

A Comprehensive Multilevel Analysis of the Bucharest Early Intervention Project: Causal Effects on Recovery From Early Severe Deprivation

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Objective: The Bucharest Early Intervention Project is the first randomized controlled trial of foster care as an alternative to institutional care. The authors synthesized data from nearly 20 years of assessments of the trial to determine the overall intervention effect size across time points and developmental domains. The goal was to quantify the overall effect of the foster care intervention on children's outcomes and examine sources of variation in this effect, including domain, age, and sex assigned at birth.

Methods: An intent-to-treat approach was used to examine the causal effects of the randomized controlled trial for 136 children residing in institutions in Bucharest, Romania (baseline age, 6–31 months) who were randomly assigned to either foster care (N=68) or care as usual (N=68). At ages 30, 42, and 54 months and 8, 12, and 16–18 years, children were assessed for IQ, physical growth, brain

electrical activity (EEG), and symptoms of five types of psychopathology.

Results: Participants provided 7,088 observations across follow-up waves. Children assigned to foster care had better cognitive and physical outcomes and less severe psychopathology than did those who received care as usual. The magnitude of these effect sizes remained stable across development. The foster care intervention most influenced IQ and disorders of attachment/social relatedness.

Conclusions: Young children benefit from placement in families after institutional care. The benefits of foster care for previously institutionalized children were remarkably stable across development.

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Over and above basic needs like nutrition, shelter, and safety, infants require psychosocial care, including nurturance and stimulation, for healthy development. Unfortunately, millions of children being raised without parents experience severe deprivation in the context of institutional care, where high child-to-caregiver ratios and lack of nurturing care lead to psychosocial neglect even when survival needs are met (1, 2). Psychosocial deprivation is not limited to institutions; neglect is the most common form of maltreatment identified by U.S. child protective services agencies (3). Given that psychosocial deprivation both in institutional and family-based contexts is linked to delays in cognitive, physical, and socioemotional development (2, 4–6), understanding the impact of interventions that aim to promote recovery from early neglect is a public health priority.

Studying children's developmental functioning during and after exposure to institutional care provides insight into the effects of deprivation relevant to neglected children

across contexts (7). Specifically, examining children's outcomes following placement in family-based care enhances knowledge of developmental plasticity, including the degree to which lasting improvement following early deprivation is possible (8). The Bucharest Early Intervention Project (BEIP) was initiated in 2001, and it remains the only randomized controlled trial of foster care as an alternative to institutional care (9). The goal of the BEIP was to examine the impact on development of high-quality family-based care following exposure to institutional care in early life (10). The trial enrolled 136 abandoned Romanian children at a mean age of 22 months. After randomization to foster care or to care as usual, children were assessed across multiple developmental domains at baseline and at ages 30, 42, and 54 months (at which point the trial concluded and support of the foster care network was transferred to the Romanian authorities) (11). Follow-up assessments were conducted at ages 8, 12, and 16–18 years. Notably, over the intervening years, many

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children experienced placement changes (for example, many care-as-usual children received family placements; some foster care group children experienced placement disruptions; and some children in each group returned to biological families). The ethical dimensions of this study have been widely discussed by the study team and others (4, 11–13).

The effects of the foster care intervention across development have been documented extensively (e.g., 14–19). However, in keeping with scientific conventions, findings published to date largely focus on specific outcomes at discrete time points. Consistent with the aims of meta-science techniques such as meta-analysis, by aggregating data across nearly 20 years of follow-up assessments, it is possible to provide a more accurate determination of the overall intervention effect size and identify sources of variation in this effect. By using a common approach to analyze data from multiple informants, time points, and developmental domains, we can address concerns about the robustness of scientific findings (20, 21). This approach may, furthermore, help guide future research and policy by documenting the potential strengths and limitations of the intervention through capturing the relative breadth and stability of its effects across outcome domains and developmental stages.

In this study, we comprehensively analyzed over 7,000 observations of children's outcomes across domains of development collected from infancy through adolescence in participants of the BEIP. First, using intent-to-treat analyses, we quantified the overall causal effects of the foster care intervention on children's functioning across assessment waves and the domains of cognitive functioning, physical growth, brain electrical activity (EEG: relative alpha power), and psychopathology. Second, we explored moderators of the overall effects of the intervention, testing whether an enhanced foster care intervention has broad or specific effects on the development of children exposed to severe early deprivation. We assessed whether the effect of intervention varied as a function of outcome domain, age, and biological sex. Finally, we examined sources of variation in functioning among children randomized to foster care, allowing us to examine whether the timing and stability of family-based care were associated with children's outcomes.

METHODS

Study Design and Participants

In this randomized controlled trial, 187 children 6–31 months of age residing in six institutions in Bucharest were initially screened for participation. Of these, 51 were excluded from the study because of medical conditions severely compromising development (e.g., genetic syndromes, signs of fetal alcohol syndrome, microcephaly). Thus, the final sample included 136 children who had been abandoned at or shortly after birth and placed in institutions. Their mean age at baseline was 20.74 months (range = 5.39–31.76), and 51% were female. Half of these children were randomized to the foster care group and the other half to the care-as-usual group (i.e., continued institutional care). Within the foster care group,

the mean age at placement into a study-sponsored foster care family was 22.63 months (range = 6.81–33.01).

Figure 1 is a CONSORT diagram of the flow of participants for the analyses. Children completed follow-up assessments at ages 30, 42, and 54 months and at ages 8, 12, and 16–18 years. Of the 136 participants, 130 (65 in the foster care group and 65 in the care-as-usual group) completed at least one of these follow-up assessments. Overall, these 130 participants (48% of them female) provided 7,088 observations (3,628 in the foster care group and 3,460 in the care-as-usual group) between the 30-month and 16- to 18-year follow-up waves across the domains of cognitive functioning, physical growth, brain electrical activity, and psychopathology. Here, an observation refers to a single score for a given assessment at a given wave (for example, each IQ score at each wave is a single observation). Across all waves and outcome domains, participants could complete a total of 68 possible assessments; on average, they completed 55 (80%) assessments. Supplementary analyses indicated that missing data were not differentially associated with intervention group or baseline characteristics. Children randomized to the foster care and care-as-usual groups did not differ in demographic variables, percentage of lifetime in institutional care, cognitive functioning, or physical growth at baseline (see Table S1 in the online supplement; King et al., unpublished 2022 data).

Within the foster care group, the stability of placement with the original study-sponsored foster family has previously been linked with children's outcomes (17, 22). In the present analyses, for each assessment, participants assigned to the foster care group were identified as “stable” if they remained with their original foster family at the time of the assessment or as “disrupted” if they no longer resided with the family at that assessment. At the time of the 16- to 18-year assessment wave, 37 of the 65 (57%) foster care participants who completed at least one of the follow-up assessments had been disrupted from their original foster family. Two participants assigned to the foster care group were reunited with their biological families prior to placement in a study-sponsored foster family and are not included in stability analyses, given that they were neither stably placed in nor disrupted from foster care. Children who were identified as “disrupted” and “stable” in later childhood and adolescence did not differ at baseline in symptoms of psychopathology or measures of IQ or physical growth (see the online supplement).

Randomization

Young children living in institutions were assessed at baseline (mean age, 22 months) and were randomized in a 1:1 ratio to high-quality foster care or care as usual. Assignment to group was done using slips of paper with subject identifiers written on them (sibling pairs were included together) and drawn from a hat. Because foster care was extremely limited in Bucharest when the study began, the investigators, in collaboration with Romanian officials, created a foster care network (9, 23). After advertising and subsequent screening, 56 foster families were selected to care for the 68 children randomized to the foster care group.

Procedures

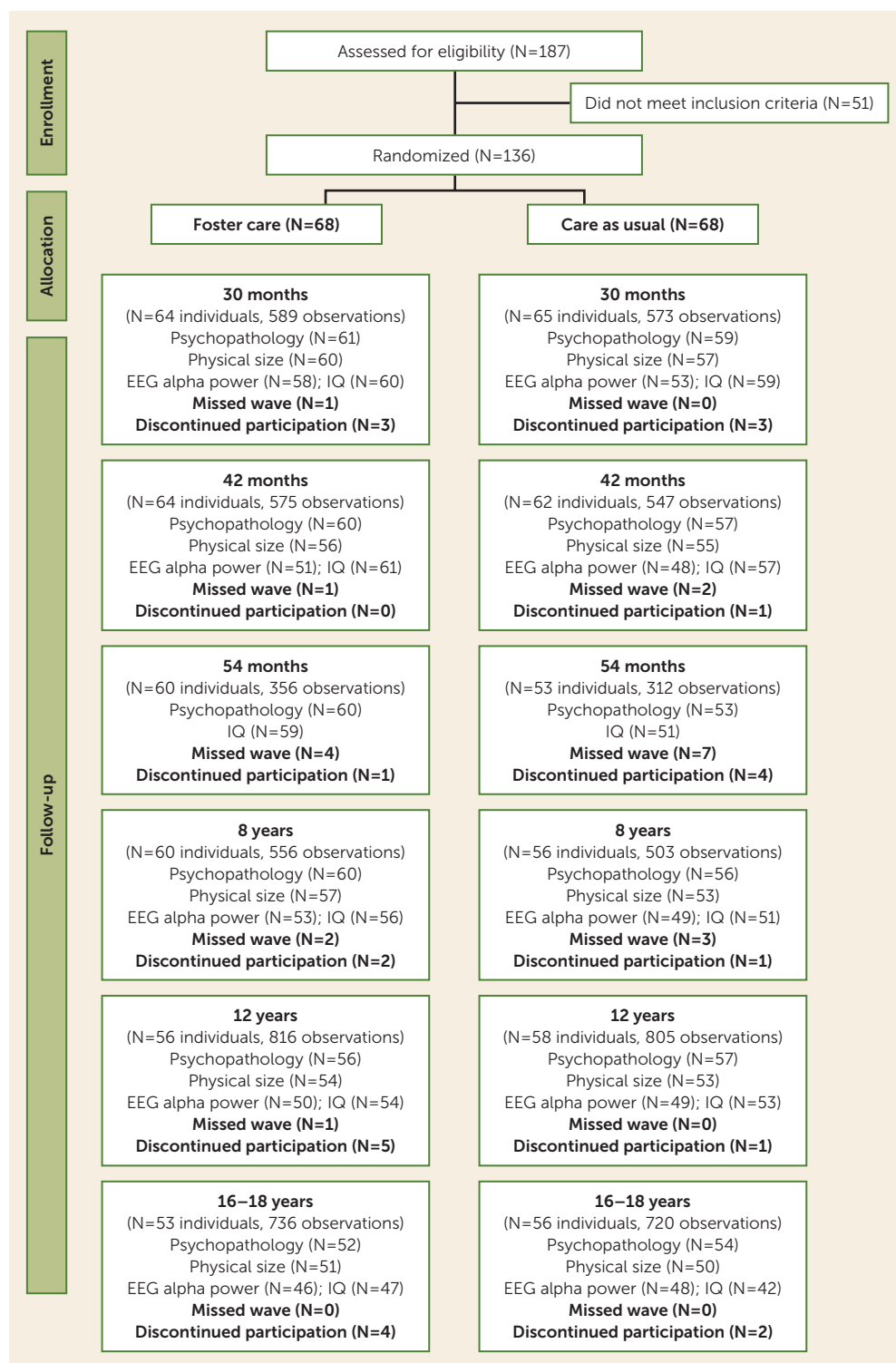
Children's legal guardians provided signed informed consent (children age 8 years and older provided written or verbal assent). Ethics approval was obtained from the institutional review boards of the three principal investigators' universities and from the local Commissions on Child Protection in Bucharest.

The foster care intervention was designed to be affordable, replicable, and grounded in findings from developmental research on enhancing caregiving quality. BEIP social workers, who received regular consultation from U.S. clinicians, supported the foster parents to provide child-centered care that emphasized meeting children's physical and psychological needs. This included how to understand children's behavior in the context of their prior experience in the institution and their developmental stage (9, 23). All decisions regarding placements after randomization were made by child protection authorities, and no child was retained in institutional care solely because of the study. As a result of the evolution of child protection efforts in Romania, all but 13 children in the care-as-usual group were placed into family care by age 18 years. At age 54 months, the trial itself concluded, and support of the foster families was assumed by the Romanian government.

Outcomes

Primary outcomes for the randomized controlled trial included several measures of cognitive functioning, physical growth, and psychopathology. For the present analyses, the primary outcomes were cognitive functioning, physical growth, brain electrical activity, and symptoms of five forms of psychopathology. Children were assessed for these

FIGURE 1. CONSORT diagram of the flow of participants in an analysis of the Bucharest Early Intervention Project^a



^a“Discontinued participation” indicates the number of participants who withdrew from the study after the previous wave. “Missed wave” indicates the number of participants who were unavailable for assessment.

outcomes at every follow-up wave except at 54 months, when physical growth and brain activity were not assessed. We chose these outcomes because they were assessed consistently across waves, allowing for estimation of the overall effect of the

intervention across ages. Given many potential outcomes, we down-selected outcomes to ensure the feasibility and digestibility of the analyses while maximizing their usefulness for interpreting the impact of the BEIP in the context of the existing literature. Importantly, the metrics included here may differ from those reported in previous publications. We provide detailed information about each of the measures, as well as histograms, in the online supplement.

Cognitive functioning was operationalized as IQ, assessed with the Bayley Scales of Infant Development (24) (at 30 and 42 months), the Wechsler Preschool and Primary Scale of Intelligence (25) (at 54 months), and the Wechsler Intelligence Scale for Children, 4th ed. (26) (at 8, 12, and 18 years). Physical growth was operationalized as height, weight, and head circumference. Brain electrical activity was operationalized as relative EEG power in the alpha frequency band, defined consistently with past BEIP reports (at age 30–42 months, 6–10 Hz [27]; at age 8 years, 7–12 Hz [28]; at ages 12–16 years, 8–13 Hz [29, 30]) averaged across 10 electrode sites (F3, F4, C3, C4, P3, P4, T7, T8, O1, and O2) collected at rest with eyes open. Relative alpha power, which minimizes interindividual differences in absolute power due to factors such as skull thickness, was computed as the proportion of absolute power in the alpha band relative to the total power across 1–45 Hz.

Psychopathology was operationalized as signs and symptoms of disorders of attachment/social relatedness (disinhibited social engagement disorder and reactive attachment disorder), attention deficit hyperactivity disorder (ADHD), externalizing problems (excluding symptoms of ADHD), and internalizing problems. Disinhibited social engagement disorder and reactive attachment disorder symptoms were measured using the Disturbances of Attachment Interview (31) (at all waves; caregiver report). ADHD, internalizing, and externalizing symptoms were measured using the Infant-Toddler Social and Emotional Assessment (32) (at 30 and 42 months; caregiver report), the Preschool Age Psychiatric Assessment (33) (at 54 months; caregiver report via interview), the MacArthur Health and Behavior Questionnaire (34) (at 8, 12, and 16 years; caregiver and teacher report), and the Diagnostic Interview Schedule for Children, 4th ed. (35) (at 12 and 16 years; caregiver report). All measures of psychopathology are well validated in severely deprived children.

Statistical Analysis

Analyses were performed in R, version 4.2.0 (36), and were two-tailed, with an alpha of 0.05. Multilevel (i.e., mixed-effects) models were implemented using the *lme4* package (37). Prior to all analyses, scores on the outcome variables were standardized within wave and measure to account for the use of different measures across waves and so that values measuring different outcomes were on the same scale. Therefore, our analyses preclude examination of growth curves (i.e., within-individual change in outcomes across time) and instead yield information about between-individual

differences. Further, between-individual differences in effect sizes based on age at assessment must be interpreted relative to the measures used at those ages. For all models, we computed bootstrapped parameter estimates and 95% confidence intervals (1,000 iterations) using the *parameters* package (38). We performed F tests for interactions using the *anova* function from the *lme4* package (37), using Satterthwaite's method for calculating degrees of freedom.

Overall Effects of the Foster Care Intervention

We used multilevel models to quantify the overall effect of the foster care intervention on children's IQ, physical growth, EEG relative alpha power, and psychopathology across assessment waves. We used two separate models, corresponding to cognitive, physical, and neural outcomes (i.e., IQ, physical size, EEG power) and symptoms of psychopathology, respectively. Given that higher scores on IQ, physical size, and EEG power are interpreted as indicating healthier functioning whereas higher scores on each form of psychopathology indicate more difficulties, this grouping of outcome measures accomplished our goal of estimating overall effects of the foster care intervention while allowing straightforward interpretation of effect sizes. The dependent variable in each model was the standardized value on each measure at each assessment wave for the outcomes included in that model, such that the model of cognitive, physical, and neural outcomes contained 2,789 observations (1,425 in the foster care group and 1,364 in the care-as-usual group) and the model of psychopathology contained 4,299 observations (2,203 in the foster care group and 2,096 in the care-as-usual group). In addition to modeling the effect of intervention group (foster care group vs. care-as-usual group, dummy coded) on these values, we included terms for domain of psychopathology (effect coded), exact age at assessment in years (mean centered; see the online supplement), sex assigned at birth (effect coded), a random intercept for participant, and a random intercept for biological family (to account for nonindependence of data from six sibling pairs). For the model of psychopathology, we also covaried for informant (caregiver vs. teacher; effect coded). In summary, this modeling approach allowed us to estimate the overall effect of the intervention across outcomes while accounting for variation across psychopathology.

Sources of Variation in the Effects of the Intervention on Children's Outcomes

We tested whether outcome domain/type of psychopathology, exact age at assessment, or sex moderated the effect of the foster care intervention on children's outcomes by modeling interactions between these variables and the effect of intervention group. These interactions were tested in separate models from those of the overall effects of randomization to foster care, and all interactions were included simultaneously in a single model. In the presence of a significant interaction, we probed simple effects by examining the effect of intervention group at different levels of the moderator(s) in a series of multilevel models. Given our goal of characterizing

sources of variation in the effect of the foster care intervention, we did not adjust for multiple comparisons when testing simple effects of significant interactions. Thus, *p* values for simple effects should be interpreted as nominal.

Sources of Variation Among Children in Foster Care: Timing and Stability of Placement

Among children in the foster care group, we tested the associations of age at placement and stability of foster care placement with children's cognitive, physical, and neural outcomes and their symptoms of psychopathology (see the online supplement for additional information about age and placement stability variables). While causality may be inferred from analyses testing the effects of intervention group on children's outcomes, analyses of sources of variation in outcomes among children in the foster care group are correlational in nature. Placement stability was treated as a time-varying dummy-coded variable. Given that the likelihood of disruption from the original foster care family increased with age (see the online supplement), this variable was interpreted only in interaction with age at assessment, so that parameter estimates reflected the difference in functioning between currently stable and disrupted children at a given assessment occasion.

RESULTS

Descriptive statistics of the measures for each outcome as well as correlations among outcome scores averaged across assessment waves are provided in the online supplement.

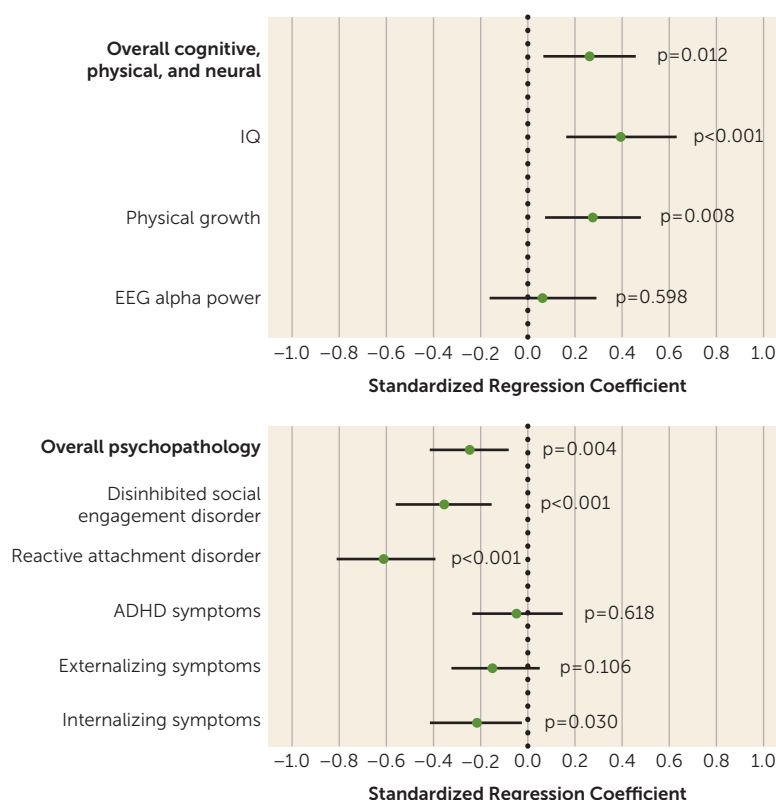
Overall Effects of Foster Care on Children's Outcomes

Results for analyses of the overall effects of the foster care intervention are presented in Figure 2.

Cognitive, physical, and neural outcomes. We found an overall effect of the foster care intervention on cognitive, physical, and neural outcomes when considered collectively across assessment waves ($\beta=0.26$, 95% CI=0.07, 0.46). Compared with children in the care-as-usual group, those in the foster care group had significantly higher scores on the combined IQ, physical growth, and EEG relative alpha power measures.

Psychopathology. We found an overall effect of the foster care intervention on symptoms across all five types of psychopathology combined and across assessment waves ($\beta=-0.25$, 95% CI=-0.42, -0.08). Children in the foster care group had significantly lower symptoms of psychopathology than children in the care-as-usual group.

FIGURE 2. Overall and domain-specific standardized mean differences between children randomized to the foster care intervention compared with children randomized to care as usual^a



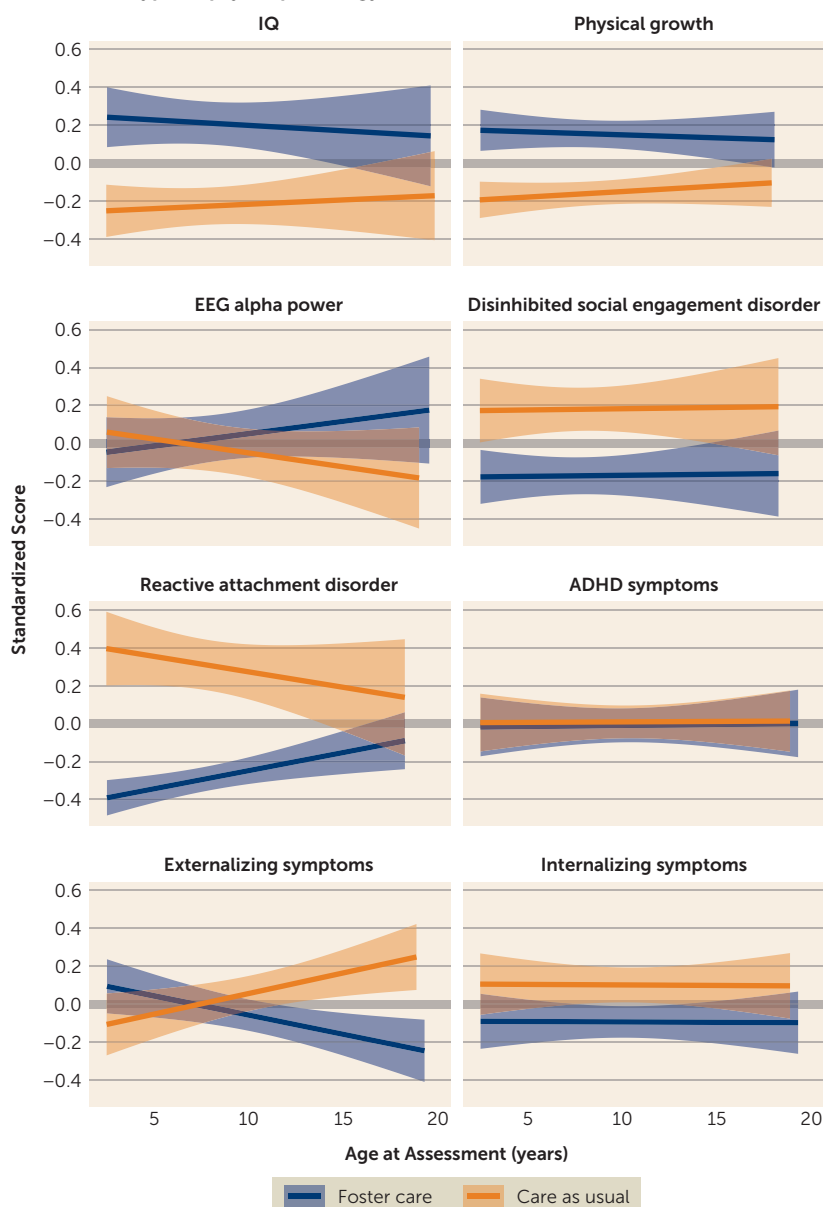
^a The graphs show standardized regression coefficients and 95% bootstrapped confidence intervals from multilevel models, controlling for covariates. ADHD=attention deficit hyperactivity disorder.

Sources of Variation in the Effects of the Intervention on Children's Outcomes

Results of analyses examining variation in the effects of the intervention based on outcome domain and type of psychopathology are summarized in Figure 2. Standardized scores over time for each group, outcome domain, and type of psychopathology are summarized in Figure 3.

Cognitive, physical, and neural outcomes. We found that outcome domain moderated the strength of the effect of the foster care intervention on children's cognitive, physical, and neural outcomes when considered collectively across assessment waves ($F=5.57$, $df=2$, 2664.99, $p=0.004$). There were significant effects of the intervention on IQ ($\beta=0.39$, 95% CI=0.16, 0.63) and physical growth ($\beta=0.28$, 95% CI=0.07, 0.48) but not on EEG relative alpha power ($\beta=0.06$, 95% CI=-0.16, 0.29). Children in the foster care group had significantly higher average IQ scores and were physically larger on average than children in the care-as-usual group. The effects of the intervention on IQ and physical growth were significantly larger than on EEG alpha power, but there was no significant difference between the effects on IQ and physical growth (see the online supplement).

FIGURE 3. Standardized scores for children randomized to the foster care intervention and to care as usual across ages at assessment for each outcome domain and type of psychopathology^a



^a Because scores are standardized within assessment wave, plots do not show within-individual change across time but depict between-individual differences. The graphs show linear regression lines of best fit, with shaded areas indicating standard error. ADHD=attention deficit hyperactivity disorder.

In two-way interactions, neither age at assessment ($F=0.44$, $df=1$, 2718.16 , $p=0.506$) nor sex ($F=0.01$, $df=1$, 124.13 , $p=0.916$) significantly moderated the effect of the intervention on cognitive, physical, and neural outcomes. However, there was a significant three-way interaction between intervention group, outcome domain, and sex. The effect of the intervention on physical size was similar for male and female children, whereas the effect on IQ was larger for female than male children (see the online supplement).

Psychopathology. We found that type of psychopathology moderated the effect of the foster care intervention on children's symptoms of psychopathology ($F=11.85$, $df=4$, 4157.60 , $p<0.001$). Children in the foster care group had significantly lower symptoms of disorders of attachment/social relatedness (disinhibited social engagement: $\beta=-0.35$, 95% CI = -0.56 , -0.15 ; reactive attachment: $\beta=-0.61$, 95% CI = -0.81 , -0.39) and internalizing problems ($\beta=-0.22$, 95% CI = -0.42 , -0.03) than did children in the care-as-usual group. In contrast, there was no significant overall effect of the foster care intervention on symptoms of ADHD or externalizing problems (ADHD symptoms: $\beta=-0.05$, 95% CI = -0.24 , 0.15 ; externalizing problems: $\beta=-0.15$, 95% CI = -0.32 , 0.05). The effects of the intervention on symptoms of disinhibited social engagement disorder and reactive attachment disorder were significantly larger than the effects on ADHD and externalizing symptoms; further, the effect of the intervention on reactive attachment disorder symptoms was significantly larger than the effects on symptoms of internalizing and disinhibited social engagement disorder (see the online supplement).

In two-way interactions, neither age at assessment ($F=2.16$, $df=1$, 4261.80 , $p=0.142$) nor sex ($F=2.37$, $df=1$, 114.50 , $p=0.127$) moderated the effect of the foster care intervention on symptoms of psychopathology. However, there was a significant three-way interaction between intervention group, type of psychopathology, and age at assessment. Whereas effect sizes for disinhibited social engagement disorder, ADHD, and internalizing symptoms were similar across ages at assessment, the effect of the intervention on externalizing symptoms was close to zero at younger ages but medium in magnitude and significant in adolescence. In contrast, the effect of the intervention on reactive attachment disorder symptoms, although significant throughout development, was larger at younger ages than in adolescence (see the online supplement).

Sources of Variation Among Children in Foster Care: Timing and Stability of Placement

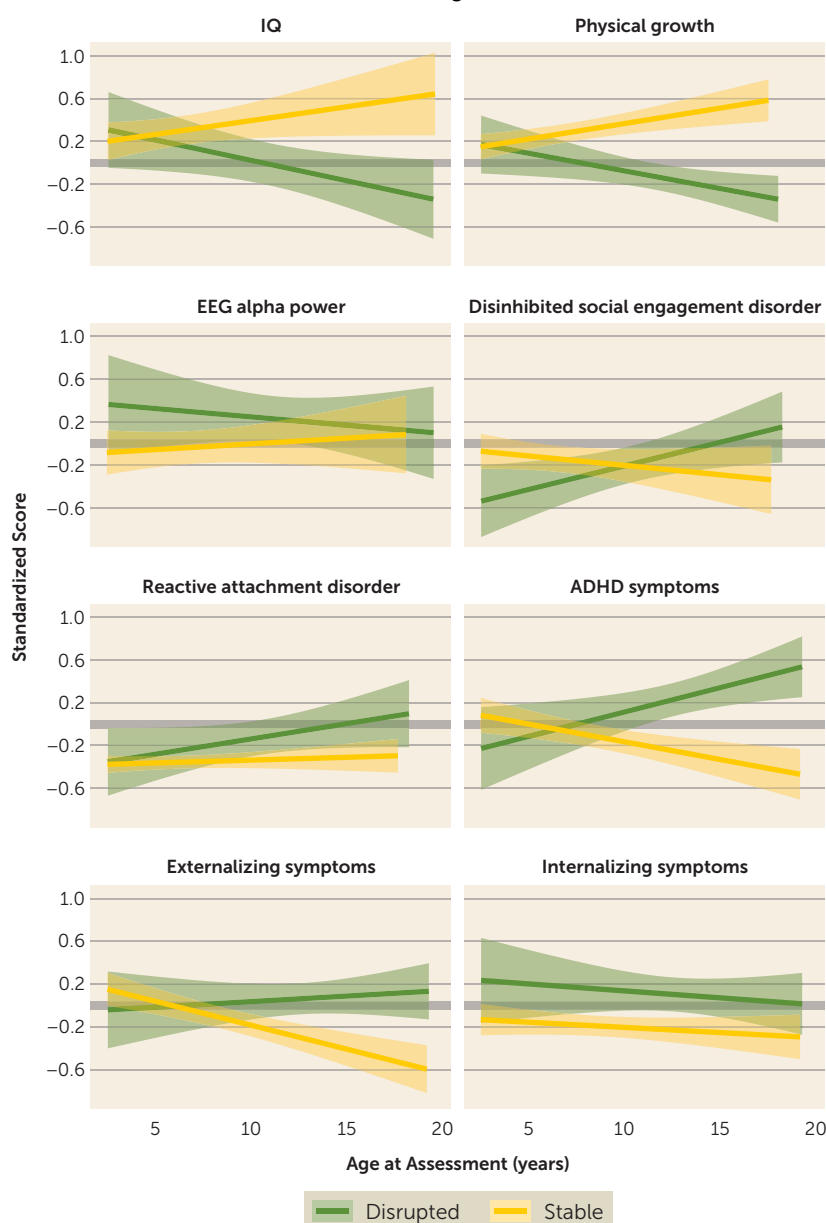
The associations of placement stability with scores for each cognitive, physical, and neural outcome and type of psychopathology by age at assessment are summarized in Figure 4. The associations of age at placement with scores for

each cognitive, physical, and neural outcome and type of psychopathology are summarized in Figure S15 in the online supplement.

Cognitive, physical, and neural outcomes. We found a significant overall effect of age at placement in foster care on children's cognitive, physical, and neural outcomes ($\beta = -0.18$, 95% CI = $-0.35, -0.03$, $p = 0.016$). On average, across assessment waves and outcome domains, children placed in foster care earlier within the range of 6–33 months had better cognitive, physical, and neural outcomes than did children placed in foster care later within this range. Outcome domain ($F = 4.71$, $df = 2$, 1325.48 , $p = 0.009$) and age at assessment ($F = 5.51$, $df = 1$, 1354.20 , $p = 0.019$) each moderated the association between age at placement in foster care and children's cognitive, physical, and neural outcomes. The magnitude of the effect of age at placement in foster care was largest for IQ ($\beta = -0.30$, 95% CI = $-0.48, -0.13$, $p < 0.001$), followed by EEG relative alpha power ($\beta = -0.21$, 95% CI = $-0.40, -0.03$, $p = 0.008$) and physical size ($\beta = -0.12$, 95% CI = $-0.29, 0.03$, $p = 0.116$). The effect of age at placement on IQ was significantly larger than on physical size but did not differ significantly between IQ and EEG alpha power or between EEG alpha power and physical size (see the online supplement). Further, age at placement was more strongly negatively associated with children's outcomes at younger compared with older ages (early childhood [42 months]: $\beta = -0.23$, 95% CI = $-0.40, -0.08$, $p = 0.002$; middle childhood [8 years]: $\beta = -0.18$, 95% CI = $-0.35, -0.03$, $p = 0.018$; adolescence [16 years]: $\beta = -0.09$, 95% CI = $-0.27, 0.08$, $p = 0.306$; see the online supplement). Sex did not moderate the effect of age at placement in foster care on children's cognitive, physical, and neural outcomes.

In interaction with age at assessment, placement stability explained variation in children's cognitive, physical, and neural outcomes ($\beta = 0.21$, 95% CI = $0.09, 0.33$, $p < 0.001$). Placement stability was not associated with children's cognitive, physical, and neural outcomes in early childhood ($\beta = -0.11$, 95% CI = $-0.31, 0.10$, $p = 0.344$) or middle childhood ($\beta = 0.07$, 95% CI = $-0.10, 0.23$, $p = 0.448$), but in adolescence, children who remained with their original foster family had better outcomes when examined across the broad cognitive, physical, and neural domain than children who had been disrupted from this family ($\beta = 0.37$, 95% CI = $0.16, 0.57$, $p < 0.001$).

FIGURE 4. Associations of placement stability among children randomized to foster care with outcomes in each domain across ages at assessment^a



^a Because scores are standardized within assessment wave, plots depict between-individual differences but do not show within-individual change across time. The graphs show linear regression lines of best fit, with shaded areas indicating standard error. ADHD=attention deficit hyperactivity disorder.

Psychopathology. There was no significant overall association of age at placement in foster care with children's symptoms of psychopathology when considered collectively across types of psychopathology and assessment waves ($\beta = 0.06$, 95% CI = $-0.06, 0.19$, $p = 0.296$). Age at assessment moderated the association between age at placement in foster care and symptoms of psychopathology ($F = 15.30$, $df = 1$, 2118.47 , $p < 0.001$). Age at placement in foster care was positively associated with symptoms of psychopathology in early childhood ($\beta = 0.14$, 95% CI = $0.01, 0.27$, $p = 0.032$) but was not associated with symptoms in middle childhood ($\beta = -0.08$,

95% CI = $-0.05, 0.20$, $p = 0.236$) or adolescence ($\beta = -0.04$, 95% CI = $-0.17, 0.09$, $p = 0.530$) (see the online supplement). Neither type of psychopathology nor sex moderated the association of age at placement in foster care with children's symptoms of psychopathology.

In interaction with age at assessment, placement stability was associated with children's symptoms of psychopathology ($\beta = -0.11$, 95% CI = $-0.20, -0.02$, $p = 0.019$). Placement stability was not associated with children's symptoms of psychopathology in early childhood ($\beta = 0.01$, 95% CI = $-0.16, 0.18$, $p = 0.944$) or middle childhood ($\beta = -0.09$, 95% CI = $-0.22, 0.04$, $p = 0.200$), but in adolescence, children who remained with their original foster family had fewer symptoms of psychopathology than children who had been disrupted from their original family ($\beta = -0.25$, 95% CI = $-0.40, -0.09$, $p = 0.002$).

DISCUSSION

In this study, we analyzed over 7,000 observations collected from 136 BEIP participants assessed from infancy through adolescence. Our goal was to quantify the overall effects of this randomized controlled trial of high-quality foster care as an alternative to institutional care on children's functioning across multiple developmental domains. We also examined sources of variation in children's outcomes. Using intent-to-treat analyses, we found that children who were randomized to foster care had better cognitive and physical outcomes and less severe symptoms of psychopathology than did their peers who remained in care as usual and experienced more prolonged exposure to psychosocially depriving conditions. The benefits of family-based care were remarkably consistent across development. Nonetheless, outcomes also differed on the basis of developmental domain, the life stage in which children were placed in family-based care, and whether this care was stable across childhood and adolescence.

Although the benefits of the foster care intervention overall have been narratively summarized (4, 10), the present analyses reflect the first quantitative synthesis of individual-level data from the BEIP across domains. Our findings provide the most robust and comprehensive evidence to date that children exposed to severe early psychosocial deprivation benefit substantially when they receive enriching, family-based care. We found causal effects of the foster care intervention on IQ, physical growth, symptoms of disorders of social relatedness (reactive attachment disorder and disinhibited social engagement disorder), and internalizing symptoms. Among these domains, IQ and disorders of social relatedness were most sensitive to the benefits of the intervention (standardized coefficients ranged from 0.35 to 0.60). The strong effects of the intervention on IQ are noteworthy, given that the foster care intervention was not specifically designed to improve cognitive functioning but rather to improve caregiver-child relationships. The BEIP offers a model for the types of placements to be supported for children who are abandoned or orphaned (see reference 39 for a review of the policy and practice recommendations). The

model of foster care used in the BEIP (4) encouraged foster parents to make a psychological commitment to the child, and thus differs from the model currently used in the United States, which emphasizes only instrumental care needs. The BEIP model also included regular support from trained social workers and U.S.-based psychologists to help foster parents meet the needs of children vulnerable to developmental and socioemotional difficulties.

The enhanced level of care for children after institutionalization may partially explain why the BEIP intervention outperformed in some domains the effects found in a recent meta-analysis of observational studies of recovery from institutionalization (2). For instance, although the BEIP findings are consistent with other studies indicating substantial recovery for cognitive development and physical growth, in contrast to the present findings of improved symptoms of psychopathology on average, the meta-analysis of observational studies does not indicate recovery in children's socioemotional functioning. Importantly, these observational studies generally did not include assessments of reactive attachment or disinhibited social engagement disorder, which have specific etiology in caregiving deprivation (40). In the present analyses, the effect of the intervention on internalizing problems was smaller in magnitude compared with the effects on disorders of social relatedness. Additionally, the effect of the intervention on externalizing problems (which excludes ADHD) emerged only in adolescence. Differences in findings between these observational studies and the BEIP may be related to the experimental design of the BEIP, which controlled for confounders (e.g., bias in selection of children for deinstitutionalization), and to the foster care intervention possibly delivering higher-quality care than is typical following deinstitutionalization (2).

When viewed through the conceptual lens of developmental cascades, early competence can generate further well-being, such that positive functioning spreads to other domains over time (41, 42). Generally, however, our intent-to-treat analyses did not reveal cascading positive effects of the foster care intervention. Instead, with the exception of externalizing problems, for which we observed a sleeper effect consistent with previous analyses in subsets of these data (17, 43), we found that the benefits of foster care were similar throughout development. Specifically, the positive effects of the intervention on children's functioning persisted across nearly two decades of follow-up assessments, during which children in both the intervention and care-as-usual groups experienced changes to their caregiving environments. Thus, the impact of the intervention can be described as rapidly apparent by age 30 months and sustained through late adolescence, with minimal evidence of fade-out over time. It is important to consider, however, that the intervention may have catalyzed subsequent positive experiences among children in the foster care group that are partially responsible for its enduring effect. Lasting group differences are likely both a product of early exposure to family-based care and the longer-term experiences this exposure initialized.

Consistent with previous analyses of discrete time points and domains (15–17, 19, 29), we found that among children who received the intervention, individual differences in timing of placement into foster care between ages 6 and 33 months and the stability of this placement were associated with outcomes in several areas. The present analyses enhance specificity in our understanding of these individual differences. While there was an overall association of age at placement with children's cognitive, physical, and neural functioning, such that children placed earlier fared better, this association depended on the outcome domain. Children placed into foster care earlier had significantly higher IQ scores and relative alpha power but did not differ in physical growth from children placed later. Further, for both symptoms of psychopathology and cognitive, physical, and neural outcomes, the effect of age at placement varied from infancy to adolescence. Specifically, the benefits of earlier placement into foster care were apparent in early childhood but faded out by adolescence, possibly as later life experiences diminished the potency of earlier events. Importantly, however, all children in the intervention group were placed "early" by most definitions (i.e., by age 33 months), which was likely a key aspect of the overall success of the intervention. Thus, the diminishing effect of age at placement should not be interpreted as evidence that early intervention is not important.

In contrast to the waning effect of age at placement, the effect of placement stability was largest in adolescence, when, overall, children who remained with their original foster families had better cognitive and physical outcomes and less severe symptoms of psychopathology relative to children who experienced placement disruptions. The emergence of the effect of placement stability later in development is likely related both to the fact that more children had experienced disruptions by adolescence and that disruptions have harmful consequences (44). Although it is possible that children who experienced placement disruptions differed to begin with from children with stable placements, supplemental analyses indicated that children with disrupted placements in later childhood and adolescence were similar at baseline to those who remained stable in terms of psychopathology, cognitive functioning, and physical growth. However, we cannot rule out the possibility of bidirectional effects between preexisting child characteristics that contributed to placement disruption and the harmful role that placement disruptions have on child functioning. Outside the context of deinstitutionalization, our findings are consistent with the literature documenting the importance of placement stability for the well-being of children placed in foster care following maltreatment in their families of origin (45–47).

It is important to note that we identified robust benefits of foster care as an alternative to institutional care. Findings regarding which domains of development were more or less sensitive to the intervention may be partially due to informant and/or measurement choices. For example, foster parents may be more likely to provide positive reports of their children than informants for children in institutional care. In

terms of measurement, to facilitate comparison of effect sizes across ages, we processed EEG data from each assessment wave using a common protocol and focused only on data recorded from electrode sites sampled at every wave. To reduce the number of analyses, we examined only relative alpha power. It is possible that different processing choices or alternative indices of brain electrical activity would have revealed significant effects of the foster care intervention. Nonetheless, we did identify an association of age at placement into foster care with relative alpha power, suggesting that this measure is sensitive to the timing of intervention. Because specific assessment tools changed based on age at assessment, we were not able to examine trajectories of children's functioning, which would have provided important information about within-individual development, such as the rate of growth and the shape of growth curves. Relatedly, between-individual differences in effect sizes based on age at assessment are relative to the specific assessment tools used at those ages and could be partially driven by differences in those tools. Given limitations of statistical power for three-way interaction analyses within the foster care group, we did not test the associations of timing and stability of placement with outcomes; thus, we cannot determine whether these associations varied based on the confluence of multiple factors, such as domain and developmental stage. Further, specific features of the institutional care or foster care environment in Bucharest at the time of the study may limit the degree to which the findings are generalizable to other institutional and foster care settings. Finally, although the BEIP provides firm causal evidence of the benefits of family placements for children after early institutional care, many questions remain unanswered, including fully understanding how aspects of the prenatal, early institutional, and eventual family environments influence recovery.

CONCLUSIONS

Millions of children worldwide experience psychosocial deprivation in institutions, and many more are neglected in their families of origin. Against this backdrop, 6.7 million children have lost a parent or caregiver as a result of the COVID-19 pandemic (48–50). As the only randomized controlled trial of foster care as an alternative to institutional care, the BEIP provides unique evidence for the causal effects of deprivation and subsequent caregiving enrichment on development. By quantitatively synthesizing data from the BEIP across nearly 20 years of follow-up assessments, this study addresses potential concerns about the robustness of the effects of this intervention. Specifically, using a common analytic approach for all outcomes and time points, we provide strong and conclusive causal evidence that children exposed to early deprivation benefit from high-quality family-based care, and, more broadly, that the nature of the early caregiving environment has an extensive and lasting impact on development. In line with recent policy recommendations (39), our findings indicate that providing high-quality and

stable family-based care, which includes biological, foster, or adoptive families, is critical for children's well-being, and, in turn, the well-being of society.

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Data sharing: Anonymized participant data can be made available through GitHub (https://github.com/lucysking/BEIP_comprehensive_analysis/tree/master).

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REFERENCES

- Desmond C, Watt K, Saha A, et al: Prevalence and number of children living in institutional care: global, regional, and country estimates. *Lancet Child Adolesc Health* 2020; 4:370-377
- van IJzendoorn MH, Bakermans-Kranenburg MJ, Duschinsky R, et al: Institutionalisation and deinstitutionalisation of children 1: a systematic and integrative review of evidence regarding effects on development. *Lancet Psychiatry* 2020; 7:703-720
- US Department of Health and Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau: Child Maltreatment 2019. Washington, DC, US Department of Health and Human Services, Children's Bureau, 2021. <https://www.acf.hhs.gov/cb/research-data-technology/statistics-research/child-maltreatment>
- Nelson CA, Fox NA, Zeanah CH: Foster care intervention; in Romania's Abandoned Children: Deprivation, Brain Development, and the Struggle for Recovery. Cambridge, Mass, Harvard University Press, 2014, pp 94-123
- Norman RE, Byambaa M, De R, et al: The long-term health consequences of child physical abuse, emotional abuse, and neglect: a systematic review and meta-analysis. *PLoS Med* 2012; 9:e1001349
- Strathearn L, Giannotti M, Mills R, et al: Long-term cognitive, psychological, and health outcomes associated with child abuse and neglect. *Pediatrics* 2020; 146:e20200438
- King LS, Humphreys KL, Gotlib IH: The neglect-enrichment continuum: characterizing variation in early caregiving environments. *Dev Rev* 2019; 51:109-122
- Zeanah CH, Gunnar MR, McCall RB, et al: Sensitive periods (chapter 6 of *Children Without Permanent Parents: Research, Practice, and Policy*). *Monogr Soc Res Child Dev* 2011; 76:147-162
- Zeanah CH, Nelson CA, Fox NA, et al: Designing research to study the effects of institutionalization on brain and behavioral development: the Bucharest Early Intervention Project. *Dev Psychopathol* 2003; 15:885-907
- Zeanah CH, Humphreys KL, Fox NA, et al: Alternatives for abandoned children: insights from the Bucharest Early Intervention Project. *Curr Opin Psychol* 2017; 15:182-188
- Millum J, Emanuel EJ: The ethics of international research with abandoned children. *Science* 2007; 318:1874-1875
- Zeanah CH, Fox NA, Nelson CA: The Bucharest Early Intervention Project: case study in the ethics of mental health research. *J Nerv Ment Dis* 2012; 200:243-247
- Miller FG: The randomized controlled trial as a demonstration project: an ethical perspective. *Am J Psychiatry* 2009; 166:743-745
- Almas AN, Degnan KA, Nelson CA, et al: IQ at age 12 following a history of institutional care: findings from the Bucharest Early Intervention Project. *Dev Psychol* 2016; 52:1858-1866
- Fox NA, Almas AN, Degnan KA, et al: The effects of severe psychosocial deprivation and foster care intervention on cognitive development at 8 years of age: findings from the Bucharest Early Intervention Project. *J Child Psychol Psychiatry* 2011; 52:919-928
- Guyon-Harris KL, Humphreys KL, Fox NA, et al: Course of disinhibited social engagement disorder from early childhood to early adolescence. *J Am Acad Child Adolesc Psychiatry* 2018; 57:329-335.e2
- Humphreys KL, Gleason MM, Drury SS, et al: Effects of institutional rearing and foster care on psychopathology at age 12 years in Romania: follow-up of an open, randomised controlled trial. *Lancet Psychiatry* 2015; 2:625-634
- Smyke AT, Zeanah CH, Gleason MM, et al: A randomized controlled trial comparing foster care and institutional care for children with signs of reactive attachment disorder. *Am J Psychiatry* 2012; 169:508-514
- Nelson CA, Zeanah CH, Fox NA, et al: Cognitive recovery in socially deprived young children: the Bucharest Early Intervention Project. *Science* 2007; 318:1937-1940
- Barch DM, Yarkoni T: Introduction to the special issue on reliability and replication in cognitive and affective neuroscience research. *Cogn Affect Behav Neurosci* 2013; 13:687-689
- Nosek BA, Hardwicke TE, Moshontz H, et al: Replicability, robustness, and reproducibility in psychological science. *Annu Rev Psychol* 2022; 73:719-748
- Guyon-Harris KL, Humphreys KL, Miron D, et al: Early caregiving quality predicts consistency of competent functioning from middle childhood to adolescence following early psychosocial deprivation. *Dev Psychopathol* 2021; 33:18-28
- Smyke AT, Zeanah CH, Fox NA, et al: A new model of foster care for young children: the Bucharest Early Intervention Project. *Child Adolesc Psychiatr Clin N Am* 2009; 18:721-734
- Bayley N: Bayley Scales of Infant Development, 2nd ed. New York, Psychological Corp, 1993
- Wechsler D: Wechsler Preschool and Primary Scale of Intelligence. San Antonio, Tex, Harcourt Assessment, 2000
- Wechsler D: The Wechsler Intelligence Scale for Children, 4th edition (WISC-IV). San Antonio, Tex, Psychological Corp, 2003
- Marshall PJ, Reeb BC, Fox NA, et al: Effects of early intervention on EEG power and coherence in previously institutionalized children in Romania. *Dev Psychopathol* 2008; 20:861-880
- Vanderwert RE, Marshall PJ, Nelson CA III, et al: Timing of intervention affects brain electrical activity in children exposed to severe psychosocial neglect. *PLoS One* 2010; 5:e11415
- Debnath R, Tang A, Zeanah CH, et al: The long-term effects of institutional rearing, foster care intervention and disruptions in

- care on brain electrical activity in adolescence. *Dev Sci* 2020; 23:e12872
30. Vanderwert RE, Zeanah CH, Fox NA, et al: Normalization of EEG activity among previously institutionalized children placed into foster care: a 12-year follow-up of the Bucharest Early Intervention Project. *Dev Cogn Neurosci* 2016; 17:68–75
 31. Smyke A, Zeanah CH: Disturbances of Attachment Interview. New Orleans, Tulane University School of Medicine, 1999
 32. Carter AS, Briggs-Gowan MJ, Jones SM, et al: The Infant-Toddler Social and Emotional Assessment (ITSEA): factor structure, reliability, and validity. *J Abnorm Child Psychol* 2003; 31:495–514
 33. Egger HL, Erkanli A, Keeler G, et al: Test-retest reliability of the Preschool Age Psychiatric Assessment (PAPA). *J Am Acad Child Adolesc Psychiatry* 2006; 45:538–549
 34. Essex MJ, Boyce WT, Goldstein LH, et al: The confluence of mental, physical, social, and academic difficulties in middle childhood, II: developing the MacArthur Health and Behavior Questionnaire. *J Am Acad Child Adolesc Psychiatry* 2002; 41:588–603
 35. Shaffer D, Fisher P, Lucas CP, et al: NIMH Diagnostic Interview Schedule for Children, Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *J Am Acad Child Adolesc Psychiatry* 2000; 39:28–38
 36. R Core Team: R: A Language and Environment for Statistical Computing. 2021. <https://www.r-project.org/>
 37. Bates D, Mächler M, Bolker B, et al: Fitting linear mixed-effects models using lme4. *J Stat Softw* 2015; 67:1–48
 38. Lüdtke D, Ben-Shachar MS, Patil I, et al: Extracting, computing, and exploring the parameters of statistical models using R. *J Open Source Softw* 2020; 5:2445
 39. Goldman PS, Bakermans-Kranenburg MJ, Bradford B, et al: Institutionalisation and deinstitutionalisation of children 2: policy and practice recommendations for global, national, and local actors. *Lancet Child Adolesc Health* 2020; 4:606–633
 40. Zeanah CH, Smyke AT: Disorders of attachment and social engagement related to deprivation; in Rutter's Child and Adolescent Psychiatry, 6th ed. Edited by Thapar A, Pine DS, Leckman JF, et al. Hoboken, NJ, John Wiley & Sons, 2015, pp 793–805
 41. Masten AS, Tellegen A: Resilience in developmental psychopathology: contributions of the Project Competence Longitudinal Study. *Dev Psychopathol* 2012; 24:345–361
 42. Masten AS, Cicchetti D: Developmental cascades. *Dev Psychopathol* 2010; 22:491–495
 43. Wade M, Fox NA, Zeanah CH, et al: Effect of foster care intervention on trajectories of general and specific psychopathology among children with histories of institutional rearing: a randomized clinical trial. *JAMA Psychiatry* 2018; 75:1137–1145
 44. Fisher PA, Mannering AM, Van Scoyoc A, et al: A translational neuroscience perspective on the importance of reducing placement instability among foster children. *Child Welfare* 2013; 92:9–36
 45. Clemens EV, Klopfenstein K, Lalonde TL, et al: The effects of placement and school stability on academic growth trajectories of students in foster care. *Child Youth Serv Rev* 2018; 87:86–94
 46. Rubin DM, O'Reilly ALR, Luan X, et al: The impact of placement stability on behavioral well-being for children in foster care. *Pediatrics* 2007; 119:336–344
 47. Villodas MT, Litrownik AJ, Newton RR, et al: Long-term placement trajectories of children who were maltreated and entered the child welfare system at an early age: consequences for physical and behavioral well-being. *J Pediatr Psychol* 2016; 41:46–54
 48. Hillis SD, Unwin HJT, Chen Y, et al: Global minimum estimates of children affected by COVID-19-associated orphanhood and deaths of caregivers: a modelling study. *Lancet* 2021; 398:391–402
 49. Hillis SD, Blenkinsop A, Villaveces A, et al: COVID-19-associated orphanhood and caregiver death in the United States. *Pediatrics* 2021; 148:e2021053760
 50. Unwin HJT, Hillis S, Cluver L, et al: Global, regional, and national minimum estimates of children affected by COVID-19-associated orphanhood and caregiver death, by age and family circumstance up to Oct 31, 2021: an updated modelling study. *Lancet Child Adolesc Health* 2022; 6:249–259

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Examination Questions for “A Comprehensive Multilevel Analysis of the Bucharest Early Intervention Project: Causal Effects on Recovery From Early Severe Deprivation”

1. What was the value in conducting a randomized controlled trial of foster care as an alternative to institutional care?
 - A. To assess the impact of neglect on children's emotional well-being
 - B. To allow for causal determinations about the impact of the intervention
 - C. To investigate the impact of early psychosocial deprivation on physical growth
 - D. To test for sex differences in the intervention's effectiveness
2. Which statement best captures the general effect of the intervention across children's development?
 - A. The intervention's impact tended to increase as children grew older
 - B. The intervention had the greatest effect during early infancy
 - C. The intervention was most effective during adolescence
 - D. For most domains, the intervention had a consistent effect throughout children's development
3. What domain(s) of psychopathology did the intervention demonstrate the largest overall effects?
 - A. Reactive attachment disorder and disinhibited social engagement disorder
 - B. Internalizing symptoms
 - C. Externalizing symptoms
 - D. ADHD symptoms