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The neurobiological impact of postpartum maternal depression: prevention and intervention approaches

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Abstract

The lasting negative impact of postpartum depression (PPD) on offspring is well established. PDD appears to impact neurobiological pathways linked to socio-emotional regulation, cognitive and executive function, and physiologic stress response systems, systems also associated with toxic stress and negative health trajectories across the life course. Perinatal depression is expected to have significant consequences for offspring given the shared biological processes during pregnancy and the subsequent primacy of the early maternal-child relationship in shaping the child's neurobiological development. A substantial body of literature has examined prevention and intervention efforts during the prenatal period, including the challenges associated with the medication use during pregnancy. ^{1,2} Recognizing the expansive nature of the existing literature, this review take a novel focus, specifically examining the current state of research defining the effect of universal, selected and indicated interventions for PDD on *infant* neurodevelopment. This focus was selected because of the unique nature of this time-period for the interaction of maternal psychopathology and infant development, acknowledging that both prenatal and parental depression at later developmental times points can influence child outcomes. We begin by providing a general overview of PPD and the rapid neurodevelopmental changes occurring during the first years of life. Building upon this foundation, we then discuss the specific evidence linking postpartum depression to neurobiological consequences in the offspring. We focus on the development of neural pathways with established associations those aspects of maternal caregiving most impacted by depression, including feeding and nutrition, sleep, health monitoring, play and language, and maternal sensitivity and engagement. Lastly, we discuss specific evidence related to the efficacy of current PPD efforts on infant neurobiological outcomes, highlighting existing research gaps as well as the utility of research in this area to impact long-term health

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trajectories. Given the established lasting, and potentially intergenerational, negative implications of maternal depression enhanced efforts targeting increased identification and early intervention approaches for PDD that impact health outcomes in both infants and mothers represents a critical public health concern.

Keywords

postpartum depression; psychotherapy; dyadic interventions; neurobiology; early life stress; infants

INTRODUCTION

Postpartum depression represents a significant public health problem with prevalence estimates ranging from 12–19% and clear negative implications for both maternal and infant health and wellness.³ Although risk factors for postpartum depression are generally similar to those for depression at other time points in the life course, the substantial neuroendocrine changes which occur in the mother immediately after birth and the significant increase in contextual stressors that accompany caring for an infant may compound these risks.^{3–6} For instance, using data from the National Epidemiological Survey of Alcohol and Related Conditions, Le Strat, Dubertret, and Le Foll (2011) compared characteristics of women currently or within the past-year pregnant with and without depression. Demographically, depressed women were more likely to be unmarried, multipara, and ethnic minority status. As compared to non-depressed women, depressed mothers also were more likely to be under the age of 25, have lower income levels, and be less educated. Depressed mothers were significantly more likely to use substances and were 8 times more likely to also suffer from other psychiatric disorders than non-depressed women or non-depressed mothers.⁷ Repeatedly, risk for postpartum depression has been linked to increased exposure to stressful life events.⁸ Demographic stressors, like teenage parenthood⁹ or military involvement (e.g. military wives)¹⁰ have also been associated with elevated post-partum depression. Exposure to both early life adversity as well as current life stressors, such as unemployment, change in marital status, death of a loved one, or disease, seems to increase risk for postpartum depression particularly among women with presumed genetic vulnerability and with limited access to protective resources (e.g., social support, financial support).¹¹ Unfortunately, these same risk factors may affect maternal caregiving, potentially resulting in a synergistic negative effect on infant neurobiological development.

Given the significant number of maternal-infant dyads affected by PPD there is a growing interest in developing better population wide and demographically focused efforts to increase PPD identification and implement effective treatment. Public health approaches to preventive interventions distinguish among universal, selective and indicated interventions.¹² Universal interventions include health promotion efforts and intervention efforts aimed at a broad population. Public service messages addressing PPD, for example, might help women recognize how PPD differs from more typical symptoms of exhaustion, sleep disruption and emotional lability that are prevalent in the weeks following delivery of a child. Selective interventions target members of a group who have high lifetime or high

imminent risk for depression. Some estimates indicate that almost 40 percent of women with children under the age of 3 years old and who live in stressful urban environments, for example, have elevated levels of depressive symptoms.¹³ An intervention to prevent depression that targets impoverished, inner city mothers after the birth of a child would be a selective intervention. Finally, indicated preventions target those who manifest depressive symptoms that may later become a full-blown disorder. Referral of women who screen positive on the Edinburgh Postnatal Depression Scale (EDS),¹⁴ or similar measure, at the 6-week postpartum check-up to a perinatal intervention program would be an indicated intervention.

Particularly for pediatric health care providers, including mental health, the public health relevance of PPD extends beyond mothers to include the effects of both the illness itself as well as intervention efforts on their infants. With this in mind, preventive interventions can also be evaluated in their ability to buffer the impact of maternal depression on her offspring. Despite the clear links between maternal PPD and negative child outcomes, the impact of current efforts targeting the prevention and/or treatment of PPD to also diminish the negative impact on *child outcomes* remains limited. In older children, evidence of the positive effects of treatment of parental depression for both children and parents have been reported, although for the most part this has been limited to examination of the effects on child psychopathology without exploration of other health and biological outcomes.^{15,16} For young children, where maternal depression is more likely to substantially influence caregiving and the dyadic relationship, the few existing studies that have explored the direct impact of PPD interventions on infant short and long-term outcomes suggest that current approaches are insufficient to protect or buffer offspring from the harmful effects of PPD.¹⁷

This review focuses on infant neurodevelopmental outcomes associated specifically with PPD and its treatment. The neurodevelopmental and health effects of medication use, specifically selective serotonin reuptake inhibitors (SSRI), on prenatally exposed infants remains a highly prolific area of research that is covered in depth elsewhere and is beyond the scope of this review (for reviews please see^{18–20}). In examining the impact of interventions on neurobiological outcomes in offspring, we propose that a focus consistent with the Research Domain Criteria²¹ on neural systems and biological pathways, as opposed to diagnostic categories, will provide greater insight into needed next research steps. Despite established links between PPD and a myriad of negative health outcomes across the life-course, the mechanisms and specific pathways through which this elevated risk is embedded remain poorly defined. Disentangling mechanisms and moderators that include shared and independent genetic liability; familial environment, such as social support, paternal factors, and parental discord; infant temperament and other factors is a needed, albeit complex, next step with significant public health and policy implications. Delineating the modifiable factors, aspects of pre-existing risk, and specific treatment components associated with improved child outcomes, is expected enhance the efficacy of PPD interventions, not only for reducing maternal symptoms but also for promoting infant health and development. Given the challenge, particularly in young children, of eliciting data about psychological symptoms from sources other than caregivers, and the potential impact of depression symptoms on parent report of child behavior, establishing biomarkers

of both vulnerability and resilience in infants exposed to maternal PPD is critical. The pressing need for these advances is further highlighted by the existing literature, albeit limited, suggesting that treatment of maternal depression does not necessarily result in improved maternal-child interactions, one of the key proposed mechanisms through which PPD negatively impacts infant outcomes.²²

Infant neurodevelopment

The intricate development of the human brain begins only a few short weeks after conception and continues for decades. During the first years of life, there is tremendous overgrowth and differentiation of the neural substrate. Multiple processes are involved in this initial period of rapid brain growth including cellular migration, neurogenesis, dendritic branching and axonal formation. It is upon this basic early architecture of the brain that subsequent neurodevelopment and function depends. Following an initial overgrowth and proliferation, the shaping and refining of neural circuits through synaptogenesis, apoptosis, and myelination occurs in an experience dependent manner. That is, synapses that are stimulated repeatedly tend to strengthen, creating consolidated circuits that are then myelinated. Synapses that do not receive repeated stimulation are lost, a process called pruning, which subsequently results in apoptosis, or programmed cellular death. The rate by which the refining of these neural circuits occurs differs throughout the brain, with protracted refinement in some areas, such as the prefrontal cortex, well into adolescence and early adulthood. The refining of these circuits is directly influenced by experience and, particularly during infancy and early-childhood, is intricately linked to the young child's experience of caregiving.

The impact of maternal care on neurodevelopmental processes is an area of active research, both in terms of understanding the consequences of appropriate, contingent and sensitive caregiving and in relation to defining the lasting negative consequences of atypical caregiving, including the effects of maternal depression.^{3,16,23–26} Mothers, both in humans and across mammalian species, serve as potent external regulators of infant neurodevelopment, physiology, and emotion regulation.^{27–31} As such, variations or deviations in the expected caregiving experience, such as often occurs with PPD, is expected to influence an infant's developing neurobiological processes likely resulting in life-long alterations.

Postpartum depression and the spectrum of postpartum disorders

The emergence of postpartum depression may begin with the appearance of the postpartum blues. Postpartum blues typically occurs during the first 2 weeks of childbirth, with the strongest link to the physiologic drop in levels of circulating hormones and massive diuresis following delivery. Symptoms are generally short-lived and include crying, confusion, mood lability, anxiety, and sadness.⁴ No demographic or cultural factors have been demonstrated to significantly increase risk for postpartum blues.³² Currently, no available evidence links postpartum blues not escalating to PPD to any adverse effects on children. Given that postpartum blues *on its own* is fleeting and relatively minor in impairment, the condition will not be the focus of subsequent discussion. Its chief importance is that approximately, 20 percent of women who experience postpartum blues will subsequently develop PPD, as such

postpartum blues represents an important risk factor.³³ An alternative perspective, to date unexplored, is that an enhanced understanding of the 80% of women who do not develop PDD may provide novel insight into preventive approaches.

Differing from postpartum blues, PPD symptoms match those of a major depressive episode and include: sadness, loss of interest in previously pleasurable activities, sleep disturbance, loss of energy, weight changes, concentration problems, agitation, feelings of worthlessness or guilt, or thoughts of suicide and meet similar duration and intensity criteria to typical depression.³⁴ In very rare cases, new mothers exhibit a severe, postpartum disorder known as *postpartum psychosis*, involving delusions, hallucinations, and gross functional impairment.³⁵ Postpartum psychosis typically appears during the first three months after childbirth.⁴ Symptoms are often consistent with a bipolar disorder.^{36,37} Postpartum psychosis represents the rarest form of the major three postpartum disorders, with an incidence rate of 1–2 cases per 1000 births.³⁷

Neurodevelopmental impact of maternal postpartum depression

The impact of PPD crosses multiple domains for both the mother and the infant.^{3,26,38} In addition to health impacts, the impact of maternal depression has also been evaluated in terms of its economic impact in relation to elevated health care utilization as well as other costs such as lost wages, increased costs associated with special education, etc. factors of heightened relevance in the current economic climate.^{39,40} Negative effects of PPD on offspring include increased risk of insecure attachment and poorer cognitive, language, social-emotional, and behavioral development.^{26,41} In smaller prospective studies and larger epidemiologic samples, PPD has been associated with increased risk for internalizing symptoms at 18 months of age as well as increased rates of internalizing disorders throughout childhood and adolescence.^{42–45} Elevated rates of externalizing symptoms, including physical aggression, also have been reported across childhood, suggesting that PPD impacts multiple neural pathways.^{2,46–48} Other neurobiological consequences of PPD have been reported including decreased diurnal cortisol, altered stress cortisol reactivity, inattention, social disengagement, lower IQ, and language delays.^{49–54} Infants of mothers with PPD are reported to exhibit less positive facial and vocal expressions and be more irritable and avoidant.⁵⁵ Additionally, there is evidence of the association between PPD and poor infant physical growth across the first year of life, an effect that was stronger than socioeconomic status and remained even after controlling for infant birth weight.⁵⁶ While much of the work summarized here reflect findings specific to PPD, distinguishing between the effects of prenatal and postnatal exposure and the delineation of moderating and mediating pathways is challenging.^{26,57,58}

The relation between maternal depression and infant negative outcomes has been explained, in part, by the impact of depression on maternal interactional behaviors and distorted maternal cognitions about her infant and about parenting.⁵⁹ Meta-analyses of studies reporting on the impact of maternal depression on maternal behavior note that depressed mothers are more irritable and/or hostile, less engaged with their infant, play less with their infant and demonstrate decreased positive emotion and warmth.^{60,61} Depressed mothers also may be more aggressive in their parenting strategies and less emotionally responsive to their

offspring. Infants and toddlers of mothers with depression have been found to exhibit increased rates of insecure attachment, reduced social engagement, increased negativity and poor fear regulation.^{43,50,62,63} One interesting unanswered question is whether maternal difficulties in establishing relationships with infants, or a diminished positive experience of the relationship, is reflective of the underlying neurobiology of depression or a pre-existing risk factor that contributes to the development of PDD.²²

PPD also influences other caregiving and health related practices, which independently may effect neurobiological development, suggesting innovative targets for universal, targeted and selected interventions.⁶⁴ At the extreme, studies have examined the impact of maternal depression on early childhood neglect and aggression/discipline.⁶⁵ Depressed mothers are more likely than their non-depressed counterparts to engage in neglectful behaviors, such as leaving children home alone.^{66–68} Depressed mothers also are more likely to report being irritable,⁶⁹ have increased negative emotions, feel less invested, and use more physical discipline with their children than non-depressed mothers.^{70–73}

In addition to elevated risk of abuse and neglect, mothers with PPD are more likely to engage in less optimal feeding practices, including decreased rates of breast feeding, increased rates of inappropriate feeding habits, like introducing cereal and juice earlier than recommended, decreased rates of well-child visits and fewer vaccinations.⁷⁴ Mothers with PPD have decreased rates of reading, playing and talking with infant as well as less adherence to daily routines.^{64,75} The impact of PPD on these other aspects of caregiving may play a role in infant neurodevelopmental disruptions. For instance, lower rates of reading to children may influence the development of language deficits associated with PPD, a model that has yet to be examined.⁷⁵ Despite the likelihood that these other dimensions of caregiving can compound the negative impact of PPD, traditional psychotherapy and/or pharmacotherapy do not routinely address them. Although it appears intuitive that effective treatment of maternal depressive symptoms is needed to prevent or ameliorate the negative effects on offspring, this remains to be empirically tested in well-designed studies, and in part, would rely on data defining the mechanisms through which PPD results in negative neurobiological outcomes.^{2,76}

UNIVERSAL, SELECTED, and INDICATED EFFORTS FOR MATERNAL POSTPARTUM DEPRESSION

The ideal goal of all public health efforts centers on prevention. In the case of the lasting impact of PPD on infant neurodevelopment, prevention efforts may serve to prevent both maternal depression and the negative effects on infant neurodevelopment and health. Given evidence supporting the intergenerational risk of depression,^{77,78} particularly associated with early childhood abuse,^{79,80} prevention efforts focused on enhancing maternal sensitivity and contingent caregiving among mothers with a history of child abuse, a substantial risk factor for both PPD and caregiving deficits regardless of their own depressive status, may provide an innovative approach to intergenerational protection. In the next section we discuss non-pharmacologic treatment of PPD, providing a broad overview of the efficacy of universal, targeted and indicated efforts on PPD, with specific attention to the limited number of studies that have examined the impact of these interventions on infant

outcomes. We identify the strengths and weaknesses of data at each level as well as the gaps in the research. Lastly, we propose a targeted research agenda that leverages evidence for best approaches and suggest novel biological indicators that may provide enhanced evidence of the efficacy of these approaches.

Universal

Universal efforts focus on health promotion and/or efforts aimed at a broad population. One of the primary approaches for PPD has been the implementation of universal screening of mothers for PPD by a variety of health care providers including obstetricians, pediatricians, nurses, lactation consultants, birthing centers, and WIC agencies that are the most likely care providers for screening for PPD. The World Health Organization, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists recommend universal screening at all postpartum and well-child visits.^{1,81,82} To be effective universal screening must be both practical and accurate. Studies have examined the utility of a range of different screening of very brief (e.g., 2 or 3 questions) and longer questions screens, finding that both short and longer screens are effective in identifying postpartum depression, particularly within the primary care setting.⁸³ While the implementation of universal screening within primary care settings has resulted in significant increased PPD identification and referrals,⁸¹ to date the impact of these screening on actual maternal depression levels is equivocal,⁸⁴ and the downstream effect on neurobiological outcomes in offspring has yet to be studied.

Universal screening—In May 2015 the American College of Obstetricians and Gynecologists released a committee opinion regarding screening for perinatal depression. This report noted that PPD symptoms often go under-recognized and under-reported due to the failure of both providers and mothers to differentiate between normal physiologic changes and pathologic symptoms.^{1,85} The consequences of perinatal maternal depression for infant development is pervasive, prompting efforts to improve screening and treatment efforts, including ACOG recommendations for implementation of systems to ensure follow up for diagnosis and treatment are needed.¹ Screening efforts using a variety of established measures (CES-D, EDS, and BDI) have been found to successfully identify major and minor depression during pregnancy and offer established and relatively simple measures to incorporate within routine prenatal care for medical providers, including obstetricians and pediatricians.⁸⁶ Screening tools are generally more accurate in detecting major depression as compared to minor depression.⁸⁴ Despite the established risks associated with PPD and the availability of practical screening measures, the use of validated tools to identify PPD is rare in obstetric practices. Overall screening rates often fall below 50 percent and the percentage of mothers actually entering treatment, once identified, is even lower.^{86–88} When considering a targeted goal of ameliorating the negative neurobiological impact of PPD on offspring, an alternative venue in which to implement universal screening is a well-child visits, particularly as pediatricians may be the only medical providers routinely encountered by mothers during the child's first years of life.⁸¹ Similar to screening within obstetrics the need for rapid, practical screens and referral options is critical to effective universal efforts at this level.⁸⁹

Universal interventions—In addition to universal screening, universal prevention efforts have been explored. Interventions include educational, peer support, massage, group support, and structured psychotherapies. The effectiveness of these interventions, however, varies. Analyses suggest that universal preventive efforts have not been cost-effective and are significantly less effective than targeted or indicated efforts.^{90–94} To date few of these have evaluated the impact of preventive interventions on infant neurobiological outcomes. Evidence of the positive impact on infants of universal interventions targeting anticipatory guidance about breast feeding, playing, sleep, book reading/talking and nutrition have been reported. Unfortunately, examination of the impact on maternal mood in these studies is absent. Universal intervention studies that focus on parental behaviors known to be impacted by predisposing factors associated with PPD, (e.g., previous depressive episode, age, child maltreatment) that concurrently measure the impact on both maternal mood and infant neurobiological development are needed.

A variety of different universal home visiting and community support intervention programs have been studied, with varying levels of scientific rigor. In a randomized study examining both the impact and the cost-effectiveness of a community in-home support on PPD, no evidence of effectiveness was found.⁹³ Data combined with other studies suggesting that *universal* home visiting programs are neither effective nor cost-effective, and instead interventions targeting specific, at-risk, populations, are needed, and have demonstrated efficacy (see below).^{95–98} Interestingly, in a low-risk, universal home visiting intervention, women who had low levels of depression symptoms at six weeks post-partum showed significant reductions in depressed mood, suggesting a stronger protective effect of these interventions among low risk mothers.⁹⁹

Cognitive behavior therapy (CBT) is an empirically supported treatment for prevention and treatment of depression across the life course. A recent meta-analysis examined studies of CBT for treatment and prevention of perinatal depression, including PPD.¹⁰⁰ While CBT demonstrated some evidence of efficacy for maternal depressive symptoms when administered at the community level, its impact was small when administered prenatally. Greatest evidence of efficacy for PPD was found when CBT was provided to highest risk individuals, administered postnatally, and provided as individual therapy as opposed to group therapy.¹⁰⁰ However, the impact of CBT on infant neurobiological outcomes remains unknown.

In conclusion, despite widespread recognition of both the frequency and the negative impact of PPD, current approaches to implementing both universal screening and universal prevention efforts have demonstrated only minimal impact on maternal outcomes.^{90,101} Well-designed studies of universal interventions have not yet evaluated the impact on infant neurodevelopment. With this body of evidence in mind, efforts to decrease the negative impact of PPD on infant outcomes will likely need to be either selected or indicated to be efficacious.

Selected

Selected interventions require identification of individuals at heightened risk. In the case of PPD, the risks are, in general, similar to those for major depression and include: previous

history of depression, elevated financial stress and strain (e.g., unemployed status, financial hardship, and poverty), heightened marital stress and strain (e.g., marital conflict, separation, and divorce), diminished social support, and a family history of depression.^{5,6,102,103} Moreover, women reporting low socioeconomic status, defined as a combination of low income, less than a college education, being unmarried and being unemployed, were at an 11-fold greater risk for postnatal depression compared to women reporting high socioeconomic status.⁶ Strong evidence indicates that women with history of neglect, sexual abuse, and other early traumatic life events are at particular risk for perinatal depression, a risk moderated by both current life stressors and potentially maternal race.^{5,104,105} This relationship between elevated risk of PPD in women with a history of child maltreatment may be compounded as maltreatment is also associated with altered immunologic and neuroendocrine regulation, factors that are independently linked to both poor birth outcomes and PPD.^{106,107} Increased risk for PPD is associated with preterm delivery and infant care in the neonatal intensive care unit (NICU). Exposure to abuse during childhood is a risk factor for maternal depression during the perinatal period, and subsequently maternal depression, in the perinatal period, is associated with elevated risk of both child maltreatment and depression in her offspring.^{108,109} This cyclic, and intergenerational impact, suggests that careful assessment of the effects of child maltreatment on maternal neurobiology and mothering behavior, irrespective of depressive status, might identify mechanistic pathways contributing to multi-generational risk for depression. Evidence is accumulating to suggest that pregnant women and mothers of young children should be screened for history of childhood abuse and offered interventions to improve their own well-being, ideally preventing serious long-term health disparities in their offspring, and potentially subsequent generations as well.

One targeted population with significantly elevated rates of PPD is mothers whose infants are in the newborn intensive care unit (NICU). Rates of PPD are substantially higher among mothers of children in the NICU, as are rates of post-traumatic stress disorder and other anxiety disorders.¹¹⁰ Although recognizing the need for enhanced identification of PPD in the NICU, to date it is unclear who are the best providers to implement this screening.¹¹¹ Targeted interventions may decrease PPD among these mothers, with some, but not all, interventions demonstrating moderate efficacy.^{112–115} Infant outcomes positively impacted by these interventions include increased rates of secure attachment,¹¹⁶ improved feeding behaviors,¹¹³ decreased irritability and colic,¹¹⁷ and enhanced cognitive functioning at two years of age.¹¹⁸ Additionally, while other attachment and dyadic focused interventions have demonstrated efficacy in improving infant neurobiological outcomes with preterm babies,^{119,120} these interventions did not assess the impact on maternal mood, despite evidence that disrupted maternal-infant relationships are related to PPD risk. Future studies to examine potential bidirectional effects are warranted.

Selected interventions—In a recent review of PPD preventive interventions by Werner and colleagues, of the 37 RCTs only 17 were found to be effective, and of these 13 were targeted to at-risk populations, supporting the hypothesis that the greatest efficacy for prevention is associated with selected populations. Several important barriers to these interventions have been proposed including inconsistent measurement of PPD and high rates

of attrition, potentially as a consequence of stigma, accessibility, and a sole focus on the mother.^{94,121} Feasibility of web and smartphone based interventions for PPD to address accessibility challenges have been piloted and represent innovative future directions.^{122–126} Examples of larger selected interventions targeting depression after the first year of life have found that improvement in maternal depression symptoms mediated the effect of family based treatment on toddler externalizing and internalizing symptoms, however this was not specific to PPD.¹²⁷

Despite evidence that universal CBT was, for the most part, ineffective in decreasing PPD risk, CBT provided to selected high-risk populations appears to have some efficacy in decreasing depression risk as well as mood regulation and coping, factors expected to have direct implications for maternal caregiving.^{3,128–130} The effects in the majority of studies are modest, however, likely due to high rates of attrition and flaws in study design.³ Feasibility trials of cognitive behavioral based on-line interventions for at-risk mothers may result in greater efficacy given that accessibility of treatment has been identified as a primary barrier to effective selected interventions.^{124,131} In at least one study, CBT has demonstrated unique effects on infant neurobiological outcomes, specifically cortisol levels.¹²⁹ In this study, high-risk mothers, defined by past history of depression or elevated depressive symptoms during the second trimester, were randomized to CBT or usual treatment. A positive effect on both maternal and infant cortisol levels was detected at 6 months postpartum, suggesting a joint neurobiological effect.¹²⁹

Home based interventions for at-risk mothers have been evaluated, and while several studies have demonstrated positive effects on depression, this has not been universal.¹³² Quite unexpectedly, a study of low-income mothers who received a home-based, peer support, intervention with education about maternal-infant interactions found that the control group demonstrated greater reductions in depressive symptoms and better maternal infant interactions, the opposite of expected outcomes. The authors ascribe these discrepant results to the use of peer, rather than professional, home visitors. No impact on infant IQ or salivary cortisol was detected.¹³³ In a tiered home visiting program, with specialty trained home visitors, home visiting appeared to be protective against PPD through 18 months of age, however the impact of this intervention on infant outcomes was not evaluated.¹³⁴ The preventive impact of telephone-based peer mentoring for at-risk mothers has also been explored. While efficacy of decreasing depressive risk was reported, to date the impact on infant outcomes has not been reported.⁹¹ Fussy Babies, a tiered individualized intervention,¹³⁵ has demonstrated positive effects on maternal well-being, depression and parenting stress among women who received the intervention compared to wait list control, however, to date, the impact on infant neurobiological or health outcomes has not been evaluated (personnel communication).

Although a significant number of psychotherapeutic and educational approaches have been studied as selected interventions for PPD, alternative interventions targeting infant behavior or caregiving factors associated with elevated PPD risk also have been proposed. Infant sleep problems, for example, appear to have a bi-directional relationship with maternal PPD, with evidence of poor sleep practices among mothers with PPD as well as elevated risk of PPD among mothers with infants experiencing sleep problems.^{136,137} Further, infant sleep

problems are independently associated with poor maternal-infant attachment, less sophisticated child cognitive development and elevated risk of child maltreatment.¹³⁸ Several randomized trials have examined the impact of sleep interventions on both maternal mood and child developmental outcomes, demonstrating consistent evidence of a positive effect on maternal mood, child sleep and child behavior problems.^{136,139,140} The long-term neurobiological and health effects of these interventions beyond the toddler years has yet to be examined. Despite the evidence of efficacy of infant sleep strategies, to date this has not been integrated into other indicated or selected interventions for PPD. Another small pilot study examined the impact of problem solving education on low-income mother of preterm infants, finding decreased rates of PPD, but this study failed to concurrently explore infant outcomes.¹¹²

In conclusion, selected interventions have demonstrated modest efficacy in decreasing PPD in selected, high-risk, populations. To date, there is insufficient evidence to suggest that one type of intervention is more efficacious than another in preventing PPD. Intuitively, dyadic-based interventions might be expected to demonstrate enhanced positive effects on infant outcomes compared to interventions specifically targeting mothers, however, this has yet to be empirically tested. Few studies have examined the impact of selected interventions on infant outcomes, an area much in need of research. Based on the existing, albeit limited data, it appears that CBT selected interventions show promise for neurobiological effects on infants and mothers.^{129,133} The positive findings associated with sleep interventions suggest that integration of sleep education and support into other interventions may have particular utility. Given the growing evidence of efficacy for selected interventions on maternal depression, there is now a clear need to evaluate the short and long-term impact on both maternal and infant neurobiological outcomes. Future research that focuses on selected interventions targeting maternal biological markers of elevated PPD depression risk, including genetic liability or neuroendocrine markers, are innovative and needed next research steps, particularly as genetic and neurobiological markers may have shared influences on both mother and infant.^{141,142}

Indicated

The established links between PPD and negative infant outcomes suggests that treatment of PPD should result in improvement in maternal-infant interactions and infant behavior, health and neurobiology. In contrast to the wide variability in efficacy for universal and selected interventions, indicated non-pharmacologic interventions for PPD have demonstrated modest efficacy in decreasing maternal depressive symptoms.¹⁴³ These interventions include support groups, home visiting, peer volunteer telephone support, cognitive behavioral therapy (CBT), psychodynamic therapy and interpersonal therapy (IPT).^{3,17,22,144–146} Therapeutic interventions for PPD also differ widely on their focus relative to the infant and the mother-child relationship, with some only including the mother and some specifically focusing on the dyad.

A meta-analysis of the impact of psychotherapy for maternal depression on child outcomes identified nine studies that met inclusion, with five of these studies focused on PPD and young children.¹⁴⁷ Overall, positive effects on both infant behavior and maternal-infant

interactions were detected. CBT and IPT were not significantly different from each other in terms of infant outcomes, consistent with an earlier comprehensive review that found that treatment of PPD resulted in improved maternal-infant interactions as reported by mothers.²² Very few of these studies examined the impact maternal treatment on direct measures of infant cognition, behavior and health, as opposed to maternal report, a potential confound that warrants future study.²²

Maternal Psychotherapeutic interventions—Interpersonal therapy (IPT) is an established treatment for depression, including PPD, in both individual and group settings.^{17,148,149} However, while IPT decreased parenting stress, at least one study did not find improvement in maternal report of infant attachment, behavior or temperament, suggesting that IPT alone is not sufficient to protect infants from the negative impact of PPD.¹⁷ A more recent study of IPT found effectiveness not only for maternal symptoms but also mother-infant interactions assessed through trained observers.¹⁵⁰ Interestingly, similar to the effect of toddler parent psychotherapy, genetic factors appear to moderate maternal response to IPT.¹⁵¹ An intriguing future direction of research might be to explore whether infant genotype moderates the impact of PPD treatment on infant outcomes.

CBT also has significant evidence to support its use to treat maternal depression including PPD. Improvement in infant cognitive outcomes has been demonstrated following treatment of PPD in several studies, but not all, that evaluated CBT and other therapies.^{145,152,153} In a RCT comparing CBT, non-directive supportive therapy, and psychodynamic therapy with routine primary care for low-risk mothers with PPD, improvement in social emotional and cognitive measures were found in all three treatment groups at 18 months of age. However, these effects did not persist to 5 years of age. The investigators suggest that selecting mothers from a relatively low-risk cohort may account for these findings; selecting higher risk mothers may have resulted in larger and more persistent findings. The authors also suggested that for higher risk women there was not significant difference between interventions with specialists. From an economic cost effectiveness perspective, using non-directive supportive therapy may be beneficial. In another randomized trial of group CBT, mother-toddler groups, and no treatment, no group differences for mothers of older toddlers, no effect of intervention on depression was detected.¹⁵³ Although some evidence of greater decline in child psychological symptoms were suggested in the CBT group, the authors noted this should be interpreted with caution.

One intervention for prenatal and postnatal anxiety and depression that does not seem to have been studied to date is mindfulness. This is a surprising omission given the increasing number of mindfulness interventions in the field of psychiatry at large. Levels of maternal mindfulness during pregnancy was associated with fewer infant self-regulation problems and less negative affectivity after birth. While the study only focused on maternal anxiety, this work should be extended to maternal depression and could be applied in universal and selected interventions as well as indicated.¹⁵⁴

Dyadic interventions—Given the significant evidence that PDD negatively impacts maternal-infant interactions several studies have reported on the effectiveness of therapies focused on the maternal-infant relationship, administered both pre and postnatally, as well as

dyadic therapies.¹⁵⁵ Toddler-parent psychotherapy (TPP), provided weekly over the course of a year has been found to impact attachment classification as well as IQ in infants of depressed mothers.^{146,151,156} The improvement in IQ was limited to verbal IQ, and persisted after controlling for covariates. In this study, a significant proportion of the impact was moderated by subsequent maternal depressive episodes indicating that heightened monitoring and booster sessions ought to be included over the first five years of life. Insecure attachment, elevated among mothers with depression, also decreased with TPP. In fact, depressed mothers who received treatment actually demonstrated higher rates of secure attachment than control mothers, hinting that the relationship between PPD and insecure attachment may be bidirectional.¹⁴⁶ Similar to initial risk for PPD, genetic variability appears to impact treatment efficacy, again suggesting that specific women may be more vulnerable to PPD, but also more responsive to interventions, as may their offspring.¹⁵¹

Child Parent Psychotherapy (CPP) is an evidence-based therapy for traumatized mother-child dyads with established effectiveness of maternal functioning in women with a history of complex trauma and/or current exposure to interpersonal violence, factors often associated with maternal depression as well as other psychopathology such as PTSD. The improvement in maternal functioning, particularly in relation to her parenting and sensitivity should have positive effects on infant neurodevelopmental processes. Ideally, effective treatment would mitigate the lasting negative consequences of maternal depression. In a more recent study, CPP was administered prenatally to mothers with depression and/or PTSD. Improvement in mothers' symptoms was strongly correlated with maternal self-report of attachment to their unborn child. Specifically, the greatest improvement in symptoms was found among mothers who pre-treatment reported less attachment to their infant.¹⁵⁷ This finding is consistent with the attachment based model upon which CPP is based. For mothers with less prenatal attachment, an attachment derived therapy administered prenatally may significantly improve emerging mother-infant attachment relationships. Evaluation of the impact of this type of intervention on maternal sensitivity, contingent parenting and dyadic attachment classification in future studies would be useful, as would examinations of neurobiological outcomes in these same infants. A recent pilot randomized controlled trial of Triple P Positive Parenting in women with PPD found that while triple P was highly acceptable in women with depression, no significant differences between active treatment and control groups in maternal-infant interactions or depressive symptoms were reported.¹⁵⁸

Infant Massage—Consideration of a range of alternative treatment approaches for PPD is increasing, likely in light of concerns about medication use in pregnancy and breastfeeding and challenges to treatment adherence. Evidence is accumulating to suggest that maternal massage administered prenatally, as well as infant massage postnatally, may not only decrease maternal depressive symptoms but also improve infant neurobiological outcomes.^{159–161} In a trial comparing support group to maternal-infant massage for PPD, both groups demonstrated decreased depressive symptoms, but at one year post-delivery symptoms were still elevated compared to non-depressed mothers.¹⁵⁹ Interestingly in non-pregnant studies massage therapy has been suggested to decrease cortisol, ACTH and increase oxytocin, although some debate exists.^{162,163}

A number of individual and dyadic therapies have demonstrated positive effects on postnatal maternal depressive symptoms. Particularly for dyadic interventions, there appears to be positive effects on maternal-infant interactions and beginning support for positive neurobiological effects in infants as well. In light of the limited effectiveness of universal and selected interventions, investment in indicated treatments for PPD, with extended monitoring for recurrence of PPD, is likely the most promising direction for additional research.

CONCLUSIONS

Maternal depression is a pervasive public health problem with substantial economic and health costs mothers and their offspring. Although universal screening efforts appear to increase PPD identification, to date these interventions have been relatively ineffective at reducing PPD and no data exists demonstrating positive downstream impacts on infants. Given this, research focused on defining existing barriers to effective PPD treatment by women identified by universal screening is a high priority. Selected interventions have demonstrated minimal effectiveness on maternal mood symptoms and maternal-infant interactions, unfortunately there is no evidence of a positive impact on infant neurobiological outcomes, again highlighting needed next research steps. Both dyadic and individual psychotherapies have demonstrated efficacy in the treatment of PPD. A growing body of research indicates that these treatments also improve maternal-infant interactions. However, there remains a paucity of research exploring the short and long-term neurobiological consequences of these interventions on infants. This research gap is somewhat striking given the increasing focus on health and neuroscience across medicine and funding agencies. Studies specifically designed to capture both maternal and infant outcomes are needed. Novel therapies that leverage evidence based existing dyadic therapies and integrate alternative therapies that address caregiving behaviors influenced by PPD, such as sleep, nutrition, and play, may have synergistic benefits for both mothers and their infants. Efforts to determine shared neurobiological pathways linked to elevated risk for PPD, maternal exposure to child maltreatment, and decreased maternal sensitivity with her own children has the potential to uncover innovative preventive and therapeutic targets. As burgeoning data suggest that the impact of PPD may also span generations, improved efficacy of interventions may result in lasting effects across future generations.

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Key Points

- Postpartum depression is a highly prevalent public health concern with implications for infant neurobiological outcomes.
- To date evidence for universal and selected interventions is limited in terms of efficacy for the treatment of postpartum depression, and there is a dearth of evidence of this level of intervention on infant neurobiological outcomes.
- A small, but growing, body of research, suggests that indicated psychotherapeutic interventions have positive effects on infant neurobiological outcomes.
- Greater incorporation of biological outcomes in both the infant and mother is needed to improve long-term infant and maternal outcomes in women at risk for postpartum depression.