Aaron van Dorn (00:07):

Welcome to AJP Audio for August, 2023. I'm Aaron Van Dorn. Today, on the podcast, I spoke with Dr. Lucy King, at the time a postdoc at the Department of Psychiatry and Behavioral Sciences at Tulane University of New Orleans, and Dr. Kathryn Humphreys, Assistant Professor of Psychology and Human Development at Vanderbilt University in Nashville. Psychiatric experiments involving children instantly require us to ask important questions regarding the ethics and morality of the studies being conducted. Dr. King and Dr. Humphreys are authors of a paper looking back on the effects of one such experiment, a randomized controlled trial known as the Bucharest Early Intervention Project, which looked at the affects of institutionalization versus family care on infants and children in Bucharest, Romania. They'll join us to discuss what made this trial so unique, how that trial navigated the ethical issues that arose, and what their work in analyzing the results of the trial found and the long-term impacts of the trial on participants. Dr. King, Dr. Humphreys, welcome to AJP Audio.

Dr. Kathryn Humpreys (00:57):

Hello.

Dr. Lucy King (00:59):

Hi.

Aaron van Dorn (00:59):

We'll start with Dr. King. Your paper is an analysis of the Bucharest Early Intervention Project, a randomized controlled trial which sought to investigate the impact of foster care, where children are cared for in a family home, and institutional care, where children are cared for in an institutional setting, such as an orphanage. But before we discuss that, can you tell us a little bit about the impact of neglect and deprivation on the development of children, especially young children?

Dr. Lucy King (01:19):

So neglect is actually the most prevalent form of child maltreatment in the US. It accounts for about 75% of all identified maltreatment victims. So it's a pervasive issue, and there are different types of neglect. And those might have different consequences. So there's physical and medical neglect, so not providing the instrumental care needs that children require to survive, so food, shelter, medical care. And those kinds of neglect pose immediate safety concerns. They threaten the survival of the child immediately. There's also psychosocial neglect, and that means when children are deprived of the cognitive and social and emotional input from their caregivers. That's really important for their development. And that kind of neglect doesn't have as immediate consequences of wellbeing, but it can have long-term consequences. And that's actually the kind of neglect that children participated in the BEIP project were most exposed to.

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The reason that that has long-term consequences is that, particularly in infancy and young childhood, we're almost totally dependent on our caregivers to help regulate our emotions. So we cry, we express a feeling, and that feeling is communicating something about the input we need, and we require our caregivers to respond to that, to soothe our distress, to provide interaction. And when we don't receive that kind of contingent response to our expressions, the neurobiological and behavioral systems that govern how we'll respond to stress and process our emotions in the future might develop atypically. And so, problems in those systems are really evident in attachment relationships, the bonds we form with our caregivers in early life. And neglected children are far more likely to develop insecure or

disorganized attachment relationships and also psychiatric disorders that specifically follow from not having those kinds of attachment relationships. And those can be characterized by problems in relating to other people and emotion dysregulation.

(03:39):

On top of that, there's also the deprivation of that cognitive enrichment. So playing with our caregivers, talking with our caregivers, our caregivers providing us with varied interactions with other people and places. So when we don't get that kind of input, our opportunities for learning are really constrained. And that can lead to challenges later on in cognitive functioning and with language and communication. And on top of that, all of this is happening, if it's happening in early life, in a really sensitive period of development when the brain's rapidly changing and therefore, really sensitive to the type of environmental input it's receiving. And so, without sufficient exposure to interactions with our caregivers during that period, our brain development can go awry in a way that could have lasting consequences.

Aaron van Dorn (04:32):

Dr. Humphreys, let's turn to the Bucharest Early Intervention Project that we mentioned earlier. What were they investigating? What did they find? And what were the ethical concerns with conducting a randomized controlled trial on one of the most vulnerable populations imaginable?

Dr. Kathryn Humpreys (04:43):

Thank you for that question. I'll give some context, for the BEIP trial, which is in Romania, after the fall of Nicolae Ceaucescu, there were a number of orphans living in institutions. Well over a hundred thousand orphans were living in these institutional settings, which we just learned from Dr. King, are sources of great psychosocial deprivation. And the government in Romania was trying to determine the best policies for caring for these children who were abandoned or orphaned. Orphanage care or institutional care is used around the world in many countries to care for children who have been abandoned or orphaned. And Romanian officials were trying to figure out, "What are the consequences of this type of care? And are there alternatives to providing care for these children?" So three investigators, who are the principal investigators of this study, were invited by the Minister of Child Protection in Romania to conduct this study.

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So the three principal investigators are Dr. Charles Nelson, Nathan Fox, and Charles Zeanah. And the goal was to try to figure out, is there evidence that family-based care, provided through foster care, is it better than the kinds of care that the kids are receiving in institutional care? And would there be better outcomes for these children who were randomized to the foster care conditioner arm? I'll note that there were prior studies, finding that kids who were placed into family care, following institutional care, tended to fare better than children who remained in institutional care. But one issue with those studies is the possibility of a selection bias, such that children who were being adopted or placed into families may have differed from the children who remain in institutional care, in ways that are not random. So a family who was going in to adopt a child may have selected a child who was higher functioning to begin with, rather than any given child in an orphanage.

(06:42):

And so, in order to be confident that the outcomes were associated with family-based care, those better outcomes were associated with family-based care, one would need to be confident that it's due to the family care and not due to potential preexisting differences. And so, the best way to draw those kinds of

causal conclusions regarding an intervention is through randomized controlled trials. Now, several ethicists have weighed in on the Bucharest Early Pntervention Project trial design, which did several things that were important to mention. One is that there is minimal harm with any of the instruments we use to assess how children were doing. So the actual study procedures involved minimal harm. Although we randomized children to receive family care in the foster care arm, no child was required to remain in institutions. And in fact, many of the children who were randomized to the care as usual condition, which is often remaining in institutional care for longer durations of time, those children often ended up in family-based placements at some point during their childhood.

(07:42):

I'll also note that there wasn't an existing foster care system for children in Romania. And so, the study team had to create a foster care network by recruiting foster parents to participate in the study. And so, at best, children were being randomized into receiving family-based placements. And at worst, the child wasn't required to do anything different than would've normally happened without the study taking place. So as I've noted before, several ethical commentaries have been written about the study, including from the investigative team, as well as ethicists outside of the investigative team, that can be used to read more about the ethics. I'll just say that it is a very vulnerable population, and we were paying a lot of attention to, how can we provide evidence to support the placements of children in family care? And the value of the randomized controlled trial is to provide that really clear concrete evidence whether the intervention was superior to care as usual, and that evidence could then be used to inform placement decisions for children in Romania, as well as children around the world.

Aaron van Dorn (08:45):

How did your group go about creating a strategy for gathering and analyzing a diverse data set collected at various points and using various methods over the course of two decades, obviously creating a much different data and a much more complicated dataset?

Dr. Lucy King (08:57):

Yeah, it's a really complex, interesting dataset, so it includes a six follow-up assessments, following a baseline assessment that occurred in 2001 when the trial was initiated. And those follow-up assessments have occurred at 30, 42, and 54 months of age for the children, as well as eight, 12, and 16 to 18 years. As you mentioned, it's a diverse data set. Lots of different domains of development have been assessed over that time period, and it's a complex data set, as you mentioned. Children had different experiences following the end of the formal intervention, and some went in and out of their foster care or institutional settings. We used an intent to treat approach to analyze the data, and that means that, in our main analyses, all children who were originally assigned to receive the foster care group were analyzed as being in the foster care group. Whereas all children who were randomly assigned originally to be in care as usual were analyzed as being in that group, regardless of where they were placed at later ages.

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And so, that's a more conservative approach to analyze the data. We can get to in a bit that we did look at some individual differences at the experiences of those children in the foster care group, specifically both at the timing of their placement in foster care. All children who were randomized to the foster care group were placed between the ages of six to 33 months old, but there was some variation in that time period that we examined. And we also looked at the stability of their placements. So not all children... Actually, by the end, by 16 to 18 years, most of the children, a majority, a small majority, 60% of the children in the foster care group were no longer with their original study sponsored foster family. They

had gone to another family or potentially returned to an institution for various reasons, so we looked at stability of that placement as well.

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So our analyses for this paper focused on those six follow-up waves from toddlerhood, 30 months, up to 16 to 18 years, to understand the degree to which children in the foster care group evidenced recovery from their experience of early institutionalization, compared to those children who had been assigned to the care as usual group. Publications analyzing data from this project had previously focused on specific domains of development at specific time points. So for example, understanding differences in symptoms of psychopathology when children were eight years old or understanding differences in IQ when children were 12 years old. And there had also been narrative reviews of the effects. So just synthesizing, reading across those papers, the overall effects of the intervention, but there had not been a quantitative synthesis of the effects. And we wanted to be able to directly quantify the overall impact of the intervention on children's recovery from early institutionalization and also, examine sources of variation in that impact.

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So for example, whether there was a greater effect on certain domains of development than others and whether the effect was stable across development or whether it changed across time. So we first needed to identify the constructs we wanted to include in this quantitative synthesis. And so, we focus on constructs that had been assessed consistently across all of those assessment waves. And also, planning to cover, as much as possible, multiple domains of development, that had been focused on in previous publications. So that included cognitive functioning, which we assessed as IQ in this paper, physical growth, including weight and height and head circumference, symptoms of psychopathology, including symptoms of internalizing, externalizing, symptoms of disorders of social relatedness, including reactive attachment disorder and disinhibited social engagement disorder, as well as ADHD symptoms. And we also looked at a metric of brain function, in terms of overall EEG alpha power.

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So these were all constructs that had been examined in previous papers, but again, hadn't been directly compared to each other or synthesized across all of the waves. And this approach was inspired by meta-analysis or meta science, in which you would take effect sizes published in lots of previous papers, usually not from a single project, but from kind of field of literature, and try to understand what the overall average effect size it was. And so, instead of doing that from lots of previous papers here, we were doing that on the raw data collected from the 20 years of this project, which accounted for over 7,000 observations of these children. And by using a common analytic approach to analyze all of that data, we could estimate these overall effects, and we could also examine those sources of variation in the effects. Every time a different researcher analyzes a data set, they might take a slightly different perspective on it or make different analytic choices.

(14:49):

And so, it can be difficult to interpret differences across papers for that reason. And using a common analytic approach kind of evens out those different choices that you might make, so you can make direct comparisons between different effect sizes and analyses. The actual strategy we used is called... We used a mixed effects model or also known as multi-level modeling. And that allows you to combine data across many time points and constructs, in order to estimate that overall effect, while also examining sources of variation in that effect and accounting for important dependencies in the data, so that data from the same person collected across multiple time points is dependent on each other, as well as data collected about the same constructs. And so, then we examined those sources of variation, which

included the domain of development, whether the effect size would vary based on that, as well as time point. So whether was smaller or larger at different ages. And again, as I mentioned that, within the foster care group, we looked at individual differences, in terms of age of placement and the stability of placement.

Aaron van Dorn (16:03):

Why did you choose to look back at this particular trial?

Dr. Kathryn Humpreys (16:05):

So the BEIP is one of the most influential studies regarding the recovery of children from deprivation. So it's told us many things about the potential for recovery. We know that deprivation can have really severe impacts on children's development, but can children benefit from family placements after exposure to early institutional care? Some of the most striking findings from the beginning stages of the study were that those who were randomized for the foster care intervention had dramatic gains in their IQ scores, relative to those who were randomized to the care as usual condition. And in fact, after the study team presented their findings to the Romanian government, there was a law passed that banned the institutionalization of young children in Romania. Originally 24 months of age, no child was allowed to be placed in institutions. Was later changed to 36 months, and now, is seven years.

(17:01):

So there's this possibility that research can be used in this way to influence policy, but that's really specific to the Romanian context. Given how rare randomized controlled trials are for children in institutional care, we really wanted to see whether there could be more gained from what we've learned from this trial. A lot of studies that have focused on early intervention in other contexts have found that the promising effects of an intervention tend to fade out across time and across development, suggesting the possibility that those early gains that we saw may not last into later childhood and into adulthood. That was highly motivating for me about the potential long-term impacts of this trial. And we did so using that conservative intent to treat approach that really can underestimate the true effect of the intervention.

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So if we still see effects of the intervention, even using that conservative approach, it suggests that family-based care is really superior to institutional care, and it would allow us to see, is the intervention effect stable across time? Is there that fade out effect? Is it constant across these different domains of development? Has children changed in their placements over time? Did we see any differences in their functioning, regarding where they were living and whether they were living with their original foster care family? With the hope that this might be useful for improving our understanding of the best care practices for children who've been orphaned or abandoned.

Aaron van Dorn (18:31):

So what did your analysis find about the long-term impacts of the Bucharest trial? Did your analysis differ from the original conclusions of the trial appreciably, especially given the passage of time?

Dr. Lucy King (18:39):

The short answer is no. It didn't differ from the original conclusions appreciably. We were excited that we did find these overall significant effects of the intervention. So we looked at overall across cognitive ability, physical growth, and neural functioning, and collapsing across all those time points across 20

years, whether the intervention had a significant effect. And it did. And similarly, across all those types of psychopathology, the intervention did have a significant effect. And the effect sizes for all those domains were similar in magnitude. When collapsing across the domains, the effect size was around 0.25, which is about a small to medium effect size. We also found that there were sources of variation in those overall significant effect sizes. So specifically, it mattered the domain of development we were examining. And understanding which domains were most affected by the intervention was a new contribution of this paper.

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So specifically, we found that the intervention had the largest effect on cognitive ability measured by IQ score. There were also significant effects on physical growth. We didn't find an overall significant effect on EEG alpha power, which was our only measure of brain functioning. Also, large effects on those disorders of social relatedness that specifically follow from disruptions in attachment relationships. That's reactive attachment disorder and disinhibited social engagement disorder. That understanding of which domains of development are most influenced by this intervention was a new contribution. A really important finding was that we didn't find very many effects of age of assessment, meaning that the effect of the intervention appeared remarkably stable across development. It didn't change. So the size of the effect in early life was similar to the size of the effect much later in life. So as Kate was mentioning, we didn't find evidence of fade out as children grew older.

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And again, that's particularly noteworthy, given by the later assessments in adolescents, many children in both groups had experienced changes in caregiving environments. Many children in the foster care group were no longer with that original study sponsored foster family. So we described the impact of this intervention to improve the caregiving environment as rapid. So it was evident already by age 30 months, and it lasted through adolescence. And I think this speaks to the importance of the early caregiving relationships for our long-term development. So it's both the provision of those relationships in early life. We also think likely that getting those relationships early on might have helped catalyze more positive experiences for children in the intervention group. So for example, having a positive caregiving relationship might have opened up other positive social, cognitive, and emotional experiences for those children. We also found some interesting effects when we looked within the foster care group, investigating how individual differences in the stability of their placement with the foster family were associated with their long-term outcomes.

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And importantly, when looking within the foster care group, we're looking at correlational findings, rather than causation here, because it's individual differences within that group, rather than comparing the randomized control trial groups. So again, the stability of placement refers to whether children remained with the original foster care family they were placed with for the intervention or were disrupted from that placement. Meaning they moved to a different family or might have returned to an institutional setting. And by late adolescence, about 60% of children in the foster care group had been disrupted from their original family. And by that time, we saw a potential negative impact of disruption. So by adolescence, children who were no longer with that family weren't doing as well as the children who had been able to remain with that family. That provided greater evidence that remaining with your original family, not experiencing those disruptions in the bond with a family, are really critical for long-term development.

Aaron van Dorn (23:22):

So what were the limitations of your study?

Dr. Lucy King (23:22):

Yeah, so as I was mentioning before, we did have to make some choices about the domains of development and measures that we were going to focus on in this paper. There are limitations to all measures. They don't perfectly capture the constructs as they are in reality. So many of our measures of psychopathology were measured by asking caregivers to report on the children's symptoms, and it's possible that there might be bias in those informants. So for example, it's possible that caregivers of children in foster care might report differently on children than caregivers of children in institutions or other settings. We also, in particular, looked at one specific measure of brain function, that EEG alpha power measure, and brain function can be measured in many different ways. And so, I wouldn't take the findings of this project to indicate that institutionalization does not affect brain function.

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Brain function, of course, underlies most of the behavioral or all of the behavioral effects of institutionalization. It mediates our experiences and how we behave. So we believe it does affect brain function, but we're not able to detect that with the measure that we selected for this project. It may not be sensitive enough or it might not have been the right measure to examine. We also, because we had different measures across time, because measures change depending on the child's developmental stage, so you don't use the same measure to measure externalizing symptoms in early childhood as you do in adolescence, we weren't able to look at growth trajectories, so within individual changes over time in children's functioning.

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And that would allow you to look at the rate and shape of change within individuals. We could only look at between individual differences in this project. So for example, whether the effect size was larger at older versus younger ages versus whether, within individuals, functioning grew or diminished. There are also many more features of the environment, of course, that we didn't examine in this analysis. That includes the prenatal environment, the features of the institutional environment, and features of family-based environments. So for example, the quality of the care one receives in a family is very likely to affect outcomes. That's not something we examined in this set of analyses, but we believe it's likely important.

Aaron van Dorn (26:11):

Are there any immediate clinical or policy implications for your findings relating to children in foster and institutional settings?

Dr. Lucy King (26:16):

Yeah, I can start this, Kate, and then, if you want to weigh in. So the overall conclusion and has been the conclusion of many previous papers and other researchers studying institutionalization is that institutions are just not appropriate settings for raising children. Even when the quality of care within institutions is improved, they're still associated with poorer outcomes and difficulties for children. So the major policy implication of this work is that family-based care is the appropriate setting for children, and institutions are not. The fact that we didn't find a fade out of the effect over time is really important. It suggests that providing this high quality care beginning early in life can have long lasting positive consequences, even for children exposed to severe early adversity, but also, that the stability of that care is important. So it's important to get children into family placements that they can remain in and develop those long lasting bonds and also, not experience the disruption of having to change families and try to reinstate those bonds with others.

(27:31):

Another piece of this is, sometimes, we might think about neglect as physical neglect and think that physical neglect is the type of neglect that we should care most about, because it has this immediate effect on survival, this imminent threat. But our findings show that psychosocial neglect and providing children with psychosocial input following early neglect is really important. Not receiving that kind of input can have these long lasting negative effects, but providing it early in life, intervening to make sure children receive it, can also have long lasting benefits and promote their recovery.

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So intervening early is important, both for limiting the duration of exposure to neglect and also, for providing children with healthy environments within that window of sensitive development, that would allow them to recover from early negative experiences and form the brain connections important for their lifelong development. So I think, going back to this idea of social neglect, identifying it in family-based cares can be challenging. Physical neglect might be more obvious, but it's a very important aspect of neglect to focus on. And we really need to support families struggling with this type of maltreatment. Doing so would prevent a lot of suffering and allow a lot more children to thrive.

Dr. Kathryn Humpreys (28:57):

I have one thing to add too, which is something special about the Bucharest Early Intervention type of foster care. So foster care in the United States is often really focused on meeting kids' instrumental care needs, making sure that kids have food, shelter, clothing. Those kinds of things are obviously important, but they're not sufficient for helping children to grow and thrive. And so, one thing that's really special about the foster care created by the BEIP team is that it really encouraged the foster care parents to make a psychological commitment to the children, to love them as if they were their own, to provide them simulating and nurturing care, not just meeting their survival needs.

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And we think it's really important that it was this type of high quality foster care system that was created, that allowed these children to really recover from a lot of the dramatic impacts of early institutional care. And so, as countries are thinking about what policy choices they have available to them, to provide children care who have been orphaned or abandoned, it's not only placing them within families, although of course, that's a great start, but making sure that those families are making a psychological commitment and that are engaging in child-centered ways, that really promote stimulating and nurturing environments, that we think children need to really to thrive in their environments and to recover from early exposure to adversity.

Aaron van Dorn (30:16):

So what's next for your research?

Dr. Kathryn Humpreys (30:18):

Well, there's kind of two things that I want to mention here. One is that we're still following these trial participants from the BEIP. They're now in early adulthood. And so, we're able to bring them back into the lab, see how they're doing in many of the domains that we studied in this large paper. We're also able to ask new questions about how they transition to more independent stages of life, in terms of going to school, getting careers, living independently, forming relationships, maybe having children of their own. And so, we're excited to see how this new phase of development is working out for these child participants and seeing whether we still see the same sorts of large gains that we were happy to

find for the previous waves of development. So that's one thing our team is doing. And then, in addition, because psychosocial deprivation is not only occurring in institutional care, in orphanage care, we're really interested in how families vary in the kind, enriching, nurturing, and stimulating care they provided children in their everyday lives.

(31:18):

Lucy and I have been thinking about this as really on a continuum from severe psychosocial deprivation all the way to highly enriching, stimulating, and nurturing environments. And so, within families in the United States, we're trying to come up with ways to better assess and capture the variation that occurs naturally in just typical family environments to see whether we see these same sorts of associations with more enriching, nurturing, and stimulating care associated with better outcomes, in terms of mental health, social functioning, cognitive functioning, as well as healthier physical development. So the goal in our lab right now is to really think about tools to better capture everyday variation in kids' lives, so we might be able to see whether we see these same types of patterns in family-based settings as we see in institutional care.

Aaron van Dorn (32:06):

Dr. King, Dr. Humphreys, thank you very much for your time today.

Dr. Lucy King (32:09):

Thank you.

Dr. Kathryn Humpreys (32:10):

Thank you for inviting us.

Aaron van Dorn (32:11):

That's all for AJP Audio for this month, but be sure to check out our other podcasts offered by the APA, including Psychiatric Services From Pages to Practice, Psychiatry Unbound, and others at psychiatryonline.org/podcasts or wherever you get podcasts. The views and opinions expressed in this podcast are those of the individual speakers only and do not necessarily represent the views of the American Psychiatric Association. The content of this podcast is provided for general information purposes only and does not offer medical or any other type of professional advice. If you're having a medical emergency, please contact your local emergency response number.