



Published in final edited form as:

J Nerv Ment Dis. 2012 March ; 200(3): 243–247. doi:10.1097/NMD.0b013e318247d275.

Case Study in Ethics of Research: The Bucharest Early Intervention Project

Charles H. Zeanah, M.D.,

Institute of Infant and Early Childhood Mental Health, Tulane University School of Medicine

Nathan A. Fox, Ph.D., and

College of Human Development, University of Maryland

Charles A. Nelson, Ph.D.

Developmental Medicine Laboratory, Children's Hospital Boston, Harvard Medical School

Abstract

The Bucharest Early Intervention Project is the first ever randomized controlled trial of foster care as an alternative to institutional care for young abandoned children. This paper examines ethical issues in the conceptualization and implementation of the study, which involved American investigators conducting research in another country, as well as vulnerable participants. We organize discussion of ethical questions about the study around several key issues. These include the nature and location of the vulnerable study population, the social value of conducting the study, risks and benefits of participating in the study to participants, and the post-trial obligations of the investigators. In discussing how these questions were addressed as the study was designed and after it was initiated, we describe our attempts to wed sound scientific practices with meaningful ethical protections for participants.

Keywords

randomized clinical trial; institutional rearing; orphaned and vulnerable children

1. The Research Project

The Bucharest Early Intervention Project (BEIP) was a randomized controlled trial of foster care as an alternative to institutional care for young children conducted between 2000 and 2005 (see Zeanah et al., 2003). Follow-up assessments of the children are ongoing. Three U.S. investigators served as Principal Investigators (PIs), and they partnered with an NGO in Romania in order to complete assessments of infants and children, create a foster care network, and develop an administrative structure that could employ study personnel for the duration of the study. The purpose of the study was to determine if removing young children from institutional care and placing them in foster care would enhance their developmental outcomes as assessed by brain and behavioral functioning. The scientific and humanitarian components of the study were supported largely by the John D. and Catherine T. MacArthur

Foundation through the Research Network on “Early Experience and Brain Development,” chaired by Charles A. Nelson, Ph.D.

The chief goal in designing the intervention was to implement high quality foster care for young, abandoned children that was affordable, culturally sensitive and replicable in other settings. The foster care model has been described in detail elsewhere (Nelson et al., 2007, SOM; Smyke et al., 2009), but it involved training 3 project social workers to oversee 56 foster homes. They were trained to encourage the enhancement of social relationships between the foster parents and the child and to oversee the quality of care in the foster home environment. There are compelling data substantiating that qualities of the child parent relationships in the early years are predictive of important outcomes in later childhood and beyond. Importantly, these social workers received weekly consultation from experienced psychologists in the U.S. throughout the life of the project to help them respond effectively to foster parents and the children they cared for.

A total of 136 children between 6 and 31 months old who were being raised in all of the 6 institutions for young children in Bucharest, Romania, participated in the study. They were assessed comprehensively at baseline on a variety of cognitive, language, social, psychiatric measures, as well as measures of brain functioning (Zeanah et al., 2003). These measures included psychological tests, interactional assessments between caregiver and child, interactional assessments between examiner and child, physical measurements such as height and weight, and brain electrical activity measured by electroencephalograms and event related responses. Following baseline assessments, 68 children were randomly assigned to care as usual (continued institutional care) and 68 to placement into the foster family homes..

In addition, 72 children with no history of institutional rearing were recruited from pediatric clinics in Bucharest to serve as a comparison group for the children with histories of institutional rearing. This group was needed because the investigation involved measures that had not been used previously in Romania and their performance allowed us to determine how typically developing Romanian children performed in relation to those who had experienced institutional rearing.

Though the overall pattern of results clearly favors the children placed in foster care, the effectiveness of the intervention varied across developmental domains (Nelson et al., 2009). The results have examined main effects of the intervention, degree of catch up or recovery among children with institutional rearing, and the question of timing of enhanced environments on outcomes.

Regarding main effects, for most domains of development, foster care produced significant gains compared to care as usual. Further, these results are probably conservative estimates of the advantages of family care versus institutional care, because of the data analytic strategy we used, known as “intent to treat.” This type of analysis compares groups of participants based on the initial treatment intent rather than the placement conditions the children experienced. Although, as the study continued, the care as usual group included children who were adopted domestically, who were returned to their biological parents and children

who were placed in government sponsored foster care, this group of children was considered as one group---randomized to remain in the institution.

Second, for most domains, the foster care children did not attain levels of functioning comparable to the community raised Romanian children. This suggests that foster placement made possible some but not complete recovery following early deprivation. However, it is important to remember that the children placed in institutions had many risk factors that the never institutionalized children did not have, and this may well have contributed to their incomplete recovery.

Third, timing of the intervention mattered for some domains but not others, compatible with sensitive periods in brain development. That is, for brain activity and attachment, children placed in foster care prior to 24 months had significantly better outcomes than children placed after 24 months. On the other hand, psychiatric symptomatology was reduced by placing children in foster care, but earlier or later placement did not affect results. Obviously, timing results have significant implications for policies regarding orphaned, abandoned, and maltreated children.

2. Background: Care for Abandoned Children in Romania

Foster care barely existed in Romania at the time the study began. Poverty was widespread, and the Romanian dictator, Ceausescu, had imposed coercive pronatalist policies on women of reproductive age. As result, there were tens of thousands of children being raised in state run institutions.

For many years in Romania, abandoned children were cared for in “Leagans,” institutions for young children from birth to age three years. Following the Communist takeover in 1945, institutional rearing increased due to coercive pro-natalist policies of Nicolae Ceausescu. In addition, a rigid system of care was implemented. At age three years, the children were assessed by a psychiatrist and a psychologist, and based on results, they were sent either to children’s homes or to institutions for handicapped children. The former were smaller group homes with rotating staffs in which the children had some personal space and may have even attended public preschools. The latter were often large institutions with limited resources, rotating staff and regimented care.

There had been some limited foster care in Bucharest in the 1990s, but these homes were mostly run by international adoption agencies. Because international adoption from Romania was banned by the government in 2001, these homes no longer existed when the project began. Therefore, creating a foster care network involved starting without an existing infrastructure and with social workers who had no previous experience with child welfare.

3. Ethical Issues

To discuss the ethical dimensions of BEIP, we begin by stating that the case involves American investigators conducting a study with an extremely vulnerable population in a country with fewer protections for human subjects than the US. The study addressed a number of scientific and policy questions. Among the scientific questions was whether there

were sensitive periods for the development of specific cognitive and social skills such that young children who were living in institutions during these age periods would benefit less from intervention than those removed from conditions of extreme deprivation and placed into foster homes prior to the end of this sensitive period. Among the policy questions addressed by the study was which form of care is preferable for abandoned children (institutional vs. family centered), even though there is widespread consensus among most child protection professionals about the answer to that question.

This case study of the BEIP is organized around a series of questions about the ethical soundness of the study, drawn from the concerns outlined above. In responding to the questions, we describe how we considered and addressed each of them, either before or during the study. Many of these issues have been discussed previously (Miller, 2009; Millum & Emmanuel, 2007; Nelson et al., 2007; Wassenaar, 2006; Zeanah et al., 2006a; Zeanah et al., 2006b).

3.1. Study Population: Location

Why was the study conducted in Romania? Couldn't the study be conducted in the United States?—For more than 100 years, U.S. child welfare policy has endorsed that children should be raised in families rather than institutions, and that if institutions are necessary, they should be as family like as possible. As a result, there are few young children placed in group settings in the U.S. According to data from the Child Welfare League of America (2007), fewer than 0.5% of children less than 3 years old in care in the U.S. are in group care settings, and virtually all of these are intended to be short-term placements. Thus, there were an insufficient number of young children in group care in the U.S. to make a study feasible. In addition, there is no policy debate in the US about the best approach for abandoned children, although group care is sometimes still used (Jones Harden, 2002).

In contrast, in Romania at the time of the onset of the BEIP study, the question of foster care vs. institutional care was far from settled. In fact, the investigators were originally invited to conduct the study by the Secretary of State for Child Protection in Romania because of a debate there about the most appropriate care for abandoned children. At the time of Ceaucescu's ouster in the revolution of 1989, there were perhaps 150,000 children living in institutions in Romania (Rosapepe, 2001). So, the question of how best to care for these children was a significant policy dilemma. On one side of the debate were those who argued that institutional care had been practiced for more than 100 years and that trained professional caregivers were preferable to untrained foster parents. In addition, there was deep suspicion among some about the motives of foster parents -- rumors of pedophilia or child trafficking were widespread. On the other hand, others believed that Romania needed to close their institutions and move to family based care, as had been done in some other countries such as the U.S. and the U.K. Publicity about the conditions of thousands of children housed in poorly staffed and materially deprived institutions also created pressure for developing alternatives to institutional care.

We conducted the study in Romania because at the time there were tens of thousands of children being reared in institutions there, because the best form of care for these children

was a matter of debate rather than a settled policy question, and because we were invited originally by a government official who requested a scientific investigation to inform policy.

3.2. Study Population: Abandoned Children

How can we justify studying abandoned children? Who can consent for them and who will speak on their behalf with regard to research activities?—It would be hard to find a more vulnerable population than preverbal, abandoned young children. In any research study involving minors, legal guardians, such as a child's biological parents, must consent. For children lacking parents, there may be concern that their legal guardians may be less vigilant about ensuring protection. In Romania, local commissioners on child protection were the legal guardians of abandoned children and had to provide consent for their participation. Clearly, research involving vulnerable children needs to pay scrupulous attention to adequate protection.

With regard to the BEIP study, there were two additional layers of protection for institutionalized children. The first was that Institutional Review Boards at each of the U.S. universities for the three PIs had to approve the study prior to implementation. Two key questions considered by the IRBs involving concerns about exploitation were who would provide informed consent for the institutionalized children in our study, and whether the activities and procedures of the study entailed more than minimal risk. Given the difficulty in obtaining consent from the child's biological parents, consent had to be obtained by local commissioners. And, the IRBs wanted demonstration that the research would provide either direct or indirect benefit to the study population. Minimal risk, that is, risk that is comparable to routine daily activities was also important for similar reasons. Vulnerable children certainly should not be exposed to risks that exceed those typically asked of family reared children. For this reason, BEIP included only measures and procedures that had been used with hundreds (or more) of children being raised by their biological parents. All three IRBs agreed that the BEIP studied abandoned, institutionalized children because the scientific questions being addressed and was focused squarely on the best interest of these children. In addition, all three Institutional Review Boards at the home institutions of each of the PIs universities reviewed and approved the protocols as involving no more than minimal risk, that is, the kind of risks likely to be encountered in everyday life.

The second layer of protection for subjects in the BEIP study was that institutional caregivers or foster parents had to assent to the specific activities and procedures involved in the study in addition to the local commissioners' consent. Because they know the children best and may have more psychological investment in them than distant government officials, they were deemed to be in the best position to decline or terminate any activity or procedure that they deemed too unpleasant or undesirable for the child. For example, several young children objected to wearing a cap containing electrodes for recording EEGs and ERPs. Research assistants made determinations about whether to persist, but caregivers accompanying the child always had the final word about terminating the procedure due to the child's distress.

3.3. Social Value: Equipoise

Didn't we already know that foster care is better than institutional care? Was the study really necessary?—The principle of clinical equipoise is that there ought to be genuine uncertainty among experts about whether a proposed intervention is better than standard care in order for research to be ethical. Why subject participants to any risk, one may ask, in order to conduct a study when the outcome is all but a foregone conclusion? As noted, in the U.S., official policy had concluded many years ago that foster care is more desirable than institutional care.

These considerations actually contain two different questions about foster care vs. institutional care. First, is there a consensus about which form of care is preferable, and who shares that conclusion? And second, how convincing are the data upon which expert opinion rests? That is, is there a disconnect between a prevailing zeitgeist and what the evidence actually indicates?

With regard to the first question, deciding between institutional care and foster care as a societal intervention for abandoned children was decidedly *not* settled in Romania at the time the study began. In fact, institutional care for orphaned, abandoned and maltreated children had prevailed there for several hundred years, as it has much of the world. Thus, the question is far from settled as a matter of policy, regardless of what U.S. psychological researchers or child welfare professionals may have concluded (Zeanah, Smyke & Settles, 2006). BEIP was uniquely positioned to provide data relevant to the question of whether foster care offered advantages over institutional care for children who were abandoned and placed in institutions in the Romanian context. With such data, we believed, Romanian policy makers could make more informed decisions. The Romanian Secretary of State for Child Protection who invited the study originally believed that if data from a study within Romania favored foster care, skeptics about foster care would be more readily convinced.

With regard to the second question, it is worth asking about the data base on which that opinion rests. It turns out that there were fewer than a dozen, mostly small descriptive studies that had ever compared children raised in foster care to children raised in institutions. All of them indicated that the children in foster care were developing more favorably than children in institutions and that there were negative effects to being raised in an institution early in life (Zeanah, Smyke & Settles, 2006). On the other hand, none of the studies used random assignment, hence the selection of children for placement into groups may have been systematically biased. It is plausible that children who were developing more favorably would be placed in families, and those with delays or handicapped would remain in institutions. On balance then, we concluded that the data base for this important policy question was remarkably thin.

Furthermore, Miller & Brody (2003) have argued that the principle of clinical equipoise is flawed and should not be applied as a standard for ethical clinical trials. Clinical equipoise, they note, equates clinical research with clinical care and holds investigators studying participants to the same standards as clinicians providing care to patients. Clinical research, they argue, is not a therapeutic activity devoted to the care of patients but rather is designed

for answering scientific questions to produce knowledge that will be of benefit to society rather than to any individual participant.

Therefore, in our view, a randomized controlled trial was not only justifiable but also required to examine the question of which caregiving approach was most advantageous for young children who were abandoned and placed in institutions. This knowledge was generated to benefit the larger society rather than each individual participant.

3.4. Risks and Benefits

How can we justify randomizing children to an intervention that experts widely believe to be inferior (i.e., institutional care)? Doesn't this mean that the risk/benefit ratio was unfavorable for at least half of the participants? If the investigators got a clear sense early on that foster care was more favorable, why not employ a "stop rule?"

Here, an important question is whether the risks involved are increased because of participation. This would raise significant concerns, particularly because BEIP involved a vulnerable population.

In fact, half of the study population in BEIP were randomized to not receive the intervention. Nevertheless, this was a continuation of their current life circumstance-- they were not placed in institutions by the BEIP. Importantly, no child remained in institutional care *because of* the study. If children had been assigned to remain in institutional care for purposes of the study, the risk benefit ratio would clearly be unfavorable for that group. But that was not the case for BEIP. In fact, no child remained in institutional care *because of* the study; we employed a rule of noninterference regarding placement. That is, whatever plan for a child's placement that was made by the local Commissions on Child Protection were implemented without regard to their study participation. This was true for all 136 children, and indeed, some children in the foster care group also were returned home to their biological parents or adopted domestically.

The Commissions reviewed each child's placement every 3 months and made decisions about custody and placement as usual. Participation in the BEIP did not limit or affect in any way removal of children in the institutional group from institutions or their placement in foster care, if foster homes other than those we supported became available. In fact, at the time of the assessment at 54 months of age, 28 children in the care as usual group were still institutionalized, 9 had been adopted within Romania, 18 were in government foster care that did not exist when the study began, 11 had been returned to their biological families, and 2 were placed with extended family.

Furthermore, if the research had not been conducted, more of the children would have experienced more time in institutional care. Foster care was not an option at the time the study began for abandoned young children living in Bucharest. No research participants had their risk increased by the research, except for the risks associated with foster placement. In fact, since half of the children were randomized to foster care, arguably, they were better off than if the study had not been conducted. And, all participants potentially benefited from an initial physical exam and referral for identified problems.

An additional factor to consider in assessing risk benefit ratios is the overall benefit to society. If risks to participants are low, as they were in BEIP (since without the study all of the children would have experienced extended institutional care), then advantages that accrue from knowledge gained from research becomes an important consideration. In Romania, for example, although much progress has been made in developing alternatives for abandoned children, many thousands of children remain in institutions. How best to care for these children is an especially important question there. Therefore, the results of this study have many potential benefits for the larger population of institutionalized children in Romania and perhaps those in other parts of the world, as well. Policy makers concerned about how best to enhance the long term outcomes of abandoned children should attend closely to research comparing different forms of care. Furthermore, there are millions of abandoned children worldwide, and many are being raised in institutions (Browne et al., 2006; NGO Working Group on Children without Parental Care, 2006; Zeanah et al., 2006). The BEIP results, with appropriate cross cultural cautions, have implications for many of these children.

In studies of drugs developed to treat a specific medical condition, randomized controlled trials are stopped if preliminary data suggests clear advantages for the drug being evaluated. At that point, the treatment is made available to those participants who were originally randomized to the placebo arm of the trial. This ensures that participating in the trial does not preclude or unnecessarily postpone obtaining effective treatment.

Unfortunately, we were not able to employ a stop rule because of the cost of foster care and the limitations of project funding. Instead, when we analyzed early returns of the effects of the intervention, and we found that foster care appeared to be beneficial, we arranged to report results at a press conference to which we invited ministers of departments concerning child well being (e.g., Ministry of Health, Ministry of Child Protection, Ministry of Education). Our presentations at the press conference were introduced by the U.S. Ambassador to Romania, who urged that the government of Romania make use of the findings. We also obtained funding for and hosted a meeting for 350 professionals from all over Romania in 2002 and again in 2003, and we presented some of our early findings at those meetings.

3.5. Post-trial Obligations

What about after the study ended? Isn't it a problem to implement a study and then after obtaining results, withdraw the intervention?—There are reasonable concerns about investigators who study high risk or vulnerable populations, collect the data they need, and then leave the study population with little to show for their participation when the study ends. From the outset, we were determined to avoid this pitfall.

We enacted two approaches to ensure that the study population and others would enjoy benefits beyond the life of the study. First, we attempted to ensure that no child randomized to foster care would be returned to institutional care after the study ended. This meant making a long term commitment to continued foster care for the 68 children randomized to foster care. We attempted to negotiate agreements with each of the sectors in Bucharest (governmental districts) that they would assume support of foster homes after the study

concluded. Four of the five sectors agreed to this condition. Our administrative partner, an NGO called SERA, agreed to provide back up for any foster parents for whom the government failed to assume support. In fact, at the formal conclusion of the trial, all the remaining children in BEIP foster homes had been transferred to the government, mostly because the government assumed support of the foster homes formerly supported by the Project.

We also obtained start up funding for the creation of a Child Development Institute in Romania. The vision is that this Institute will oversee clinical services, research and policy proposals relevant to high risk children. We obtained matching funds from one of the sectors in Bucharest for renovation of space that now houses the Institute. We are working with Romanian partners to develop sustainable funding for this effort that in our view could contribute substantially to Romania's child welfare needs.

4. Conclusions

Ethical considerations were widely discussed from the inception of the BEIP and were monitored throughout the implementation of the intervention and during follow-up assessments. The questions posed above were discussed at length within our group and with a number of other investigators as well as with three university IRBs. The conclusions of those deliberations were described above as answers to the questions posed.

References

- Author. Development of international standards for the protection of Children deprived of parental care. The NGO Working Group on Children without Parental Care. Child Rights, the Role of Families and Alternative Care Policies Developments, Trends and Challenges in Europe International Conference; 2–3 February; Bucharest. 2006. www.crin.org, retrieved June 27, 2009
- Browne KD, Hamilton-Giachritsis CE, Johnson R, Ostergren M. Overuse of institutional care for children in Europe. *British Medical Journal*. 2006; 332:485–487. [PubMed: 16497769]
- Child Welfare League of America. Special Tabulation of the Adoption and Foster Care Analysis Reporting System. Washington, DC: Author; 2007. Children in group homes and institutions by age and state, 2004.
- Harden BJ. Congregate care for infants and toddlers: Shedding new light on an old question. *Infant Mental Health Journal*. 2002; 23:476–495.
- Miller FG. The randomized controlled trial as a demonstration project: An ethical perspective. *American Journal of Psychiatry*. 2009; 166:743–745. [PubMed: 19570933]
- Miller FG, Brody H. A critique of clinical equipoise: Therapeutic misconception in the ethics of clinical trials. *Hastings Center Report*. 2003; 33:19–28. [PubMed: 12854452]
- Millum J, Emanuel EJ. The ethics of international research with abandoned children. *Science*. 2007; 318:1874–1875. [PubMed: 18096792]
- National Authority for Child Protection and Adoption. *Protectia copilului: Intre rezultate obtinute si prioritati pentru viitor*. Bucharest: Government of Romania; 2004.
- Nelson CA, Furtado E, Fox NA, Zeanah CH. The deprived human brain. *American Scientist*. 2009; 97:222–229.
- Nelson CA, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, Guthrie D. Cognitive recovery in socially deprived young children: The Bucharest Early Intervention Project. *Science*. 2007; 318:1937–1940. [PubMed: 18096809]
- Rosapepe, JC. Half way home: Romania's abandoned children ten years after the revolution. Report to Americans from the U.S. Embassy; Bucharest, Romania: 2001.

- Smyke, AT.; Zeanah, CH.; Fox, NA.; Nelson, CA. Psychosocial interventions: Bucharest Early Intervention Project. In: Schechter, D.; Gleason, MM., editors. *Infant and Early Childhood Mental Health, Child and Adolescent Psychiatric Clinics of North Carolina*. Vol. 18. Philadelphia: Saunders; 2009. p. 721-734.
- Stativ , E.; Anghelescu, C.; Mitulescu, R.; Nanu, M.; Stanciu, N. The situation of child abandonment in Romania. Geneva: UNICEF; 2005.
- UNICEF. *Children in institutions: the beginning of the end? The cases of Italy, Spain, Argentina, Chile and Uruguay*. Florence, Italy: UNICEF Innocenti Research Centre; 2003.
- Wassenar DR. Commentary: Ethical considerations in international research collaboration: The Bucharest early intervention project. *Infant Mental Health Journal*. 2006; 27:577–580.
- Zeanah CH, Koga SK, Simion B, Stanescu A, Tabacaru C, Fox NA, Nelson CA. the BEIP Core Group. Ethical issues in international research collaboration: The Bucharest early intervention project. *Infant Mental Health Journal*. 2006; 27:559–576.
- Zeanah CH, Koga SK, Simion B, Stanescu A, Tabacaru C, Fox NA, Nelson CA. the BEIP Core Group. Ethical dimensions of the BEIP: Response to commentary. *Infant Mental Health Journal*. 2006; 27:581–583.
- Zeanah CH, Nelson CA, Fox NA, Smyke AT, Marshall P, Parker SW, Koga S. Designing research to study the effects of institutionalization on brain and behavioral development: The Bucharest Early Intervention Project. *Development and Psychopathology*. 2003; 15:885–907. [PubMed: 14984131]
- Zeanah, CH.; Smyke, AT.; Settles, L. Children in orphanages. In: McCartney, K.; Phillips, D., editors. *Blackwell handbook of early childhood development*. Malden, MA: Blackwell Publishing; 2006. p. 224-254.

Further Reading

Selected examples of publications of results from BEIP are listed below

- Nelson CA, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, Guthrie D. Cognitive recovery in socially deprived young children: The Bucharest early intervention project. *Science*. 2007; 318:1937–1940. [PubMed: 18096809]
- Ghera M, Marshall PJ, Fox NA, Zeanah CH, Nelson CA. The effect of early intervention on young children’s attention and expression of positive affect. *Journal of Child Psychology, Psychiatry and Allied Disciplines*. 2009; 50:246–253.
- Zeanah CH, Egger H, Smyke AT, Nelson C, Fox N, Marshall P, Guthrie D. Institutional rearing and psychiatric disorders in Romanian preschool children. *American Journal of Psychiatry*. 2009; 166:777–785. [PubMed: 19487394]
- Smyke AT, Zeanah CH, Fox NA, Nelson CA, Guthrie D. Placement in foster care enhances attachment among young children in institutions. *Child Development*. 2010; 81:212–223. [PubMed: 20331663]

Previous discussions and commentaries about BEIP Ethical Issues may be found in

- Miller FG. The randomized controlled trial as a demonstration project: An ethical perspective. *American Journal of Psychiatry*. 2009; 166:743–745. [PubMed: 19570933]
- Millum J, Emanuel E. The ethics of international research on abandoned children. *Science*. 2007; 318:1874–1875. [PubMed: 18096792]
- Wassenar DR. Commentary: Ethical considerations in international research collaboration: The Bucharest Early Intervention Project. *Infant Mental Health Journal*. 2006; 27:577–580.

Children Raised in Institutions

- McCall R, Groark CJ, Nikoforova NV, Muhammedrahimov R, Palmov OI. The effects of early social-emotional and relationship experience on the development of young orphanage children *Monographs of the Society for Research*. *Child Development*. 2008; 73(3):1–297.

Zeanah, CH.; Smyke, AT.; Settles, L. Children in orphanages. In: McCartney, K.; Phillips, D., editors. Blackwell handbook of early childhood development. Malden, MA: Blackwell Publishing; 2006. p. 224-254.

Regarding Ethical Issues in Research with Children

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Research Involving Children: Report and Recommendations. Washington, D.C: U.S. Government Printing Office; 1977. [Online] Available: http://bioethics.georgetown.edu/pcbe/reports/past_commissions/Research_involving_childrenpdf.

Kopelman L. Children as research subjects: A dilemma. Journal of Medicine and Philosophy. 2000; 25:745–64. [PubMed: 11262635]