Walking the Moral Tightrope: Respecting and Protecting Children in Health-Related Research

PAUL B. MILLER and NUALA P. KENNY

Introduction

Special moral, regulatory, and scientific questions surround the inclusion of children in health-related research. These questions arise from a fundamental moral tension between the obligation to expose children to research participation to ensure that they share in the benefits that arise from it and the obligation to protect them from the harms associated with their inappropriate involvement in research. This tension is felt in the development of moral and regulatory frameworks for the protection of child research subjects and in the implementation and interpretation of these frameworks by institutional review boards (IRBs).

The tension arising from this coupling of obligations also permeates the process through which parents, children, and clinical caregivers work together to determine whether research participation is in the best interests of an individual child. At this level, this moral tension is accompanied, and at times modified, by another tension: that between the obligations to respect *both* the authority of parents *and* the need for children—whose capacity for independent decisionmaking is developing—to be involved in making decisions that affect their care.

There are many persons and parties responsible for making decisions regarding the participation of children in research. The levels at which these decisions are to be made are most often not distinguished, which adds undue complexity to difficult questions of the distribution of responsibility for respectfully including children in beneficial research and for protecting them from harm. We aim presently to establish a preliminary framework through which levels of decisionmaking are distinguished, as are the moral and legal issues, roles, and responsibilities appropriate to each. It is hoped that these considerations will also shed light on the relationships of responsibility obtaining between persons and parties involved in decisionmaking at different levels.

We shall proceed by first establishing the grounds for the obligations to involve children in research and to protect them from the harms posed by their involvement. We shall then consider how the thematic moral tensions set in play by these obligations are, or ought to be, reflected in the distribution of responsibility among those involved in decisionmaking at national, institutional, and clinical levels.

The authors would like to thank Charles Weijer for his comments on an earlier draft of this paper.

Cambridge Quarterly of Healthcare Ethics (2002), **11**, 217–229. Printed in the USA.

The Need for the Involvement of Children in Research

It has long been recognized that health-related research is of great importance in improving the health and well-being of children, individually and collectively. Until recently, however, many have presumed that children can benefit from research without being exposed to the risks of research participation. In its *Policy and Guidelines on the Inclusion of Children in Research Involving Human Subjects*, the U.S. National Institutes of Health cites a statement from the House Appropriations Committee in which it is recognized that "most research on the cause, treatment and cure of diseases which affect children rely primarily on adults as subjects in clinical trials."[1]

Although in some circumstances the results of research involving adults might significantly inform our understanding of the etiology and treatment of disorders affecting children, more often the direct involvement of children in research is imperative for improving their care. Ironically, the protective impulse to shield children entirely from harms of research participation has the potential to cause them significant harm. History tells of the dangerous consequences of presuming treatments tested on adults to be safe and efficacious for children:

- The antibiotic chloramphenicol was first used for the prevention and treatment of neonatal sepsis, in the dosage (1000 mg/kg) used for older children and adults. Many neonates died from chloramphenicol toxicity.[2] It was subsequently learned that the hepatic microsomal enzyme systems responsible for the metabolism and detoxification of chloramphenicol are markedly less active in the immediate neonatal period.
- Sulfasoxazole also was used, along with penicillin, in the prevention of neonatal sepsis. A controlled clinical trial of this "established" treatment demonstrated a lower incidence of infection.[3] However, nine times as many of these infants would die from kernicterus—the deposition of bilirubin in the brain. This problem was specifically and only identified in newborn infants because of their immature metabolism of bilirubin.
- The changes in metabolism of drugs due to alterations in hepatic enzyme activity and renal function occur in relation to postnatal age so that, for many drugs, a dosage that is appropriate on Day 1 of life is different from a dosage that may be appropriate at 1 week, 1 month, or 1 year of life. These variations are compounded by the fact that dosages often differ for drugs that are structurally quite similar.[4]
- There are certain disorders that affect older members of the pediatric age group and adults but that present special problems in pediatrics. Type I, insulin-dependent or juvenile-onset diabetes mellitus is one such example. The physiologic and hormonal changes that occur during growth and at time of puberty increase blood glucose lability and result in a need to tailor therapy specifically to the pediatric age group.[5] Results of research involving adults cannot possibly be extrapolated to reflect such age-related phenomena.

For scientific and ethical reasons, children should receive wherever possible only those treatments that have been adequately evaluated on children. The moral imperative and justification for the inclusion of children in such research is found in the scientific evidence of the importance of their involvement to

maintaining and improving standards of clinical care. Reliance on the results of research involving adults as the knowledge base from which to develop the care of children may make the provision of such care unnecessarily dangerous.

Justice demands the equitable distribution of certain basic social benefits and burdens.[6] Among the most valued of social benefits is access to healthcare. Justice requires equitable access to healthcare. This equitability depends, in turn, on equitability in the *quality* of healthcare delivered. Justice thus demands that children have equitable access to quality healthcare. In the interests of just distribution of the benefits of research, it will be necessary for children to assume some of the burdens attending research participation.

The Need for Special Protections That Clearly Identify and Demarcate Roles and Responsibilities

The obligation to respectfully include children in research must be balanced against the obligation to protect them from the harms attending research participation. Children are dependent on adults for protection, nurturing, and care. In recognition of their dependence, the state requires parents to safeguard the interests of their children until they are capable of independent decision-making. As Loretta Kopelman notes, it is "well established that parents and the state have duties to children that set non-negotiable thresholds."[7] These thresholds are to ensure the protection of children from exploitation, abuse, and neglect, whether at the hands of parents or others.

Parents are assisted in fulfilling their obligations to their children through consultation with others, including healthcare providers who, in turn, have fiduciary obligations to children under their care. Institutions and the state are obligated to take reasonable measures to ensure that parents and healthcare providers are aware of their obligations as they relate to the participation of children in research. Clearly, the obligation to protect children from the harms associated with research is founded and distributed widely.

Recognition of the need for special public-policy protections for child subjects of research is by no means a recent development.[8] However, an unmet challenge in the development and interpretation of these policies is that of demarcating the roles and responsibilities of those involved in research and research review. Particularly unclear are the beginning and end points of the responsibilities of IRBs and clinical caregivers.[9] A full response to this challenge would require the identification of:

- the levels at which decisions regarding the participation of children are to be made, and the moral and procedural norms which are to guide decisionmaking at each level
- the limits of decisional authority appropriate to each level
- overlapping responsibilities and appropriate mechanisms for communication and cooperation between decisionmakers at different levels
- the appropriate sequence in which ethical issues related to research participation are to be addressed at each level of decisionmaking
- how, at all levels, the fulfillment of these obligations is to be undertaken in a way that is respectful of children's developing capacity to participate in decisionmaking.

We could not possibly treat thoroughly all of these issues here. We aim, through the remainder of this paper, to present a framework that might provide the basis for the development of a more coherent picture of the roles and responsibilities of governmental and other policymaking bodies, IRBs, parents, children, and healthcare providers in making decisions regarding the participation of children in research.

The Role of Policymaking Bodies

In civil societies, state governments are recognized to have a responsibility to protect the welfare of their citizenry through promulgating and enforcing legal and regulatory codes. It is also generally recognized that governments bear increased responsibilities in this respect for protecting the welfare of their more vulnerable citizens.

A manifestation of the recognition of this responsibility is seen in the development, by state governments throughout the world, of moral and legal/regulatory frameworks for the protection of human subjects of research. In many cases, additional or supplementary codes or clauses for the protection of potentially vulnerable subjects (including children, the mentally ill or incapacitated, etc.) have been promulgated.

The protective frameworks formulated by governments should set forth *both* moral norms that are sufficiently general as to be compatible with prevailing moral pluralism *and* procedural norms offering substantive protection to heterogenous subject populations. The experience of policymaking bodies in the United States to this end is instructive for both its successes and its failings.

Through the *Belmont Report*, the U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (hereafter: the National Commission) articulated a moral framework for the consideration of ethical issues in research.[10] Established philosophical and religious moral systems were eschewed in favor of a prima facie principles approach, consisting of three guiding principles: respect for persons, beneficence, and justice.[11] Recognizing the unique problems posed by the involvement of vulnerable subjects in research, the National Commission prepared reports on research involving children, fetuses, prisoners, and persons institutionalized as mentally infirm.[12] With the notable exception of the latter report, much of the National Commission's work was eventually reflected in U.S. federal regulations for the protection of human subjects (the *Common Rule*).[13]

In its *Research Involving Children* report, the National Commission considered the quandaries posed by the involvement of children in research, and reported on the debate over how to address these through existing and innovative regulatory mechanisms. The work of the National Commission in this report prepared the way for the development of special regulatory protections for children (*Common Rule*, Subpart D). Similar supplemental protections are found in many other research ethics policies worldwide.[14]

In Canada, the United States, and many other countries, governmental policymaking bodies have delegated to IRBs the responsibility for implementing research ethics policy. This delegation of responsibility is founded in the belief that local committees provide the most effective and informed arena

within which to bring protective policies to bear on the conduct of research. IRBs are to ensure that research carried out within their respective institutions is in agreement in spirit and letter with the norms set forth in public policy. In most cases, governments remain responsible for providing for oversight and the informational and educational needs of IRBs.

There has been considerable debate over the adequacy and integrity of the institutional ethics review system in Canada and the United States.[15] Public controversies and academic debates in both countries have drawn attention to problems relating to conflicts of interest, resources for monitoring, expertise, accountability, and composition. In the United States, these developments have led the Office of the Inspector General to investigate the institutional review system and to conclude that it is in need of reform.[16] Further, widespread criticism of federal oversight of research protections has led to reform of the U.S. agency responsible for performing this function.

Some such problems could have been avoided had policymakers been more explicit in delineating the moral and legal responsibilities of institutions, institutional committees, researchers, and clinical and nonclinical caregivers. Further, the establishment of clear mechanisms for communication could improve ethics review and oversight. These improvements would ultimately require amendments to existing policy; regular provision of continuing ethics education at institutional, regional, state, and national levels; and the establishment of formal networks of cooperation among policymaking and oversight bodies, research institutions, institutional committees, and bioethics organizations.

It is important to note that problems arising from confusion surrounding the distribution of responsibilities for protecting research subjects are exacerbated when research is conducted in an international context. Where research is carried out across the boundaries of nation states (as is increasingly the case), it is often not clear who has jurisdiction over the conduct of research and thus the responsibility for protecting research subjects. In some instances, there is the frightening prospect of research being carried out on children without any legal or regulatory mechanisms for their protection in place.

In a timely new book, philosopher Onora O'Neill dwells on questions relevant to our consideration of the problems associated with delineating the authority and obligations of those involved in making decisions regarding the participation of children in research.[17] O'Neill encourages us to reconsider the way we think about justice and the fixity of boundaries, ideological, social, political, and otherwise. In particular, she argues that the actual porosity of boundaries makes the establishment of limits on moral and legal obligations troublesome. We affirm and extend her argument here. We find in it support for our call for reflection on the way in which responsibilities of bodies and persons at various levels of decisionmaking overlap, requiring communication and collaborative decisionmaking.

To our analysis of roles and responsibilities at national, institutional, and clinical levels of decisionmaking, we might have added a section on decisionmaking at the international level. However, it must suffice to have raised the question of whether we ought to follow O'Neill's lead in working to extend beyond state boundaries responsibilities for upholding justice and preventing injustice in research. Whether and how this might be achieved will continue to loom as an ominous, yet essential, issue for further attention.

The Role of the Institutional Review Board

Members of the IRB are responsible for interpreting and implementing at the *local*, *institutional* level public policy for the protection of human subjects of research. They thus perform an essential social oversight function.[18] To ensure that the mandate of social oversight is fulfilled in a democratic manner, IRBs are *representative* bodies, with voting members drawn from the health and legal professions, academia, and the public at large.

In the United States, the *Common Rule* assigns to IRBs the responsibility for ensuring that *all* proposed research involving human subjects meets certain basic moral and procedural norms *before* subjects are asked to consider participation. IRB review is structured according to the procedural norms of the *Common Rule* and is guided by the moral norms of the National Commission's *Belmont Report*. Among other things, IRBs are to ensure that in all research: adequate provision is made for consent or permission; benefits and burdens of research participation are fairly distributed; and risks are minimized, risks and benefits of therapeutic research procedures are acceptably balanced, and risks of nontherapeutic research procedures are acceptable in relation to the knowledge expected to result from the research.

Developed on the basis of the work of the National Commission, Subpart D of the *Common Rule* assigns the IRB increased responsibility in reviewing research involving children. In addition to the above requirements, IRBs are to ensure that children are exposed to no more than a "minor increase over minimal risk" purely for the purposes of research.

In the interest of becoming clearer on its role and responsibilities, it is important to emphasize that the moral decisionmaking occurring at the level of the IRB is concerned with the implementation of public policy and that it is generally *prior to* and *separate from* that which occurs at the clinical level between parents and children, in consultation with clinical caregivers and researchers. The IRB is not responsible for deciding whether the risks posed by participation in research to a *particular* child are acceptable. Rather, the IRB must ensure that research meets certain basic ethical requirements as a condition for the research to proceed. Except for the purposes of monitoring, after ensuring that proposed research meets the basic ethical standards set forth in public policy, the IRB does not, and should not, be involved in the process by which parents and children, with the assistance of clinical caregivers, decide whether risks of participation are acceptable given the overall situation of the particular child.

Freedman and colleagues suggest that one of the first tasks facing IRBs is to demarcate therapeutic and nontherapeutic elements of the research in question.[19] IRBs are to assess separately the risks posed by therapeutic and nontherapeutic procedures and only then consider whether researchers have made adequate provisions for obtaining consent or permission, for protecting privacy and confidentiality, and so on.

Therapeutic procedures are those undertaken with the promise of direct medical benefit to the child (e.g., the administration of a new drug). Nontherapeutic procedures promise no direct medical benefit to the child, but are, rather, administered solely for the purposes of research (e.g., extra blood draws).

Procedures undertaken with therapeutic warrant are subject to a harm–benefit assessment and are justified on the basis of the requirement for clinical

equipoise.[20] To find that a given protocol satisfies this requirement, the IRB must determine that the relevant expert medical community is in a state of "honest, professional disagreement" as to whether the standard or experimental treatment presents the favorable balance of benefit to harm. To be ethical, a trial must have the potential to disturb this state of "equipoise" and thereby change practice.

Risks associated with all nontherapeutic procedures in a study are to be minimized, to be subject to a risk-knowledge assessment, and, additionally in the case of pediatric research, are to fall under the "minor increase over minimal risk" threshold.[21] In finding risks to have been minimized, the IRB is to determine that only those methods and procedures necessary to answer the research question have been employed. In the risk-knowledge assessment, the IRB is to determine that the knowledge to be generated by the nontherapeutic procedures is of sufficient importance to justify the risks that they pose.[22] In determining that risks posed by nontherapeutic procedures are no more than a minor increase over minimal, the IRB must find that these risks are only incrementally higher than those unthinkingly assumed in the everyday life of a typical subject. The minor increase over minimal risk threshold essentially formally requires IRBs to consider the central moral issue in research involving children, insofar as its purpose is to allow beneficial research to proceed while protecting subjects from exposure to serious research risk without compensatory direct medical benefit.

Although the minor increase over minimal risk threshold is intended only to limit risks associated with nontherapeutic procedures, it is often taken to limit the risks of research in general.[23] Misunderstood in this way, the threshold is thought to limit the level of risk to which a subject can be exposed for therapeutic purposes. If this interpretation were correct, the consequences would be severe, for much, if not most, research would be deemed impermissible. For this reason, it is essential to bear in mind the independence of standards governing IRB assessment of risks of therapeutic and nontherapeutic procedures.

On determining the risks of research to be acceptable, the IRB has in essence decided that it meets standards requisite to its being presented to individuals and/or families as a *reasonable choice*. The IRB must then proceed to scrutinize the consent documentation for completeness and legibility. It must finally assess and approve the provisions made by researchers for subject selection, reporting adverse events, maintaining confidentiality, and obtaining consent. Only after having passed through these stages of review is the choice of participation to be presented to subjects and their caregivers.

In sum, we argue that the IRB is a social oversight mechanism charged with ensuring that research involving human subjects meets general standards of ethical acceptability. The ethical standards, and the level of responsibility assigned to the IRB in upholding them, are heightened when research involves populations of potentially vulnerable subjects. But despite its heightened responsibility, the authority and the protective function of the IRB in reviewing research involving children are limited in scope.

IRB review should not be seen as usurping the decisionmaking authority of parents and children. The IRB does not decide for particular persons whether or not participation in research presents a favorable balance of harm and benefit. The harms and benefits associated with participation in research must necessarily be assessed at both institutional and clinical levels.

We will proceed through the remaining sections to consider the roles and responsibilities of persons involved in making decisions regarding the participation of individual children in research. We will find that among these persons, clinical caregivers have a unique status, inasmuch as their role in decisionmaking is consultative rather than decisive and insofar as their day-to-day observation of research puts them in a position to assume an essential role in ensuring that protections mandated by public policy, and implemented as conditions by the IRB, are upheld in the practice of research.

The Role of Clinical Caregivers

Health research involving children occurs in many and diverse contexts. Research is conducted on health promotion and injury prevention, disease prevention, growth and development, and on innovative treatments for diseases ranging from acne to childhood cancers. This range of research necessarily involves children widely varying in health status, from the healthy to the seriously ill. IRBs must take into account these features of the institutional context of research: that is, the differences between types of research, and the demographics of the typical subject population.

Institutional context is, however, not clinical context. Once IRB approval has been given to a research protocol, the decision about whether participation would be in the best interests of a given child must made in light of even more numerous and complex contextual considerations.

To date, research ethics guidelines and educational materials have been developed to assist members of the IRB in interpreting and implementing public policy. As such, they fail to clearly address the issues facing those involved in decisionmaking at the clinical level. In the present section, we work toward redressing this problem in providing an outline of the roles and responsibilities of clinical caregivers.

Because of the fact that judgments of harm and benefit in clinical contexts require expert opinion on the merits of research given the medical situation of particular subjects, clinical caregivers must be involved in determining whether participation in research is in the best interests of particular children. Indeed, parents and children often base their decisions on their trust in the information and advice of clinical caregivers. In research contexts, caregivers bear at least two kinds of responsibility: first, to assist parents and children in making informed decisions about whether or not participation is in the child's best medical interests; and second, to monitor the child's well-being during participation.

Of particular importance in fulfilling both responsibilities is that the caregiver understands the moral salience of the distinction between therapeutic and nontherapeutic research procedures and ensuring that this is understood by parents (and, to whatever extent possible, the child). This is particularly crucial where research involves children with severe chronic and life-threatening illnesses. Researchers, parents, and children are all susceptible to the "therapeutic misconception" in which the aims of care (served by therapeutic procedures) are confused with the aims of research (served by nontherapeutic procedures).

In primary care settings, caregivers have a duty to assist parents and children in making informed decisions regarding participation in research. The caregiver's knowledge of the child, the family, and the nature of the research must

be regarded as an invaluable resource for the making of such decisions. Apart from assisting in determining whether research participation is in the best medical interests of a child, caregivers can also help parents in determining the appropriate involvement of the child in the decisionmaking process.

In hospital-based and specialist care contexts, a host of other important considerations may influence the determination of the appropriate role and level of responsibilities of clinical caregivers. Among them:

- The child participant will most likely suffer from a serious, complex, and/or life-threatening illness.
- Some children will have acute, emergent conditions requiring rapid responses to requests for participation in research.
- Some children with chronic illness and/or life-threatening conditions will have established relationships with clinical caregivers; these relationships may engender special insight and unique responsibilities.
- Different clinical caregivers may come to different conclusions regarding the appropriateness of a particular child's participation in research; as a result of these differences, parents and families may receive conflicting advice.
- Some children, especially those with chronic illness, may be enrolled in multiple research projects; the cumulative risks may not be evident to a given research team. Caregivers may alone be aware of multiple enrollment and the risks attending it.
- The role of the child in decisionmaking may be expected to change substantially over time, particularly for children with chronic illness enrolled as infants or as young children. The caregiver will often be ideally situated to help to assess the appropriateness of the child's increased involvement.

Clinical caregivers have a critical role to play through fulfilling consultative and oversight responsibilities. In addition to ensuring that moral and procedural norms are upheld in the practice of research, they consult with parents as to whether research is in the best interests of their child and, where appropriate, encourage and facilitate the respectful involvement of children in the decisionmaking process.

The Role of Parents and Families

Parents and families will rely on caregivers to assist in making clinically sound decisions regarding their child's participation in research. Caregivers must be aware, however, of the salient nonclinical individual, familial, and social factors shaping the substance and context of decisionmaking. For example, one must explore and assess with parents the child's physical, emotional, and developmental status, unique personality, life experience, social and moral maturity, and cognitive capacities. One must seek also to understand the religious, cultural, and economic features of the familial context, as well as to appreciate the influence of such social factors as patterns of positive and negative bias within the society. Contextual elements of this sort will come into play as parents and guardians decide whether it is in their child's best interests to participate in a particular research project and/or the decisionmaking process itself.[24]

Society holds parents primarily responsible for protecting and promoting their children's interests. Children below a certain age legitimately expect that parents will care for them by making appropriate decisions on their behalf. Parents who are not neglectful, exploitive, or abusive of their children are thus generally granted wide discretion in making decisions for their children. There are many reasons for granting such discretion. Among them: parents are the persons most likely to know their children's interests; they are most likely to be committed to promoting them; and they stand to bear at least some of the consequences of decisions made on behalf of their children.

It should be expected that, consistent with their prerogative, parents will guide the child to decisional maturity in varying ways. Some are generally very protective; others actively promote independence from an early age. For most activities of daily living, a delicate balance is forged (and often, especially in adolescence, contested) between the parent's and the child's role in decision-making. It should be no different in the case of research. And here, too, how this balance is ultimately to be struck is at the parent's discretion.

The Role of Children and Youth

It is widely accepted that, in principle, children's expressed wishes regarding research participation should be respected.[25] In practice, however, the involvement of children in such decisions is neither routine nor standardized. There are many reasons for this lack of fit between principle and practice. Among them are: lack of clear criteria for balancing the respective roles of parents and children; the legitimate desire to protect children; inappropriate emphasis on decisionmaking capacity as the sole criterion for the involvement of children in decisionmaking; and general reluctance to recognize mature children as persons fully capable of providing an independent consent or refusal to research participation. The Declaration of Helsinki illustrates the problem. There, it is stipulated that

> In case of legal incompetence informed consent should be obtained from the legal guardian in accordance with national legislation. . . . Whenever the minor child is in fact able to give consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.[26]

Note that the requirement here is that the child's consent be obtained in addition to, not in lieu of, the consent of the legal guardian. Are two consents better than one?

In addition to the above-cited reasons for the discrepancy between principle and practice on child consent are concerns about liability. The lack of clarity in law and morality on the decisionmaking authority of children with respect to research seems to be mutually reinforcing. Inconsistent and arbitrary age-related legal thresholds of legal competence reflect the difficulty in practice of making moral judgments of the weight to be assigned choices made by children with developing decisionmaking capacities.

In societies in which informed consent and choice are privileged, what is the appropriate means by which to recognize the developing capacity of children? Assent and dissent have been widely employed as compromise concepts.[27]

These concepts are, however, internally contradictory and difficult to apply in practice. The general tendency has been to conflate consent with assent and dissent with refusal. As Baylis and colleagues recognize,

> if a parent's legal and morally valid authorization can be overridden by a child's dissent, then it appears that a dissent by a person with developing decision-making capacities has the same moral force as a refusal by a person with decision-making capacities. This is perplexing, for while it is undeniably important to heed a child's objections, it is not clear that these objections should be authoritative in the same way and for the same reasons that a refusal by a person with decision-making capacity is generally regarded as authoritative.[28]

Debates about the proper role of children in decisionmaking have been focused overly narrowly on decisional authority—that is, on the question "Is the child capable of making the participation decision?" Children can and should have a role in making decisions about their participation in research, but this imperative need not hinge on a polar determination of decisional authority. There are reasons for involving children in discussions about their possible involvement in research that have nothing to do with seeking their authorization or assent.

We believe that considerations in policy and practice of the role for children in decisionmaking ought to instead be focused on the question "What is respectful involvement of children in health decisionmaking?"[29] Through this reformulation is introduced the possibility of conceiving the role for children in nonpolar terms.

We conclude with the suggestion that progress toward the end of the respectful involvement of children in decisionmaking can be made through participative assessment of: (1) what the child wants to know; (2) what the child can understand; (3) what is the child's decisionmaking capacity; and (4) what the child needs to know to participate appropriately.[30] The interactive and iterative characteristics of this process are essential for assessing both the relevant substantive issues (e.g., what the child wants or needs to know) and the relevant procedural issues (e.g., how the communication should take place).

Conclusion

We have argued that the tension between the obligations to involve children in potentially beneficial research and to protect them from avoidable and excessive research-related harms is pervasive in debates surrounding involvement of children in research. This tension and the efforts to balance its constitutive concerns are further complicated with recognition of the need to be respectful of children's capacity for involvement in making decisions regarding their participation in research. Requisite to adequate negotiation of these tensions in policy and practice is greater effort on the part of those involved in policy development and implementation to more clearly distinguish the distribution of responsibilities for the protection of children at different levels of decisionmaking.

We have sought to present a framework for making these distinctions. With this end in mind, we have argued that policymakers at national (and possibly

international) levels are responsible for protecting the general welfare of potential child participants through overseeing the development and implementation of protective public policy, through facilitating communication, and through providing for the continuing education needs of IRB members and researchers. Institutions are responsible for establishing ethics review and monitoring committees and, through these, for ensuring that all research carried out in their institution meets the norms mandated by policy before proceeding. Clinical caregivers are responsible for assisting national and institutional authorities in ensuring that ethical standards continue to be met in practice, and for consulting with parents and families in determining whether it is in the best interests of their child to participate in research and how best to include children in the decisionmaking process. Parents and families, with the assistance of clinical caregivers, are responsible for making decisions regarding the acceptability of participation in research for individual children who are not yet capable of mature decisionmaking. The discretion accorded to parents in making such decisions is not without limits but is considerable, consistent with the widely held view that parents are in the best position to make decisions in the best interests of their dependent children. As children are able and interested, their appropriate involvement in decisionmaking should be promoted.

The presentation of our framework and our framing throughout of problems for future research are guided by one concern: to demonstrate that and how policymakers, IRB members, and clinical caregivers must work both independently, and together with parents and children, in ensuring that children are respectfully involved in beneficial research and are protected from its avoidable and excessive harms. Clearly, much work remains to be done in clarifying the nature of the responsibilities of all parties involved. Only through such work might we make attributions of authority and responsibility within distinct, yet porous bounds and thereby illuminate for decisionmakers their responsibility for stretches of the moral tightrope whereupon the welfare of child subjects rests.

Notes

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