Certain aspects of the study itself also influence a parent's participation.^{28,29} For example, studies that involve a greater-than-minimal risk deter parents. Parents dislike subjecting their child to additional injections or blood draws. Research recruitment in emergency settings also deters parents, which is consistent with the previous findings about unpressured decision-making. Finally, and predictably, placebos deter parents.

Finally, factors regarding the investigator can also affect a parent's decision.³⁰⁻³⁴ Trust and confidence in the investigator helps, as does the investigator's ability to communicate study information.

Recommendations

Let us begin with the recruiting materials. Identify both the direct and indirect benefits of the study. Make sure these benefits inform the development of the recruiting materials. Similarly, explain the altruistic aspects of the study — how it will advance science, and to what purpose. Parents want to know how they are contributing to science. More than half of the parents endorsed this item. When creating recruitment materials, identify how the study does this specifically and bring altruism to the forefront. At the opposite extreme, carefully consider stipends and other such incentives, and what you will say in recruiting materials. Think about how incentives separately influence parents and children. Obtain ethical guidelines from the institutional review board (IRB).

Clearly quantify or assess the risks of the study in all the materials, not just in the consent form. Highlight risks of most potential concern to the parents, rather than presenting them all. Think about how parents will react when learning about the risks. Present risks with benefits in a balanced, objective manner. In doing so, you can mitigate trust issues that some parents have with investigators. Saving the risks and costs for the consent process can diminish the parents' trust in the investigator as a purveyor of a bait-and-switch study.

Recruitment materials are not just flyers and advertising copy, but also the letters that go out to parents and the telephone scripts used by study coordinators and recruiters. Enrollment of a child is usually a family decision, so distribute a number of brochures at the initial visit. Armed with this information, children and their parents may also recruit their friends for the study. (The technical term is "snowball recruiting.")

Does the text of the recruiting material, particularly the brochure, explain what the study involves? Does it address why we need the study and how the study will benefit those with the condition? Does it address how it will advance medical research? Does it present the benefits to the study subjects? The brochure should also introduce to the reader to who the researchers are and which aspects of the subject's care will be in the study and which in the regular clinic.

Making studies acceptable for parents goes far beyond the recruiting materials. Studies involving children must attend to study design issues to improve their palatability to parents, without diminishing the scientific quality of the study. Minimize all but essential visits. Minimize the "hassle factor" and impact on family life. Furthermore, make the study an educational opportunity for the parents. Build in additional educational efforts, as discussed below.

During the study, how are you communicating to improve trust? Use culturally sensitive materials. Consider a newsletter that addresses frequently asked questions and provides information about new findings concerning the condition. Always plan a "thank you" communication to parents at the end of the study. Your IRB may require a review of retention materials, just as it requires a review of recruitment materials.

Obtain end-of-study outcome information. By outcome information, I mean data like lab results, not just visible signs and symptoms that you can assess yourself. Three levels of outcome information exist. First, in some studies, you will have the ability to share with subjects both individual assignments and individual outcomes, but this is infrequent. Second, in many studies, you can report the individual assignment after the study is over, the data are locked, and the code is broken. In most cases, you will not learn the individual outcomes, such as antibody levels at different time points in a vaccination trial. But, you can share group outcomes. Third, in some studies, you never learn individual assignments or see individual outcome information, but you obtain group outcomes that can guide future care. At the time of study initiation, investigate what outcome information you will be able to share with study subjects. Plan to transmit that information to the parents at the end of the study. Budget for it. Staff for it. Parents love to see the study completed and new findings learned. Both the IRB and the sponsor will need to approve the release of information about individual assignment and individual outcome, as well as address the timing, the level of granularity, the tone and content, and the need to involve the subject's primary care physician or medical home. Later on, when the study results are published, consider how you might communicate the publication, at least in summary form, to the parents.

When the results are complex, you may wish to enlist the subject's primary care provider to help in the education process. Consider how you can use a shared medical record or give the subject a letter to bring to the provider. Here is an example of an opening sentence that might work for a letter about the results:

Dear _____, Thank you for permitting your child to participate in the Avian Influenza Vaccine Study. All the children have now completed their participation. We have entered all the data for analysis and now have the results to share with you. Until this time, neither you nor I knew to which group the study assigned your child. We now know that the study assigned your child to the X group. Overall, the X

group did well with this response to the vaccine, generating Y% of immunity. The study sponsor has not shared with us your child's individual test results.

Such communications increase the trust parents have in the researcher and in medicine, in general. These parents are more likely to participate in future studies because they better understand the benefits of participation and how studies work. Positive "word of mouth" will support your research program, as well as that of others.³⁵

Conduct an in-study satisfaction survey near the end of each subject's participation to help identify obstacles to recruiting and retaining subjects. Consider a standardized, validated, previously published, and freely available questionnaire, such as the RRPQ-C and the RRPQ-P for child and parent, respectively.³⁶ There are twelve questions to rate, for example: "I was told the truth about the study before it closed." The respondent rates the statement with a "1" for no, a "5" for yes, and a "3" for somewhere in the middle. However, the RRPQ-C and the RRPQ-P questionnaires were developed for observational, rather than interventional studies, so they may require modification for your purposes. Questionnaires for therapeutic clinical trials are also available, but they are unvalidated.^{37,38} They can be modified for pediatric use.

Consider adopting long-range approaches to building trust. For example, employ community-based participatory research.^{39,40} Here, the participation of the parents who may enroll their children shapes the very purpose and design of the study. When a community can come together to design a research approach to a problem, the investigators will be more successful in overcoming recruitment barriers. A realistic alternative for many investigators is to create a board of community research advisors. Such boards work better with studies that cannot be significantly modified or where community participation otherwise cannot be obtained. Experts also recommend employing research personnel who are ethnically representative of the community.^{41,42} A research team of Caucasian males enrolling children of African-American mothers may face substantial recruiting and retention problems unless it can build bonds in other ways.

Summary

Parents generally support clinical research. The devil, as usual, is in the details. In particular, parents make decisions on whether their child should participate in the study by weighing the risks and costs versus the potential benefits they perceive. Parents seek to be altruistic, as well as to give their child personal health benefits from the study. Their decision process is handicapped unless they can trust the investigator. Thus, embrace the role of the parents and appeal to their motivations. Give them the information they need before, during and after the study. With these efforts, your study will succeed and the parents will thank you for offering their children opportunities through your research.

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Author

Robert M. Jacobson, MD, is Professor and Chair of the Department of Pediatric and Adolescent Medicine at Mayo Clinic. Contact him at 1.507.266.4598 or jacobson.robert@mayo.edu.