

Virtual Mentor

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Journal discussion

Parental consent for pediatric research

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Despite an historic emphasis on protecting children from research risks, over the last few decades medicine has come to recognize the need to include children in systematic efforts to evaluate treatments in order to ensure their safe and effective medical care. In her new book, “Children in Medical Research: Access Versus Protection,” Lainie Friedman Ross, MD, assesses the state of human subjects protections in pediatric research [1]. Ethical analyses of U.S. federal regulations and research practices are supplemented by case studies and a rich variety of empirical data. Questioning whether federal policies and initiatives overemphasize access at the expense of adequate protection, Ross challenges the ethics of greater acceptable research risk for children with acute or chronic illness, critiques current policies on parental consent and child assent, discusses the debate regarding subject payment in pediatric research and examines the meaning of “prospect of direct benefit.”

In Chapter 5, “Informed Consent in Pediatric Research,” Ross addresses the unique aspects of informed consent in research with children, focusing on parental rights. In pediatric research, the informed consent process includes two elements: parental (or guardian) permission and child assent, where “assent” means an affirmative agreement to participate and *not* mere failure to object. Regulations guiding research with children are outlined in Subpart D (Additional Protections for Children Involved as Subjects in Research) of the Common Rule (Protection of Human Subjects, 45 CFR 46) [2]. In most research, permission from one parent and provisions for soliciting child assent are required. Additional provisions are necessary for research involving: (a) greater than minimal risk but presenting the prospect of direct benefit to individual subjects, or (b) a minor increase over minimal risk and no prospect of direct benefit.

Child dissent may be overridden (either for an individual child or for all children in a particular study) in certain cases, for example, if the child is not capable of providing assent (due to age, maturity, psychological state, etc.) or when the prospect of direct benefit from a particular treatment is available only through research. In the latter case, child dissent may be overridden even if the child is deemed capable of

providing assent. Parents' rights to be involved in the decision may be waived if an institutional review board (IRB) determines that contacting parents or mandating permission would potentially harm or fail to protect subjects (as in the case of neglected or abused children).

The ethical justification for requiring parental permission for children's research participation is grounded in respect for parental decision-making authority. Because parents know their children intimately and care deeply for their welfare, parental decisions can be reasonably assumed to promote children's best interests. Ross argues that parents also have the right to raise their children according to their own standards and values without state intervention. She believes that over-regulation is not in children's best interest and that parents ought to be the primary decision makers regarding their children's health care.

Children should play an active role in health care decision making, and their voices should have greater weight in research decisions than in those that concern clinical care. Federal guidelines do not suggest specific age limits, but it is generally agreed that efforts to involve children in health-related decision making should begin around age seven; assent or dissent should be given more serious consideration as the child enters adolescence (around age 12). While in most states 18 is the legal age of consent for health care decisions, exceptions are made to the need for parental permission for those under 18 for certain types of treatment such as reproductive health or substance abuse treatment or for mature minors (e.g., minors who are themselves parents).

Ross argues, however, that the requirement for parental permission should not be waived in pediatric research if there is no prospect of direct benefit for the child. While regulations allow waiving the requirement for parental permission to protect children who need medical care and whose parents are unavailable, unable or unwilling to consent, Ross does not believe that this justification should be extended to the research setting, especially where there is no prospect of direct benefit to the child.

According to Ross, applying the principle of respect for persons to children by soliciting assent for research participation is not—as it is for competent adults—about self-determination, voluntariness and comprehension; it is about respecting the *developing* autonomy of the child. For example, parents may compel research participation against a child's wishes in order to respect the child's future autonomy by forcing him or her to undergo potentially life-saving medical treatment. In the case of a sick child, study participation may offer the possibility of direct benefit by treating a rare disease or disorder for which there is no effective treatment available outside of the research context. Parents may coerce a healthy child, who, out of fear, may be hesitant to serve as a case-control subject for an ill sibling, into participating in order to promote altruism, family unity and, again, the well-being of the autonomous adult that child will become.

Alternately, parents may prohibit their child from participating in a study even if the child assents. For example, a child may want to participate in a nontherapeutic asthma study that pays \$50 but involves two extra doctor visits. It is reasonable that a parent may not want to give permission for this because the time conflicts with other commitments such as piano lessons or family dinners that will be of greater benefit to the future adult than the \$50 they forgo now.

Ross acknowledges that parents who give permission for their child's research participation may be misguided regarding the therapeutic value of the protocol but argues that parental discretion must be respected unless it is abusive or harmful. When research does not offer the prospect of direct benefit to the child, Ross supports limiting parents' rights to override the child's dissent.

Ross's work prompts discussion of the reasons why parents agree or refuse to enroll their children in medical research, how they understand the potential for benefit or harm and how they balance risks against potential benefits. Several interesting studies published in the last few years shed light on these questions and complement Ross's ethical analyses [3-7]. In a study of children participating in clinical anesthesia and surgery research, Tait et al. found that many parents had inadequate understanding of the research as it was presented to them during the informed consent process [3]. Parents who consented had greater understanding than those who did not. Factors shown to be significantly associated with greater parental understanding included age over 30, higher education level, lower anxiety, greater perceived clarity of information, greater degree of listening to the explanation of the research, greater degree of reading the consent document and perceptions of the study's importance, risks and benefits [3].

In a study of parents with children in leukemia trials, approximately half failed to understand random assignment at the time of enrollment and six months later [4]. Factors associated with better understanding in this study included being a member of a majority ethnic group, higher socioeconomic status, presence of a nurse during informed consent, parental reading of the consent document and physician discussion of specific components of the randomized controlled trial [4].

Among other determinants of parents' decisions (beyond their understanding of the proposed research) their perceptions about its risks and benefits and their opinions about the importance of the research seem to carry the most weight [5]. A study comparing parents who consented to their child's research participation to those who declined to give permission found that the consenters exhibited less uncertainty in their decision making, were more trusting of the medical system and believed that the environment in which the consent was sought was less pressured [5]. Rothmier et al. discovered that, although many parents exhibit altruistic motives such as a desire to contribute to medical knowledge, the most compelling motive for parents who enroll their child in clinical research is learning more about their child's illness [6].

Cost was another factor in decisions about whether to participate. While payment for participation was not found to play a significant role in parental decisions, obtaining free medications gained importance as socioeconomic status declined [6]. Hulst et al. learned that, although illness severity did not decrease the probability of obtaining parental permission for observational research, parents of children with a history of disease and parents who perceived that the research would be burdensome to the child were significantly less likely to consent [7].

Ross argues that federal policies governing pediatric research should focus on minimizing risks and that respect for parental autonomy and family privacy should limit state interference in parental decision making. Nevertheless, review of the data suggests that, although parents may have their child's best interests in mind when enrolling them in research, much could be done by institutions and investigators to improve the quality of parental decision making. Parents may not understand the potential risks of the research, they may refuse participation in potentially beneficial research because they do not adequately understand what is being asked of them, or they might decide about research participation before listening to and understanding the specifics.

Some factors shown to influence parental decision making that are amenable to intervention include anxiety; inadequate reading of the consent form or inadequate attention to the researcher's explanation of the research (these may be issues of time or timing); trust in the medical profession; and perceptions of risks, benefits and burden. Other factors that affect understanding, such as parental age and education level, are not amenable to intervention. Researchers may need to spend more time discussing potential study enrollment with parents or developing innovative strategies to improve understanding among certain parent populations.

Questions for discussion

- Do you think parental permission for participation in pediatric research should be allowed to override child dissent? When, if ever, should the need for parental consent be waived?
- What circumstances might lead a researcher to consider refusing to enroll a child in (or withdrawing a child from) a pediatric study even if the child meets the inclusion criteria?
- What changes to the parental permission or child assent processes are suggested by the empirical data discussed above?

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