

Psychiatric Outcomes Following Severe Deprivation in Early Childhood: Follow-Up of a Randomized Controlled Trial at Age 16

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Objective: Early psychosocial deprivation is associated with increased risk for psychopathology, yet few studies have examined outcomes in adolescents. **Method:** At baseline (M age 22 months), 136 children from Bucharest, Romania, living in large institutions, were randomized into foster care (FCG) or to care as usual (CAUG). Caregivers completed psychiatric interviews regarding their children (52 FCG; 51 CAUG) at age 16 years ($M = 16.67$ years; $SD = 0.78$) to assess past year diagnoses and symptom counts. In addition, never-institutionalized community comparison children ($n = 47$) were included. **Results:** Ever-institutionalized children had higher rates of meeting criteria for any psychiatric disorder and higher symptom counts of internalizing, externalizing, attention-deficit/hyperactivity, and substance use disorders compared to never-institutionalized children ($ps < .05$). Using intent-to-treat analyses, we found that children in the CAUG had more than twice the rate of psychiatric disorders than children in the FCG ($OR = 2.48$, 95% CI [1.12, 5.48]). Furthermore, children in foster care who remained in their original placement did not significantly differ in their rates of psychiatric disorders compared to never-institutionalized children. **Conclusions:** There are many ways children can be separated from parents, including placement into institutional care. The current findings indicate that such placements are associated with significant risks for psychopathology. Moreover, we provide causal evidence for the long-lasting positive effect of foster care in reducing the risk of psychopathology in adolescence, especially among those in stable placements. These results provide strong evidence that early and stable placements into quality foster care may mitigate risk for psychopathology following severe early psychosocial deprivation.

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What is the public health significance of this article?

This randomized controlled trial finds causal effects of a foster care intervention on rates of psychiatric disorder in adolescence. Placement into long-term family-based care is associated with decreased risk for psychopathology among those with exposure to early adversity.

Keywords: randomized controlled trial, institutional care, psychopathology, adolescence

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Infants and young children are reliant on caregivers for survival, as well as species-expected nurturance and enrichment. In most cases, that caregiving is provided in the context of a family, with one or two caregivers (typically parents) who care for the child. Yet some children experience a deviation from this expected environment in the form of psychosocial deprivation or neglect (Humphreys & Zeanah, 2015; King, Humphreys, & Gotlib, 2019; McLaughlin, Sheridan, & Nelson, 2017; Nelson & Gabard-Durnam, 2020; Nelson, Zeanah, & Fox, 2019; Sheridan & McLaughlin, 2014). The absence of this species-expected experience, including insufficient responsive interaction with, and attention from, a caregiver, is common among children reared in institutional settings (e.g., orphanages). Experiences of psychosocial deprivation are associated with long-term negative outcomes (Nelson, Fox, & Zeanah, 2014; Rutter, Sonuga-Barke, & Castle, 2010; Zeanah, Gunnar, McCall, Kreppner, & Fox, 2011; Zeanah, Smyke, & Settles, 2006), including increased risk for psychopathology (Colvert et al., 2008; Humphreys, Gleason, et al., 2015; Wiik et al., 2011; Zeanah et al., 2009). While there is heterogeneity in the outcomes of children exposed to institutional care (Humphreys et al., 2018; Kreppner et al., 2007; Vorrria, Ntouma, & Rutter, 2015), it is important to identify malleable external factors in order to promote resilience following significant early adversity. This is particularly urgent given recent estimates that indicate that over five million children worldwide reside in institutions (Desmond, Watt, Saha, Huang, & Lu, 2020).

The Bucharest Early Intervention Project (BEIP) is the first and only randomized controlled trial of foster care for children reared in institutions (Nelson et al., 2014). Prior evidence from the BEIP indicated that children assigned to the foster care group (FCG) had lower rates and symptoms of psychopathology relative to those with prolonged institutional care (care as usual group; CAUG) at 54 months of age (Zeanah et al., 2009). However, children were assessed and placed into families at a mean age of 22 months, and thus the effects of early placements may fade over time as children experience placement changes such as adoptions and disruptions. Please see the [Appendix](#) for a Data Transparency statement regarding related publications from the BEIP.

Furthermore, adolescence is a period of heightened risk for psychopathology (Lee et al., 2014), including higher rates of internalizing, externalizing, and substance use disorders (SUDs) in this period (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Merikangas et al., 2010). Given that early adversity is a known risk factor for psychopathology (McLaughlin, Green, et al., 2012), those with a history of institutional care may be particularly vulnerable during this developmental period. It is unclear whether,

and to what degree, placement into foster care early in life may mitigate this risk.

In the present study, we conducted a follow-up of participants from the BEIP to examine rates of psychiatric disorders at age 16 years, the most recent age of assessment (after randomization, assessments were conducted at 30, 42, and 54 months, with follow-up assessments at 8, 12, and 16 years). This report has two primary and three exploratory aims.

Primary Aim 1: Examine Rates of Disorder at Age 16 Years by History of Institutional Care

We hypothesized that children with a history of institutional care would have greater psychopathology relative to never-institutionalized children, given that early exposure to psychosocial deprivation may be associated with long-term psychiatric difficulties (Golm et al., 2020; Rutter & Sonuga-Barke, 2010; van IJzendoorn et al., 2020).

Primary Aim 2: Examine Rates of Psychiatric Disorder at Age 16 Years Following Randomization of Institutionalized Young Children Into High-Quality Foster Care

Second, using an intent-to-treat (ITT) approach, we examined whether those assigned to the FCG differed from the CAUG 12 years after the trial concluded at age 54 months. From the BEIP, our previous reports on psychiatric outcomes from assessments at ages 54 months (Zeanah et al., 2009) and 12 years (Humphreys, Gleason, et al., 2015) indicated that children randomized to the FCG fared better than their counterparts randomized to the CAUG, although the domains in which these differences were found shifted from internalizing disorders to externalizing disorders across development. We hypothesized that randomization into families in early childhood would be associated with lower rates of disorders at age 16 years, and if so, would provide evidence that placement into families in early life is associated with more prolonged positive outcomes in mental health.

Exploratory Aim 1: Examine Rates of Psychiatric Disorder at Age 16 Years Based on Disruption From Foster Care

Third, there is evidence that placement changes or disruptions are associated with poorer well-being in foster children, even when considering baseline child behavior problems (Rubin, O'Reilly, Luan, & Localio, 2007). Furthermore, given findings from the BEIP linking placement disruption to psychopathology at age 12

years (Humphreys, Gleason, et al., 2015), we examined whether psychopathology outcomes differed as a function of the stability of foster care placement. Based on prior findings, we hypothesized that those children in stable placements in foster care would have lower rates of psychiatric disorder compared to those assigned to the FCG who experienced disruption from their foster placement.

Exploratory Aim 2: Examine Rates of Psychiatric Disorder at Age 16 Years by Sex

Based on previous findings of sex differences in disorder rates in this sample (Humphreys, Gleason, et al., 2015; Zeanah et al., 2009), and on types of disorder more prevalent in boys versus girls (Costello et al., 2003), we conducted exploratory analyses in which the above aims were rerun within each sex separately.

Exploratory Aim 3: Examine Rates of Psychiatric Disorder Change From Age 12 to 16 Years

Given that there is evidence of normative increases in psychopathology across adolescence (Paus, Keshavan, & Giedd, 2008), we examined whether rates of psychiatric disorder changed over this period and as a function of group. While psychopathology among children was expected to increase between the ages of 12 and 16 years, we hypothesized that those children with greater experiences of psychosocial deprivation would exhibit larger increases in psychopathology across this period.

Method

Participants

The participants in this investigation were 150 children who were assessed at a mean age of 16.67 years ($SD = 0.78$) as part of the BEIP study (Zeanah et al., 2003). Of the original 136 children, 103 were included in this follow-up (76%; Figure 1). The remaining 47 children were a never-institutionalized group (NIG) of Romanian children from the community. At baseline, 72 children who had never been institutionalized were recruited using birth records at the same maternity hospitals where the ever-institutionalized children had been born. Their parents were approached by personnel from the Institute for Maternal and Child Health in Bucharest, Romania, at the children's routine clinic visits and invited to participate. They were matched to the other groups by child age and sex. Given attrition of this community comparison group, at the age 8 follow-up, an additional 61 children were recruited from local elementary schools, the Institute of Maternal and Child Health clinics, and related pediatric clinics in Bucharest. Children in this group were matched on age, sex, and ethnicity to study participants. These clinics are part of the National Health Service in Romania and are attended by families ranging from poor to upper-middle class; they draw children from all sectors of Bucharest and are representative of the city's population. Sixty-one percent of the sample was of Romanian ethnicity (for ethnicity by group, see Table 1).

Of the originally recruited sample, attrition was largely due to participants selecting to opt out from further assessments when contacted by the study staff. In some cases, the participants had moved away from Bucharest or our team was no longer able to

contact them. As noted in the online supplemental materials (see supplemental Tables 1–2), those with and without psychopathology data at age 16 did not significantly differ by sex, gestational age at birth, age at entry into institutional care, or percent time in institutional care.

Following approvals by the institutional review boards of the three principal investigators' universities (University of Minnesota; University of Maryland; Tulane University School of Medicine) and by the local Commission on Child Protection in Bucharest, the study commenced in collaboration with the Institute of Maternal and Child Health of the Romanian Ministry of Health. A data safety monitoring board in Bucharest reviewed the assessments for the current follow-up. Consent was obtained and signed by each child's legal guardian and assent was obtained from each child. Written [or verbal] informed consent was obtained from all participants. Ethical considerations are discussed in detail elsewhere (Millum & Emanuel, 2007; Zeanah, Fox, & Nelson, 2012). The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human participants were approved by institutional review boards at Boston Children's Hospital, Tulane University School of Medicine, and the University of Maryland. Participants received modest financial compensation for their visit.

Randomization and Masking

Following baseline assessments, children were randomly assigned to the CAUG or FCG by drawing participant numbers from a hat. Following randomization (occurring at mean age = 22 months), the study had a noninterference policy and all subsequent placement decisions were made by Romanian child protection authorities. At baseline, children who would later be randomized to FCG and CAUG were comparable on all measures, including caregiver reports of behavior problems (Zeanah et al., 2003). In the years following randomization, in addition to some CAUG children obtaining family placements, some FCG children were returned to the parents who had abandoned them, some were placed in later emerging government foster care, and some were later readmitted to institutions (see Figure 1).

The ITT groups at age 16 years comprised 51 children in the CAUG and 52 children in the FCG. As noted above, there were 47 comparison children in the NIG (see Table 1). In addition to considering the original randomization groups for those children ever institutionalized, we further divided children randomized to the FCG based on their current placements to gauge potential differences related to long-term placement stability. Among those 52 children originally assigned to the FCG, at the age 16 assessment, 24 remained with the study-sponsored foster family with whom they were originally placed (or moved to another study-sponsored foster family within 12 months of the study launch). We considered these children as having a stable foster care placement and grouped them as FCG-Stable. The 27 children assigned to the study-sponsored foster care but no longer were residing with that family at the age 16 assessment were considered to have had one or more placement disruptions, and therefore were grouped as FCG-Disrupted. One child assigned to the FCG was reunited with her biological family prior to placement and therefore was not



BEIP: CONSORT at Age 16

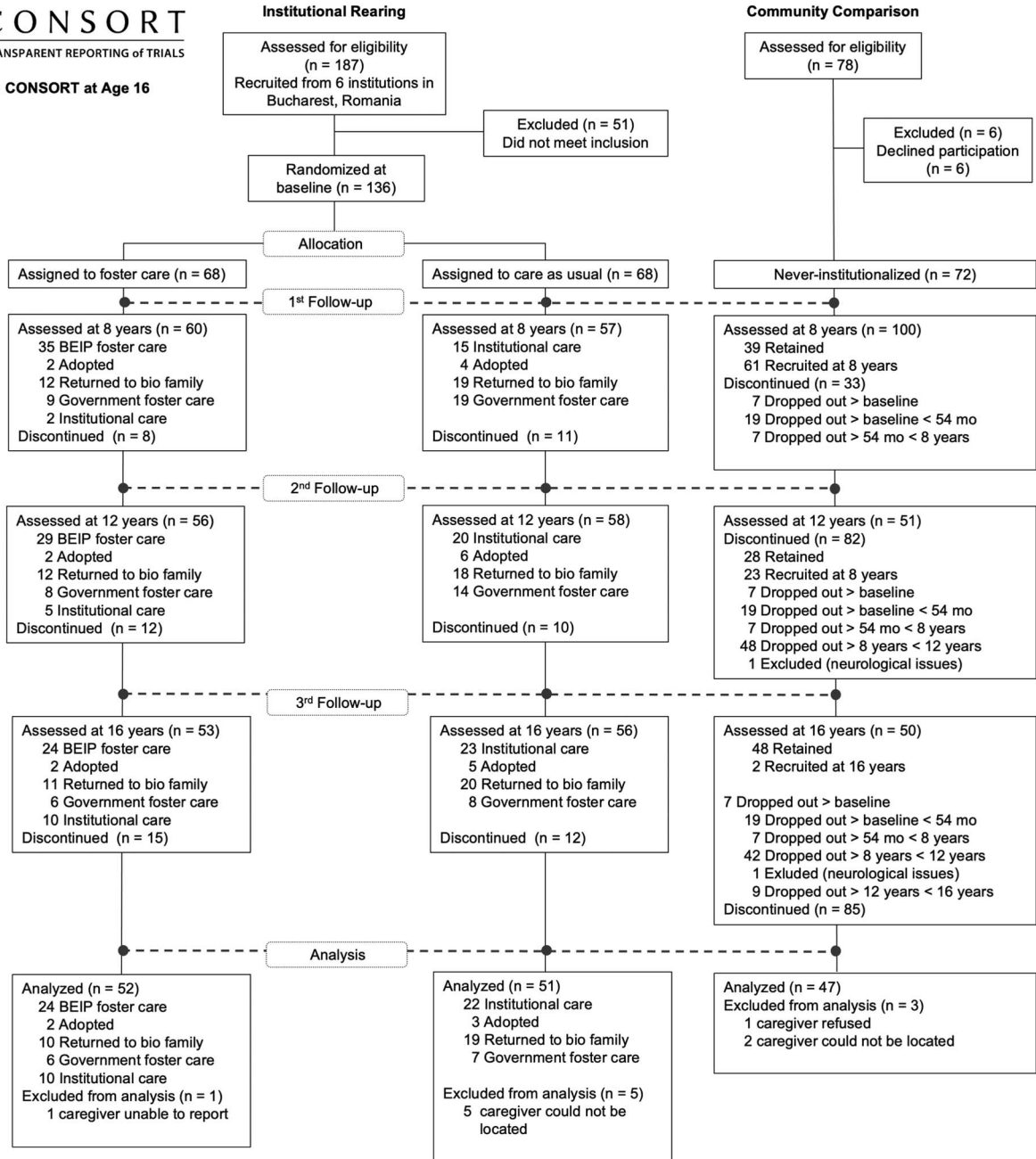


Figure 1. Group status at age 16 years for children living in Romanian institutions who were assigned to usual care or foster care (CONSORT).

included in stability analyses given that this child was neither stably placed in foster care nor disrupted from a foster family placement.

Measures

We administered the computerized Diagnostic Interview Schedule for Children, 4th edition (DISC-IV; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) to each caregiver to ascertain DSM-IV (American Psychiatric Association, 1994) diagnostic cri-

teria for ADHD, alcohol use disorder, anorexia nervosa, bipolar disorder, bulimia nervosa, conduct disorder, dysthymia, generalized anxiety disorder, marijuana use disorder, major depressive disorder, nicotine dependence, obsessive-compulsive disorder, oppositional defiant disorder, other SUD, panic disorder, posttraumatic stress disorder, separation anxiety disorder, social phobia, schizophrenia, and tic disorder within the past year. Specific phobia was not included in the present analyses. This structured interview probes symptom levels, duration/persistence, age of on-

Table 1
Demographic Characteristics by Care as Usual, Foster Care, and Never Institutionalized Groups

| Group | Sex | | Age | | Romanian ethnicity | |
|--|------------------------|-----------------------|----------|-----------|--------------------|----|
| | Girls (<i>n</i> = 79) | Boys (<i>n</i> = 71) | <i>M</i> | <i>SD</i> | <i>N</i> | % |
| Care as usual (<i>n</i> = 51) | 25 | 26 | 16.56 | 0.78 | 25 | 49 |
| Foster care (<i>n</i> = 52) | 25 | 27 | 16.48 | 0.71 | 30 | 58 |
| Disrupted (<i>n</i> = 27) ^a | 13 | 14 | 16.53 | 0.76 | 13 | 48 |
| Stable (<i>n</i> = 24) | 11 | 13 | 16.45 | 0.64 | 16 | 67 |
| Never institutionalized (<i>n</i> = 47) | 29 | 18 | 16.98 | 0.76 | 36 | 95 |

^a One foster care participant is not included in stability groupings because she was reintegrated into her biological family prior to placement in the study sponsored foster care.

set, and functional impairment. The DISC was translated into Romanian, back-translated into English, and assessed for meaning at each step by bilingual research staff. For children living with biological parents or foster parents, the mother reported on the child's behavior. For children living in institutions, an institutional caregiver who worked with the child regularly and knew them well reported on the child's behavior. The number of symptoms endorsed for each diagnosis was recorded, and composite scales were calculated. "Internalizing disorders" comprised depression and anxiety disorders. "Externalizing disorders" comprised oppositional defiant disorder and conduct disorder. ADHD was considered independently. SUD included nicotine dependence, alcohol use disorder, marijuana use disorder, and any other SUD.

Intervention

Because foster care was extremely limited in Bucharest at the outset of the study, the investigators, along with Romanian collaborators, created a foster care network. The foster parents were supported by social workers in Bucharest who received regular consultation from U.S. clinicians. Fifty-six foster families were selected to care for 68 children. Foster care was designed to be affordable, replicable, and grounded in findings from developmental research on enhancing caregiving quality (see Nelson et al., 2014, and Smyke, Zeanah, Fox, & Nelson, 2009, for more details). Foster parents were recruited by BEIP staff, consented to background checks, and were trained by a nongovernmental organization in Bucharest. In addition, most foster parents visited institutions and learned about the routines and typical behaviors of the children there. All foster parents had at least a high school education, but most had additional vocational training or had completed college. A small percentage (5%) had never been previously employed, and 27% were retired. Single-parent families accounted for 46% of the foster families.

The BEIP model of foster care was attachment-based and child-centered, emphasizing understanding and valuing each child as an individual. It emphasized the importance of making a long-term commitment to the child given that it was unclear at the outset of the study if any children would return to their biological families. Three social workers on the BEIP study team oversaw foster care, helping foster parents manage the complex and challenging behaviors of postinstitutionalized infants and toddlers. Training content included basic behavioral management techniques, language stimulation approaches, and fostering attachment between young

children and foster parents. BEIP social workers received regular weekly consultation from experienced U.S. clinicians via video calls to maintain consistency in their approach, adapt to unforeseen challenges, and feel supported in their challenging assignments (see Nelson et al., 2014, and Smyke et al., 2009, for more details).

Statistical Analysis

For primary aims 1 and 2 and exploratory aim 1, disorder prevalence was obtained for each group and presented as raw data (i.e., prior to adjustment for covariates). Furthermore, omnibus tests of the effect of group as Wald chi-square values, degrees of freedom, and *p* values, along with 95% confidence intervals (CIs) of group differences, are presented from generalized linear models covarying participant age and sex. For exploratory aim 2, the above approach was implemented with the exception that sex was not included as a covariate given that analyses were conducted in girls and boys separately. We specified a binary logistic outcome given that all disorder level variables were coded as 0 = no disorder, 1 = disorder. Additional analyses on symptom level outcomes can be found in the supplement. For these we used a negative binomial regression, a type of generalized linear model used to model count data. Lastly, for exploratory aim 3 we examined changes in the rates of disorders and symptoms by domain from the age 12 and 16 assessments (see online supplemental materials for more details). For our primary aims, we implemented the Benjamini-Hochberg adjustment (Benjamini & Hochberg, 1995) to reduce the risk for Type I errors (selecting a 10% false discovery rate). For our exploratory analyses, no adjustments were made for multiple comparisons given that these analyses are intended to be descriptive, and we emphasize effect sizes rather than *p* values.

Results

Disorder Rates by History of Institutional Care

For primary aim 1, we first examined rates of meeting diagnostic criteria for any disorder (i.e., presence or absence of one or more disorder). The ever-institutionalized group (EIG; i.e., CAUG and FCG considered jointly) had higher disorder rates than the NIG (Wald $\chi^2 = 22.03$, *df* = 1, *p* < .001; see Table 2), after including sex and age at assessment in the model. However, there was no difference between EIG and NIG on rates of internalizing

Table 2

Rates of Psychiatric Disorders at Age 16 by Intent to Treat Groupings and Institutional Care History Groupings

| Disorder category | Care as usual (<i>n</i> = 51) | Foster care (<i>n</i> = 52) | Difference [95% CI] | <i>p</i> value | Ever placed in institution (<i>n</i> = 103) | Never placed in institution (<i>n</i> = 47) | Difference [95% CI] | <i>p</i> value |
|-------------------|-----------------------------------|---------------------------------|------------------------|----------------|--|--|------------------------|-----------------|
| Any disorder | 61% | 39% | .23 [.04, .42] | .020 | 50% | 15% | .35 [.20, .49] | <.001 |
| Any internalizing | 18% | 4% | .14 [.02, .25] | .021 | 11% | 4% | .07 [−.02, .15] | .129 |
| Any externalizing | 42% | 28% | .15 [−.04, .33] | .126 | 35% | 11% | .24 [.11, .37] | <.001 |
| ADHD | 24% | 21% | .02 [−.14, .18] | .780 | 22% | 0% | .22 [.14, .30] | <.001 |
| SUD | 2% | 6% | −.04 [−.11, .04] | .322 | 4% | 0% | .04 [.00, .08] | .042 |

Note. Psychiatric disorder %. ADHD = attention-deficit/hyperactivity disorder; SUD = substance use disorder. Age at assessment and sex were included as covariates for presentation of group differences and 95% CI. Tests comparing groups with 0 cases involved quasi-complete separation and the validity of the statistics are uncertain. Values are provided for illustrative purposes. *p* values in boldface are statistically significant after applying a Benjamini-Hochberg adjustment with a 10% false discovery rate to avoid Type I errors. The correction was calculated separately for the five tests between care as usual and foster care groups and the five tests between ever placed in institution and never placed in institution.

disorders (Wald $\chi^2 = 2.30$, $df = 1$, $p = .129$). Rates of externalizing disorders, ADHD, and SUDs differed significantly between EIG and NIG children (Wald $\chi^2 = 13.04$, $df = 1$, $p < .001$; Wald $\chi^2 = 27.09$, $df = 1$, $p < .001$; Wald $\chi^2 = 4.15$, $df = 1$, $p = .042$, respectively). In all cases, higher rates were found among those with histories of institutional rearing. It should be noted that for some cells, there were no cases (i.e., zero children who met criteria for a given disorder), and statistical results from these analyses should be interpreted with caution. Instead, we suggest readers focus on the magnitude of the rates of disorder within each group as a better indicator of group differences.

Disorder Rates by Intent-to-Treat Grouping

For primary aim 2, we examined rates of meeting diagnostic criteria for disorders based on initial group assignment of those ever institutionalized. Individuals randomized to FCG had significantly lower rates of meeting diagnostic criteria for any disorder relative to those randomized to CAUG (Wald $\chi^2 = 5.41$, $df = 1$, $p = .020$; see Table 2). Similarly, individuals in the FCG had lower rates of internalizing disorders than those in the CAUG (Wald $\chi^2 = 5.29$, $df = 1$, $p = .021$). Although the pattern was similar, group differences did not reach statistical significance for externalizing disorders (Wald $\chi^2 = 2.34$, $df = 1$, $p = .126$). No differences were found in rates of ADHD (Wald $\chi^2 = 0.08$, $df = 1$, $p = .780$) or SUD (Wald $\chi^2 = 0.98$, $df = 1$, $p = .322$) between FCG and CAUG.

Disorder Rates by Placement Stability

Exploratory aim 1 examined rates of psychiatric disorder by placement stability. Given that there were substantial changes in placement following initial randomization, we examined the potential association of placement stability in the FCG, setting aside the original ITT grouping. We examined two groups of children from the FCG: (1) those who remained in their original study-sponsored foster placement (or were placed within the first 12 months of the study with this family; FCG-Stable), and (2) those who were placed in a study-sponsored foster family and no longer resided with this family at the age 16 follow-up (FCG-Disrupted). Given evidence that children who experience more placement disruptions may differ in characteristics that may increase the risk for disruption (e.g., behavioral difficulties; Leathers, 2006), we

sought to explore the potential for preexisting child differences or “child effects” in examining which children ultimately were or were not disrupted from their foster care placement. We compared these two groups based on psychiatric symptoms, IQ scores, and percent time in institutional care at age 54 months (i.e., the age at which the randomized controlled trial was completed and transfer of the foster care network was made to Romanian authorities). We found no group differences in total psychiatric symptoms assessed at age 54 months (mean difference 95% CI [−1.95, 8.67]), full scale IQ at age 54 months (mean difference 95% CI [−14.34, 10.50]), or percent time spent living in institutions through age 54 months (mean difference 95% CI [−10.31, 11.76]), indicating that significant differences between these groups were not present at the end of the trial. Such findings bolster the idea that if differences are found at age 16 years, they may be better explained by the placement disruption than preexisting child differences.

Analyses examining individuals based on four groups (CAUG, FCG-Disrupted, FCG-Stable, and NIG) revealed a significant omnibus test for group on meeting criteria for any psychiatric disorder at age 16 (Wald $\chi^2 = 24.25$, $df = 3$, $p < .001$; see Table 3). Pairwise comparisons adjusting for age and sex indicated that the CAUG and FCG-Disrupted had higher rates of psychiatric disorder than the FCG-Stable and NIG children, and within each set, groups did not differ from one another.

The omnibus test did not reach statistical significance for internalizing disorders (Wald $\chi^2 = 6.54$, $df = 3$, $p = .088$). However, pairwise comparisons indicated that the CAUG had significantly higher rates of internalizing disorder than all other groups.

A significant group effect was found for externalizing disorders (Wald $\chi^2 = 13.12$, $df = 3$, $p = .004$). Participants in the CAUG and FCG-Disrupted had significantly higher rates of externalizing disorders than those in the NIG. In addition, the CAUG had significantly higher rates of externalizing disorders than did the FCG-Stable.

There was no significant omnibus effect for ADHD (Wald $\chi^2 = 2.13$, $df = 3$, $p = .546$). However, pairwise comparisons found that those in the CAUG and FCG-Disrupted had significantly higher rates of ADHD than those in the NIG.

The omnibus test for group was not statistically significant for SUDs (Wald $\chi^2 = 1.20$, $df = 3$, $p = .752$). No pairwise comparisons within groups reached statistical significance.

Table 3
Rates of Psychiatric Disorders at Age 16 for Care as Usual, Disrupted Foster Care, Stable Foster Care, and Never-Institutionalized Groups

| Disorder category | Care as usual (n = 51) | Disrupted foster care (n = 27) | Stable foster care* (n = 24) | Never placed in institution (n = 47) | Usual vs. disrupted (differences [95% CI]) | Usual vs. stable (differences [95% CI]) | Usual vs. never (differences [95% CI]) | Disrupted vs. stable (differences [95% CI]) | Disrupted vs. never (differences [95% CI]) | Stable vs. never (differences [95% CI]) |
|-------------------|------------------------|--------------------------------|------------------------------|--------------------------------------|--|---|--|---|--|---|
| Any disorder | 61% ^a | 56% ^a | 21% ^b | 15% ^b | .05 [-.18, .29] | .41 [.20, .62] | .46 [.29, .63] | .35 [.10, .60] | .40 [.19, .62] | .05 [-.14, .25] |
| Any internalizing | 18% ^a | 4% ^b | 4% ^b | 4% ^b | .14 [.01, .27] | .13 [.00, .27] | .13 [.01, .26] | .00 [-.11, .10] | -.01 [-.10, .09] | .00 [-.10, .10] |
| Any externalizing | 42% ^a | 39% ^{ab} | 17% ^{b,c} | 11% ^c | .04 [-.20, .27] | .25 [.05, .46] | .31 [.15, .48] | .22 [-.02, .46] | .27 [.07, .48] | .06 [-.12, .23] |
| ADHD | 24% ^a | 30% ^a | 13% ^a | 0% ^b | -.06 [-.27, .15] | .11 [-.06, .28] | .23 [.11, .35] | .17 [-.04, .39] | .29 [-.12, .47] | .12 [-.01, .25] |
| SUD | 2% ^a | 8% ^a | 4% ^a | 0% ^a | -.06 [-.17, .06] | -.02 [-.12, .07] | .02 [-.02, .06] | .04 [-.10, .17] | .08 [-.03, .19] | .04 [-.04, .13] |

Note. Psychiatric disorder %. ADHD = attention-deficit/hyperactivity disorder; SUD = substance use disorder. Age at assessment and sex were included as covariates for presentation of group differences and 95% CI. Groups with matching superscripts did not significantly differ from one another. Tests comparing groups with 0 cases involved quasi-complete separation and the validity of the statistics are uncertain. Values are provided for illustrative purposes.

* One FCG was excluded from these analyses as she was reunited with her biological family prior to placement into a study-sponsored foster placement.

Analyses by Sex

For exploratory aim 2 we examined rates of psychiatric disorder within each sex (see [supplemental Table 5](#)). Briefly, descriptive information shows that more ever-institutionalized boys met criteria for any disorder than girls (57% vs. 42%). Institutional care history was associated with increased rates of psychiatric disorder among both girls and boys, however, although the magnitude of the intent-to-treat effect was similar in both sexes, only among girls was the group difference statistically significant.

Age 12 to 16 Years Rates of Disorders

Given the same diagnostic interview was used at ages 12 and 16 years, for exploratory aim 3 we examined changes in disorders across these two assessment waves. As seen in [supplemental Table 7](#), only among the CAUG did rates of meeting diagnostic criteria for any psychiatric disorder increase significantly from age 12 to 16 years. Furthermore, at the domain level, increased rates of internalizing disorders were found for the CAUG from age 12 to 16 years.

Discussion

The present study examined rates of psychiatric disorder in adolescence (age 16 years) from BEIP study participants. Our primary aims established that those ever institutionalized, as a group, experienced greater rates of psychiatric disorder than those never institutionalized. Furthermore, foster care placement for infants and toddlers who had previously experienced severe psychosocial deprivation in institutional care had a causal effect in reducing psychiatric problems in adolescence. The BEIP trial ended when children were age 54 months, and this follow-up of participants at age 16 years demonstrates the persistent benefits of the intervention during a developmental period in which psychopathology is known to increase (Lee et al., 2014). Indeed, our results show that, while the proportion of children who meet criteria for any disorder increases from age 12 to 16 years, this increase appears to be driven by CAUG participants. These findings underscore the power of early family placement in mitigating the risks posed by early psychosocial deprivation in that those randomized to care as usual were at over twice the risk ($OR = 2.48$, 95% CI [1.12, 5.48]) for meeting criteria for a psychiatric disorder at age 16 years than were those children randomized to foster care.

Institutional Care Exposure

These findings build on the growing literature documenting increased risk for psychopathology in adolescence for those exposed to institutional care in early life (Golm et al., 2020; Sonuga-Barke et al., 2017; Wade, Fox, Zeanah, & Nelson, 2018). Results from primary aim 1 underscore that adolescents with and without institutional care exposure are likely to differ in rates of psychiatric disorder. The majority of research on psychopathology among children with a history of institutional care consists of adoption studies, in which families in the U.S. or U.K. adopt children who resided in institutions for the early months or years of life. For example, rates of clinically concerning inattention/overactivity in early adolescence are much higher among Romanian children

adopted into the U.K. following at least six months of deprivation relative to U.K. adoptees or Romanian children who spent less than six months in institutional care (Stevens et al., 2008). Of course, when comparing children with and without exposure to institutional care, one cannot be certain that differences are fully explained by institutional care exposure. Community comparison children, including in our study, likely differed in other important ways (e.g., prenatal care, diet, genetic risk) given that parents who do and do not place their children in institutional care likely differ in their levels of resources, stress exposure, and other characteristics.

Causal Effects of the Intervention

Our primary aim 2 examined whether, using a conservative intent-to-treat approach, we found a causal effect of the foster care intervention being protective for psychiatric disorder risk. Given that functional impairment is a requirement to meet criteria for a psychiatric disorder, these findings highlight not only the higher levels of symptoms experienced among those randomized to the CAUG, but also that symptoms interfere with the functioning of these adolescents in at least two settings. This is an approach not available when considering the structure of psychopathology (see Wade et al., 2018, for psychopathology structure within this sample). When considering psychiatric disorders in this sample (Zeanah et al., 2009), children were first assessed at age 54 months (at the formal end of the intervention trial). Preschool-age children with a history of institutional care had higher rates of any disorder than those in the community comparison group (53% vs. 22%). In addition, rates were higher among the CAUG relative to the FCG (62% vs. 46%). At age 12 years, rates of meeting criteria for any psychiatric disorder were lower than those found at age 54 months, although differences persisted based on institutional care history and ITT group (Humphreys, Gleason, et al., 2015). Furthermore, given the number of placement changes since the formal end of the intervention, we examined the stability of the foster care placement, finding large differences in rates of psychopathology as a function of stable placement. The findings from the present study replicate and extend these earlier papers from the study. In terms of extensions, we demonstrate that in mid-adolescence (i.e., age 16 years), a developmental period characterized by higher rates of disorders (Lee et al., 2014), we continue to see differences based on the randomized controlled trial grouping.

Stability of Foster Care Placement

Importantly, we find evidence that events that occurred postrandomization (i.e., foster care placement disruptions) are a meaningful predictor of risk for psychopathology in mid-adolescence. Specifically, we found that children placed in foster care who remained with the same family through age 16 did not significantly differ in disorder risk or symptom levels compared to never-institutionalized children. These findings are bolstered by the fact that there were no differences detected at the trial's conclusion between those who were later disrupted and those who remained in stable placements, compatible with the idea that disruptions led to increased psychopathology rather than the reverse. This work is in line with prior research from U.S. foster care, in which placement disruptions predicted more negative outcomes (Rubin et al., 2007).

This does not preclude the possibility that unmeasured child or foster family characteristics may have contributed to these differences, as other work finds that children's baseline behavioral difficulties are associated with increased risk for placement disruption (Leathers, 2006). In particular, children with significant emotional and behavioral difficulties are at increased risk for disruption, and merit particular attention in finding permanent placements (Redding, Fried, & Britner, 2000). However, if poorer outcomes derive from placement disruptions driven by factors unrelated to child characteristics, this provides guidance about mitigating long-term risk for children who experienced severe early adversity. Specifically, these findings indicate that ensuring stable family placements may be critically important for children removed from adversity and placed in foster care. Further evidence of the negative consequences of placement disruptions comes from the results comparing those disrupted with those in the CAUG, as rates of disorder and levels of symptoms were comparable in these two groups at age 16 years.

Although the context of the foster care in this study differs in meaningful ways from foster care in the U.S. (i.e., the foster families in the study were asked to psychologically commit to the child and love the child as if they were their own; this may be a useful model to improve U.S. foster care that typically is considered a temporary intervention focused on meeting instrumental care needs), the findings regarding placement stability resonate across both contexts (and are consistent with other work indicating placement longevity rather than type [e.g., adoption, foster] is more important for child well-being; McSherry, Fargas Malet, & Weatherall, 2016). Children fare best with stable, consistent, and supportive caregivers, and movement between placements is likely to be associated with significant psychological adjustment (for additional discussion of parent-child separation, see Humphreys, 2019). In addition, evidence that the duration of time with a current family is associated with better outcomes in children who experienced placement disruptions (Fernandez, 2009) suggests that other factors among those in the FCG-Disrupted group may be relevant for understanding variation in child outcomes. Children who experience foster care in the U.S. have, on average, poorer outcomes than do comparison samples (Gypen, Vanderfaeillie, De Maeyer, Belenger, & Van Holen, 2017; Turney & Wildeman, 2016), although it is difficult to disentangle the contributions of early care history, removal from attachment figures, and subsequent experiences in foster care when explaining variability in child functioning.

Sex/Gender

Although findings were similar across sexes, different patterns were found relative to rates of any psychiatric disorder in those disrupted from foster care. Specifically, boys who were disrupted fared worse than disrupted girls in terms of percent with any disorder (71% boys vs. 39% girls), while those in stable foster care had similar disorder rates (23% boys vs. 18% girls). There is mixed evidence for sex-specific vulnerability to adversity (Humphreys et al., 2018; Ordaz & Luna, 2012), and these findings point to the potential for boys to be more sensitive to placement disruptions. Generally, we observed lower rates of psychopathology among girls relative to boys, regardless of the history of psychosocial deprivation, which is similar to other work focused more

broadly on competent functioning following adversity (e.g., McGloin & Widom, 2001), as well as work from this sample finding that girls from the NIG, FCG, and CAUG were more likely to be functioning competently than their male counterparts (Humphreys et al., 2018).

Changes From Age 12 to 16 Years

Our analyses examining changes in psychopathology from ages 12 to 16 years indicated that rates of psychiatric disorders are increasing during this period, although this increase was only statistically significant among the CAUG (rates of meeting criteria for any disorder increased 8% and 9% for the FCG and NIG individuals, respectively, while rates in the CAUG jumped 19% from ages 12 to 16 years).

Attention-Deficit/Hyperactivity Disorder

Persistent elevations in ADHD symptoms and diagnoses have been documented in this study across the children's developmental stages (Humphreys, Gleason, et al., 2015; McLaughlin et al., 2010; Zeanah et al., 2009), and, unlike both internalizing and externalizing symptoms, foster care did not result in ADHD symptom reduction. Despite language in the *DSM-5* indicating that the early environment is unlikely to play an etiological role in the development of ADHD, the high rates in this sample (and other samples of children experiencing stress and adversity) underscore the strong possibility that early environmental experiences may set into motion increased risk for ADHD (see Humphreys et al., 2019; Humphreys & Zeanah, 2015). The results from this study do not find that later family care is able to reduce ADHD symptoms, suggesting that a sensitive period for environmental influences on ADHD may be in early infancy.

Persistence Versus Fadeout

Of particular interest to those considering the long-term effects of interventions in early childhood, the findings here offer a counterexample to those disappointed by the fade-out for early interventions that is often documented (i.e., initial gains related to the intervention are lost at follow-up; for discussion of these issues, see Bailey, Duncan, Odgers, & Yu, 2017). One reason we continue to see long-term persistence in effects of foster care is likely due to the sustained nature of the intervention. These children are not only being placed into family care where more responsive and child-centered experiences occur, but also the stability affords the formation of secure attachment relationships and meets far more than instrumental care needs through a consistent, long-term relationship. While the primary aim of this article was to document whether the intervention had persisting effects, there are several plausible mechanistic explanations linking foster care to reduced psychopathology that our group has previously considered, including attachment security (McGoron et al., 2012; McLaughlin, Zeanah, Fox, & Nelson, 2012), caregiver responsiveness to child distress (Humphreys, McGoron, et al., 2015), and executive function (McDermott et al., 2013; Troller-Renfree, Zeanah, Nelson, & Fox, 2018; Wade, Zeanah, Fox, & Nelson, 2020). Additional mechanistic pathways may include neurobiological effects of quality caregiving, perhaps including stress response and brain structure and function.

Limitations

Several limitations merit comment, including the small number of participants with complete participation in the trial follow-up, attrition of community comparison participants, and the large number of statistical tests run. While the retention of 76% of initial trial participants in the context of this longitudinal study is a strength, we acknowledge that sample size is related to the power available to detect statistical significance. We included the Benjamini-Hochberg correction for multiple comparison for our primary analyses, and for the exploratory analyses emphasize the size of the effects (e.g., percent of children from each group who meet criteria for a given disorder) rather than statistical significance. In terms of study attrition, although we did not find evidence that those from the EIG who did and did not remain in the study differed in important baseline measures, selective attrition could affect findings, particularly for the NIG, which as a group dropped out at a higher rate. Another limitation is related to our decision to set aside ITT to examine the FCG in terms of current placement (FCG-Stable vs. FCG-Disrupted). Although meaningful, these groups were small, particularly when examined within each sex. The quality, duration, and number of family experiences of these children, as well as the CAUG, are likely to predict outcomes in a manner that we were unable to parse in the current study. We were unable to consider the quality of care within each placement a child experienced across their childhood, especially as several children moved multiple times between follow-up assessments. However, unmeasured caregiving characteristics very likely play a meaningful role in predicting adolescent psychopathology. Lastly, we conducted these analyses based on caregiver report. Caregivers' familiarity with each child may have differed as a function of placement type (i.e., caregivers of children in institutional care settings will likely have spent fewer years with that child than those living with their original study-sponsored foster family), and seven children experienced a placement change within the past 12 months. Thus, some reporters may not have had as much knowledge of the child, and concerns related to bias may have influenced the degree to which the same behaviors could be seen as problematic in different children. Adolescents are often capable of reporting on their psychiatric symptoms, but the cognitive impairment associated with severe psychosocial deprivation is likely to reduce the validity of some participants' self-report information, and thus for consistency across participants these data were not included here. It should be noted that differences between child and caregiver reports about symptoms may indeed be a predictor of placement disruption (Strijker, Van Oijen, & Knot-Dickscheit, 2011). Ideally, multiple adult informants would be preferred along with the child when possible. In the case of our participants, not all would have more than one adult with sufficient knowledge to provide this information (e.g., many children were not in regular school, limiting the ability to use teacher report for diagnostic purposes).

Conclusion

Parent-child separations occur in many forms, and in many countries institutional care remains the primary mode of providing care for children separated from or abandoned by their caregivers. Placement into institutional care is associated with long-term negative psychiatric outcomes. These results provide

robust support for high-quality and stable family-based care in order to promote resilience following early adversity. These findings coincide with efforts in child protective services to emphasize children's needs beyond safety and prioritize finding children permanent placements with the goal of improving child well-being (Zeanah & Humphreys, 2018). Most urgently, they provide guidance for governments around the world housing the estimated five million children who live in institutions (Desmond et al., 2020).

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Appendix

Data Transparency

The study from which this paper draws began in 2001 and has resulted in over 100 publications from the multiple waves of data collection. Please note that this manuscript is the first to include psychiatric assessments (i.e., diagnostic interview results) from the age 16 follow-up of the randomized controlled trial. There are papers that contain diagnostic information from age 54 months (Zeanah et al., 2009) and at age 12 years (Humphreys et al., 2015). In the supplement of the current article we compare the rates of disorder from age 12 to 16 years. In addition, other papers from

this sample examine P factor based on dimensionally-reported data (e.g., Wade et al., 2018) from age 16 years, although importantly, the P factor approaches do not include formal diagnoses including assessment of functional impairment.

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