
**COMMENTARY: ETHICAL CONSIDERATIONS IN
INTERNATIONAL RESEARCH COLLABORATION: THE
BUCHAREST EARLY INTERVENTION PROJECT**

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Ethical issues in international collaborative research are multiple and complex, and the applicable ethical guidance is diverse and sometimes contradictory (Council for International Organizations of Medical Sciences (CIOMS), 2002; Nuffield Council on Bioethics, 2002; World Medical Association, 2004). Research with children is similarly fraught with ethical conundrums, competing guidelines, and legislation. An intervention study, which is both international and involving children, is thus bound to be riddled with ethical issues. The authors of the Bucharest study (BEIP) (Zeanah, Koga, Simion, Stanescu, Tabacaru, Fox, & Nelson, this issue) are thus to be commended for publishing some ethical reflections on their study to supplement the basic research findings. Such ethical reflections are rare in the research literature. A useful and comprehensive framework for conceptualizing ethical issues in international collaborative research was published by Emanuel, Wendler, Killen, and Grady (2004). This framework attempts to embody the central ethical principles applicable to international health research in a format that is accessible to researchers rather than just to bioethicists. The authors (Zeanah et al., this issue) of the BEIP refer to this framework in their paper and cite it as an appendix, but regrettably do not apply it in structuring their discussion of their ethical issues. This could be seen as a shortcoming of the paper itself, as the application of the framework to this Commentary will hopefully illustrate. Each of the headings below represents one of the major categories of ethical discussion contained in the Emanuel et al. framework.

COMMUNITY PARTICIPATION

In this domain the BEIP appears to have had extensive contact and active cooperation with national and local authorities and with those closely involved in the care of the children, and this, to some extent, is exemplary.

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SOCIAL VALUE

The BEIP presents extensive international and some local evidence in support of the study, justifying the research in terms of its potential local and international value and significance. There is no question, given the detailed background of the study, that empirical evidence is needed regarding deinstitutionalization and its potential impact on national policies in the best interests of children in need of surrogate care.

SCIENTIFIC VALIDITY

The BEIP authors correctly assert that the randomized controlled trial (RCT) is the gold standard for evaluating the efficacy of biomedical and social intervention research. The intervention is thus based on this design, with some ethically acceptable dilutions allowing sample attrition, e.g., allowing children from either arm of the study to be removed if they were able to be placed back with family members or foster parents. However, the study is compromised by the omission of one central element of most RCTs: blinding. The evaluation of multiple developmental outcomes, based on information provided in the report, was not conducted by blind raters. The nature of the study precludes a double- or triple-blind design, but the scientific strength of the study would have been enhanced if at least some of the evaluations conducted to evaluate the developmental comparisons between the two groups had been conducted by blind raters. This applies to both some of the “soft” psychosocial evaluations, which are notoriously subject to rater bias, and some of the more “objective” physical evaluations conducted on developmental parameters. Such blinding would have strengthened the scientific validity of the study and the degree of confidence that could be placed in the findings, and furthermore should have been discussed by the authors in their own ethical and methodological reflections, particularly in view of their expressly stated bias favoring deinstitutionalization. Biomedical RCT studies routinely include blinding, even where the outcomes are far more “objective” than in the BEIP. Blinding is done to eliminate speculation about conscious and unconscious investigator bias, and would have done so for this important study. A further question warranting comment is the sample size and the degree of statistical confidence that can be placed in this small sample relative to biomedical RCT samples.

FAIR SELECTION OF STUDY PARTICIPANTS

This dimension is satisfactorily dealt with: those selected for the study were those most likely to benefit from its findings. The vulnerability of the participants is also recognized.

FAVORABLE RISK-BENEFIT RATIO

The study reviews considerable literature favoring the deinstitutionalization of children, suggesting that if anything, the deinstitutionalized group would not be adversely affected by the intervention. There is some consideration of possibly ulterior motives and accompanying harms that might impact negatively on the fostered group, but this seems limited to financial motives and omits other considerations such as paedophilia, pornographic abuse, and child prostitution, which are global concerns in the child literature. In this respect the BEIP does not provide sufficient detail of the screening of the foster parents for suitability to attempt to reduce the likelihood of such harms. This is a serious ethical concern. Further speculation

about the possible adverse effect on staff morale in the affected institutions should also have been presented to allay concerns that deteriorating staff morale, due to declining numbers of children in the control institutions, might have impacted negatively on the quality of care in those settings, thereby accounting for some of the more negative outcomes in the control group. This is both a scientific and an ethical issue that warranted some comment. The authors describe the financial constraints impacting on the study and the institutional context, particularly where the authors mention that the local and national authorities could not guarantee that the results of the study would be nationally implemented if the findings favored foster care, as they did. This is clearly beyond the resources of the investigators. However, it would have been valuable to know if the investigators at least tried to negotiate foster placements for the institutional control group if the intervention was shown to be effective. Although considerable, the financial implications of this seem within the realm of persuasive negotiation and advocacy, and ethically very important. No evidence is presented of such efforts, and we are left with the impression that the approximately 67 control subjects, subjected to batteries of physical and psychosocial evaluations for over 4 years, languish in these institutions to this day. Most ethical guidelines require that in comparative interventions, the intervention, if beneficial, should be offered to the control group(s) after that study. Failure to discuss this issue is a major omission of the paper, and a major ethical concern.

INDEPENDENT ETHICAL REVIEW

The study addresses the problems with this dimension in some detail, outlining the difficulty of obtaining formal local ethical review because of the absence of such structures in Romania, notwithstanding the approval of government agencies for the study. U.S. approvals were obtained, but in international collaborative research the local approvals are often those most informed by local conditions requiring careful scrutiny. At least one guideline (CIOMS, 2002) and a European Commission (EC) opinion (European Commission (EC), 2003) assert that international collaborative research should build local ethical review capacity in support of proposed studies. This point thus warranted some comment in view of the paucity of evidence documenting such ethics capacity development.

INFORMED CONSENT

This issue is fully commented on, given the complexities of intervention research with very young children.

ONGOING RESPECT FOR PARTICIPANTS AND COMMUNITIES

This is expressed in various ways throughout and after the study, such as ensuring ongoing support for those in foster care and providing feedback on study outcomes to involved parties, which seems to have been done. It is also expressed in careful protection of the confidentiality of individuals (and if necessary, communities), which is also not problematic in the BEIP. Respect was also shown in enabling control children to leave the study if favorable placement opportunities arose, but a shortcoming is the failure to secure foster placements for the institutional control group, as mentioned above. The paper's conclusions would benefit from

some frank discussion of ethical “lessons learned,” which could assist future studies of this nature: What would the investigators do differently in the future to address some of the concerns they identified?

In conclusion, the authors are to be commended for supplementing their original study with some careful ethical deliberations. It is hoped that others will follow this example and that the comments above supplement the efforts of the investigators.

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