Preschool-Onset Major Depressive Disorder as a Strong Predictor of Suicidal Ideation and Behaviors Into Preadolescence

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Abstract

Objective: Suicidal thoughts and behaviors (STBs) in children are an escalating public health concern. This study focused on 1 understudied candidate risk factor, namely, preschool-onset major depressive disorder (PO-MDD), as a predictor of persistent and emerging STBs from early childhood into preadolescence.

Method: Participants were 137 children 8 to 12 years of age who met criteria for PO-MDD when they were 3 to 6 years of age, and a nondepressed sample of 53 age-, income-, and sex-matched peers. STBs were reported by caregivers (preschool, preadolescence) and children (preadolescence) using age-appropriate diagnostic interviews.

Results: By preadolescence, children who had PO-MDD were 7.38 times more likely than their peers to have endorsed STBs after early childhood ($p < .001$; 67.9% vs 22.6%), including 6.71 times more likely to have engaged in suicide behaviors/attempts ($p = .012$; 21.9% vs 3.8%); they were also 8.98 times more likely to have endorsed STBs over the prior month ($p = .005$; 26.3% vs 3.8%). Similar findings emerged when limiting the PO-MDD group to children without preschool STBs, and when controlling for externalizing comorbidities, implicating PO-MDD as a unique diagnostic predictive risk factor. However, children who had PO-MDD with STBs were 3.46 times more likely than children who had PO-MDD without STBs to endorse later STBs ($p = .018$; 83.1% vs 54.2%), indicating substantial continuity of preschool STBs alongside strikingly high rates of emerging STBs into preadolescence.

Conclusion: PO-MDD is a strong risk factor for the emergence and persistence of STBs into preadolescence. Children with PO-MDD would likely benefit from increased suicide screening, proactive safety planning, and early interventions.

Suicidal thoughts and behaviors (STBs) in childhood have been escalating in recent years and now represent a pressing public health concern. Rates of suicide in youth have nearly tripled since 2007,[1] with suicide now the second leading cause of death in individuals 10 to 14 years of age in the United States.[2] Emergency department visits for suicidality have also increased sharply, with 1 study finding a 24.5% increase in visits for suicidal ideation by children 5 to 13 years of age between 2016 and 2021,[3] straining health care systems and highlighting the child mental health crisis. Recent population estimates further indicate that by 9 to 10 years of age, 14.5% of children have experienced STBs, and 1.3% have made a suicide attempt,[4] elucidating the scope of the public health problem. Despite these dramatic rises in STB rates, there has been little investigation of the prevalence, timing of onset, or correlates of STBs in school-aged children. Moreover, despite a multitude of studies investigating predictors of STBs in adolescence and adulthood, meta-analytic work demonstrates that our current abilities to identify risk factors that predict STBs are only slightly better than chance.[5] This finding underscores the need for new approaches to identifying predictors of later STBs to inform targeted prevention and consideration of whether developmental timing of risk predicts onset and maintenance of childhood STBs.[6]

Early-onset psychopathology, including both internalizing and externalizing disorders, represents a key pathway for the emergence of childhood STBs.[7–11] As early as the preschool period, psychopathology and STBs are positively associated, with some evidence for continuity with later STBs and psychopathology into adolescence.[8] Preschool-onset major depressive disorder (PO-MDD),[12] in particular, provides a potentially relevant risk pathway, with 1 recent study finding that 19.1% children 3 to 6 years of age who were enrolled in a treatment study for PO-MDD experienced STBs.[13] These preschoolers with STBs presented with higher depressive symptom severity, preoccupation with death, and increased violence exposure relative to depressed peers without STBs. Furthermore, depressed preschoolers with STBs also had a more advanced understanding of death than their peers,[14] and those with active suicidal ideation depicted more violence and suicide

in conflict resolution during narrative play,[15] demonstrating meaningful differences in the thoughts and behaviors of very young children with STBs.

Prevalence estimates of PO-MDD for children 3 to 5 years of age are 1% to 2%,[16–18] with 1 more recent study documenting rates of depression 6.2% (32 of 516 children) by age 6 years in a community sample.[19] That study, by Silver *et al.* (2022), found that depression (including MDD, dysthymia, and depression not otherwise specified [NOS]) by age 6 years predicted current STBs at 1 or more follow-up assessments that occurred when children were 9, 12, and 15 years of age. However, because STBs during the preschool period were not reported or assessed in this study, it is possible that these findings reflect continuity of preschool STBs that might already have been present in children with preschool depression rather than new-onset STBs. The small number of depressed children and the heterogeneity in depression diagnoses further limit the ability for this study to address specific diagnostic predictors of adolescent STBs or to differentially assess risk for suicidal ideation, behaviors, or attempts.

A separate small body of research has reported associations between children who present with suicidal ideation or suicide behaviors and presence of concurrent depressive symptoms.[20–23] For example, early work by Pfeffer and colleagues found that depression, hopelessness, and worthlessness were significantly correlated with suicidal behaviors in children 6 to 12 years of age.[24] However, because these studies do not assess STBs prior to these associations, they are not able address the potential causal impact of depression on STBs. Thus, further work starting in early childhood and documenting the developmental course of STBs in children is needed.

The current study examined suicidality and related outcomes in preadolescents 8 to 12 years of age who met criteria for PO-MDD based on a research diagnostic assessment between ages 3 and 6 years from a prospective study. Specifically, rates of STB endorsement were assessed (1) in preadolescents who had PO-MDD relative to preadolescents in a matched, nondepressed sample to establish relative risk of PO-MDD for experiencing STBs into preadolescence; and (2) as a function of preschool STBs, to examine both the continuity of STBs into preadolescence and to investigate whether PO-MDD without STBs is a risk factor for STB onset after the preschool period. To estimate the independent contributions of PO-MDD to childhood STBs, the present analyses controlled for externalizing comorbidities, as research suggests these symptoms may also be linked to the development of STBs.[7,11] To better characterize the PO-MDD sample and to test additional predictors of risk, trauma exposure, and post-traumatic stress disorder (PTSD) diagnoses, were investigated based on prior findings linking violence exposure and violence in play to preschool STBs.[14,15] Family history of suicide or suicide attempt was also investigated as a risk factor for STBs based on evidence in the literature about familial transmission of STBs[25,26] and more specific findings by Sheftall *et al.* demonstrating that children 6 to 9 years of age with suicidal ideation were more likely to have a family history of suicide or suicide attempt than peers without suicidal ideation.[7] Global functioning was also examined to provide a broad indicator of preadolescents' current functioning across peer, school, and family contexts. Finally, we explored the impact of early intervention—that is, children's response to a

depression-focused, parent–child psychotherapy during the preschool period—on risk for continuing and/or new-onset STBs.

METHOD

Participants

The Pediatric Suicidality Study (PED-SI) included 137 children with PO-MDD who initially participated in a randomized controlled trial (RCT) for parent–child psychotherapy at 3 to 6 years of age (mean = 5.31, SD = 1.02, range = 3.03–6.99) and who were recently recaptured for a preadolescent follow-up assessment at 8 to 12 years of age (mean = 10.14, SD = 1.01, range = 8.02–12.20). Demographic information is presented in Table 1. All preadolescents (N = 137) had a primary caregiver who completed the Kiddie Schedule for Affective Disorders and Schizophrenia—Early Childhood[27] (K-SADS-EC) in early childhood and the K-SADS—Present and Lifetime[28] (K-SADS-PL) at the follow-up; the majority of preadolescents (n = 128) also completed the depression/suicide, generalized anxiety disorder (GAD), social phobia, and PTSD modules of the K-SADS-PL at follow-up. The preadolescent K-SADS-PL was limited to these internalizing modules, given time constraints and because parent-report has been deemed more reliable for externalizing disorders.[29]

Original Sample Ascertainment and RCT Details.—Prior to inclusion in the preschool RCT, a clinician-administered K-SADS-EC interview was used to assess child psychopathology at baseline (ages 3–6 years). Children who met criteria for PO-MDD (N = 229) were randomized to either the treatment or waitlist group. Upon completion of the treatment (20 sessions over ~18 weeks) or comparable time for the waitlist, a post-assessment was conducted to reassess PO-MDD diagnosis, symptoms, and other psychopathologies by interviewers blinded to treatment status. Then children on the waitlist were offered the treatment (for the follow-up sample, 70% of waitlist group completed 50% of treatment relative to 91% of the treatment group), with a second post-assessment conducted for all children following the completion of treatment after waiting. Key post-treatment findings from the RCT included lower rates of PO-MDD, depression severity, comorbid psychopathologies, improved neural response to reward, and functional impairment in children who received the treatment relative to the those who were on the waitlist; however, outcomes specific to STBs were not directly assessed at the post-treatment assessment. Detailed findings from the RCT are reported in Luby *et al.* (2018), Barch *et al.* (2018), and Luby *et al.* (2020).[30–32]

Nondepressed Peer Sample.—A separate sample of 53 nondepressed peers served as a comparison at follow-up. Nondepressed peers were initially recruited as a control group for key baseline measures, participated in an abbreviated baseline session when they were 4 to 6 years of age (n = 82, mean = 5.23, SD = 0.90, range = 4.01–7.44), and completed the preadolescent follow-up at 8 to 12 years of age (n = 53, mean = 10.05, SD = 0.90, range = 8.33–31 11.87; 57% boys). At baseline, these children scored in the normal/non-clinical range on measures of depression (Supplement 1, available online). They were also matched for mean age, sex, and socioeconomic indicators to the original PO-MDD sample. At

follow-up, there were also no significant differences between the PO-MDD and peer sample on these demographic factors (Table 1). Procedures and measures at the follow-up were identical to those described for the PO-MDD sample.

Sample Attrition.—At follow-up of the original RCT, approximately 4 to 6 years after the RCT (mean = 4.80 years, SD = 0.81), sample retention was 59.8% for children who had PO-MDD and 64.6% for nondepressed peers. All children who participated in the original study were eligible to participate in the follow-up, with multiple attempts made to contact and recapture each family. There were no significant differences between preadolescents with and without a follow-up assessment for any key demographic variables (both groups) or pre/post-treatment MDD severity (PO-MDD group; Table S1, available online). Of note, follow-up data collection took place from fall 2019 to spring 2022 and had substantial overlap with the COVID-19 pandemic, which likely contributed to a decrease in study retention.

Consent.—Written informed consent and assent was obtained from caregivers and preadolescents respectively. Study procedures were approved by Washington University's Institutional Review Board, #201306070. Detailed safety protocols were in place to address reported STBs.

Measures

Suicidal Thoughts and Behaviors.—The K-SADS-PL, a semi-structured age-appropriate diagnostic interview for the *DSM-5* disorders, was administered separately to the primary caregiver and preadolescent by a trained researcher. Caregivers reported on their child's symptoms for 2 primary periods: (1) since the preschool period (ie, after participation in the RCT and associated post-treatment assessments), and (2) current (over the prior month). Preadolescents reported on their own lifetime and current symptoms. Presence or absence of the following suicidality constructs were captured: (1) passive suicidal ideation (eg, a wish to be dead, a wish they had never been born); (2) active suicidal ideation (a desire to kill oneself); (3) suicidal behaviors (preparations or planned attempt, such as acquiring a means, or a suicide attempt); and (4) suicide attempt (a subset of suicidal behaviors that requires engagement in self-injurious behaviors, such as trying to strangle oneself with scarf/rope or jumping from a high place, with the intent of dying from the behavior). For suicide attempts, lethality of method (eg, specific object height) was not considered, but context of behavior (the behavior had to occur in context of suicidal expression or child-reported intent) was considered. Examples of passive suicidal ideation included preadolescents describing a general wish to be dead or to fall asleep and never wake up, or describing specific things happening that make them want to die. Passive suicidal ideation, active suicidal ideation, and suicidal behaviors were not mutually exclusive (ie, children could have both). Interrater reliability was good/very good for parent ($k = 0.75$) and child ($k = 0.93$) STBs (present/absent). In the present analyses, each suicide construct is considered present (1) if it was endorsed by either parent or child, and absent (0) if it was not endorsed by either parent or child.

MDD Symptoms.—An MDD symptoms score was the sum of 8 current core depression symptoms captured by the K-SADS-PL (depressed mood, anhedonia, appetite changes, insomnia/hypersomnia, motor agitation/retardation, fatigue, guilt, cognitive changes) reported by either parents or children, and excludes suicide variables.

Externalizing Comorbidities.—Dichotomous scores (present/absent) were created to capture any externalizing diagnosis (ie, attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder) obtained from the parent K-SADS during the preschool period (PO-MDD group) and lifetime (both groups).

Global Functioning.—The Children's Global Assessment Scale (CGAS),[33] a standardized clinician-rated measure scored from 0 to 100, was used to assess children's global functioning based on the parent assessment. Higher scores indicate better functioning.

Traumatic Events and PTSD.—The Life Events Checklist,[34] administered to caregivers, measured the number of traumatic lifetime events experienced by the child. Dichotomous scores (present/absent) were created to capture a PTSD diagnosis obtained from information gathered across the parent and child K-SADS interviews.

Parental History of Suicide/Attempt.—The Family Interview for Genetic Studies (FIGS),[35] a semi-structured interview, was used to assess parental history of suicide and/or suicide attempts, coded dichotomously (present/absent).

Statistical Plan

The first set of analyses examined PO-MDD as a risk factor for experiencing STBs into preadolescence. Binary logistic regressions were conducted to determine whether preadolescents who had PO-MDD were more likely than nondepressed peers to experience each type of STB (1) since the preschool period, and (2) currently. Using these same procedures, the second set of analyses limited the PO-MDD to children without preschool STBs to test whether any potential risk for later STBs observed in the first set of analyses could be accounted for by preschool STBs. The third set of analyses limited the STB outcome measures to preadolescent-only endorsements to test whether potential risk for STBs as a function of PO-MDD (assessed via parent-report during the preschool period) could be captured by preadolescents' own STB endorsements during the preadolescent period. The fourth set examined the relative risk, within the PO-MDD sample, of experiencing STBs into preadolescence by presence of preschool STBs.

All analyses included child's age at follow-up and sex as covariates; however, sex was removed from the final analyses after no significant effects were detected. The Benjamini–Hochberg procedure was used to correct for false discovery rate (FDR) across each timepoint. When "current" models were statistically significant, secondary analyses were performed that controlled for concurrent MDD symptoms (with STBs removed) and parental history of suicide/attempt. For the first and third set of analyses, secondary models were tested that (1) controlled for lifetime externalizing comorbidities (preschool externalizing diagnoses were not available for the peer sample), and (2) restricted the PO-MDD sample to children without externalizing comorbidities. These covariates were chosen based on prior

literature and our particular sample characteristics (eg, high rates of preschool externalizing comorbidities) as factors with the strongest likelihood of accounting for STB outcomes in the present sample.

To further characterize preadolescents' current functioning and select psychopathology symptoms and risk factors based on their history of PO-MDD and STBs, the following 4 groups were created: (1) "no-STBs" (no preschool STBs, no later STBs); (2) "emerged" (no preschool STBs, later STBs); (3) "remitted" (preschool STBs, no later STBs); and (4) "persistent" (preschool STBs, later STBs). To examine functioning outcomes, MDD symptoms, and number of trauma events experienced, univariate analyses of variance with group as the independent variable, function score as the dependent variable, and age as a covariate were conducted with the 4 PO-MDD and peer groups. Pairwise comparisons (FDR corrected) were used to probe group differences in models with a significant group main effect. Logistic regressions were used to explore MDD diagnosis, PTSD diagnosis, parent suicide/attempt history, and preschool and lifetime externalizing comorbidities.

Finally, we explored whether treatment response in the RCT had an impact on STB onset or continuity after the preschool period.

RESULTS

PO-MDD Status as a Predictor of STB Endorsement Into Preadolescence

Prevalence and types of STBs experienced by children are reported in Table 2. By preadolescence, 67.9% of children 8 to 12 years of age who had PO-MDD endorsed STBs after the preschool period (by either parent or child), including 26.3% over the prior month. In contrast, 22.6% of nondepressed peers endorsed STBs by preadolescence, including 3.8% over the prior month.

Relative to nondepressed peers, preadolescents who had PO-MDD were 7.38 (3.49–15.57) times more likely to have endorsed any STBs after the preschool period (B = 2.00, SE = 0.38, χ^2[df = 1, n = 190] = 27.46, $p < .001$) (Table 3). Specifically, preadolescents who had PO-MDD were 5.83 (2.78–12.21) times more likely to have endorsed passive SI (B = 1.76, SE = 0.38, χ^2[df = 1, n = 190] = 21.82, $p < .001$), 6.14 (2.08–18.16) times more likely to have endorsed active SI (B = 1.81, SE = .55, χ^2[df = 1, n = 190] = 10.75, $p = .002$), and 7.03 (1.60–30.91) times more likely to have endorsed suicidal behaviors including attempts (B = 1.95, SE = 0.76, χ^2[df = 1, n = 190] = 6.65, $p = .012$). This latter finding remains significant when restricting analyses to suicide attempts, such that preadolescents who had PO-MDD were 8.03 (1.04–62.23) times more likely than peers to have made a suicide attempt after the preschool period (B = 2.08, SE = 1.04, χ^2[df = 1, n = 190] = 3.97, $p = .046$). Methods of attempts included cutting/stabbing neck, wrist, or heart with a knife (n = 9), wrapping a scarf, rope, or belt around the neck (n = 7), jumping from height (n = 4), running into busy street (n = 2), jumping out of moving car (n = 2), or pill overdose (n = 1). Actions coded as suicidal behaviors (that did not reach threshold for an attempt) included multiple instances of children grabbing a kitchen knife or trying to get a knife and being stopped by an adult (in the context of expressing active SI), holding a knife/scissors to the neck but not leaving a mark, and writing a suicide note.

Preadolescents who had PO-MDD were also 8.98 (2.07–39.05) times more likely to have endorsed current STBs (B = 2.20, SE = 0.75, χ^2[df = 1, n = 190] = 8.57, p = .005) than nondepressed peers, including 7.63 (1.75–33.22) times more likely to have endorsed passive SI (B = 2.03, SE = 0.75, χ^2[df = 1, n = 190] = 7.34, p = .010). These findings remain significant when including current MDD symptoms (with STBs removed) in the model (Table S2, available online), and when including parent history of suicide/attempt in the model (Table S3, available online). Moreover, all past and current findings remain largely unchanged when controlling for lifetime externalizing comorbidities and when restricting the PO-MDD sample to preadolescents without preschool externalizing comorbidities (n = 52), indicating that externalizing symptomatology does not drive these results (Tables S4 and S5, available online).

PO-MDD Status (Without STBs) as a Predictor of STB Endorsement Into Preadolescence

Preadolescents who had PO-MDD without STBs (n = 72) were 4.27 (1.91–9.56) times more likely than nondepressed peers to endorse STBs after early childhood (B = 1.45, SE = 0.41, χ^2[df = 1, n = 125] = 12.47, p = .002), including 3.65 (1.63–8.18) times more likely to have endorsed passive SI (B = 1.30, SE = 0.41, χ^2[df = 1, n = 125] = 9.92, p = .004), 4.21 (1.33–13.39) times more likely to endorse active SI (B = 1.44, SE = 0.59, χ^2[df = 1, n = 125] = 5.94, p = .025); and were marginally more likely to endorse suicide behaviors/attempts (B = 1.47, SE = 0.80, χ^2[df = 1, n = 125] = 3.38, p = .082). Preadolescents with PO-MDD without STBs were also 7.74 (1.65–36.27) times more likely to have endorsed current STBs than nondepressed peers (B = 2.05, SE = 0.79, χ^2[df = 1, n = 125] = 6.74, p = .014), including 7.00 (1.49–32.88) times more likely to have endorsed passive SI (B = 1.95, SE = 0.79, χ^2[df = 1, n = 125] = 6.07, p = .014) (Table S6, available online).

PO-MDD Status as a Predictor of Child STB Endorsement Into Preadolescence

Overall, 59.4% of caregivers endorsed STBs for their child since preschool, whereas 43.8% of preadolescents endorsed lifetime STBs (k = 0.33); in addition, 19.5% of caregivers endorsed current STBs whereas 15.6% of preadolescents endorsed current STBs (k = 0.33). When limiting the STB outcome variables to preadolescent-only endorsements, findings broadly replicated the primary findings that used the combined parent–preadolescent STB outcome variable. Preadolescents with PO-MDD were 5.00 (2.09–11.97) times more likely than nondepressed peers to endorse STBs after early childhood (B = 1.61, SE = 0.45, χ^2[df = 1, n = 181] = 13.05, p = .002), including 4.12 (1.72–9.86) times more likely to have endorsed passive SI (B = 1.41, SE = 0.45, χ^2[df = 1, n = 181] = 10.07, p = .004), 5.77 (1.31–25.43) times more likely to endorse active SI (B = 1.75, SE = 0.76, χ^2[df = 1, n = 181] = 5.37, p = .034); and were marginally more likely to endorse suicide behaviors/attempts (B = 2.02, SE = 1.05, χ^2[df = 1, n = 181] = 3.73, p = .067). Preadolescents with PO-MDD were also 9.36 (1.22–71.80) times more likely to have endorsed current STBs than nondepressed peers (B = 2.24, SE = 1.04, χ^2[df = 1, n = 181] = 4.63, p = .049), including 7.79 (1.01–60.17) times more likely to have endorsed passive SI (B = 2.05, SE = 1.04, χ^2[df = 1, n = 181] = 3.87, p = .049) (Table S7, available online). Finally, exploratory analyses demonstrated that older age predicts decreased parent–child concordance for the current period (B = –0.91, SE = 0.27, χ^2[df = 1, n = 128] = 11.20, p < .001), but not for the overall period since preschool (B = –0.21, SE = 0.19, χ^2[df = 1, n = 128] = 1.28,

$p = .259$). For context, in the current period, 11 preadolescents endorsed STBs when the caregiver did not (30% of STB endorsements), whereas in the overall period since preschool, 18 preadolescents endorsed STBs when the caregiver did not (18% of STB endorsements).

Preschool STB History as Predictor of STB Endorsement Into Preadolescence

Table 4 shows STB prevalence by STB history. Within the PO-MDD sample, 65 children (47.4%) had preschool STBs and 72 children (52.6%) did not have preschool STBs. Children who had PO-MDD with STBs were 3.46 (1.51–7.91) times more likely than children who had PO-MDD without STBs to endorse STBs after early childhood (B = 1.24, SE = 0.42, χ^2[df = 1, n = 137] = 8.65, $p = .018$), including 2.78 (1.29–6.00) times more likely to have endorsed passive SI (B = 1.02, SE = 0.39, χ^2[df = 1, n = 137] = 6.75, $p = .027$). However, there were no significant differences in endorsement of active SI or suicide behaviors/attempts since early childhood, or current STB endorsement between the PO-MDD with STB and PO-MDD without STB groups (Table S8, available online). Moreover, findings remain significant when controlling for children's preschool and lifetime externalizing comorbidities (Tables S9 and S10, available online).

Global Functioning, Psychopathology, and Related Constructs as a Function of STB Timing

Across the PO-MDD sample, 76% endorsed STBs by age 12 years, with 28.5% emerging after the preschool period. Within the PO-MDD without STB group, 54.2% endorsed STBs after preschool (emerged), including 20.8% currently. Within the PO-MDD with STB group, 83.1% endorsed STBs after preschool (persistent), including 32.3% currently (Table 4). Only 16.9% of children who endorsed STBs in preschool did not continue to endorse them after preschool (remitted).

Descriptive statistics for CGAS/functioning, MDD symptoms, MDD diagnosis, PTSD diagnosis, traumatic events, parent history of suicide/attempt, and externalizing disorders by group are reported in Table 5. There were main effects of group for CGAS/functioning ($F_{4,184} = 10.14$, $p < .001$), MDD symptoms ($F_{4,184} = 8.34$, $p < .001$), MDD/MDD-NOS diagnosis (χ^2[df = 4, n = 190] = 31.81, $p < .001$), and lifetime externalizing comorbidities (χ^2[df = 4, n = 190] = 38.22, $p < .001$), but not for number of traumatic lifetime events ($F_{4,182} = 0.94$, $p = .440$), parent history of suicide/attempt (χ^2[df = 4, n = 187] = 1.48, $p = .831$), or preschool externalizing comorbidities (χ^2[df = 3, n = 135] = 1.00, $p = .800$). The model for PTSD diagnosis could not be tested, as all preadolescents with a PTSD diagnosis (n = 5) were in the persistent group. As might be expected, pairwise comparisons indicated lower global functioning in the persistent group relative to the no-STB group, and in the persistent and emerged groups relative to nondepressed peers (p values <.010). In addition, they also indicated increased current MDD symptoms and MDD/MDD-NOS diagnosis in the persistent and emerged groups relative to the no-STB group, and the persistent and emerged groups relative to nondepressed peers (p values <.015), and increased lifetime externalizing comorbidities in all PO-MDD groups relative to nondepressed peers (p values <.001).

Impact of Treatment Response on Future STBs

For children with a baseline and post-treatment assessment (n = 114), children who achieved remission after treatment (defined as no PO-MDD and 50% reduction in MDD severity) were less likely to experience STBs after preschool ($\chi^2 = 7.59$, $p = .006$). This finding remained significant when limiting the analysis to children with PO-MDD+STBs ($\chi^2 = 5.16$, $p = .023$), but not to children with PO-MDD–STBs ($\chi^2 = 0.69$, $p = .407$), suggesting that treatment remission reduced the likelihood of persistent STBs but did not impact new-onset STBs (Table S11, available online).

DISCUSSION

This study found strikingly high endorsement of STBs in preadolescents with a history PO-MDD: since the preschool period, 67.9% of children who had PO-MDD endorsed subsequent STBs, with 26.3% of those children continuing to endorse STBs within the past month. These rates were far higher than those of a nondepressed peer sample, indicating that PO-MDD is a strong risk factor for experiencing later STBs. Critically, in addition to predicting passive and active SI, PO-MDD also predicted suicidal behaviors and attempts, which is notable given the serious nature of these events, despite their relative rarity. The overwhelming majority of children (83.1%) who had PO-MDD and who experienced preschool STBs continued to experience STBs into later childhood and preadolescence. However, a significant number of children who had PO-MDD and who did not experience preschool STBs endorsed new-onset STBs in later childhood and preadolescence (54.2%) compared to lower rates of STBs endorsed by nondepressed peers (22.6%), further supporting the claim that PO-MDD is a diagnostic risk factor for later STBs. Together, these findings provide compelling evidence for the continuity of STBs across childhood in a population with early-onset depression (even after accounting for comorbid externalizing disorders) and suggest a common etiology for preschool and adolescent STBs. Importantly, these longitudinal data allowed for the detection of new-onset STBs, including suicide attempts, in children with PO-MDD, overcoming a major limitation of past work.

Previous history of STBs is a known risk factor for future STBs, as is depression. However, our findings, albeit consistent with this previous work, are novel for several reasons. First, our sample is much younger than in the bulk of previous empirical work on STBs, with clinically significant depression beginning during the preschool period. Although this diagnosis has been validated,[12] it is still often missed or overlooked in clinical settings. Attention to its detection is made even more important by the finding that this early-onset diagnosis may represent 1 high-risk trajectory for the emergence and continuation of STBs in later development. Indeed, here we find higher rates of STB endorsement in children with PO-MDD histories than has been documented in children with other forms of early-onset psychopathology including externalizing disorders[36,37] and in non-clinical samples.[4,38] Notably, these effects appear to be driven by PO-MDD and not comorbid externalizing symptoms. We also provide evidence that PO-MDD, which is diagnosed based on parent interviews during the preschool period, predicts children's self-reported STBs in preadolescence, further strengthening the validity of these findings. In addition, this study is the first to comprehensively assess preschool suicidal ideation and behaviors/attempts

and to longitudinally follow those children into preadolescence to document the emergence (and remittance) of STBs in a high-risk mood sample. Related studies, such as that by Silver *et al.*,[19] which followed a community sample of children 3 and 6 years of age into adolescence, either did not capture or report on child STBs during the preschool period, and thus were unable to account for the possibility that preschool STBs specifically, rather than an overarching depression diagnosis, might have driven the association that they found between preschool depression and later STBs.

These findings add to the growing literature linking preschool-onset STBs with STBs later in development—an issue worthy of increased clinical attention, screening, and prevention efforts. These findings also provide evidence of continuity of STBs across childhood (measured via parent-report) and into preadolescence (measured via both parent- and child-report), suggesting that early-onset STBs are not only developmentally valid but are also likely to be a marker of future risk, and therefore should not be ignored or discounted as clinical signs. Finally, we were able to document differences in preadolescents who never endorsed STBs compared to those who continued to endorse them across childhood. These 2 groups differed in overall functioning and severity of MDD symptoms. However, no significant differences were found between individuals who "remitted" from previously reported STBs and those who endorsed them after preschool. Perhaps prior STBs may continue to impair functioning and symptomatology, consistent with a scar hypothesis, even after STBs themselves are no longer present. This intriguing possibility warrants additional research with longitudinal samples.

When compared to nondepressed peers, children with PO-MDD differed regarding type of STB endorsement. Specifically, not only were children who had PO-MDD more likely to endorse later STBs, they were more likely to endorse severe STBs leading to possible attempts. However, few differences emerged in STB type as a function of STB history. That is, among preschoolers, who had PO-MDD and STBs compared to those who had PO-MDD without STBs, current endorsement of STB type was mostly equivalent. This may be due to our limited sample size and to relatively fewer children endorsing more severe STBs; alternatively, more severe STBs may increase with age and have yet to peak in our sample. Future research with larger, clinically enriched samples is needed to further probe these questions. In addition, in-depth content analysis of preadolescents' STB endorsements might provide further insight into suicide risk.

Of note, 22.6% of the nondepressed peer sample endorsed lifetime STBs by preadolescence, which is substantial and alarming, yet aligned with the results of other recent studies.[4,38] For example, the population-based Adolescent Brain and Cognitive Development (ABCD) study found STB rates of 14.5% for children 9 and 10 years of age (combined parent/child endorsement in a slightly younger sample than ours),[4] and a large representative sample of students 11 to 14 years of age in Maryland reported STB rates of 23% (child endorsement only in a slightly older sample).[38] Given the rapidly rising rates of childhood STBs, along with the far-reaching socioemotional and health impacts of the COVID-19 pandemic, the inclusion of an age-matched cohort of peers recruited at the same time as children with PO-MDD provides a particularly potent comparison in the present work.

The American Academy of Pediatrics' recent "Blueprint for Youth Suicide Prevention" recommends universal suicide screening by pediatric health clinicians for youth 12+ years of age and targeted screening for those 8 to 11 years of age when clinically indicated (ie, primary behavioral complaints, child or caregiver raising concern, history of STBs, or displaying suicide warning signs).[39] Although general STB screening is not indicated for children under age 8 years, suicide assessment should be conducted if warning signs such as mood disturbances are present. Our work further suggests that children with PO-MDD would likely benefit from increased suicide screening and proactive safety planning that includes reducing access to lethal means. Caregivers should also be counseled about warning signs, with resources for treatment and support provided. Moreover, our finding that discordance between parent and child endorsement of current STBs increased with age across preadolescence suggests that obtaining both parent and child reports may be important to ascertain a full STB history, and that increasing attention should be paid to child self-reported current STB endorsements with age.

The finding that children with PO-MDD who achieved remission following parent–child psychotherapy were less likely to experience STBs after the preschool period is novel and noteworthy, as the treatment did not specifically target STBs but, rather, more generally targeted emotional development. Although remission status did not predict new-onset STBs, it did predict a decrease in continuing STBs, raising the possibility that the presence of or knowledge about preschool STBs allows them to be targeted during treatment. However, despite this promising finding, the high rates of STB continuity make it clear that current therapies focused broadly on PO-MDD are not sufficient and suggest that modifications to this treatment to directly target STBs may be worthwhile. Modifications might include a focus on teaching early coping strategies for intense negative emotion, and encouraging adaptive alternatives to self-harm.

Other key future directions include examining whether these findings extend to other early-onset clinical populations, such as young children with attention-deficit/hyperactivity disorder, and the role of comorbidities on risk trajectories. Although the present study demonstrates that later STB risk in children who had PO-MDD is not driven by early externalizing comorbidities, the extant literature suggests that such comorbidities present additive or interactive risks.[40] Research examining the validity of retroactive assessment of PO-MDD by caregivers and/or children may aid in risk assessment, as these high-risk children with PO-MDD are less likely to be detected clinically at early ages, given that their symptoms are more internal/self-focused and less disruptive. PO-MDD and related symptoms are frequently unrecognized by parents, teachers, and clinicians, placing these children at even higher risk for STB continuity and ongoing impairment. It was also interesting that neither experiences of traumatic events nor parent history of suicide/attempt related to new-onset or persistent or STBs in this sample, which may be more of an indicator of the potency of PO-MDD as a risk factor than a meaningful assessment of the role of these variables in suicide risk. Furthermore, the finding that the few preadolescents who met diagnostic criteria for PTSD (n = 5) all had persistent STBs does suggest that children's reactions to traumatic events may relate to suicide risk. This is consistent with literature showing links between PTSD and suicide risk in adolescence,[41,42] and should be further explored in future studies with samples higher in trauma exposure.

Several study limitations should be noted. First, STB endorsement and psychiatric diagnoses were not systematically collected from the nondepressed peer sample during the preschool period, limiting the comparisons and inferences that can be drawn about that group. Second, this sample included mostly White children, potentially limiting generalizability to minoritized children—an important issue, as suicide rates in Black children are increasing,[43,44] alongside evidence indicating differences in STB patterns and suicide risk factors between Black and White youth.[45,46] Specifically, recent evidence that traditional risk factors—including mental health problems and suicidal ideation—are less likely to precede suicide behaviors in Black youth[41] raise the possibility that PO-MDD might not be as strong of a risk factor in Black children as in White children. Empirical studies of this issue in more diverse samples are warranted to address this question. Third, although we did not detect any significant differences between children with and without a follow-up assessment on key demographic variables or MDD severity, it is important to acknowledge that approximately 40% of the original sample did not participate in the follow-up, and might have differed from the follow-up group in aspects that were not available in the dataset, somewhat limiting the generalizability of these findings. In addition, given the relatively small sample size (albeit large for the unique characteristics under study), it is possible the odds ratios identified may be an overestimate of actual effects, and the confidence intervals wider than would be identified in a larger sample. Fourth, children in the PO-MDD study group were all offered parent–child psychotherapy, with most families completing a majority of the 20 therapy sessions. As the therapy appeared to reduce continuing STBs, the present findings might underestimate the link between PO-MDD and STBs in non–therapy-seeking children. Fifth, relatively few children with preschool STBs did not continue to endorse STBs in later childhood, limiting analyses of resilience factors. However, children who fit this profile might be of particular interest for future work in resiliency and preventive intervention.

Studying individuals with or at risk for STBs early in development holds promise for identifying at-risk children for targeted preventive intervention to alter risk trajectories away from persistent or escalating STBs.[47] This study highlights PO-MDD as a strong risk factor for the emergence and persistence of STBs into preadolescence, and advances our understanding of STB onset in children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Demographics for Preschool-Onset Major Depressive Disorder (PO-MDD) and Nondepressed Peer Samples

	PO-MDD (n = 137)	Peer (n = 53)	Statistic
	Mean (SD)	Mean (SD)	
Age at follow-up	10.14 (1.01)	10.05 (.90)	$F_{1,186} = 0.36, p = .551$
Income-to-needs	3.09 (1.01)	2.99 (1.01)	$F_{1,186} = 0.36, p = .551$
	n (%)	n (%)	
Sex (male)	92 (67.2)	30 (56.6)	$\chi^2 = 1.85, p = .174$
Race			Fisher exact, $p = .513$
Asian	1 (.7)	2 (3.8)	
Bi/Multi-Racial	13 (9.5)	5 (9.4)	
Black	12 (8.8)	4 (7.5)	
White	111 (81.0)	42 (79.2)	
Ethnicity			Fisher exact, $p = .320$
Hispanic	7 (5.1)	5 (9.4)	

TABLE 2

Suicidal Thoughts and Behaviors (STB) Endorsement for Preschool-Onset Major Depressive Disorder (PO-MDD) and Nondepressed Peer Samples Across Key Time Periods

| | PO-MDD (n = 137) | | | | | | Nondepressed PO-MDD (n = 137) | | | |
| | Preschool[b] | | Since preschool | | Current | | Lifetime | | Current | |
	n	%	n	%	n	%	n	%	n	%
STB endorsement (any)	65	47.4	93	67.9	36	26.3	12	22.6	2	3.8
Passive SI	54	39.4	86	62.8	32	23.4	12	22.6	2	3.8
Active SI	31	22.6	46	33.6	8	5.8	4	7.6	0	0.0
Suicide behaviors	10	7.3	30	21.9	7	5.1	2	3.8	0	0.0
Attempts	5	3.6	19[a]	13.9	2	1.5	1	1.9	0	0.0

Note: Since preschool includes current endorsements. PO-MDD = preschool-onset major depressive disorder; SI = suicidal ideation.

[a] Two children in the PO-MDD group had a suicide attempt but no reported SI prior to or at the time of the attempt.

[b] Of note, rates of preschool STBs in the PO-MDD sample are higher than previously reported, as we now report STBs endorsed at any session of the RCT, whereas prior papers only included STBs endorsed at baseline. [13,15]

TABLE 3

Logistic Regressions to Predict Suicidal Thoughts and Behaviors (STBs) Since Preschool and Currently as a Function of Preschool-Onset Major Depressive Disorder (PO-MDD) Covarying for Age (n = 190)

Since Preschool	B/Est.	SE	χ^2	df	p	FDR p	OR	95% CI
Any STBs								
Age	0.37	0.17	4.88	1	.027		1.45	1.04–2.00
PO-MDD vs peers	2.00	.38	27.46	1	<.001	<.001	7.38	3.49–15.57
Passive SI								
Age	0.35	0.16	4.76	1	.029		1.42	1.04–1.96
PO-MDD vs peers	1.76	0.38	21.82	1	<.001	<.001	5.83	2.78–12.21
Active SI								
Age	0.36	0.18	4.16	1	.042		1.44	1.01–2.03
PO-MDD vs peers	1.81	0.55	10.75	1	.001	.002	6.14	2.08–18.16
Suicidal behaviors								
Age	0.62	0.22	7.94	1	.005		1.85	1.21–2.84
PO-MDD vs peers	1.95	0.76	6.65	1	.010	.012	7.03	1.60–30.91
Suicide attempt								
Age	0.69	0.27	6.51	1	.011		1.99	1.17–3.36
PO-MDD vs peers	2.08	1.04	3.97	1	.046	.046	8.03	1.04–62.23
Current (prior month)[a]	B/Est.	SE	χ^2	df	p	FDR p	OR	95% CI
Any STBs								
Age	0.46	0.20	5.39	1	.020		1.59	1.07–2.34
PO-MDD vs peers	2.20	0.75	8.57	1	.003	.005	8.98	2.07–39.05
Passive SI								
Age	0.35	0.20	2.96	1	.085		1.41	.95–2.10
PO-MDD vs peers	2.03	0.75	7.34	1	.007	.010	7.63	1.75–33.22

Note: All scores in boldface type remained significant after corrections for multiple comparisons. B/Est. = B/Estimate; FDR = false discovery rate; OR = odds ratio; SI = suicidal ideation.

[a]Models did not converge for Active SI, Suicidal Behaviors, or Suicide Attempts.

TABLE 4

Suicidal Thoughts and Behaviors (STBs) in Early Adolescence as a Function of STBs in the Preschool Period

| | PO-MDD −STBs (n = 72), no preschool STBs | | | | PO-MDD +STB (n = 65), preschool STBs | | | |
| | Since preschool | | Current | | Since preschool | | Current | |
	n	%	n	%	n	%	n	%
STB endorsement (any)	39	54.2	15	20.8	54	83.1	21	32.3
Passive SI	36	50.0	14	19.4	50	76.9	18	27.7
Active SI	18	25.0	3	4.2	28	43.1	5	7.7
Suicidal behaviors	10	13.9	1	1.4	20	30.8	6	9.2
Suicidal attempts	6	8.3	0	0.0	13	20.0	2	3.1

Note: PO-MDD = preschool-onset major depressive disorder; SI = suicidal ideation.

TABLE 5

Global Functioning, Current Major Depressive Disorder (MDD) Symptoms and Diagnosis, Parent History of Suicide/Attempt, and Preschool and Lifetime Externalizing Disorders as a Function of Experiencing Suicidal Thoughts and Behaviors (STBs) During and/or After the Preschool Period

	No STBs (n = 33)		Emerged (n = 39)		Remitted (n = 11)		Persistent (n = 54)		Statistic	Peers (n = 53)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		Mean	SD
CGAS	70.82^a	16.92	64.00	17.80	68.09	18.60	56.98^b	16.49	$F_{4,184} = 10.14, p < .001$	78.74^c	17.68
MDD symptoms[d]	$.67^b$	.99	1.77^a	1.99	1.00	1.79	2.06^a	1.89	$F_{4,184} = 8.34, p < .001$	$.45^e$	.82
No. of lifetime traumatic events	3.78	3.45	3.64	3.62	5.00	4.78	4.07	3.98	$F_{4,182} = 0.94, p = .440$	2.94	2.58
	%	n	%	n	%	n	%	n		%	n
MDD/MDD-NOS diagnosis[f]	12.1^b	4	46.2^a	18	27.3	3	63.0^a	34	$\chi^2 = 31.81, df = 4, p < .001$	3.8^e	2
PTSD diagnosis	0.0	0	0.0	0	0.0	0	9.4	5	—	0.0	0
Parent suicide/attempt history	12.5	4	21.1	8	0.0	0	13.2	7	$\chi^2 = 1.48, df = 4, p = .831$	13.2	7
Preschool externalizing disorder	57.6	19	56.4	22	54.6	6	69.2	36	$\chi^2 = 1.00, df = 3, p = .800$	—	—
Lifetime externalizing disorder	60.6	20	71.8	28	63.6	7	75.9	41	$\chi^2 = 38.22, df = 4, p < .001$	7.6^g	4

Note: CGAS = Children's Global Assessment Scale; NOS = not otherwise specified; PO-MDD = preschool-onset major depressive disorder; PTSD = post-traumatic stress disorder.

[a] Indicates groups that are significantly higher than [b].

[b] Indicates groups that are significantly lower than [a].

[c] Peer sample is significantly higher than emerged and persistent groups.

[d] MDD symptoms includes 8 core symptoms of depression captured by the Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime version, reported by either parents or children, and excludes suicide variables.

[e] Peer sample is significantly lower than emerged and persistent groups.

[f] MDD/MDD-NOS diagnostic categories are based on DSM-V criteria reported by either parents or children and include suicide variables.

[g] Peer sample is significantly lower than no STBs, emerged, remitted, and persistent groups.