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Impact of the COVID-19 pandemic on developmental care practices for infants born preterm

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ARTICLE INFO

Keywords:

Developmental care
Premature infants
COVID-19

ABSTRACT

Objectives: To assess the impact of the COVID-19 pandemic on rates of hospital visitation and rates and durations of developmental care practices for infants born preterm.

Methods: We analyzed electronic medical record data from 129 infants born at less than 32 weeks gestational age (GA) cared for in the Lucile Packard Children's Hospital neonatal intensive care unit (NICU) in a COVID-19-affected period (March 8, 2020 to Nov 30, 2020, $n = 67$) and the analogous period in 2019 ($n = 62$). Rates of family visitation and of family- and clinical staff-delivered developmental care were compared across cohorts, adjusting for covariates.

Results: Families of infants visited the hospital at nearly half of the rate during 2020 as during 2019 ($p = 0.001$). Infants experienced developmental care less frequently in 2020 vs. 2019 (3.0 vs. 4.3 activities per day; $p = 0.001$), resulting in fewer minutes per day (77.5 vs. 130.0; $p = 0.001$). In 2020, developmental care activities were 5 min shorter, on average, than in 2019, $p = 0.001$. Similar reductions occurred in both family- and staff-delivered developmental care. Follow-up analyses indicated that effects persisted and even worsened as the pandemic continued through fall 2020, despite relaxation of hospital visitation policies.

Conclusions: The COVID-19 pandemic has negatively impacted family visitation and preterm infant developmental care practices in the NICU, both experiences associated with positive health benefits. Hospitals should create programs to improve family visitation and engagement, while also increasing staff-delivered developmental care. Careful attention should be paid to long-term follow up of preterm infants and families.

1. Introduction

Each year, approximately 380,000 infants in the United States and 15 million worldwide are born preterm (before 37 weeks of gestation) [1]. Preterm children, especially those born very preterm (<32 weeks gestational age, GA) are at high risk for adverse health and neurodevelopmental outcomes that persist far beyond the newborn period [2]. Over the last 20 years, advances in perinatal developmental care practices, such as positive touch, skin-to-skin holding (kangaroo care), swaddled holding, massage, music therapy, and reading, have led to substantial improvements in health and neurodevelopmental outcomes of preterm children, including reduced rates of infections, and improved

cardiovascular health, growth, and behavioral organization [3]. Studies have also shown that developmental care practices reduce parent and infant stress and improve parent-infant bonding and rates of breastfeeding [4]. Due to the COVID-19 pandemic, however, there is substantial concern that preterm infants may be deprived of access to developmental care activities and may therefore be more at-risk for poor health and long-term neurodevelopmental outcomes than preterm infants born prior to the pandemic [5–7].

As a consequence of the COVID-19 pandemic, healthcare centers, including our center, instituted restricted visitation policies [8–10], guided by recommendations from national experts at the Centers for Disease Control and Prevention, similar to many facilities globally [9].

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<https://doi.org/10.1016/j.earlhumdev.2021.105483>

Received 1 March 2021; Received in revised form 9 September 2021; Accepted 30 September 2021

Available online 4 October 2021

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These policies, combined with other factors that may limit families' ability or willingness to visit their preterm infant in the neonatal intensive care unit (NICU) (e.g., concerns about disease transmission and/or limited access to childcare for siblings), may limit preterm infants' access to developmental care activities, thereby, reducing opportunities for associated health benefits. In the present study, we sought to assess the impact of the COVID-19 pandemic on rates of family visitation and rates and durations of developmental care practices on infants born preterm delivered by both families and clinical staff. We hypothesized that families would have reduced rates of visitation and less engagement in developmental care activities in the COVID-19 period than in a similar period the year prior. We also hypothesized that clinical staff would deliver reduced amounts of developmental care as compared to those in previous period due to psychological aspects of physical distancing under the COVID-19 pandemic, but that their reduction in activities would be less than that of families, whose physical presence in the NICU was impacted. We also examined the impact of hospital policy change which occurred June 1, 2020, which liberalized parental visitation from a single parent per day to allow both parents to visit daily. We hypothesized that relaxing visitation rules would improve rates of visitation and developmental care provided by parents in the NICU compared to the preceding more restricted period.

2. Methods

2.1. Participants

Participants were infants ($N = 129$; 58 females, 71 males) born very preterm (<32 weeks GA). Based on information in the Electronic Medical Records (EMR), all infants were either born or transferred for hospitalization in the NICU at Lucile Packard Children's Hospital (LPCCH) within one week of their birth and stayed for at least seven days during the study period in 2019 (March 8–November 30, 2019 cohort, $n = 67$) and 2020 (March 8–November 30, 2020 cohort, $n = 71$). An additional 29 infants were excluded from analyses because the number of days during the study period was less than seven days ($n = 3$), the infant was admitted more than one week after birth ($n = 17$), or both ($n = 9$). These exclusions sought to ensure similar postmenstrual age (PMA) between cohorts, with similar expected patterns of developmental care activity and an adequate representative period of hospitalization in which developmental care activities could occur.

Table 1 shows that the sexes of the infants were distributed equally among the cohorts, as were the race and ethnicity distributions. About half of the families in both cohorts used public, rather than private, health insurance. The infants were about 28 weeks GA, on average, with no difference between cohorts. Mean PMA at first day within the study period was marginally significantly older for infants in the 2019 cohort than those in the 2020 cohort. Because PMA is likely to affect the types and frequency of and developmental care activities, it is used as a covariate in all analyses. We also controlled for proportion of possible days during the study period as this was significantly different across cohorts.

To determine comparability in the health status of the infants in the 2019 versus the 2020 cohorts, several clinical variables were accessed from the EMR. As shown in Table 1, the incidences of medical or surgical Necrotizing Enterocolitis (NEC), Bronchopulmonary Dysplasia (BPD), defined as treatment with supplemental oxygen at 36 weeks postmenstrual age (PMA), and Intraventricular Hemorrhage (IVH), defined as presence of IVH grade 1 or higher, were similar across the two cohorts.

2.2. Procedure and measures

2.2.1. Study period

Visitation and developmental care (DC) activities were retrospectively analyzed based on the EMR during the COVID-19 pandemic (March 8–November 30, 2020) and during an analogous period prior to

Table 1

Demographic and clinical factors of infants followed during study period in 2019 ($n = 67$) and 2020 ($n = 62$).

	Cohort		t or χ^2	p
	2019	2020		
Female: n (%)	29 (43.3)	29 (46.8)	0.16	0.72
Race: n (%)			4.19	0.38
White	8 (11.9)	12 (19.4)		
Asian	8 (11.9)	10 (16.1)		
Pacific Islander	1 (1.5)	1 (1.6)		
Other/unknown	50 (56.2)	39 (43.8)		
Ethnicity: n (%)			0.83	0.66
Hispanic	29 (43.3)	23 (37.1)		
Non-Hispanic	22 (32.8)	25 (40.3)		
Other/unknown	16 (23.9)	14 (22.6)		
Public insurance: n (%)	29 (43.3)	29 (46.8)	0.16	0.72
GA at birth (weeks) ^a	28.5 (2.4)	28.0 (2.6)	1.03	0.30
PMA ^b	209.0 (24.9)	201.9 (19.7)	1.8	0.07 [#]
Days in NICU ^c	0.37 (0.24)	0.46 (0.27)	2.05	0.05 [*]
NEC: n (%) ^d	10 (14.9)	13 (20.4)	0.80	0.49
BPD: n (%) ^e	20 (29.9)	12 (19.4)	1.90	0.22
IVH: n (%) ^f	17 (25.3)	14 (22.5)	0.14	0.84

^{*} $p < 0.05$.

[#] $p < 0.07$.

^a Gestational age (GA) in weeks at birth.

^b Post-menstrual age (PMA) at start of study period.

^c Proportion of possible days of NICU hospitalization during study period.

^d Presence of medical or surgical Necrotizing Enterocolitis (NEC).

^e Presence of Bronchopulmonary Dysplasia (BPD) defined as treatment with supplemental oxygen at 36 weeks PMA.

^f Presence of Intraventricular Hemorrhage (IVH) of grade 1 or higher.

the pandemic (March 8–November 30, 2019). This study period was selected because March 8, 2020 was the first day on which pandemic-related visitation policies were implemented at LPCCH. Prior to March 8, 2020, parents and family members were permitted to visit at any time of the day, except during nursing sign out (7:00–7:30 a.m./p.m.). Between March 8, 2020 and June 1, 2020, state and county guidelines resulting from the COVID-19 pandemic required that LPCCH visitation policies change. During that period, visitation was limited to parents only. On March 30, 2020, only one parent was allowed to visit per infant for the entire hospital stay. By May 7, 2020, parents could alternate days visiting but could not come together. On June 1, 2020, these policies were partially relaxed such that both parents could again visit their infant but no other family members. This policy remained in effect until December 2020. To allow for exploration of the effects of these policy differences, we tabulated visitation and developmental care activities separately for two periods (March 8 to May 31 and June 1 to November 30). Data were combined to derive total values across the entire study period.

In addition to changes to visitation policies, physical distancing protocols for clinical staff were in effect starting March 8, 2020 with some members working remotely, reducing on-site clinical support. These policies were in effect across the entire study period. To offset hospital revenue loss, clinical staff took paid time off, further reducing developmental team and social work staffing. These changes did not impact bedside nursing ratios but reduced on-site family support services. No explicit restrictions to DC activities were implemented during either period. Family members and clinical staff were required to perform hand hygiene and to avoid the NICU with signs of illness (both 2019 and 2020 cohorts) and, additionally, to universally wear a mask (2020 Cohort). In December 2020, clinical staff began receiving vaccination to COVID-19, creating another possible shift in staff behavior, thus we limited our analysis to the end of November 2020.

Routine daily charting of all visitation and DC activities observed by staff in the EMR was instituted on May 1, 2018 and therefore was well-established by the onset of the pre-pandemic study period in 2019. Visitation policy changes implemented due to the COVID-19 pandemic

did not directly affect protocols regarding the charting of visitation and DC activities and therefore procedures required of clinical staff were identical for the 2019 and 2020 cohorts.

2.2.2. Family visitation

To determine family visitation rates, each instance of family visitation was determined from the EMR. Family visitation rate was defined as the number of family visitation instances logged by clinical staff out of all days during each infant's length of hospital stay during the study period. A visitation rate near 1.0 would indicate that families visited on a daily basis. A visitation rate greater than 1.0 would indicate that families visited, on average, more than once per day, whereas, a visitation rate of less than 1.0 would indicate that families visited less often than once per day, on average.

2.2.3. Developmental care

As part of routine daily charting practice, clinical staff are trained to regularly document the occurrence of each instance of DC, the approximate duration, and who was involved, for seven types of DC activities: Kangaroo Care, Holding, Touch, Massage, Music, Talking, and Singing. Instances of DC were collapsed across type, given the differences in the PMA of the infants and hence which specific types of DC activities might be more or less likely to occur. However, all parents at LPCH are taught a range of DC activities appropriate for their infant so that all infants in this sample were offered some type of DC during the study period. *Frequency* was defined as the number of instances of DC out of number of days during study period, capturing the rate of DC per day normalized for each infant's length of stay during the study period. *Amount* was the sum of all minutes of DC out of number of days during the study period, capturing the minutes per day of DC. *Duration* was the mean number of minutes per DC activity, calculated as the sum of all DC minutes out of the number of DC instances. Each measure was sub-categorized by who was involved in the activity to derive frequency, amount, and duration of DC involving *Family* or *Clinical Staff*.

2.3. Analytic strategy

We first present descriptive statistics for visitation rates, and the frequency, amount, and duration of DC by cohort across the entire period (2019 vs. 2020). To explore cohort differences, we conducted univariate analyses of co-variance (ANCOVA) with cohort (2019 vs. 2020) as the between-group factor. To explore differences in DC activities as a function of who delivered the care, we conducted mixed ANCOVAs on each measure with delivery source (Family vs. Clinical Staff) as the within-group factor and cohort (2019 vs. 2020) as the between-group factor. Follow-up analyses were conducted to determine whether measures of DC were different in the two sub-periods of 2020 that corresponded with changes in hospital visitation policies. All models control for PMA at start of study period and proportion days in study window. Effect sizes were estimated using Cohen's *d*, expressed in SD units, or partial eta squared (η_p^2). Significance levels were set at $p < 0.05$. The protocols were approved by the Stanford University Institutional Review Board. Participants were not required to provide consent, because this study was based on a retrospective chart review.

3. Results

Table 2 shows that, on average, visitation rates for the families in the 2019 cohort were nearly daily. During 2020, rates of visitation dropped significantly to almost half that rate ($d = 0.82$). In addition, the frequency of DC activities for infants in the 2019 cohort was approximately 4.3 DC instances per day, compared to approximately 3.0 DC instances per day in the 2020 cohort, on average, a reduction of approximately 1.3 DC instances per day ($d = 0.64$). Moreover, infants in the 2019 cohort experienced more amounts of DC, with 50 more minutes of DC per day, than infants in the 2020 cohort ($d = 0.72$), with each DC

Table 2

Estimated marginal means (SD) and group comparisons for rates of visitation and frequency, amount, and duration of developmental care (DC) by 2019 ($n = 67$) and 2020 ($n = 62$) cohort.

	Cohort		<i>F</i> (1,124)	<i>p</i>
	2019	2020		
Family visitation ^a	0.95 (0.41)	0.58 (0.41)	25.13*	0.001**
Frequency ^b	4.26 (1.65)	3.03 (1.65)	17.43	0.001**
Amount ^c	130.04 (58.70)	77.50 (58.76)	25.08	0.001**
Duration ^d	29.11 (7.38)	24.29 (7.39)	13.35	0.001**

Note: Controls in the models: PMA at start of study period and proportion days in study window.

^a Number of visitation instances out of days of hospitalization during study period.

^b Frequency of DC expressed as number of instances per day during study period.

^c Amount of DC expressed as minutes per day during study period.

^d Duration in minutes of each instance of DC during study period.

* $p < 0.05$.

** $p < 0.01$.

instance having a duration lasting nearly 5 min longer in 2019, on average, than in 2020 ($d = 0.58$).

We next explored differences in the frequency, amount, and duration of DC activities delivered by *Family* versus *Clinical Staff*. Fig. 1A shows the estimated marginal means for the frequency of DC delivered by Family versus Clinical Staff for infants in the 2019 versus 2020 cohorts. A significant main effect of source, $F(1,125) = 10.78$, $p = 0.001$, $\eta_p^2 = 0.08$, reflected the fact that Clinical Staff delivered DC more frequently than family overall, and a main effect of Cohort, $F(1,125) = 17.43$, $p = 0.001$, $\eta_p^2 = 0.12$, indicated that DC occurred more frequently for infants in the 2019 cohort overall compared to those in the 2020 cohort. Importantly, the Cohort by Source interaction was not statistically significant, $F(1,125) = 0.03$, $p = 0.86$, $\eta_p^2 = 0.01$, suggesting that the reduction in the frequency of DC was the same regardless of whether Family members or Clinical Staff were delivering the care.

Fig. 1B shows a similar pattern for amount of DC expressed as minutes per day. Even though family members were likely to deliver DC less frequently than clinical staff, family members spent more time in DC and therefore, contributed more to the minutes of DC that infants experienced, $F(1,125) = 8.71$, $p = 0.004$, $\eta_p^2 = 0.07$. Infants in the 2019 cohort experienced significantly more DC minutes/day than infants in the 2020 cohort, $F(1,125) = 25.08$, $p = 0.001$, $\eta_p^2 = 0.17$. A non-significant interaction indicated that the reduction in amount of DC received in 2020 compared to 2019 was similar for both family- and clinical staff-delivered DC, $F(1,125) = 1.45$, $p = 0.23$, $\eta_p^2 = 0.01$.

Fig. 1C shows the estimated marginal means for the mean duration of each instance of DC delivered by Family versus Clinical Staff. Here, DC delivered by family was significantly longer per instance than that delivered by clinical staff, $F(1,125) = 13.24$, $p = 0.001$, $\eta_p^2 = 0.10$, and DC delivered in 2019 was significantly longer than that delivered in 2020, $F(1,125) = 4.48$, $p = 0.04$, $\eta_p^2 = 0.04$. Again, the cohort by delivery source interaction did not achieve significance, $F(1,125) = 0.41$, $p = 0.52$, $\eta_p^2 = 0.01$, suggesting that the pandemic impacted how long each DC activity lasted, regardless of whether the care was delivered by family or clinical staff.

Finally, we explored potential differences in impact of the pandemic early vs. later in the year, comparing differences during the spring vs summer/fall periods during the 2020 pandemic year. As shown in Table 3, visitation rates and the frequency and amount of DC activities were significantly lower in the later part of the year, compared to a period early in the pandemic. Effects sizes ranged from $d = 0.72$ to 1.01. Duration of DC activities remained at the same levels across both periods, $d = 0.31$. These results suggest that the impacts of the pandemic on DC were not short lived nor limited to the beginning of the pandemic when more restrictive visitation policies were in place. The pandemic

Fig. 1. Estimated marginal means (SE) for DC frequency (A), amount (B), and duration (C) by 2019 ($n = 67$) and 2020 ($n = 62$) cohort, and source (Family, Clinical Staff).

Table 3

Estimated marginal means (SD) and group comparisons for rates of visitation and frequency, amount, and duration of developmental care (DC) by earlier ($n = 25$) vs. later ($n = 37$) in the period of 2020.

	Period in 2020		$F(1,57)$	p
	March to May	June to November		
Family visitation ^a	0.79 (0.38)	0.42 (0.37)	11.54*	0.001**
Frequency ^b	4.10 (1.82)	2.11 (1.45)	15.08	0.001**
Amount ^c	99.41 (58.65)	55.65 (56.18)	7.09	0.01**
Duration ^d	22.74 (8.13)	25.11 (7.79)	1.08	0.30

Note: Controls in the models: PMA at start of study period and Proportion days in study window.

^a Number of visitation instances out of days of hospitalization during study period.

^b Frequency of DC expressed as number of instances per day during study period.

^c Amount of DC expressed as minutes per day during study period.

^d Duration in minutes of each instance of DC during study period.

* $p < 0.05$.

** $p < 0.01$.

continued to impact the lives of families with young infants for a sustained period.

4. Discussion

Our study documents lower rates of family visitation, decreased frequency, reduced amounts, and shorter durations of DC activities by both family members and clinical staff for preterm infants cared for in the NICU during a COVID-19 pandemic-affected period in 2020 compared to a similar period in 2019. Parents in the COVID-19 period

visited their infants roughly half as often as in the preceding year. Surprisingly, a similar reduction in the frequency, amount, and duration of DC activities occurred regardless if that care was provided by clinical staff or by family members. Although bedside nurses were unaffected by limitations to visitation, they were not immune to more subtle psychological impacts of a pandemic and may have felt undersupported by other staff members. The duration of individual DC activities was also impacted. Finally, contrary to our hypotheses, follow-up analyses comparing sub-periods of 2020 revealed that relaxation of hospital visitation policies did not result in increases in the rates of family visitation or in the frequency and amount of DC activities that infants experienced. In fact, the impact of the pandemic seemed to worsen over the year.

Concerns about the impacts of the COVID-19 pandemic on family visitation in the NICU and engagement have been raised [5,6]; however, our study is the first to document the concrete existence and degree of the feared impact. Although reduction in family visitation is not an unexpected finding considering the changes to hospital policies, it represents a significant threat to parent-infant bonding, the delivery of important parent-delivered care activities [11–13], and positive health outcomes for parents and infants [14–16]. DC has shown to produce positive impacts on both short-term (cardiorespiratory stability, growth, infection rates) and long-term (neurodevelopmental) outcomes [17], raising concerns that care may have been compromised in the NICU and that this impact may be long-lasting. Concerning also is the impact on parental mental health. Qualitative analysis of NICU parent surveys around COVID-19-related visitation restrictions revealed that over 50% of parents were experiencing increased sadness or anger and 25% were distressed by feelings of separation from either partners or the newborn [18]. Although minimum effective doses of DC activities are still being explored, reducing amounts of DC activities, possible decreases in the

benefits may ensue. Close tracking of disturbances in family bonding, family mental health, and infant neurodevelopmental outcomes is warranted.

Interestingly, relaxation of parental visitation policies in June 2020 did not result in improvement in visitation and rates of DC provided by parents. Although most publications have focused on hospital policies as the primary driver for reduced parent visitation and engagement [7,10,19], these restrictions represent only part of the problem. Ongoing fear of infection, job losses, challenges with childcare and episodes of potential exposure or infection necessitating home quarantine may be more important or just as important barriers to family visitation and engagement in the NICU. Multiple authors have reported impairments in parenting quality and family functioning [20–22] due to the stress of the pandemic and these effects are likely contributing to reduced parenting behaviors among high-risk preterm infants in the NICU. In these studies, families with fewer resources were particularly impacted. Programs to better support emotional needs of NICU parents are generally needed but may be of even greater importance now, particularly among those families with lower socioeconomic status.

In addition to differences in family visitation and involvement in care, we also found differences in DC activities delivered by clinical staff, who should be unaffected by restrictions in visitation policies. Fear of transmission of infection may impact clinical staff behavior, reducing contact [23] and even leading to an increase in medical errors [23]. Similar concerns were raised during the Ebola outbreak [24], where nurses felt the need for personal protective equipment (PPE) and the risks associated with touch negatively impacted the quality of their care. The importance of human touch for human wellbeing, both mental and physical, has been well described [25]. Concerns have been raised about touch starvation during the COVID-19 pandemic, particularly in adults for whom physical distancing may limit interpersonal contact [26]. Our study presents data suggesting reduced touch is occurring even in the NICU among infants who are at high risk of poor health outcomes.

Mitigation strategies should be implemented immediately. Recommendations for supporting parent-infant attachment during the COVID-19 pandemic have been reported [27], many of which our institution was following during the 2020 period, with significant impacts measured on visitation and care despite best efforts. Alteration of social factors that may contribute to reduced visitation is difficult; lack of childcare, job losses, and fear of exposure outside the home cannot be changed by hospital policy. However, clinical staff should reduce barriers for family engagement when visitation does occur so that time may be of maximum benefit and enhanced emotional support services offered to improve family functioning, particularly among families with lower socioeconomic status. Some opportunities may exist to support parent-infant attachment via technology [28]. Clinical staff may also increase DC activities they provide to reduce, albeit only partially, the absence of the parent or other family members. Structured DC programs augmented by clinical staff when family members were not able to be present, have shown health benefits for NICU infants [29]. Finally, government and hospital policymakers should carefully consider the possible negative impacts to patients and families when making decisions that may adversely affect immediate and long-term outcomes among NICU families. Although reduced visitation may decrease COVID-19 transmission risk to patients, families, and medical staff, it also impairs care that is both compassionate and medically indicated. As the COVID pandemic continues across the world, the number of infants and families impacted continues to grow. These infants and families are at risk for poorer outcomes and should be closely followed for long term effects.

Limitations to this study include its reliance on bedside charting by nurses that may provide an incomplete picture of all interactions due to inadvertent omissions. When comparing two periods, one must also consider the effects of changing clinical staff. New nurses were hired between 2019 and 2020, but nurse educational onboarding included expectations for family visitation and DC charting. However, it is possible that the differences across study period that were documented

here, at least partially, could relate to differences in nurse charting practices. Also limiting is the single-center nature of the study. Effects at our institution may or may not agree with those at other hospitals with different restrictions on family visitation or parent involvement in infant care. Some hospitals have forbidden all skin-to-skin care in their NICUs in an effort to reduce possible parent-infant COVID-19 transmission, while we have continued to allow it in asymptomatic parents who practice good hand hygiene and wear masks. Differences in visitation policies also exist across counties, cities, states and countries, creating variation in effects. Other limitations include unavailable data on parent mood, infant health outcomes, and neurodevelopment. Also unexplored due to sample size was an evaluation of socioeconomic-related health care disparities, important to include in any outcome analysis. These areas remain good avenues for future research into the effects of this pandemic on at-risk infants and families who experience a NICU stay.

The COVID-19 pandemic has had, and continues to have, a devastating impact on global health in ways both directly and indirectly measured. Although significant mortality and morbidity has been recorded particularly in adult patients, infants have been largely spared [30]. However, indirect impacts of the COVID-19 pandemic on preterm infants in the NICU and their families are significant and, until now, largely unmeasured. Careful attention needs to be paid to current infant care patterns, family support services, hospital policies, and to long-term follow up of infants in the NICU and their families. The effects of this pandemic may in fact last decades for our smallest high-risk infants and their families.

Funding/support

This research work was supported by grants from the National Institutes of Health- Eunice Kennedy Shriver National Institute of Child Health and Human Development (K.E. Travis, PI; 5R01HD08474904; H. M. Feldman, PI; 2R01- HD069150), the National Institute of Mental Health Postdoctoral Research Training in Child Psychiatry and Neurodevelopment (A. Reiss, PI; T32 MH019908), and the Stanford RISE COVID-19 crisis response faculty seed grant (K.E. Travis, PI).

Credit authorship contribution statement

Drs. Scala and Travis conceptualized and designed the study, drafted the initial manuscript, supervised data abstraction, and critically reviewed and revised the manuscript for important intellectual content. Dr. Marchman conceptualized and designed the study, supervised data abstraction, analyzed data, drafted the initial manuscript, and reviewed and revised the manuscript for important intellectual content. Dr. Brignoni-Pérez conceptualized and designed the study, acquired data from the medical record, and critically reviewed and revised the manuscript for important intellectual content. Ms. Morales assisted with acquiring data from the medical record and critically reviewed and revised the manuscript for important intellectual content. Dr. Dubner acquired data from the medical record and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article to disclose.

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