ETRICAL CONSIDERATIONS IN INTERNATIONAL RESEARCH COLLABORATION: THE BUCHAREST EARLY INTERVENTION PROJECT

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ABSTRACT: The Bucharest Early Intervention Project (BEIP) is the first ever randomized controlled trial of foster care as an alternative to institutional care for young children. It involved a collaboration between American investigators and Romanian health and child protection professionals. We present a brief description of the Romanian context and the project itself before discussing a number of ethical issues raised by the project. Organized around a discussion of exploitation, risk/benefit ratio, and cultural sensitivity, we evaluate a number of ethical issues involved in the BEIP using the Ethical Clinical Research Framework and the Fair Benefits Framework. Based on this review, we conclude that notwithstanding challenging ethical dilemmas, the benefits of the project outweighed its risks. Throughout the planning and implementation of the project, ethical issues were a central focus of discussion among the investigators and in the collaboration between Americans and Romanians. Thoughtful discussions from multiple perspectives are necessary to conduct research that is ethically sound and scientifically meaningful.

RESUMEN: El Proyecto Bucharest para una Temprana Intervención (BEIP) es el primer intento controlado al azar de ver la posibilidad del cuidado en manos de padres adoptivos socialmente como una alternativa al cuidado institucional de niños pequeños. Dicho proyecto involucra una colaboración entre los investigadores estadounidenses y los profesionales rumanos de salud y de protección al niño. Presentamos una breve descripción del contexto rumano y del proyecto mismo antes de discutir los asuntos éticos sobre los cuales el proyecto llama la atención. Centrados en una discusión sobre explotación, el promedio de riesgo/beneficio, y la sensibilidad cultural, evaluamos un número de asuntos éticos involucrados en el BEIP, usando el Marco Referencial Ético para la Investigación Clínica, así como el Marco Referencial de Beneficios Justos. Basándonos en esta revisión, concluimos que a pesar del reto de los dilemas éticos, los beneficios del proyecto pesan más que sus riesgos. A través del planeamiento y la implementación del proyecto, los asuntos éticos resultaron un enfoque central de discusión entre los investigadores y en la colaboración entre estadounidenses y rumanos. Se hace necesario tener discusiones bien pensadas desde múltiples perspectivas, con el fin de conducir una investigación que sea éticamente apropiada y científicamente significativa.

ZUSAMMENFASSUNG: Das bukarester Frühinterventionsprogramm (BEIP) ist der erste, jemals randomisierte, kontrollierte Versuch Pflegefamilien als Alternative zu einer institutionellen Pflege für junge Kinder anzubieten. Es bedeutete eine Zusammenarbeit zwischen amerikanischen Forschern und rumänischen Gesundheits- und Kinderschutzmitarbeitern. Wir präsentieren eine kurze Beschreibung des rumänischen Kontext und des Projekts selbst bevor wir eine Anzahl ethischer Fragen diskutieren, die sich aus dem Projekt ergeben haben. Angeordnet rund um eine Diskussion der Ausbeutung, einer Risiko-Vorteilsratio und kultureller Feinheit, überprüfen wir eine Anzahl von ethischen Fragen, die sich aus dem BEIP

抄録：ブカレスト早期介入プロジェクト (BEIP) は、幼い子どものための施設での養育に替わるものとしての、乳児による養育についての、全く最初のランダム化された対照試験である。これには、アメリカの研究者と、ルーマニアの健康と子どもの保護の専門家との間の、協同作業がかかわっていた。われわれは、プロジェクトにより提起された多くの倫理的な問題を議論する前に、ルーマニアの文脈とプロジェクトそれぞれ最終の記述を、簡単に提示する。探索、リスク/利益比、および文化的感受性の議論をめぐって組織化されて、われわれは BEIP にかかわる多くの倫理的な問題を、倫理的臨床研究の枠組み the Ethical Clinical Research Framework を用いて、評価する。このレビューに基づき、われわれは困難な問題である倫理的クレンジにもかかわらず、プロジェクトの利益はそのリスクよりも勝っていると結論を下す。プロジェクトの計画と実施を通して、倫理的な問題は研究者の間の、そしてアメリカ人とルーマニア人との間の協同作業における議論の中心的焦点であった。多くの観点からの思慮深い議論が、倫理的に健全で科学的に意味のある研究を実施する上で、必要である。

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INTRODUCTION

International research collaborations between more and less advantaged nations are fraught with ethical challenges. Imbalances in resources, research experience, and technical expertise are likely, as well as cultural differences between the collaborators, all of which may contribute to problems ranging from use of inappropriate measures and misunderstanding about the meaning of findings, to frank exploitation of vulnerable populations. On the other hand, international research also presents unique opportunities to enhance capacity, address interesting questions, and mutually enrich collaborating institutions of both developed and developing nations.

Much of the interest and controversy in this area have arisen from the questions about what conditions are necessary to justify and/or recommend that placebo-controlled drug trials be conducted by investigators from more advantaged nations in less advantaged nations. Nevertheless, many of the issues involved are applicable to research that extends well beyond drug trials. In fact, the issues involved are probably most complex when the participants involved are children, especially young, preverbal children. When those young children have also been abandoned by their parents and made wards of the state, the concerns about exploitation become even more paramount.

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In this paper, we describe a study of institutionalized children being conducted in Bucharest, Romania, by a group of American investigators in collaboration with Romanian colleagues from child protection and child health backgrounds. Our purpose is to illustrate a number of challenging ethical issues posed by this project and to describe how our collaborative group dealt with them. In order to appreciate the ethical and scientific issues involved, we begin by providing a description of the context of the study by reviewing briefly the historical, social, and political situation in Romania as it pertains to children in residential institutions. Next, we review the impetus for initiating the Bucharest Early Intervention Project (BEIP), and describe the process of its creation and implementation, with special attention to ethical dilemmas. Finally, we apply two proposed frameworks for ethical conduct of research in less advantaged countries and evaluate the BEIP from those perspectives.

ROMANIAN CONTEXT

Romania is a country of 22 million people, more than 80% of whom are ethnic Romanians, located in Southeastern Europe between Central Europe and the Black Sea (National Institute of Statistics, Romania, 2002). Situated at the gateway of Europe, near both Russia and the Middle East, Romania has throughout history been the battleground of rival Empires. Following Roman occupation and the invasions of migratory tribes, Romania was fragmented, divided between the Ottoman, Austro-Hungarian, and Russian Empires (Iorga, 1970; Treptow, 1997). As such, Romania has existed as a unified and independent nation for less than 200 years.

From 1945 to 1989, Romania was an Eastern European satellite under the sphere of influence of the USSR. In 1965, Nicolae Ceausescu, a former shoe cobbler, became Secretary General of the Communist Party. He instituted a number of draconian economic and social policies designed to enhance Romania’s productivity, but which instead, had devastating effects, especially on young women and families. Among these measures, he oversaw passage of a law that required all women under the age of 40 to produce five children in order to increase the number of workers by creating the “Romanian Workers Army.” This law was associated with various incentives for compliance and harsh penalties for failure to comply. These included higher income taxation for “incomplete families” and visits from a gynecological corps dubbed “the Menstrual Police,” which had free reign to interrogate and even examine young women who did not seem to be in compliance. Abortion and all forms of contraception were illegal, and carried severe punishments, so many families who were unable to support their children handed them over to be raised by the state (Moskoff, 1980).

Romania began the transition from communism a mere 15 years ago when Nicolae Ceausescu was overthrown in a revolution in 1989. At present, Romania is a democracy, committed to a free market economy, and civil rights and freedom for all citizens. However, the effects of Soviet communism combined with Ceausescu’s totalitarian rule placed Romania far below the level of development of its neighbors, and thus it continues to struggle today with economic reform, ranking among the lowest income per capita in the region. Low wages, poor living conditions, civil inequities, and judicial corruption also have slowed the process of Romania’s desired admission into the European Union (The European Union, 2004).
Orphanages in Romania

Institutions for young children in Romania date back at least to the 19th century. Nevertheless, in the Communist era, widespread poverty and coerced childbirth led to many more unwanted children. In addition, the Communist ideology destigmatized institutional care because the state, according to this rationale, could raise good and loyal workers. These factors converged and are believed to have led to significant increases in the orphanage population in the latter half of the 20th century. Thus, at a time when orphanages for young children were disappearing in the West and foster care was becoming the preferred form of care for orphaned and abandoned children (Hacsi, 1997), in Romania and other Soviet satellites, institutions for young children flourished. Although exact numbers are difficult to ascertain, estimates are that as many as 200,000 children were institutionalized in 1989 when Ceaucescu was overthrown (Rosapepe, 2001).

Despite putative ideological support, most communist orphanages in Romania were poorly financed, and children often were raised in appalling conditions of social and material deprivation. This was documented dramatically by Western media reports about Romania’s institutions soon after Ceaucescu’s overthrow, as well as by Human Rights Watch (www.hrw.org/children/abandoned.htm).

Reform efforts began in earnest with legislation in 1997 designed to encourage prevention of child abandonment by provision of social support to parents considered at high risk, and through efforts to support local governmental efforts to develop alternatives to institutional care. This was a major transformation, as institutional care had been the only form of child protection in Romania for decades and was the official State policy even after Ceaucescu was overthrown. These legislative initiatives, coupled with other forces, have led to significant changes. Over 27,000 foster homes have been developed in the past 3 years and the number of children in institutions has been reduced significantly. Although over 30,000 children remain in institutions in Romania today, many of these are older children with multiple handicaps who cannot be easily placed in family settings. As a comparison, as recently as 6 years ago, there were virtually no state-funded foster homes in Bucharest (National Authority for Child Protection and Adoption (ANPCA), Government of Romania, 2004). That is the context in which the Bucharest Early Intervention Project was conceived and initiated.

BUCHAREST EARLY INTERVENTION PROJECT

Children raised in institutions in Romania experience dramatically increased rates of a number of health, social, and behavioral abnormalities, including serious medical illnesses (Albers, Johnson, Hostetter, Iverson, & Miller, 1997; Johnson, 1997; Johnson, 2000), disturbances of attachment (Chisholm, 1998; O’Connor et al., 2000; O’Connor, Marvin, Rutter, Olrick, & Britner, 2003; Zeannah, 2000), inattention/hyperactivity (Kreppner et al., 2001), behavior problems (Fisher, Ames, Chisholm, & Savoie, 1997), and a syndrome that mimics autism (Federici, 1999; Rutter et al., 1999). Institutional care provides an extreme caregiving environment that we believed afforded an opportunity to assess the effectiveness of an intervention designed to address the social deprivation that is believed to be inherent in many institutional settings for young children.

Aware of findings about the potential reversibility of the effects of early deprivation (see

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Chisholm, 1998; O’Connor et al., 2000; Rutter et al., 1999), we were interested in examining this question more carefully than is permitted by adoption studies, since those are inherently limited by selection bias. The investigators are core group members of the MacArthur Foundation’s Research Network on “Early Experience and Brain Development,” which was created in 1998 to address questions of how the experiences of infancy are incorporated into the structures of the developing brain, and how, in turn, those changes in the structures of the brain influence behavior (Nelson et al., 2002). Aside from BEIP, the network initiated a variety of research projects on sensitive periods of brain development and neural and behavioral plasticity.

Establishing Collaborative Partnerships for the Project

The BEIP was designed as a longitudinal, randomized controlled trial of foster care as an intervention for children in institutions in Bucharest. From the outset, the BEIP was conceived as a scientific study and as a humanitarian undertaking. Over half of the resources of the project were committed to the intervention, and fewer than half to the actual study.

The groundwork for the BEIP was established in a preliminary visit to Romania in December of 1998, when the minister for Child Protection expressed an interest in research aimed at developing alternatives to institutionalization. In a follow-up visit in June of 1999, we conducted a preliminary pilot study and learned that the government of Romania was actively exploring alternatives to institutionalization for abandoned children. The visit concluded with the local child protection authorities pledging full cooperation in implementing a larger intervention study with institutionalized children. In order for the study to be meaningful and ethically sound, it had to be conducted with scientific and ethical integrity and provide useful information to the local and central government authorities managing child protection. It also had to be affordable within available resources of the funding agencies. The study design that emerged from many deliberations was a randomized control trial evaluating the effects of foster care as an alternative intervention to institutional care on the development of young children raised in institutions throughout Bucharest (see Zeanah, Nelson, Fox, Smyke, & Koga, 2003).

Foster care at that time was being discussed as an alternative to institutional care in Romania, and it had both supporters and detractors. The hope of the BEIP was to learn about recovery of young children placed in foster care after initial institutionalization, the relationship of the timing of interventions to recovery, and the relationship between brain development and behavioral functioning. These questions were of scientific interest to the U.S. investigators, but they were also of practical importance to Romanian partners interested in developing sound and humane social policies for tens of thousands of abandoned children. If Romania were going to resolve its questions about how best to care for abandoned children, we reasoned that having sound scientific data on which to base these decisions would be an important contribution of the project.

Following preliminary collaboration with the departments of child protection, we realized that we needed additional assistance. We were directed to the Institute for Maternal and Child Health, the child health specialty body of the Ministry of Health, specifically for medical and developmental expertise with institutionalized children and for help recruiting the comparison group of never institutionalized children from the Bucharest community.

We also needed administrative assistance implementing the data collection and also re-
cruiting, screening, and training foster families. For this, we sought a partnership with Soli-
darite Enfants Roumains Abandonnes (SERA) Romania, a nongovernment organization
(NGO) committed to deinstitutionalization of children throughout Romania. SERA had ex-
tensive experience with foster care development and support, and they provided an adminis-
trative partnership that proved essential to recruiting and hiring staff for the project.

In addition to addressing scientific questions about the relationships of brain and behav-
ioral development, and about critical periods in development, the study also had practical
value in the host country by informing a debate about care of abandoned young children at a
time of sweeping legislative changes in this area.

For the study, 136 children living in six Bucharest institutions aged between the ages of
5 and 31 months (who had spent at least half of their lives in institutions) were assessed at
baseline and half of them were randomly selected to be placed in foster care. The remaining
children were to be cared for by the state; meaning, institutional care. These 136 children
were compared to 72 (never institutionalized) children matched for age and gender. Children
were assessed at 9, 18, 30, 42, and 54 months of age on a variety of developmental charac-
teristics, including physical growth, cognitive function, language acquisition, social commu-
nication, social interaction, attachment, emotion expression, and discrimination of faces and
emotional expressions. In order to assess these characteristics, children were videotaped in
their natural caregiving settings, as well as at play and while carrying out tasks on their own
and together with their caregivers. They also had electroencephalograms (EEGs) and event-
related potentials (ERPs) assessed in various conditions (see Zeanah et al., 2003, for details).

By comparing children raised at home with children raised in institutions, with children
removed from those institutions (at 5–31 months, i.e., after baseline assessment and random-
ization) and raised in a foster care environment, the study had several scientific goals. First,
we wished to document what developmental differences were associated with institutional
rearing, using state-of-the-art measures. Second, we wished to know which aspects of brain
functioning that could be measured during the first few years of life were associated with
specific behavioral outcomes observed in children raised in institutions. Third, we wished to
determine the degree to which early developmental abnormalities could be ameliorated by
placing children in families (i.e., foster care). Fourth, we wished to know if specific charac-
teristics of caregiving environments, across foster families and institutions, were related to
children’s developmental characteristics. Finally, we wanted to determine whether there were
specific time periods during which placement in families is more effective, and whether there
were time periods after which the intervention would be less effective. For an overview of the
aims and design of the study, the reader is referred to Zeanah et al., 2003.

By exploring these questions, the investigators and their Romanian partners wanted to
make available scientific data to inform policy about care of abandoned children. Data rel-
vent to policy is particularly relevant in Romania, where institutionalized care has been the
accepted form of care for many years and where foster care has been regarded with some
suspicion. As noted, at the time the study began, government-sponsored foster care was quite
limited in Bucharest and throughout Romania. In fact, at the time the study began, foster care
had existed in Bucharest almost exclusively with the support of intercountry adoption agen-
cies rather than as a government-sponsored initiative. It is important to note that the study
design, a randomized controlled trial, though it raised ethical issues, is the only valid design
available for addressing the aims of the project.
Institutional Review Boards (IRBs) in the United States use the Belmont Report (Author, 1979) to evaluate the ethical conduct of research. Nevertheless, research conducted by investigators from more advantaged countries in less advantaged countries requires additional scrutiny. A number of ethical frameworks have been proposed to provide guidelines to investigators and their collaborators. Tables 1 and 2 summarize two recently published proposals.

### Table 1. What Makes Clinical Research Ethical

<table>
<thead>
<tr>
<th>Collaborative partnership</th>
<th>Develops partnerships with researchers, makers of health policies, and the community, and involves each in meaningful ways.</th>
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<tbody>
<tr>
<td>Value</td>
<td>Enhancements of health or knowledge must be derived from the research.</td>
</tr>
<tr>
<td>Scientific validity</td>
<td>Methodological rigor.</td>
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<tr>
<td>Fair subject selection</td>
<td>Scientific objectives, not vulnerability or privilege, and the potential for and distributions of risks and benefits, determine communities selected as study sites and the inclusion criteria for individual subjects.</td>
</tr>
<tr>
<td>Favorable risk/benefit ratio</td>
<td>Within the context of standard clinical practice and research protocol, risks must be minimized; potential for society must outweigh the risks.</td>
</tr>
<tr>
<td>Independent review</td>
<td>Unaffiliated individuals must review the research and approve, amend, or terminate it.</td>
</tr>
<tr>
<td>Informed consent</td>
<td>Individuals should be informed about the research and provide their voluntary consent.</td>
</tr>
<tr>
<td>Respect for enrolled subjects</td>
<td>Subjects must have their privacy protected, the opportunity to withdraw, and their well-being monitored.</td>
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### Table 2. The Fair Benefits Framework

<table>
<thead>
<tr>
<th>Fair benefits</th>
<th>Benefits to participants during the research</th>
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<tr>
<td></td>
<td>Improvements to health and health care</td>
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<td></td>
<td>Collateral health services unnecessary for research study</td>
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<tr>
<td></td>
<td>Benefits to population during the research</td>
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<td></td>
<td>Collateral health services unnecessary for research study</td>
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<td></td>
<td>Public health measures</td>
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<td></td>
<td>Employment and economic activity</td>
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<td></td>
<td>Benefits to population after the research</td>
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<td></td>
<td>Reasonable availability of effective intervention</td>
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<td></td>
<td>Research and medical care capacity development</td>
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<td></td>
<td>Public health measures</td>
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<td></td>
<td>Long-term research collaboration</td>
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<td></td>
<td>Sharing of financial rewards from research results</td>
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<tr>
<td>Collaborative partnership</td>
<td>Community involvement at all stages</td>
</tr>
<tr>
<td></td>
<td>Free, uncoerced decision making by population bearing the burdens of the research</td>
</tr>
<tr>
<td>Transparency</td>
<td>Central, publicly accessible repository of benefits agreements</td>
</tr>
<tr>
<td></td>
<td>Process of community consultations</td>
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</tbody>
</table>

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Although not available at the time that the BEIP was initiated, they provide a means of evaluating the ethical issues it involves.

**Ethical Clinical Research Framework**

Emanuel, Wendler, and Grady (2000) outlined 7 ethical requirements of clinical research. Recently, they added an eighth requirement and added specific benchmarks for their assessment (Emanuel, Wendler, Killen & Grady, 2004). The 8 requirements are listed in Table 1. These principles were derived from a synthesis of traditional codes, declarations, and relevant literature on ethical conduct of research with human participants. The authors assert that fulfilling all 8 requirements is necessary and sufficient to make clinical research ethical, assuming that they are adapted to the health, economic, cultural, and technological conditions in which clinical research is conducted.

**Fair Benefits Framework**

Participants in a conference on “Ethical Aspects of Research in Developing Countries” developed a set of guidelines that were published as the “Fair Benefits Framework” (El Setouhy et al., 2002). These guidelines (Table 2) were derived as an alternative to the “reasonable availability” requirement described in the Council for International Organizations of Medical Science (CIOMS) (1993). In essence, the reasonable availability claim is that in order to avoid exploitation, interventions proven safe and effective through research in developing countries should be made “reasonably available” to the inhabitants of those countries.

The authors emphasize that the reasonable availability standard is inappropriate in many situations, and they propose the Fair Benefits Framework as an alternative. They emphasize that it is not necessary for a project to provide all of the fair benefits outlined. Instead, the ethical imperative is to provide fair benefits overall to study participants—not equal benefits to all participants. This is particularly germane to the BEIP, as foster care is neither universally available in Bucharest, nor was it within the scope of the investigators and their sponsoring agency to make the intervention “reasonably available” in the host country. Indeed, a major purpose of the study was to make available to the government of Romania data that could inform decisions about which intervention, institutional care or foster care, they wished to make available to their citizens.

**ETHICAL ISSUES**

The preceding frameworks provide a way to evaluate the ethical issues of BEIP that were the focus of deliberations about the project within the Network and between the Network and the Romanian partners. Ethical deliberations dominated early discussions of designing the study and have remained a central focus throughout its implementation. In this section, the focus is on a series of issues and how each of them was addressed.

**Exploitation**

In many ways, this is the central dilemma confronted by the U.S. investigators and their Romanian partners, and each of the subsequent dilemmas could be considered from the
perspective of exploitation. For purposes of focusing the discussion, however, we consider exploitation here from the standpoints of Romania as a site, protection of vulnerable human participants, and what happens to children after the study ends. Throughout this discussion, we emphasize the collaboration among American investigators and Romanian government officials and child welfare professionals.

**Romania as a Site**

Romania was sought and selected as a site for this project for several reasons. First, at the time the study began, thousands of young children were institutionalized there, affording a unique opportunity to study children’s development in institutions believed to be characterized by social deprivation. The study could not be conducted in the United States because of insufficient numbers of young children in similar institutions. Although a few infants and toddlers are housed in congregate care settings in the U.S. (see Harden, 2002), the placements are usually short term and the numbers of children involved are quite small. According to data from the Child Welfare League of America, less than 1% of the children less than 3 years of age in out-of-home care in the U.S. are in institutional care, and this includes young children requiring intensive medical support (Susan Steib, personal communication, February 15, 2004). Across all 50 states, the District of Columbia, and Puerto Rico, there are fewer than 1,500 children under 3 years of age in institutions, and many of these are children with severe handicapping conditions. Further, whereas there were 205 institutions with over 100 children in Romania in 2001, there were none in the U.S. (National Authority for Child Protection and Adoption (ANPCA), Government of Romania, 2004; Susan Steib, personal communication, February 15, 2004).

Second, at the time the study began, many officials within and outside the Romanian government believed that institutional care was preferable to foster care. Though specifying the degree to which such views prevailed previously is difficult, the fact that Romania has changed so dramatically in such a short time attests to the fact that attitudes have shifted profoundly. The population of institutionalized children of all ages dropped from 60,000 in 2000 to 30,000 in 2004, and for children less than 3 years old, it dropped from 3,894 to 886 (National Authority for Child Protection and Adoption (ANPCA), Government of Romania, 2004).

In part, the belief that institutions were preferable to foster care seemed to stem from a tradition of institutional care that had existed unchallenged for over a century. In part, it seemed to be related to static “models of development” that assumed that the handicaps exhibited by institutionalized children led to, rather than resulted from, their placement. To a modest degree this is true, because it is clearly more likely that a handicapped child would be placed than a nonhandicapped child, although dramatic gains made in children adopted out of institutions suggest that caregiving environments matter considerably (O’Connor, Rutter, & the English and Romanian Adoptees (ERA) Study Team, 2000; Rutter & the ERA Study Team, 1998; Chisholm, 1998). Also, the medical tradition of residential institutions (operated under the auspices of the Ministry of Health throughout the Communist era) associated them in the public view with important medical procedures, vaccinations, and management of childhood diseases, which a foster care system supposedly could not replace. Lastly, some officials and members of the public were deeply suspicious about the motives of foster parents, worrying that they could be pedophiles, or willing to sell the children in their care to
international adoption. Some officials deeply committed to institutional care have argued that high-quality professional care in institutions is likely to be better than that provided by less well-trained foster parents. This made the assessment in the BEIP of the quality of the caregiving environments in each of the institutions, and in each of the foster homes, especially important.

On the other hand, many reformers in Romania were appalled by institutional care and quite interested in developing family care alternatives. Thus, another reason for selecting Romania was that officials within the country itself were asking questions that a methodologically sound scientific study could address. The government’s interest in research that could potentially inform their social policy was another compelling reason for conducting the study. That is, by providing data on differences in children’s development in institutions and in foster care, and possibly data on the timing of this environmental manipulation, the government could consider alternatives to institutionalization in a more informed way. Furthermore, the government could consider the economic, psychological, medical, and social risks and benefits of different approaches. This came at a time when Romania was singled out by the EU Parliament to enforce a moratorium on all intercountry adoptions, putting great pressure on the child protection system to develop a domestic/national adoptions system. The scope of the BEIP allowed it to provide evidence addressing the widespread belief that “orphanage children” are permanently damaged or “irrecuperable.”

Protection of Vulnerable Participants

Given Romania’s status as a recently established democracy attempting to recover from nearly 50 years of oppressive Communist rule, protection of human subjects is especially important. The academic and professional disciplines of psychology and social work were decimated under Ceausescu’s rule, and psychiatric research was almost nonexistent during this period. Although BEIP is focused on the most vulnerable population, abandoned children, there is no more than minimal increased risk to them as participants. The U.S. government has defined minimal risk as “the probability and magnitude if harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” (Office of the Protection from Research Risks, 2005, p. 6). Obviously, therefore, there is no application of a high-risk intervention to them because of their vulnerability.

Large-scale developmental research, such as the BEIP, is unprecedented in Bucharest, and there were no established procedures for ethical review at the time the study began. On the other hand, Romanian law outlined procedures that the investigators were required to follow.

The BEIP established principles of informed consent for all participants in collaboration with three university Institutional Review Boards in the United States and the commissions on child protection in Romania. Since Romania did not have a comparable system for review of research projects in place at the time the project began, the study was approved by the local Commissions on Child Protection in Bucharest, as well as by the Ministry of Health, by its Institute of Maternal Child Health initially, and in 2002 by an ad hoc ethics committee. In addition, it was important to the Romanian partners that the study be conducted within the principles outlined by the United Nations Convention for the Rights of the Child (www.unhchr.ch/html/menu3/b/k2crc.htm) (United Nations, 2001). Commissions on child
protection are responsible for establishing regulations and policies designed to protect children, but these regulations and policies are implemented by child protection staff working in placement centers (institutions). Thus, in the first step, the Commissions agreed to allow specific children to participate.

The investigators were required to obtain a separate consent from the birth parents of institutionalized children granting permission to place their children in foster care. Most institutionalized children in Romania have living parents who retain parental rights over them. Until recently, interpretations of the law allowed Romanian parents to demand institutionalization for their child while specifically refusing placement in alternative families (often based on fears of losing the child’s affection to another maternal figure). This requirement underscores the suspicion with which foster care was regarded at the outset of the study.

The process of informed consent also illustrated the essential role of the Romanian partners. They determined that the original consent forms developed for the project (based upon consents used in research in the U.S.) were overly long, legalistic, and ultimately inappropriate in the Romanian context. The consumer-driven approach of U.S. IRBs was not culturally sensitive in Romania. In order that the consent obtained is truly informed, the partners redrafted shorter, more explicit consent forms addressing the concerns of Romanian parents.

After the Study Ends

Another aspect of exploitation was the concern about conducting an investigation which would create an intervention that would exist only for the duration of the investigation, disappearing as soon as funding ends. From the outset, the investigators were especially concerned that children who had been removed from institutional care and placed in foster homes would not have to return to the institutions once the project ended. This stance revealed our bias that institutional care was less desirable, but this bias was by no means widely shared among Romanian officials, as noted earlier. Therefore, the investigators attempted to negotiate agreements with local government authorities to ensure that no child would have to return to institutionalization once s/he had been placed in foster care. The initial phase of the investigation has concluded, and as planned, that the Romanian government has assumed the support of all of the foster homes that were originally supported by the project.

Risk/Benefit Ratio

An important consideration in a study comparing foster care and institutional care is whether the study should be conducted at all, given the strong bias in the West against institutional care. In fact, we learned that no randomized controlled trial of foster care as an alternative to institutional care had ever been conducted anywhere. Studies that have demonstrated more favorable development among children in foster care or adoptive homes are consistent in finding more favorable outcomes for family care (see Zeanah, Smyke, & Settles, 2006, in press). On the other hand, it is not clear what factors led some children to be placed in foster care as opposed to orphanages in those studies, and children who are adopted out of institutions are unlikely to be representative of children in the orphanage. Thus, these findings are all limited because of selection bias.

In addition to the direct policy relevance of the study within Romania, the scarcity of data
on which the foster care preference rests made the study more justifiable, in the view of the investigators and partners. From an ethical perspective, the study would have been harder to justify if a large number of randomized controlled trials worldwide supported foster care over institutional care. In fact, some in the U.S. have recently advocated vigorously for a return to orphanages because of their putative advantages over foster care (see McKenzie, 1999), and institutional care for infants in a state’s custody has been reinitiated in some areas of the U.S. overwhelmed by the numbers of infants removed because of maternal substance abuse (Harden, 2002). Even in this country, there is unanimity regarding optimal placement settings.

**Randomization**

A major focus of ethical discussion involved the question of randomization. Randomization was definitely advantageous scientifically in addressing the selection bias that limits all of the previous research on institutionalized children. In fact, it is the only way to establish scientifically that foster care was causally related to putative developmental gains. On the other hand, randomization meant that half of the institutionalized children potentially would remain in institutions during the study.

Other designs were considered. A wait-list control design, frequently used in psychotherapy studies, was not feasible as it would have reduced the sample size by 50% (because the amount of support for foster care was fixed by limitations on resources) and would have led to additional problems. If foster care had been provided as it became available to all participants, a process of several months because of the logistical issues involved, the study would have involved a “subjects as their own controls” design, from which causal inferences could not be made. On the other hand, if foster care was available for all from the outset but was withheld from some participants for a specified period of time, there would be serious ethical questions about that decision.

Given limited resources and the certainty that without the BEIP intervention, all of the children would likely remain institutionalized, the investigators and their Romanian partners concluded that randomization was acceptable, with the qualifying condition of noninterference in place. The investigators pledged not to interfere with placement of any child in an alternative setting, if such a setting became available during the course of the study. These decisions always belonged, legally and ethically, to the respective Commissions on Child Protection in Bucharest who continued to manage the 136 cases independent of the BEIP study status and without any interference from BEIP staff. By Romanian law, the Commissions review the placement of each child in the state’s custody every 3 months. Therefore, children in either the institutionalized or the foster care groups are returned to their families or are adopted if the Commission so directs. BEIP participation did not limit or affect in any way removal of children from the institutional group and their placement in foster care, if foster homes other than those we supported became available. In fact, considerable changes in placement occurred, so that at the 42-month assessment, fewer than half of the institutionalized group remained in institutions. The rest had been adopted within Romania, returned to their families, or placed in government foster care that did not exist at the initiation of BEIP.
Benefits

A related consideration was the extent to which children participating in the study could benefit from it. Benefits were substantial for those randomized to foster care, in our view, and more modest for those randomized to institutional care. The more modest benefits for the institutionalized group included: (1) A careful medical examination by an expert, (2) referral as needed for identified problems, (3) reduction in the population of institutionalized children in all of the orphanages for young children in Bucharest without a concomitant reduction in staff, and (4) more careful scrutiny of each child’s legal situation, sometimes leading to better placements, including reintegration in the birth family. Benefits to the population during the project included employment and training of staff, which have contributed to enhancing the child development infrastructure in Bucharest. A legacy of the project is the creation of an Institute for Child Development that will continue training, research, and service delivery to at-risk children and serve as a resource for the entire country. This Institute holds the promise of yielding an enhanced and sustained effort to improve the lot of abandoned children in Romania.

Furthermore, the BEIP has created a precedent and a model for proactive reporting of abuses observed by project staff during the course of the study. Our reports led to the dismissal of caregivers who were observed as being physically aggressive with children, banning of smoking in infant wards, and increasing safety of outdoor play areas. The research team also organized numerous seminars for child protection and child health professionals throughout Bucharest to improve their knowledge and skills.

At a national level, the BEIP provided an important network of foster homes at a crucial time. In April of 2001, just as the BEIP was launched, the Romanian government instituted a moratorium on international adoption. As a result, all the foster homes sponsored by adoption agencies vanished, and there might have been little impetus or means to continue foster care, except for this project.

Foster parents were recruited, trained, and monitored by project personnel, and the project sponsored full-time foster parent salaries with payroll benefits (as is the model in Romania) and monthly expenses for each child. The training of foster parents was similar to the training that occurs in the U.S., but the manual was developed for and by Romanians. Those children placed in foster care remain there until a permanent plan for them can be implemented (adoption or return to their families of origin). Severely handicapped children had been excluded originally, but otherwise, all children between 5 and 31 months who were not scheduled for adoption, were included in our sample.

Risks

Ensuring that participation in the study involved no more than minimal risk of harm to the children was essential. All of the measures and procedures that the BEIP employed are measures and procedures that are noninvasive, safe, and have been used in dozens of studies with young children in the United States and other western countries. That is, we did not include in either assessments or interventions, any untested or high-risk methods.

We designed the study so that there are no children exposed to increased risk because of their participation, except for risks inherent in foster care. Although never before adequately compared to institutional care in terms of magnitude of risk, our reading of the literature was
that foster care appeared to have a reduced rather than an inflated risk when compared to institutional care. The BEIP was designed to more definitively address this question than had been possible in previous studies.

The noninterference principle that guided the study insured that there was no increased chance that children would remain in institutions any longer than they would have if the study had not been conducted. In fact, several children were reunited with their birth families as a result of contacts made with the families in order to obtain permission to place their children in care. As a direct result of contacts from BEIP personnel, these families requested and were allowed to have their children returned to them.

Finally, some pharmacological interventions include a “stop rule.” That is, if a treatment under evaluation is clearly and unmistakably beneficial compared to a control condition, then the study is stopped and the treatment is provided to all study participants. We considered a stop rule for the BEIP, but we did not have the resources to make foster care available to all participants. Instead, after preliminary results began to suggest substantial positive benefits of foster care, we scheduled a press conference to announce results of the investigation and invited all of the important ministries in the Romanian government to attend. Our hope from the outset had been to make sound data available to the appropriate Romanian government authorities so that they could develop appropriate policies with results of the BEIP available to them.

**Cultural Sensitivity**

Another ethical issue that we deliberated was cultural sensitivity. That is, there was a risk of implementing a model of parenting for Romanian foster parents that was culturally inappropriate. In particular, we did not want to assume that our American model would be acceptable without modifications. The Romanian partners obtained for us access to manuals and training courses in foster care developed by Romanians for Romanians. In addition, through ongoing consultation sessions with the BEIP native Romanian social work staff, the cultural appropriateness of all approaches were subjected to ongoing review and modification.

Another aspect of cultural relativity involved the economic disparity of relevant salaries in Romania and in the U.S. The investigators wanted to ensure that we paid salaries to the research staff and foster parents employed by the project that were commensurate with their contributions. At the same time, great care was taken to provide salaries that were reasonable, so that they would not amount to undue coercion to participate. Consultation with both governmental authorities and NGO personnel was quite helpful in this regard to ensure that salaries and other reimbursements were fair but congruent with established standards in Bucharest.

**CONCLUSIONS**

There are no universally accepted ethical guidelines covering international collaborations between more and less advantaged countries, in part because extant guidelines have been developed to cover specific situations, and new approaches emerge and are refined as new situations are encountered. Placebo-controlled drug trials may require different standards than psychosocial interventions, for example, and research with special populations may require
different standards than research with adults. Importantly, inappropriate analogies may lead to misapplication of standards and incorrect conclusions about the ethical soundness of proposed research.

Tables 1 and 2 outline two proposed frameworks from which to evaluate ethical aspects of BEIP. We recognize that other frameworks could be applied and that varied conclusions could be made about the degree to which the BEIP satisfies these guidelines. Much as the constitutionality of laws can be debated, which guidelines are most appropriate and how well the guidelines have been met are also subject to various interpretations. Furthermore, the goal of ethical decision making is not about whether endeavors are ethical or not, but rather, it is about what is the right thing to do in a particular situation.

From our perspective, the core question revolved around whether or not participants would likely be harmed more by participating than by not participating. We concluded that the benefits far outweighed the risks. Nevertheless, we recognize that others may disagree. The greatest vulnerability in the ethical soundness of the BEIP is the disparity between benefits of the foster care group and the institutional group. Arguably, an alternative study in which we compared our model of foster care to an enhanced version of institutional care could have addressed many of the same questions that the BEIP addressed.

In any case, we believe that deliberations among network collaborators and between U.S. investigators and Romanian partners, before and throughout the implementation of the BEIP, led to a careful and deliberate approach to the ethical dilemmas posed by the project. We encourage that similar projects engage in the necessary deliberations to ensure their scientific and ethical success.

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