



INFORMED CONSENT FOR PEDIATRIC RESEARCH: IS IT REALLY POSSIBLE?

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Informed consent has come to be one of the foundations of the ethical practice of medicine, and a cornerstone of efforts to protect human subjects from research risk. Despite the firmly established role of informed consent in both practice and research, many questions persist regarding its application in the context of pediatrics. At the most fundamental level is an existential question: “Can informed consent exist for pediatric research?” Pediatric ethics provides an important lens through which to examine the questions around informed consent, and its role and value for pediatricians, investigators, parents, and children.

Before the final quarter of the 20th century, traditional medical ethics had been based on a model that assumed beneficent paternalism. The concept of autonomy and the ideal of patients’ control of medical decisions gained prominence in the latter part of the century, and has been more widely embraced in American medicine than in other countries. The rise of autonomy has now completely transformed expectations and medical practice, and informed consent has been used as the means for effecting this change. Rather than patients trusting doctors to make good decisions on their behalf, the new model requires that patients become active participants in medical decisions. Along the way, informed consent became enshrined as the foundational doctrine and key mechanism by which patients and research subjects exercise their power. In the midst of this transformation, pediatric ethics was neglected. The autonomy model that may (arguably) make the most sense for adult patients is inadequate for decision-making on behalf of children.

For adults, the informed consent process represents an exchange of information between doctor and patient, or investigator and potential research subject. The dominant theoretic framework for informed consent requires 4 criteria for consent to be morally valid: *disclosure, understanding, voluntariness, and competence*.^{1*} In the ideal paradigm, exchange of information between doctor and patient leads to a decision by the patient

that reflects both clear understanding of the medical facts and an authentic decision consistent with that patient’s personal values. A similar process is envisioned for consent to research participation. Pediatric ethics is not so simple because more than two parties are involved. The geometry of pediatric ethics is best understood as a triangle with the child on the top and the parent(s) and clinician-investigator at the base to act as support. In addition to this important structural difference in pediatric ethics, the priority of ethical principles is different for decisions involving children. Pediatric ethics requires that the *best interests* of the child take precedence over the concept of autonomy. In other words, the question of *who decides*, so important in adult ethics, is less important in pediatric ethics than the question of *what decision is best for the child?*

Decisions that adults make on their own behalf may be morally robust, but decisions made for children by others cannot have the same degree of authenticity. Because pediatricians and parents are making proxy decisions, informed consent in pediatrics is necessarily less valid. This is not to say that no one can make decisions on behalf of children. Clearly, parents have both the right and the responsibility to act as surrogates for their children. The default assumption should generally be that parents are the appropriate decision makers. However, parents do not always make the best decision for their child, and society also has an important duty to protect children from foolish or dangerous decisions made by their parents. For these reasons, clinicians are obligated to initiate legal action when the actions or decisions of a parent jeopardize the well-being of a child. These considerations apply to informed consent for life-saving medical therapies, but what about consent for research?

A second problem for informed consent stems from the application of this requirement to the sometimes substantially different clinical and research contexts. Although clinical medical care is designed and intended solely for the benefit of the patient, research is defined as an effort to contribute to the development of generalizable knowledge.^{2*} The implicit expectation for research is that the knowledge generated will be applied to benefit other members of society. Deontological moral theories, such as those put forth by Immanuel Kant, would reject pediatric research that uses children as a means to the end of helping other members of society. By contrast, teleological theorists like John Stuart Mill would apply a util-

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itarian calculus to determine whether the benefits to society outweighed the potential harm to the child-subject. In general, the former would have a more restrictive, and the latter would employ a more permissive, approach to the conduct of pediatric research. The fact that most pediatric research is likely to benefit other children may also carry moral relevance.

When it is recognized that the goals of treatment are different from the goals of research, the distinction between consent for treatment and consent for research are more apparent. An important moral difference between research and medical care follows from this difference in goals. Research participation is, by definition, an optional activity. Ideally, the adult who decides to participate in research will be at least partially motivated by altruism. Although parents may, in rare cases, be compelled to permit medical care for a child, consent for research could never be considered mandatory because this would conflict with altruistic motivation. In 1944, the US Supreme Court ruled in *Prince v. Massachusetts* that "Parents may be free to become martyrs themselves. But it does not follow that they are free, in identical circumstances, to make martyrs of their children..."

The protection of subjects from research risk does not depend entirely on informed consent. Two other key protections are the integrity of the investigator and review by the Institutional Review Board (IRB). Although investigator integrity may be the single most effective means of protecting human subjects, integrity is an elusive quality that is impossible to measure or regulate. By contrast, IRB review calls for balancing the risks and harms of research participation against the potential good that may come from the research. Federal regulations suggest that potential for direct benefit to the subject be analyzed and distinguished from other benefits (ie, to society), and Subpart D provides "Additional Protections" for children that restrict IRB approval of pediatric research protocols based on this dichotomized analysis. Unfortunately, because of medicolegal and regulatory concerns, IRBs often attend to the consent document at the expense of the consent process. The assumption that an excellent consent document serves to better inform subjects or protect them from research risk may be the most egregious myth relating to informed consent. For this reason, studies of the consent process itself will fill a critical gap in the literature.^{3*}

In addition to review of the research itself, IRBs are responsible for assuring that procedures for informed consent meet regulatory standards. These more rigorous standards are not required for consent to clinical medical care, because standard therapy is presumed to be consistent with the patient's best interests. In other words, there exist at least two species of informed consent: consent for treatment and consent for research. Although these two kinds of informed consent may belong to the same genus, there are important differences.

Accurate thinking about complex issues like pediatric research ethics requires the precise use of language.^{4*} For pediatric ethics, informed consent is more properly understood as a combination of informed parental permission and (when appropriate) the assent of the child. Despite important theoretical differences, parental permission often takes the place of informed consent.^{5*} However, the ethical distinctions between the informed consent of a competent adult and the surrogate deci-

sion made by parent(s) on behalf of a child are significant. The term "parental consent" is at best an oxymoron, a frequently heard misnomer. The proper term, parental permission, may be *necessary* but is not *sufficient* for the conduct of pediatric research. First, unlike previous times in history when children were considered chattel, parents are no longer considered owners of their children. Second, multiple other criteria must be satisfied for the ethical conduct of clinical research.^{6*} Assent, a concept that allows for the participation of older children in the research decision, is a criterion that is unique to pediatric research but does not apply for competent adult subjects. Among scholars in pediatric ethics, assent is a concept that has gained favor in recent years.^{7*} Unfortunately, consensus on the role of assent in pediatric research ethics is still lacking. One recent study has shown that older children with leukemia are often excluded from research decisions, and that parents may ask fewer questions in the presence of the older child.^{8*} For research involving neonates and younger children, assent is not possible and research decisions should involve both parental permission and best interests considerations.^{9*} For older children, the supererogatory nature of research makes assent an even more significant factor for research decisions than for treatment considered the "standard of care." It is possible that the combination of parental permission and assent of the older child may even be morally superior to the simple informed consent of a competent adult. Further research on assent is clearly needed.

Although informed consent for pediatric research may not be possible in the strict philosophical sense, pediatric investigators, parents and older children have an important obligation to approximate truly informed consent to the greatest extent possible. For too many years, children (as persons and as a class) have been "therapeutic orphans," denied the benefits of clinical research.^{10*} Fortunately, we appear to have entered a new era in attitude and policy, and are making real progress toward rectifying this historical aversion to pediatric research. In this age of increased research involving children, the risk of adverse events will inevitably increase. Pediatric investigators need to recognize that, from a regulatory standpoint, research is conducted for the benefit of society and not for the sake of the child-subject. Because of this, pediatric investigators must remain vigilant in assuring that the best interests of the child-subject are never subjugated to the goals of the research protocol. We must remember that children are appropriately viewed as vulnerable subjects who require protection from research risk, and that parental permission, assent, IRB review, and investigator integrity are vital protections that, albeit imperfect, cannot be abandoned. The fact that truly informed consent may not exist for pediatric research does not relieve us of the obligation to strive for improvement. As written in the ancient rabbinical text *Ethics of the Fathers*, "The task is not yours to complete, but you are not free to desist from it."

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*References available from the author.