The Randomized Controlled Trial as a Demonstration Project: An Ethical Perspective

Zeanah and colleagues in this issue of the Journal (1) report the results of a randomized controlled trial examining the impact of institutional care on young children in Romania. Children were randomly assigned to continued institutional care or foster family care. Psychiatric outcomes for these two groups were compared with a group of never-institutionalized children. The design of this research raises important ethical issues.

The ethical evaluation of research is prospective. Socially important research findings do not justify unethically designed research. As Henry Beecher noted in 1966, “An experiment is ethical or not at its inception; it does not become ethical post hoc” (2). Two fundamental requirements of ethical research are social value and favorable risk/benefit ratio (3). Studies must be designed to answer socially valuable research questions, with promise for translation into improved medical care or public health. Otherwise, there is no justification for any risks or burdens to which research subjects are exposed. In addition, the relationship between risks to subjects and benefits either to them or to future patients and society must be reasonable. In the case of research with vulnerable children, it is imperative to avoid exploiting them unjustly for the benefit of others. How should the research described by Zeanah and colleagues be evaluated from an ethical perspective? (I set aside issues of independent ethics review and consent, as they are adequately addressed in the research report.)

It might be argued that this research is deficient, and hence unethical, on grounds of both social value and risk/benefit ratio. Do not we already know that institutional care is deleterious and inferior to foster family care, especially for very young children? Indeed, in their opening paragraph the authors list features characteristic of institutional care “which all contribute to an adverse caregiving and social environment.” Although this is the first randomized trial comparing outcomes for children who remain within institutional care versus those who receive foster care, randomized trials are not the only source of reliable knowledge. For example, we know that heart transplants and dialysis save lives despite the absence of randomized trials. Critics might contend that since the answer to the research question was already known, based on prior observational research and the extensive experience of child welfare agencies, there is no social value in conducting the research. Moreover, the children who remained within institutional care were randomly assigned to an intervention known to be inferior to foster care. The research, accordingly, violated the principle of clinical equipoise, widely regarded as an ethically necessary condition for randomized trials. There was no uncertainty among child welfare experts in the United States, including the investigators themselves, about the relative value of the two interventions with respect to outcomes for children (4). Hence, the research had an unfavorable risk/benefit ratio, both for the individual research subjects and in terms of the knowledge to be gained from the research. Although the researchers were from the United States, this research could never have ethically been conducted in the United States. Therefore, it constitutes an unethical double standard to conduct it in Romania.

Although seemingly plausible, this ethical criticism is fundamentally mistaken. In assessing the social value of the research, it is important to be clear about the precise re-

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search question. This research project was not aimed at answering the general question of whether foster care is superior to institutional care for young children. Rather, it was designed to evaluate whether young children initially placed within institutions in Romania had better outcomes after transfer to foster care than those who remained in the institution. The answer to that question was not known, and the randomized controlled trial offers the most rigorous method for answering it.

Assessing the social value of the research, furthermore, requires that it be placed within its social context. Institutional care was the standard of care in Romania for children who were abandoned or removed by child welfare authorities from the homes of their biological parents. Within Romania there was uncertainty about the relative merits of institutional and foster care; indeed, there had long been decided preference among Romanian experts for institutional care. This research constituted a socially valuable demonstration project within the Romanian setting, which is also relevant to other societies that practice institutional care of young children. As an integral part of the research, this demonstration project instituted a foster care system in Romania, which previously lacked this mode of child welfare.

Romanian officials are to be commended for inviting research investigators from the United States to their country to conduct this study, with the understanding that United States experts do not favor institutional care. Both Romanians and Americans recognized that the randomized controlled trial is not only a scientific method but also a tool of persuasion aimed at improving practice. Policy makers may need a strong method of proof to be willing to accept a given intervention, especially when it conflicts with their biases. Even if some experts claim to know, based on observational evidence or experience, that a particular intervention is effective in producing a given outcome, or is better than an alternative intervention, positive results from a well-designed randomized trial may be necessary to persuade policy makers to change standard practice.

Despite the significant policy implications of the research, potential harm to individual participants must still be considered an ethical concern, particularly because of the apparent absence of clinical equipoise. However, evaluation of the risk/benefit ratio for individual participants must also address the context in which the research was conducted. Suppose that the study had not been conducted because a research ethics committee reviewing it judged that the research was unethical. In the absence of this research and demonstration project, most, if not all, of the children randomly assigned to foster care would have remained within institutional care. In other words, the research subjects collectively were not knowingly made worse off by the research. Moreover, because each of the children had a 50% chance of being randomly assigned to foster care, the group of research subjects as a whole, arguably, had a prospect of being better off within the context of this randomized trial, on the hypothesis that foster care would have superior outcomes to continued institutional care. Whether the research was consistent with clinical equipoise is debatable. Child welfare experts in the United States probably were not in a state of uncertainty about the relative merits of institutional and foster care for young children. But in Romania, the situation was different. Whose equipoise counts? The key ethical issue, however, is not whether the trial satisfied equipoise, which has recently been challenged as a necessary ethical requirement, but whether it had a favorable risk/benefit ratio (5). Since participation in the research, at least, was not unfavorable to the children enrolled compared with the status quo outside the research, and the research question was socially important, it seems clear that this study satisfied the requirement for a favorable risk/benefit ratio.

In sum, randomized controlled trials in general, and demonstration projects in particular, should be evaluated ethically within the local context in which the research is conducted, and in terms of the relevance of potential findings to other comparable contexts. In this respect, the research reported by Zeanah and colleagues is exemplary.
References


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