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Perinatal Depression: Clinical Trial Insights and Therapeutic Advances

Ahmed Tajalsir Kandoura[1*], Greeshma Rao Koduru[2], Sankari Menon[3*] and Bhavita Tella[4]

[1]University of Medical Sciences and Technology, Khartoum, Sudan
[2]Vydehi Institute of Medical Sciences & Research Centre, Bengaluru, Karnataka, India
[3]Malabar Medical College - MMC Hospital, Modakkallur, Kerala, India
[4]Apollo Institute of Medical Sciences and Research, Hyderabad, Telangana, India

Abstract

Perinatal depression (PD) is a prevalent yet under-recognized mental health condition with profound implications for maternal and child well-being, necessitating a comprehensive review of recent advancements and persistent challenges. Despite growing awareness, gaps remain in understanding its multifaceted etiology, optimizing treatment accessibility, and addressing disparities in care-particularly for vulnerable populations. This review synthesizes current evidence to inform clinical practice, highlight innovative interventions, and advocate for systemic improvements in perinatal mental health services. By consolidating global research findings, it aims to bridge knowledge gaps and catalyze actionable solutions for this pressing public health issue. The review examines key insights from clinical trials, including the efficacy of novel pharmacological agents (e.g., zuranolone and brexanolone) and non-pharmacological approaches such as digital cognitive-behavioral therapy and microbiome-targeted interventions. It explores the neurobiological underpinnings of PD, the impact of socioeconomic factors on prevalence, and evidence-based strategies for prevention and management. Special attention is given to the developmental consequences of PD on infants, emphasizing the need for early intervention. Additionally, the review critiques systemic barriers to care, evaluates integrated care models like Massachusetts Child Psychiatry Access Project (MCPAP) for moms, and discusses the role of telehealth in expanding access. These insights collectively underscore the importance of a holistic, patient-centered approach to PD. Future research should prioritize longitudinal studies to unravel the enduring effects of PD on child development and maternal health trajectories. Investigations into biomarkers for early detection, personalized treatment algorithms, and cost-effective delivery models are urgently needed. There is also a critical demand for culturally adapted interventions and policy reforms to reduce inequities in low-resource settings. By addressing these priorities, the field can advance toward precision medicine and universal access to high-quality perinatal mental health care, ultimately mitigating the intergenerational burden of PD.

Keywords: Antenatal depression, Brexanolone, Cognitive-behavioral therapy, Maternal mental health, Perinatal depression, Postpartum depression, Psychotherapy, Zuranolone

Correspondence to: Ahmed Tajalsir Kandoura and Sankari Menon, University of Medical Sciences and Technology, Khartoum, Sudan and Malabar Medical College - MMC Hospital, Modakkallur, Kerala, India.

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Introduction

The landscape of PD research encompasses a diverse array of clinical trials and therapeutic approaches aimed at understanding and mitigating this prevalent mental health condition [1-3]. Recent studies highlight both neurobiological mechanisms and innovative treatment modalities as critical areas of investigation [4, 5]. One significant avenue of research involves exploring neurochemical interventions. Donadon et al. [6] conducted a randomized, placebo-controlled trial examining the effects of oxytocin on cognitive functions in women with postpartum depression (PPD). Their findings underscore the potential role of oxytocin in modulating emotional cognition, including facial emotion recognition, which is often impaired in PPD [6]. This aligns with prior hypotheses suggesting that neuropeptides like oxytocin may influence emotional regulation and social cognition in postpartum women.

Complementing neurochemical approaches, behavioral and integrative therapies are gaining prominence [7]. The RAINBOW trial exemplifies this trend by investigating collaborative care interventions that combine behavioral therapy with research to improve health outcomes in populations with comorbid physical and mental health issues, including depression [8]. Such integrated approaches are crucial for addressing the multifaceted nature of PD, especially considering its frequent coexistence with other health conditions. Emerging evidence also points to the potential of microbiome-targeted interventions. Toh et al. [9] outlined a protocol for the PROMOTE study, a decentralized randomized controlled trial (RCT) assessing the efficacy of *Bifidobacterium longum* NCC3001 in reducing perinatal mood symptoms [9]. This probiotic intervention represents a novel; non-pharmacological strategy aimed at modulating gut-brain axis pathways implicated in depression and stress during the perinatal period.

In addition to pharmacological and behavioral therapies, non-invasive modalities such as acupuncture are being systematically

evaluated [10-12]. Yan et al. [13] described a clinical trial protocol assessing acupuncture's safety and efficacy for chronic musculoskeletal pain in hemodialysis-dependent patients, which, while not specific to PD, exemplifies the expanding scope of alternative therapies in managing complex health conditions [13]. Furthermore, the importance of understanding underlying biological mechanisms is emphasized by Mills-Koonce et al. [14], who focus on the dysregulation of oxytocin and the hypothalamic-pituitary-adrenal axis as mediators in maternal depression transmission [14]. Such mechanistic insights are vital for developing targeted interventions and identifying biomarkers for early detection and treatment response.

Research trends also reflect a growing interest in digital and behavioral interventions. Roberge et al. [15] propose a RCT to evaluate transdiagnostic internet-based cognitive-behavioral therapy tailored for postnatal women, aiming to improve accessibility and scalability of mental health support [15]. This approach aligns with broader efforts to leverage technology for mental health care delivery in the perinatal period. Finally, the expanding global research landscape is evidenced by the increasing registration of trials related to yoga and mind-body practices. Mondal et al. [16] analyzed World Health Organization trial registry data, revealing a steady rise in yoga-related clinical trials, indicating a growing recognition of holistic and complementary therapies in managing perinatal mental health [16].

PD encompasses a range of mood disorders that can occur during pregnancy and the postpartum period [17-19]. It is a significant public health concern, affecting approximately 10 to 20% of women during this critical time. The implications of untreated PD can be profound, impacting maternal health, infant development, and family dynamics [20-22]. Recent clinical trials have explored various therapeutic interventions aimed at alleviating symptoms of PD, providing valuable insights into effective treatment strategies. In summary, current clinical trial insights into PD encompass neurochemical, behavioral, microbiome, and integrative therapies, supported by mechanistic research and innovative delivery models [23]. These multifaceted approaches reflect a comprehensive effort to improve outcomes for women experiencing depression during the perinatal period.

Prevalence and Factors

PD, encompassing both antenatal depression (AND) and PPD, is a significant global mental health concern affecting women during pregnancy and after childbirth (Table 1) [24]. The prevalence of PD varies widely across different regions and populations, influenced by socioeconomic, cultural, and healthcare factors (Figure 1) [25]. This variability underscores the need for targeted interventions and support systems to address the unique challenges faced by women in different contexts. The following details provide a detailed overview of the prevalence of PD worldwide, drawing on data from various studies.

The study Hahn-Holbrook et al. [25], a systematic review, meta-analysis, and meta-regression of 291 studies from 56 countries, revealed significant insights into the prevalence and predictors of PPD globally. The results indicate that PPD is more widespread and variable than previously understood, with economic and health factors playing a crucial role in national variations. The global pooled prevalence of PPD was found to be 17.7% (95% confidence interval (CI): 16.6 to 18.8%) based on 291 studies involving 296,284 women. When adjusted for recommended Edinburgh postnatal depression scale (EPDS) cutoffs, the prevalence was estimated at 21.0% for possible PPD and 16.7% for probable PPD. This is notably higher than the widely cited 13% prevalence from earlier meta-analyses focusing on developed countries. There was significant heterogeneity in PPD prevalence across nations, ranging from 3% (2 to 5%) in Singapore to 38% (35 to 41%) in Chile. The countries with the highest rates included Chile (38%), South Africa (37%), Hong Kong (30%), and Turkey (28%), while the lowest rates were observed in Singapore (3%), Nepal (7%), the Netherlands (8%), and Switzerland (11%). Wealth inequality, as measured by the inequality (GINI) index, was a significant predictor, explaining 41% of the cross-national variation in PPD prevalence. Nations with higher wealth inequality had higher rates of PPD. The GINI index remained statistically significant even when gross domestic product per capita was included in the model. Countries where a higher percentage of young women worked 40 h or more per week also showed higher PPD prevalence, explaining 30.9% of the variance. Together, economic predictors (GINI index, gross domestic product per capita, and women working ≥40 h per week) accounted for 73.1% of the cross-national variation in PPD prevalence.

A systematic review Al-Abri et al. [26] provides a comprehensive overview of the prevalence and associated factors of PD, highlighting several significant findings. The mean global prevalence of PD was found to be 26.3%, with a standard deviation (SD) of 11.6% and a median of 23.8%. AND had a mean prevalence of 28.5% (SD = 18.2%), while PPD had a mean prevalence of 27.6% (SD = 8.0%). The effect size for the difference between AND and PPD was small (d = 0.1). There was a notable difference in mean PD prevalence based on the assessment method used. Studies using self-reported measures reported a significantly higher mean prevalence (27.4%, SD = 12.6%) compared to those using structured interviews (17.0%, SD = 4.5%). The majority of included systematic reviews (48.1%) relied solely on self-reported measures, 50.0% used both self-reported and diagnostic assessments, and only 1.9% used diagnostic assessment alone. PD was markedly higher among potentially vulnerable populations, with a mean prevalence of 32.5% (SD = 16.7%). Examples of vulnerable groups include immigrants, HIV-infected African women, women who gave birth prematurely or whose infants had very low birth weight, those who abused substances during pregnancy, military personnel, women who experienced earthquakes, and pregnant inmates in correctional facilities. For instance, pregnant inmates in their last trimester showed an 80% prevalence of depression, attributed to lack of satisfactory medical care, isolation, stress, anxiety, maternal role transition, and parenting worries. The prevalence of PD during the COVID-19 pandemic, based on three updated systematic reviews, was 28% (SD = 6%). The review identified several major correlations (risk factors)

Table 1: Prevalence of PD by region and risk factors.

Country	Prevalence (%)	Key risk factors identified
Chile [25]	38	Wealth inequality, lack of social support
South Africa [26]	37	HIV infection, socioeconomic adversity
Hong Kong [25]	30	High work hours, marital conflict
Turkey [27]	28	Intimate partner violence, migrant status
Netherlands [25]	8	Strong social support systems
Singapore [25]	3	Low wealth inequality, healthcare access

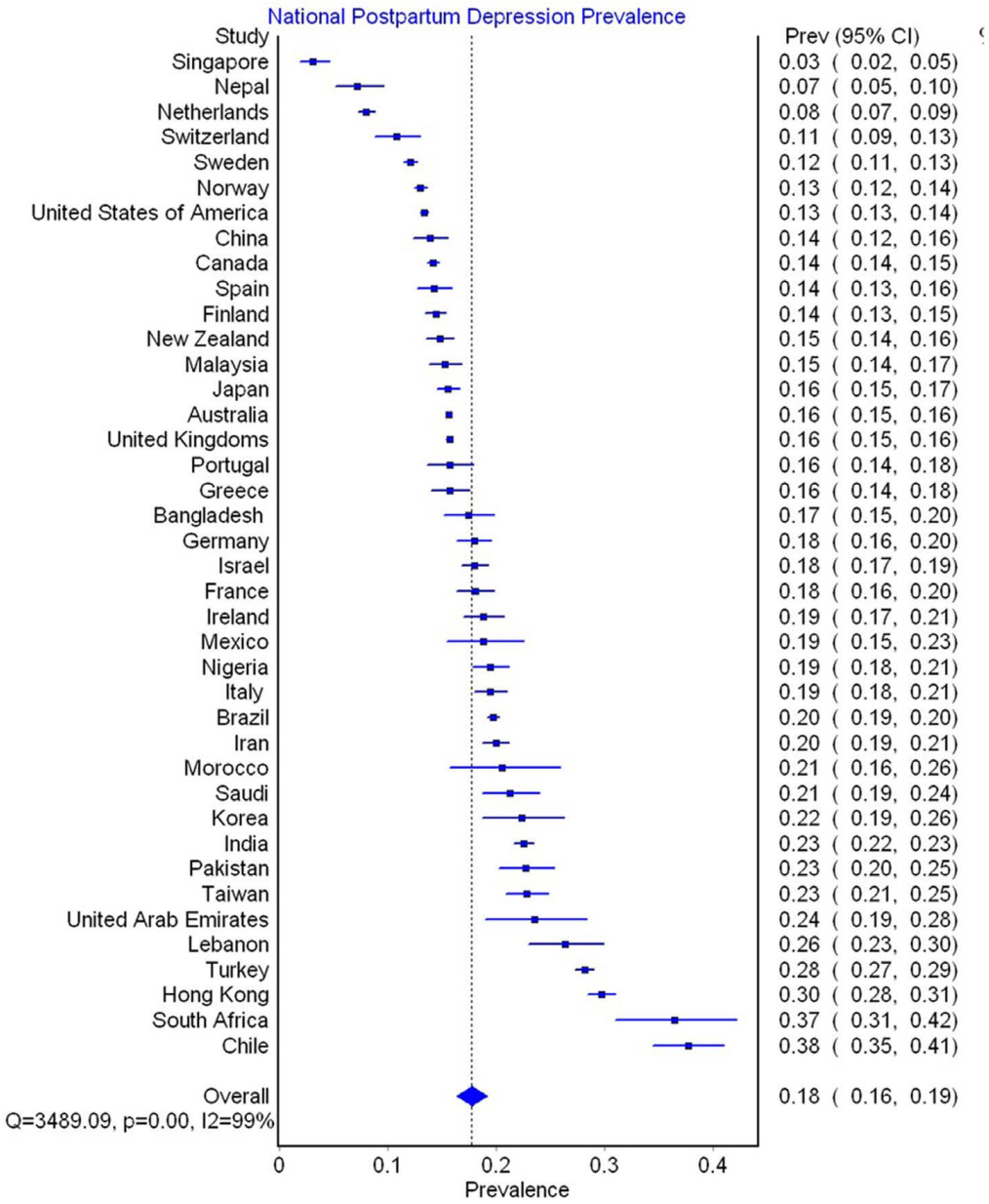

Figure 1: Meta-analytically derived PPD prevalence in 40 countries [25].

with medium to large significant effect sizes (r > 0.30). These include: (i) Personal history of mental illness (such as anxiety and depression; r = 0.30 - 0.510, (ii) childcare stress or infant temperament (r = 0.48 - 0.49 and 0.33 - 0.34, respectively), (iii) stressful life events (r = 0.36 - 0.40), (iv) Lack of social support (r = 0.37 - 0.45), (v) maternity blues (r = 0.35 - 0.37), and (iv) marital conflicts or dissatisfaction (r = 0.37 - 0.39). Lifetime history of abuse: Including childhood/adult abuse, maternal violence, or intimate partner violence, which consistently lead to an increased risk. Women experiencing intimate partner violence during pregnancy had increased odds of both antenatal (Odds ratio (OR): 1.69 to 3.76) and postnatal (Odds ratio (OR): 1.46 to 7.04) depression. Chronic medical conditions such as diabetes (Adjusted prevalence OR (aPOR) = 1.34), hypertension/heart disease (aPOR = 1.60), migraine (aPOR = 1.75), and other neurological disorders (aPOR = 1.45). Preeclampsia and pre-term deliveries: Increased the severity of PD. Exposure to second-hand smoke significantly increased the risk (OR = 1.77). Sleep disturbance, a strong predictor of PPD, with effect sizes ranging from moderate to very large (0.6 - 1.7). Gestational diabetes mellitus reported to significantly increase the risk of PPD (RR = 1.32). In summary, the paper highlights that PD is highly prevalent globally, with rates varying based on assessment methods and population vulnerability. A wide range of psychosocial, medical, and lifestyle factors are consistently associated with an increased risk of developing PD, underscoring the need for early screening and targeted interventions for at-risk groups.

A Stevenson et al. [27] systematic review and meta-analysis on perinatal common mental health disorders among migrant women revealed significant prevalence rates for various conditions, with notable differences observed between forced and economic migrants. The pooled prevalence of PD disorders across all migrant women was

found to be 24.2%. Forced migrants group exhibited a higher pooled prevalence of PD disorders at 32.5%. In contrast, economic migrants had a lower pooled prevalence of PD disorders at 13.7%. The difference in prevalence between forced and economic migrants for depressive disorders was statistically significant ($p < 0.001$). The pooled prevalence of perinatal anxiety disorders among all migrant women was 19.6%. All migrant women, the overall pooled prevalence of perinatal post-traumatic stress disorder (PTSD) was 8.9%. Forced migrants showed a significantly higher pooled prevalence of perinatal PTSD at 17.1%. Approximately one in four pregnant or postpartum migrant women experience PD, one in five experience perinatal anxiety, and one in eleven experience perinatal PTSD. The burden of perinatal mental illness is notably higher among forced migrant women compared to economic migrants, particularly for depressive disorders and PTSD. These findings underscore the critical need for community-based perinatal mental health screening and the provision of culturally sensitive interventions for migrant women, especially those who are forced migrants.

While the prevalence of PD is notably high, especially in low-resource settings and among vulnerable populations, it is important to consider the potential underreporting and variability in assessment methods across studies [28-30]. The use of different screening tools and diagnostic criteria can lead to discrepancies in prevalence estimates. Additionally, cultural factors and stigma associated with mental health may influence the reporting and diagnosis of PD [31, 32]. Therefore, efforts to standardize assessment methods and increase awareness and support for mental health in diverse cultural contexts are crucial for addressing this global health issue.

Therapeutic Interventions

PD, encompassing both AND and PPD, is a significant mental health concern affecting approximately 1 in 7 women globally [33-35]. Recent clinical trials and therapeutic advances have provided new insights into its management, highlighting both pharmacological and non-pharmacological strategies. The approval of zuranolone, the first oral medication for PPD, marks a significant advancement, although it raises concerns about accessibility and socioeconomic disparities [36-38]. Meanwhile, system-level interventions and psychotherapy continue to play crucial roles in treatment. Recent studies have investigated a variety of therapeutic approaches to manage PD (Table 2), including pharmacological treatments, psychotherapy, and alternative therapies.

Pharmacological approaches

One notable clinical trial examined the use of intraoperative ketamine as a potential intervention for PPD symptoms following cesarean delivery [43]. The study hypothesized that ketamine, known for its rapid antidepressant effects, could significantly reduce depressive symptoms in the postpartum period. The results indicated a promising avenue for further research into ketamine's role in perinatal mental health [43]. Another pharmacological approach involved omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation. A systematic review and meta-analysis of RCTs assessed the efficacy of n-3 PUFA in preventing and treating PD. Despite the inclusion of multiple studies, the findings revealed no statistically significant difference in depression scores between the n-3 PUFA and placebo groups, suggesting that while n-3 PUFA may have other health benefits, its role in PD remains inconclusive [44].

The Food and Drug Administration (FDA) approval of zuranolone offers a new oral treatment option for PPD, potentially improving accessibility compared to the intravenous brexanolone [45-47]. However, its high cost and insurance coverage uncertainties may exacerbate socioeconomic disparities in treatment access [40]. Both zuranolone and brexanolone mimic allopregnanolone, a neuroactive steroid that modulates GABAergic signaling, suggesting a role for excitation-inhibition imbalance in PPD [40]. Studies indicate that brexanolone may also exert effects through reducing inflammatory mediators like TNF-α and IL-6, linking inflammation to PPD [40].

Traditional antidepressants

- Selective serotonin reuptake inhibitors and serotonin/norepinephrine reuptake inhibitors: These remain the mainstay of pharmacological treatment for PD. They are generally considered safe, with most studies not showing increased risks of teratogenicity or neonatal complications [41, 48].

- Tricyclic antidepressants and bupropion: These are also used, though less frequently, due to concerns about side effects and safety profiles during pregnancy [41, 48].

Novel pharmacological agents

- Brexanolone and esketamine: These new medications represent a shift in treatment paradigms. Brexanolone, an intravenous formulation, and esketamine, a nasal spray, act on GABA and glutamate receptors, respectively, offering rapid relief from severe depression symptoms. However, their effects diminish after 30 days, necessitating combination with selective serotonin reuptake inhibitors for sustained efficacy [40, 42].

- Zuranolone: Recently approved by the FDA, zuranolone is the first oral medication specifically for PPD. It mimics allopregnanolone, a neuroactive steroid, and has shown significant improvement in depressive symptoms in clinical trials [40].

Psychotherapeutic interventions

Mindfulness-based interventions have gained traction in recent years. A RCT evaluated the effectiveness of smartphone-based mindfulness training on maternal PD. The results demonstrated significant improvements in depression and anxiety symptoms among participants who engaged in mindfulness training compared to those in a control group. This suggests that digital mental health interventions may offer accessible and effective support for at-risk populations [49].

Interpersonal psychotherapy (IPT) has also been explored as a

Table 2: Efficacy and tolerability of pharmacological treatments for PD.

Treatment	Efficacy (SUCRA ranking*)	Key benefits	Limitations
Estradiol [39]	94.3%	Significant symptom reduction	Limited long-term safety data
Brexanolone [40]	58.8%	Rapid action (within 48 h)	IV administration, high cost
Zuranolone [40]	58.8%	Oral administration, FDA-approved	Cost, insurance coverage barriers
SSRIs (e.g., Sertraline) [41]	64.3%	Well-tolerated, established safety	Delayed onset (2 to 4 weeks)
Esketamine [42]	N/A	Rapid relief, nasal spray format	Short-lived effects, requires adjuncts
Ketamine [43]	N/A	Non-pharmacological, safe for pregnancy	Inconclusive efficacy for PD

treatment for PD. A qualitative study investigated the mechanisms through which brief IPT alleviates depressive symptoms. Participants reported decreased interpersonal stress and improved emotional processing, highlighting the importance of therapeutic relationships in enhancing treatment outcomes [50]. IPT, particularly the brief MomCare program, has shown efficacy in reducing depressive symptoms during pregnancy, with significant improvements noted in clinical trials [51]. This therapy focuses on reducing interpersonal conflicts and enhancing social support.

Non-invasive treatments (such as repetitive transcranial magnetic stimulation and acupuncture) have shown promise in the general population and are being explored for PD. They can be used alongside pharmacotherapy to enhance treatment outcomes without the side effects associated with medications [42]. Vitamin D and mindfulness-based cognitive therapy, these integrative approaches are gaining attention for their potential benefits in managing PD, offering additional options for those seeking non-pharmacological interventions [42].

Alternative therapies

The role of probiotics in managing perinatal mood disorders has been investigated in the PROMOTE study, which aimed to assess the effects of *B. longum* NCC3001 on mood outcomes in pregnant and lactating women. This decentralized RCT sought to determine whether the probiotic could reduce symptoms of depression and anxiety during the perinatal period. While results are still pending, the study exemplifies innovative approaches to addressing perinatal mental health [9].

System-level interventions such as the MCPAP for Moms and the PRogram in Support of Moms (PRISM) have demonstrated effectiveness in reducing depression symptoms. These programs integrate mental health care into obstetric settings, though challenges remain in treatment initiation and sustainment [52]. Counseling has been effective in preventing PD, particularly among high-risk groups, though more robust evidence is needed for broader application [53]. This systematic review identified 50 studies that met the inclusion criteria, involving a total of 22,385 participants. Counseling interventions were the most frequently studied type of intervention. Compared to control groups, they were associated with a lower likelihood of PD onset. The pooled risk ratio (RR) was 0.61 (95% CI: 0.47 to 0.78). This finding was based on 17 randomized clinical trials with 3,094 participants, and an I^2 of 39.0%. The absolute difference in the risk of PD ranged from a 1.3% greater reduction in the control group to a 31.8% greater reduction in the intervention group. Health system interventions demonstrated a benefit in 3 studies involving 5,321 participants. The pooled effect size was similar to that of counseling interventions, with a restricted maximum likelihood RR of 0.58 (95% CI: 0.22 to 1.53). However, the pooled effect was not statistically significant when using a method appropriate for a small number of studies, and the I^2 was 66.3%. The absolute risk reduction for health system interventions ranged from -3.1% to -13.1%. No harms were directly reported for behavior-based interventions. In one very small randomized clinical trial (22 participants analyzed), a smaller percentage of participants prescribed sertraline experienced depression recurrence (7%) compared to those given a placebo (50%) at 20 weeks postpartum ($p = 0.04$). This benefit came with an increased risk of adverse effects for the mother. In summary, counseling interventions showed clear effectiveness in preventing PD, particularly in women at increased risk. While health system interventions also showed some benefit, the evidence base was less robust. Other intervention approaches, including antidepressants, provided some evidence of effectiveness but required further research due to limitations such as small sample sizes or reported harm.

In conclusion, while therapeutic advances and clinical trials have expanded the treatment landscape for PD, addressing socioeconomic and systemic barriers remains crucial. The integration of pharmacological and non-pharmacological therapies, alongside system-level interventions, offers a comprehensive approach to managing this prevalent condition. However, ongoing research is essential to refine these strategies and ensure equitable access to care for all affected individuals.

Clinical Studies

PD treatment clinical trials have explored a variety of interventions, both pharmacological (Figure 2) and nonpharmacological, to address this prevalent condition. The research highlights the effectiveness of several therapeutic strategies, including cognitive-behavioral therapy, IPT, and pharmacological treatments such as selective serotonin reuptake inhibitors [54-56]. These interventions aim to mitigate the adverse effects of PD on both mothers and their children.

Byatt et al. [57] the MCPAP for Moms and the PRISM interventions were found to be equally effective in improving depression symptoms among women with PD. Participants in practices allocated to MCPAP for Moms experienced a decrease in EPDS scores by 4.2 (SD 5.2) from baseline to 11 to 13 months postpartum, which was statistically significant ($p < 0.0001$). Participants in PRISM practices also showed a decrease in EPDS scores by 4.3 (SD 4.5) over the same period, which was also statistically significant ($p < 0.0001$). There was no statistically significant difference in the change in EPDS scores between the two groups. The estimated difference between MCPAP for Moms and PRISM groups was 0.1 (95% CI: 1.2 to 1.4), with a p-value of 0.87. This indicates that neither intervention was superior to the other in reducing depression symptoms. The observed 4-point decrease in EPDS score in both groups is considered clinically significant. Despite similar effectiveness, MCPAP for Moms is noted to have a lower intensity and greater population-based reach compared to PRISM. In summary, the study concluded that both system-level interventions effectively reduced PD symptoms to a clinically significant degree, with no significant difference in outcomes between the more intensive PRISM and the broader-reaching MCPAP for Moms program.

A Pettman et al. [55] systematic review (CRD42020152254) included a total of 31 studies, encompassing 5291 participants. For the meta-analysis, 26 studies were included, involving 4658 participants. CBT-based interventions showed a medium overall effect size (Hedges' $g = -0.53$ (95% CI: -0.65 to -0.40)) on symptoms of depression, though with high heterogeneity. Significant effects were also observed for anxiety, individual stress, and perceived social support. However, it is noted that few studies have examined these secondary outcomes. Subgroup analysis revealed that the type of control, type of CBT, and type of health professional were significant moderators of the main effect (symptoms of depression). The majority of the studies included presented some concerns regarding the risk of bias, with one study having a high risk of bias. The authors concluded that the results should be interpreted with caution due to high levels of heterogeneity and the low quality of included studies. In summary, CBT-based interventions appear effective for PD and some secondary outcomes, but the findings are tempered by high heterogeneity and quality concerns in the included studies, highlighting areas for future research improvement.

A Zhang et al. [39] systematic review and network meta-analysis

Study	Interventions	Location	Year	Number	Age (mean ± SD)	Baseline (HAMD-17, mean ± SD/ median, IQR)	Dosage (per day)	Follow-up (weeks)	Scales
Kanes	Brexanolone/ Placebo	Multicenter	2017	10/11	27.4 ± 5.3/28.8 ± 4.6	28.1 (27.0–30.0)/28.8 (26.0–32.0)	30-60 ug/h	30d	HAMD-17/ MADRS
Meltzer-Brody-1	Brexanolone/ Placebo	USA	2018	92/46	27.3 ± 6.1/27.8 ± 6.0 27/27.0 ± 6.0	29.1 ± 2.7/28.4 ± 2.5/28.6 ± 2.5	30-90 ug/h	30d	HAMD-17/ MADRS
Meltzer-Brody-2	Brexanolone/ Placebo	USA	2018	54/54	28.4 ± 6.1/27.4 ± 5.9	22.6 ± 1.6/22.7 ± 1.6	30-90 ug/h	30d	HAMD-17/ MADRS
Appleby	Fluoxetine/Placebo	UK	1997	43/44	26.1/24.5	14.2 (13.0-15.5) 13.9 (12.5-15.4)	NA	12	HAMD-17/EPDS
O'Hara-Iowa	Sertraline/Placebo	USA	2010	23/20	28.7 ± 5.9/ 28.1 ± 5.4	21.5 ± 4.5/20.2 ± 4.4	25-200 mg	12	HAMD-17
O'Hara-WIH	Sertraline/Placebo	USA	2010	33/33	27.8 ± 5.5/ 26.8 ± 4.9	22.1 ± 5.0/23.2 ± 4.5	25-200 mg	12	HAMD-17
Kashani	Saffron/Fluoxetine	Iran	2017	32/32	29.21 ± 7.69 32.09 ± 4.99	16.53 ± 1.48 16.65 ± 1.12	NA	6	HAMD-17
Hantsoo	Sertraline/Placebo	USA	2013	17/19	29.6 ± 4.0/31.7 ± 3.7	20.6 ± 2.8/23.2 ± 3.9	50-200 mg	6	HAMD-17/EPDS
Wisner	Sertraline/ Nortriptyline	USA	2006	55/54	NA	NA	25-200 mg/ 10-150 mg	8	HAMD-17
Yonkers	Paroxetine/Placebo	USA	2008	35/35	26.1 ± 6.5/25.9 ± 6.5	23.6 ± 4.7/24.7 ± 5.0	10-40 mg	8	HAMD-17
Li	Estradiol/Placebo	USA	2020	6/6	30.5 ± 6.2/32.7 ± 5.5	18.2 ± 7.3/18.3 ± 3.4	5 mg	6	HAMD-17/EPDS
Bloch	Sertraline/Placebo	Israel	2012	20/20	NA	18.40 ± 4.83 16.05 ± 4.84	25-100 mg	12	EPDS/ MADRS
Deligiannidis	Zuranolone/ Placebo	USA	2021	76/74	29.3 ± 5.4/27.4 ± 5.3	28.4 ± 2/28.8 ± 2	30 mg	45d	HAMD-17/ MADRS

Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; HAMD-17, 17-item Hamilton Rating Scale for Depression score; IQR, interquartile range; MADRS, Montgomery-Åsberg Depression Rating Scale; NA, not available; SD, standard deviation.

Figure 2: Details of RCTs in literature for PD [39].

evaluated the efficacy and tolerability of various pharmacotherapies for PPD. The study included 11 trials with 944 participants, examining nine different antidepressants. Only estradiol and brexanolone demonstrated significantly higher efficacy compared to placebo in reducing PPD symptoms, as measured by changes in the Hamilton Depression Rating Scale (HAMD-17) score. While all active antidepressant drugs were generally superior to placebo in reducing depression, statistical significance was only found for estradiol and brexanolone. Based on the surface under the cumulative ranking curve (SUCRA), estradiol showed the highest probability (94.3%) of being the most effective in reducing PPD, followed by paroxetine (64.3%) and zuranolone (58.8%). Although no significant differences were found between active antidepressants and placebo regarding remission or responder rates, SUCRA ranking suggested that nortriptyline, sertraline, and paroxetine had higher remission rates. Nortriptyline also had the greatest likelihood of ranking first for responder rate. Brexanolone was found to be less well-tolerated than most other antidepressants, showing a higher percentage of early dropouts compared to other treatments. Conversely, two SSRIs, fluoxetine and sertraline, were better tolerated. The study did not find any antidepressant medication to be significantly inferior to placebo in terms of early dropouts. Due to limited detailed data on common and serious side effects, a comprehensive pooling of this information was not feasible. In summary, while several antidepressants show promise for PPD, estradiol and brexanolone demonstrated significant efficacy over placebo. Estradiol, paroxetine, and zuranolone were identified as the top three in terms of overall efficacy. However, brexanolone exhibited lower tolerability compared to other antidepressants. The study highlights the need for more detailed data on side effects and acknowledges limitations due to moderate heterogeneity and the age of some included trials.

A Waqas et al. [58] systematic review and meta-regression analysis provides comprehensive insights into the effectiveness of CBT for PD, highlighting various intervention and participant-level characteristics that influence outcomes. CBT-based interventions demonstrated a strong effect size in alleviating depressive symptoms among individuals with PD, with a standardized mean difference (SMD) of -0.74 (95% CI: -0.91 to -0.56, n = 9,722). This indicates a significant positive impact on depressive symptoms. There was substantial heterogeneity in effect sizes across studies ($I^2 = 92.65\%$, $p < 0.001$). Evidence of publication bias was also observed, though sensitivity analyses did not reveal significant changes after removing outliers. CBT interventions were found to be effective across different delivery formats, including individual, group, and electronic (online) methods. This flexibility enhances the utility of CBT approaches in various settings. Interventions delivered electronically yielded strong effect sizes (SMD = -1.12, 95% CI: -1.80 to -0.63, n = 1,218). Interventions delivered individually also showed strong effect sizes (SMD = -0.63, 95% CI: -0.81 to -0.44, n = 3,589). Interventions delivered among groups similarly yielded strong effect sizes (SMD = -0.67, 95% CI: -0.96 to -0.38, n = 4,915). Treatment interventions for PND showed significantly higher effect sizes (SMD = -0.94) compared to preventive ones (SMD = -0.36). CBT interventions could be delivered effectively by both specialists and non-specialists. While interventions delivered electronically and by specialists had slightly higher effect sizes, this difference was not statistically significant.

Impact of PD on Infant and Child Development

PD has far-reaching consequences that extend beyond maternal health, significantly influencing infants and child development [59, 60]. Research indicates that maternal depression during pregnancy can alter fetal neurodevelopment through mechanisms such as increased cortisol exposure and placental dysfunction [61]. These biological

changes may predispose infants to heightened stress reactivity and emotional dysregulation, observable as early as the neonatal period. For example, infants of depressed mothers often exhibit poorer self-regulation, reduced attention spans, and atypical brain activity patterns, particularly in regions associated with emotional processing [62, 63]. Such findings underscore the importance of early identification and intervention to mitigate potential long-term effects on child development.

The impact of PD on infant attachment and bonding is another critical concern. Depressed mothers may struggle with responsive caregiving due to fatigue, emotional withdrawal, or intrusive parenting behaviors, which can disrupt the formation of secure attachments [64-66]. Studies show that insecure attachment in infancy is linked to later social and emotional difficulties, including increased risk of anxiety, aggression, and peer relationship problems [67, 68]. Furthermore, infants of mothers with PD are more likely to exhibit less positive affect and reduced engagement during social interactions, which may hinder their ability to form healthy relationships [69, 70]. These early relational challenges highlight the need for interventions that support maternal mental health and promote positive parent-infant interactions.

Cognitive and language development are also vulnerable to the effects of PD. Children exposed to maternal depression during the perinatal period often demonstrate delays in language acquisition, poorer executive functioning, and lower academic achievement [71, 72]. These outcomes may stem from reduced maternal verbal engagement, inconsistent stimulation, or chaotic home environments associated with untreated PD. Longitudinal studies reveal that the cognitive effects of PD can persist into adolescence, emphasizing the importance of addressing maternal depression early to foster optimal developmental trajectories [73-75]. Interventions such as parent-child interaction therapy and early enrichment programs have shown promise in buffering these adverse effects.

Behavioral and emotional problems in childhood are strongly associated with PD exposure. Children of depressed mothers are at higher risk for internalizing symptoms (e.g., depression, anxiety) and externalizing behaviors (e.g., hyperactivity, conduct problems) [76, 77]. These outcomes may arise from a combination of genetic predisposition, altered stress response systems, and environmental factors such as marital conflict or socioeconomic adversity. Notably, the severity and chronicity of maternal depression correlate with the degree of child psychopathology, suggesting that timely and effective treatment of PD could reduce the intergenerational transmission of mental health disorders [78-80].

Addressing the developmental consequences of PD requires a multifaceted approach. Integrating mental health support into pediatric and obstetric care, such as routine screening for maternal depression and referrals to evidence-based interventions, is essential [81, 82]. Programs that enhance maternal sensitivity, such as attachment-based therapies or home-visiting initiatives, can mitigate the negative effects of PD on child development. Additionally, public health efforts should focus on raising awareness of the long-term risks associated with PD and advocating for policies that support families [83, 84]. By prioritizing maternal mental health, society can foster healthier developmental outcomes for future generations.

Policy and Public Health Implications

PD represents a significant public health challenge that demands systemic policy changes to improve maternal and child outcomes. Current healthcare systems often fail to integrate mental health care into routine perinatal services, leaving many women undiagnosed and untreated [85]. Policymakers must prioritize universal screening for PD during prenatal and postnatal visits, coupled with streamlined referral pathways to mental health specialists. Successful models, such as the MCPAP for Moms, demonstrate how coordinated care can bridge gaps between obstetrics and mental health services [86, 87]. By adopting such frameworks globally, healthcare systems can ensure timely interventions and reduce the long-term societal costs associated with untreated PD, including increased healthcare utilization and intergenerational mental health disparities.

Socioeconomic and structural barriers further exacerbate inequities in PD care, particularly for marginalized populations [88, 89]. Women in low-resource settings, racial and ethnic minorities, and those with limited health literacy often face disproportionate challenges in accessing evidence-based treatments. Public health initiatives must address these disparities by expanding Medicaid coverage for mental health services, subsidizing innovative therapies like zuranolone for low-income families, and training community health workers to deliver culturally sensitive care. Telehealth platforms and mobile health interventions can also play a pivotal role in reaching underserved communities, but their success depends on investments in digital infrastructure and literacy programs. Policies that target social determinants of health-such as paid parental leave, affordable childcare, and housing stability-can further mitigate risk factors for PD and promote equitable access to care [88, 89].

Raising public awareness and reducing stigma around perinatal mental health are critical to fostering early help-seeking behaviors. National campaigns, akin to those for postpartum physical health, should highlight the prevalence and treatability of PD while normalizing conversations about maternal mental health [90, 91]. Schools, workplaces, and community organizations can serve as allies by providing education and resources to expectant and new mothers [92, 93]. Internationally, collaboration between governments, NGOs, and researchers is needed to adapt evidence-based interventions to diverse cultural contexts and scale promising programs. By treating PD as a public health priority one that intersects with gender equity, economic stability, and child development policymakers can create lasting change that benefits generations to come.

Challenges and Future Directions

Despite significant advancements in understanding and treating PD, several challenges persist. One major issue is the underdiagnosis and undertreatment of PD, particularly in low-resource settings and among vulnerable populations [94]. Stigma, lack of awareness, and limited access to mental health services often prevent women from seeking or receiving timely care [95]. Additionally, cultural differences in the perception of mental health can influence reporting and diagnosis, highlighting the need for culturally sensitive screening tools and interventions [96]. Addressing these barriers requires global efforts to improve mental health literacy and integrate PD screening into routine perinatal care.

Another challenge lies in the complexity of comorbid conditions, such as chronic pain or anxiety, which can complicate PD treatment [97]. Research indicates that women with comorbid conditions may experience diminished responses to standard therapies, underscoring the importance of integrated care models. Future studies should focus on personalized treatment plans that address both mental and physical health, leveraging multidisciplinary approaches to improve outcomes

[98]. For example, combining pharmacotherapy with behavioral interventions or alternative therapies like acupuncture could offer more comprehensive relief for affected women.

The socioeconomic disparities in access to innovative treatments, such as zuranolone or brexanolone, further exacerbate inequities in PD care. High costs and insurance coverage limitations restrict these therapies to privileged populations, leaving many women without viable options [99]. Policymakers and healthcare systems must prioritize affordability and accessibility to ensure that cutting-edge treatments reach all who need them. Concurrently, research into cost-effective interventions, such as digital mental health platforms or community-based programs, could help bridge this gap and expand care to underserved communities.

The COVID-19 pandemic has underscored the need for flexible and scalable treatment modalities. Telehealth and digital interventions, such as internet-based CBT, have shown promise in improving accessibility and engagement [100]. However, challenges like digital literacy and internet access remain, particularly in rural or low-income areas. Future directions should include optimizing these technologies for broader usability and evaluating their long-term efficacy in diverse populations. Moreover, leveraging mobile health apps for real-time monitoring and support could enhance early intervention and adherence to treatment [101].

Longitudinal research is critical to understanding the enduring effects of PD on maternal and child health. Studies like the Mood, Mother and Child project highlight the importance of tracking psychobiological risk factors and resilience across developmental stages [14]. Future research should also explore the role of biomarkers, such as inflammatory markers or neuropeptides, in predicting treatment response and disease progression. By identifying these mechanisms, researchers can develop targeted therapies and improve early detection strategies.

In summary, while progress has been made in PD research and treatment, addressing these challenges requires a multifaceted approach. Collaborative efforts among researchers, clinicians, policymakers, and communities are essential to advancing equitable care. Future directions should emphasize personalized medicine, innovative delivery models, and sustained investment in mental health infrastructure. By tackling these priorities, the field can move closer to mitigating the profound impact of PD on families worldwide.

Conclusions

PD remains a pressing global health issue with far-reaching implications for maternal well-being, infant development, and family dynamics. The advancements in research and treatment—ranging from novel pharmacological agents like zuranolone to innovative psychotherapeutic and digital interventions-have expanded the toolkit for addressing this condition. However, significant challenges persist, including disparities in access to care, underdiagnosis in vulnerable populations, and the need for culturally sensitive approaches. The integration of mental health services into routine perinatal care, alongside policies that address socioeconomic barriers, is essential to ensure equitable and effective treatment for all women.

Looking ahead, the future of PD management lies in personalized and multidisciplinary strategies that combine biological, psychological, and social interventions. Continued investment in longitudinal research, biomarker discovery, and scalable delivery models-such as telehealth and community-based programs-will be critical to refining these approaches. By fostering collaboration among researchers, clinicians, policymakers, and communities, society can mitigate the intergenerational impact of PD and promote healthier outcomes for mothers and their children. The journey toward comprehensive perinatal mental health care is ongoing, but with sustained commitment, meaningful progress is within reach.

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Conflict of Interest

None.

References

1. Waqas A, Nadeem M, Rahman A (2023) Exploring heterogeneity in perinatal depression: a comprehensive review. BMC Psychiatry 23: 1-16. https://doi.org/10.1186/s12888-023-05121-z
2. McNab SE, Dryer SL, Fitzgerald L, Gomez P, Bhatti AM, et al. (2022) The silent burden: a landscape analysis of common perinatal mental disorders in low- and middle-income countries. BMC Pregnancy Childbirth 22: 1-14. https://doi.org/10.1186/s12884-022-04589-z
3. Singla DR, Meltzer-Brody S, Savel K, Silver RK (2022) Scaling up patient-centered psychological treatments for perinatal depression in the wake of a global pandemic. Front Psychiatry 12: 1-5. https://doi.org/10.3389/fpsyt.2021.826019
4. Zhang K, He L, Li Z, Ding R, Han X, et al. (2024) Bridging neurobiological insights and clinical biomarkers in postpartum depression: a narrative review. Int J Mol Sci 25: 8835. https://doi.org/10.3390/ijms25168835
5. van Dijk MT, Talati A, Barrios PG, Crandall AJ, Lugo-Candelas C (2024) Prenatal depression outcomes in the next generation: a critical review of recent DOHaD studies and recommendations for future research. Semin Perinatol 48: 151948. https://doi.org/10.1016/j.semperi.2024.151948
6. Donadon MF, Martin-Santos R, Osorio FL (2021) Oxytocin effects on the cognition of women with postpartum depression: a randomized, placebo-controlled clinical trial. Prog Neuropsychopharmacol Biol Psychiatry 111: 110098. https://doi.org/10.1016/j.pnpbp.2020.110098
7. Marconcin P, Ferrari G, Marques A (2025) Physical activity and perinatal depression. In Physical Activity, Physical Fitness and Depression. Routledge, pp 79–92.
8. Venditti EM, Steinman LE, Lewis MA, Weiner BJ, Ma J (2021) Seeking a pot of gold with integrated behavior therapy and research to improve health equity: insights from the RAINBOW trial for obesity and depression. Transl Behav Med 11: 1691–1698. https://doi.org/10.1093/tbm/ibab069
9. Toh MP, Yang CY, Lim PC, Loh HLJ, Bergonzelli G, et al. (2023) A probiotic intervention with *Bifidobacterium longum* NCC3001 on perinatal mood outcomes (PROMOTE study): protocol for a decentralized randomized controlled trial. JMIR Res Protoc 12: e41751. https://doi.org/10.2196/41751
10. Zhao FY, Li L, Xu P, Zhang WJ, Kennedy GA, et al. (2024) Inadequate evidence for acupuncture as an alternative or adjunct to antidepressants/psychotherapy for postpartum depression: a Bayesian systematic review and network meta-analysis. Neuropsychiatr Dis Treat 20: 1741–1755. https://doi.org/10.2147/ndt.s484387
11. Sushmitha G, Eashwar VMA, Pandian S, Sekhar MA, Pricilla SE (2024) Non-pharmacological radical methods for treating postpartum depression around the globe: a narrative review. Cureus 16: e52916. https://doi.org/10.7759/cureus.76052
12. Li P, Zhao J, Wei X, Luo L, Chu Y, et al. (2024) Acupuncture may play a key role in anti-depression through various mechanisms in depression. Chin Med 19: 135. https://doi.org/10.1186/s13020-024-00990-2
13. Yan C, Liu HR, Kong Q, Gan JY, Liu K, et al. (2024) Effect of acupuncture intervention on chronic musculoskeletal pain in hemodialysis-dependent kidney failure patients: study protocol for a randomized controlled clinical trial. J Pain Res 17: 4289–4300. https://doi.org/10.2147/jpr.s492158
14. Mills-Koonce WR, Grewen K, O'Shea NG, Pearson B, Strange CG, et al. (2023) The mood, mother and child study: protocol for a prospective longitudinal study and randomized controlled trial. JMIR Res Protoc 12: e51132. https://doi.org/10.2196/51132
15. Roberge P, Vasiliadis HM, Chapdelaine A, Battista MC, Beaulieu MC, et al. (2025)

Transdiagnostic internet cognitive behavioural therapy for anxiety and depressive symptoms in postnatal women: protocol of a randomized controlled trial. BMC Psychiatry 25: 237. https://doi.org/10.1186/s12888-025-06636-3

16. Mondal H, Komarraju SL, Muralidharan S (2025) Global and Indian research trends on yoga: insights from WHO trial registry. Bioinformation 21: 30-34. https://doi.org/10.6026/973206300210030
17. Cantwell R (2021) Mental disorder in pregnancy and the early postpartum. Anaesthesia 76: 76–83. https://doi.org/10.1111/anae.15424
18. Meltzer-Brody S, Rubinow D (2021) An overview of perinatal mood and anxiety disorders: epidemiology and etiology. In Cox E (ed) Women's Mood Disorders: A Clinician's Guide to Perinatal Psychiatry. Springer, pp 5–16.
19. Jeličić L, Veselinović A, Ćirović M, Jakovljević V, Raičević S, et al. (2022) Maternal distress during pregnancy and the postpartum period: underlying mechanisms and child's developmental outcomes — a narrative review. Int J Mol Sci 23: 13932. https://doi.org/10.3390/ijms232213932
20. Saharoy R, Potdukhe A, Wanjari M, Taksande AB (2023) Postpartum depression and maternal care: exploring the complex effects on mothers and infants. Cureus 15: e42178. https://doi.org/10.7759/cureus.41381
21. Dessì A, Pianese G, Mureddu P, Fanos V, Bosco A (2024) From breastfeeding to support in mothers' feeding choices: a key role in the prevention of postpartum depression? Nutrients 16: 2285. https://doi.org/10.3390/nu16142285
22. Conradt E, Carter S, Crowell SE (2024) What's next for the field of multigenerational mental health? The need for deep behavioral phenotyping via a prenatal mental health registry. Dev Psychopathol 36: 2276–2284. https://doi.org/10.1017/s0954579424000099
23. Zhang W, Jia J, Yang Y, Ye D, Li Y, et al. (2025) Estradiol metabolism by gut microbiota in women's depression pathogenesis: inspiration from nature. Front Psychiatry 16: 1505991. https://doi.org/10.3389/fpsyt.2025.1505991
24. Wang Z, Liu J, Shuai H, Cai Z, Fu X, et al. (2021) Mapping global prevalence of depression among postpartum women. Transl Psychiatry 11: 543. https://doi.org/10.1038/s41398-021-01663-6
25. Hahn-Holbrook J, Cornwell-Hinrichs T, Anaya I (2018) Economic and health predictors of national postpartum depression prevalence: a systematic review, meta-analysis, and meta-regression of 291 studies from 56 countries. Front Psychiatry 8: 248. https://doi.org/10.3389/fpsyt.2017.00248
26. Al-Abri K, Edge D, Armitage CJ (2023) Prevalence and correlates of perinatal depression. Soc Psychiatry Psychiatr Epidemiol 58: 1581–1590. https://doi.org/10.1007/s00127-022-02386-9
27. Stevenson K, Fellmeth G, Edwards S, Calvert C, Bennett P, et al. (2023) Perinatal common mental health disorders among migrant women: a systematic review and meta-analysis. Eur J Public Health 33: ii102-ii103. https://doi.org/10.1093/eurpub/ckad160.262
28. Mitchell AR, Gordon H, Lindquist A, Walker SP, Homer CS, et al. (2023) Prevalence of perinatal depression in low- and middle-income countries: a systematic review and meta-analysis. JAMA Psychiatry 80: 425–431. https://doi.org/10.1001/jamapsychiatry.2023.0069
29. Chorwe-Sungani G, Chipps J (2017) A systematic review of screening instruments for depression for use in antenatal services in low-resource settings. BMC Psychiatry 17: 1-10. https://doi.org/10.1186/s12888-017-1273-7
30. Albarqi MN (2025) The impact of prenatal care on the prevention of neonatal outcomes: a systematic review and meta-analysis of global health interventions. Healthcare 13: 1076. https://doi.org/10.3390/healthcare13091076
31. Vora V, Kanyal S, Chauhan A, Agarwal P, Sethi Y (2025) Cultural perceptions and social determinants of health in perinatal mental health: an obstetric-psychiatric perspective. Int J Gynaecol Obstet 2025. https://doi.org/10.1002/ijgo.70329
32. Firth A, Haith-Cooper M, Dickerson J, Hart A (2022) Perinatal depression: factors affecting help-seeking behaviours in asylum seeking and refugee women. A systematic review. J Migr Health 6: 100128. https://doi.org/10.1016/j.jmh.2022.100128
33. Valadares G, Drummond AV, Rangel CC, Santos E, Apter G (2020) Maternal mental health and peripartum depression. In Rennó JJ, Valadares G, Cantilino A, Mendes-Ribeiro J, Rocha R, et al. (eds) Women's Mental Health: A Clinical and Evidence-Based Guide. Springer, pp 349–375.
34. Haque S, Malebranche M (2020) Impact of culture on refugee women's conceptualization and experience of postpartum depression in high-income countries of resettlement: a scoping review. PLoS One 15: e0238109. https://doi.org/10.1371/journal.pone.0238109
35. Meghani DT, Vozar TM, Maki K, Clarke UN, Bartolini E (2024) Psychological aspects of perinatal mental health. In The Routledge International Handbook of Perinatal Mental Health Disorders. Routledge, pp 26–52.
36. Patterson R, Balan I, Morrow AL, Meltzer-Brody S (2024) Novel neurosteroid therapeutics for post-partum depression: perspectives on clinical trials, program development, active research, and future directions. Neuropsychopharmacology 49: 67–72. https://doi.org/10.1038/s41386-023-01721-1
37. Barnes KN, Vogl CM, Nelson LA (2024) Zuranolone: the first FDA-approved oral treatment option for postpartum depression. Ann Pharmacother 58: 728–734. https://doi.org/10.1177/10600280231204953
38. Nashwan AJ, Rehan ST, Imran L, Abbas SG, Khan SF (2024) Exploring the clinical potentials of zuranolone in managing postpartum depression: a new therapeutic horizon. Prog Neuropsychopharmacol Biol Psychiatry 132: 110983. https://doi.org/10.1016/j.pnpbp.2024.110983
39. Zhang Q, Dai X, Li W (2022) Comparative efficacy and acceptability of pharmacotherapies for postpartum depression: a systematic review and network meta-analysis. Front Pharmacol 13: 950004. https://doi.org/10.3389/fphar.2022.950004
40. eBioMedicine (2023) Therapeutic advances and open questions in postpartum-depression research. eBioMedicine 98: 1-2. https://doi.org/10.1016/j.ebiom.2023.104925
41. McDonald M, Alhusen J (2022) A review of treatments and clinical guidelines for perinatal depression. J Perinat Neonatal Nurs 36: 233–242. https://doi.org/10.1097/jpn.0000000000000682
42. Kendall-Tackett K (2024) Treatment advances in perinatal depression: innovations and promising approaches. J Clin Med 13: 7744. https://doi.org/10.3390/jcm13247744
43. Yao J, Song T, Zhang Y, Guo N, Zhao P (2020) Intraoperative ketamine for reduction in postpartum depressive symptoms after cesarean delivery: a double-blind, randomized clinical trial. Brain Behav 10: e01715. https://doi.org/10.1002/brb3.1715
44. Suradom C, Suttajit S, Oon-Arom A, Maneeton B, Srisurapanont M (2021) Omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation for prevention and treatment of perinatal depression: a systematic review and meta-analysis of randomized-controlled trials. Nord J Psychiatry 75: 239–246. https://doi.org/10.1080/08039488.2020.1843710
45. Haris M, Mukhtar S, Mohiuddin M, Amir S, Laique F, et al. (2025) FDA-approved zuranolone: first oral treatment for postpartum depression, ushering in a new era of hope; a narrative review. Health Sci Rep 8: e70513. https://doi.org/10.1002/hsr2.70513
46. Kargbo RB (2023) Neurosteroids and postpartum depression: the mechanism, efficacy, and approval of brexanolone and zurzuvae. ACS Med Chem Lett 14: 1326–1328. https://doi.org/10.1021/acsmedchemlett.3c00388
47. Powell JG, Garland S, Preston K, Piszczatoski C (2020) Brexanolone (Zulresso): finally, an FDA-approved treatment for postpartum depression. Ann Pharmacother 54: 157–163. https://doi.org/10.1177/1060028019873320
48. Lusskin SI, Khan SJ, Ernst C, Habib S, Fersh ME, et al. (2018) Pharmacotherapy for perinatal depression. Clin Obstet Gynecol 61: 544–561. https://doi.org/10.1097/grf.0000000000000365
49. Sun Y, Li Y, Wang J, Chen Q, Bazzano AN, et al. (2021) Effectiveness of smartphone-based mindfulness training on maternal perinatal depression: randomized controlled trial. J Med Internet Res 23: e23410. https://doi.org/10.2196/23410
50. Grote NK, Lohr MJ, Curran MC, Cristofalo M (2021) Change mechanisms in brief interpersonal psychotherapy for women with perinatal depression: qualitative study. Am J Psychother 74: 112–118. https://doi.org/10.1176/appi.psychotherapy.20200039
51. Zagorski N (2023) Brief IPT found effective for perinatal depression. Psychiatr News 58: 7. https://doi.org/10.1176/appi.pn.2023.07.7.38
52. Lugo-Candelas C, Monk C (2024) System-level approaches to perinatal depression. Lancet Public Health 9: e4–e5. https://doi.org/10.1016/s2468-2667(23)00304-3
53. O'Connor E, Senger CA, Henninger ML, Coppola E, Gaynes BN (2019) Interventions to prevent perinatal depression: evidence report and systematic review for the US Preventive Services Task Force. JAMA 321: 588–601. https://doi.org/10.1001/jama.2018.20865
54. Sockol LE (2015) A systematic review of the efficacy of cognitive behavioral therapy for treating and preventing perinatal depression. J Affect Disord 177: 7–21. https://doi.org/10.1016/j.jad.2015.01.052

55. Pettman D, O'Mahen H, Blomberg O, Svanberg AS, von Essen L, et al. (2023) Effectiveness of cognitive behavioural therapy-based interventions for maternal perinatal depression: a systematic review and meta-analysis. BMC Psychiatry 23: 208. https://doi.org/10.1186/s12888-023-04547-9

56. Nillni YI, Mehralizade A, Mayer L, Milanovic S (2018) Treatment of depression, anxiety, and trauma-related disorders during the perinatal period: a systematic review. Clin Psychol Rev 66: 136–148. https://doi.org/10.1016/j.cpr.2018.06.004

57. Byatt N, Brenckle L, Sankaran P, Flahive J, Ko JY, et al. (2024) Effectiveness of two systems-level interventions to address perinatal depression in obstetric settings (PRISM): an active-controlled cluster-randomised trial. Lancet Public Health 9: e35–e46. https://doi.org/10.1016/s2468-2667(23)00268-2

58. Waqas A, Zafar SW, Akhtar P, Naveed S, Rahman A (2023) Optimizing cognitive and behavioral approaches for perinatal depression: a systematic review and meta-regression analysis. Camb Prisms Glob Ment Health 10: e22. https://doi.org/10.1017/gmh.2023.8

59. Ionescu MI, Zahiu CDM, Vlad A, Galos F, Gradisteanu Pircalabioru G, et al. (2025) Nurturing development: how a mother's nutrition shapes offspring's brain through the gut. Nutr Neurosci 28: 50–72. https://doi.org/10.1080/1028415x.2024.2349336

60. Jagtap A, Jagtap B, Jagtap R, Lamture Y, Gomase K (2023) Effects of prenatal stress on behavior, cognition, and psychopathology: a comprehensive review. Cureus 15: e38102. https://doi.org/10.7759/cureus.47044

61. Kirkpatrick M, Mandal G, Elhadidy I, Mariani N, Priestley K, et al. (2025) From placenta to the foetus: a systematic review of in vitro models of stress- and inflammation-induced depression in pregnancy. Mol Psychiatry 30: 1689–1707. https://doi.org/10.1038/s41380-024-02866-1

62. Lean RE, Gerstein ED, Smyser TA, Smyser CD, Rogers CE (2023) Socioeconomic disadvantage and parental mood/affective problems links negative parenting and executive dysfunction in children born very preterm. Dev Psychopathol 35: 1092–1107. https://doi.org/10.1017/s0954579421000961

63. Purkiewicz A, Regin KJ, Mumtaz W, Pietrzak-Fiećko R (2025) Breastfeeding: the multifaceted impact on child development and maternal well-being. Nutrients 17: 1326. https://doi.org/10.3390/nu17081326

64. Nazar-Biesman J, Matevosyan A (2024) Affective dysregulation in childhood. In Goldstein S (ed) Clinician Guide to Disruptive Mood Dysregulation Disorder in Children and Adolescents. Cham: Springer International Publishing, pp 27–51.

65. La Rosa VL, Alparone D, Commodari E (2025) Psychological and social factors influencing mother–child bonding in the first year after birth: a model for promoting infant and maternal well-being. Front Psychol 16: 1588433. https://doi.org/10.3389/fpsyg.2025.1588433

66. Dugravier R, Molenat F, Fourneret P, Salinier-Rolland C (2022) Newborns' bonding and attachment, their rhythms and needs, supporting parents appropriately: guidelines for interventions during the perinatal period from the French National College of Midwives. J Midwifery Womens Health 67: S38–S55. https://doi.org/10.1111/jmwh.13422

67. McIntosh JE, Olsson CA, Schuijers M, Tan ES, Painter F, et al. (2021) Exploring perinatal indicators of infant social-emotional development: a review of the replicated evidence. Clin Child Fam Psychol Rev 24: 450–483. https://doi.org/10.1007/s10567-021-00356-2

68. Hill J, Wright N, Sharp H, Pickles A, Steele H (2023) On the risks of secure attachment in infancy: childhood irritability and adolescent depression predicted by secure attachment and high approach behaviours at 14-months towards a caregiver living with inter-parental violence. Front Child Adolesc Psychiatry 2: 1143125. https://doi.org/10.3389/frcha.2023.1143125

69. Wendland J, Castelnau C, Déprez A, Rabain D, de Carmantrand C, et al. (2023) Borderline personality disorder in mothers, maternal sensitivity, and infant social withdrawal: a study on clinical dyads referred to perinatal mental health units. Early Child Dev Care 193: 1575–1588. https://doi.org/10.1080/03004430.2023.2266151

70. Di Giacomo E, Andreini E, Santambrogio J, Arcara A, Clerici M (2024) The interplay between borderline personality disorder and oxytocin: a systematic narrative review on possible contribution and treatment options. Front Psychiatry 15: 1439615. https://doi.org/10.3389/fpsyt.2024.1439615

71. Power J, van IJzendoorn M, Lewis AJ, Chen W, Galbally M (2021) Maternal perinatal depression and child executive function: A systematic review and meta-analysis. J Affect Disord 291: 218–234. https://doi.org/10.1016/j.jad.2021.05.003

72. Severo M, Ventriglio A, Bellomo A, Iuso S, Petito A (2023) Maternal perinatal depression and child neurocognitive development: a relationship still to be clarified. Front Psychiatry 14: 1151897. https://doi.org/10.3389/fpsyt.2023.1151897

73. Prado EL, Sebayang SK, Adawiyah SR, Alcock KJ, Ullman MT, et al. (2021) Maternal depression is the predominant persistent risk for child cognitive and social-emotional problems from early childhood to pre-adolescence: a longitudinal cohort study. Soc Sci Med 289: 114396. https://doi.org/10.1016/j.socscimed.2021.114396

74. Farewell CV, Donohoe R, Thayer Z, Paulson J, Nicklas J, et al. (2021) Maternal depression trajectories and child BMI in a multi-ethnic sample: a latent growth modeling analysis. BMC Pregnancy Childbirth 21: 10. https://doi.org/10.1186/s12884-021-04308-0

75. Bista S, Tait RJ, Straker LM, Lin A, Steinbeck K, et al. (2025) Joint developmental trajectories of internalizing and externalizing problems from mid-childhood to late adolescence and childhood risk factors: findings from a prospective pre-birth cohort. Dev Psychopathol 37: 176–191. https://doi.org/10.1017/s0954579423001505

76. Pelham WE, West SG, Lemery-Chalfant K, Goodman SH, Wilson MN, et al. (2021) Depression in mothers and the externalizing and internalizing behavior of children: an attempt to go beyond association. J Abnorm Psychol 130: 60. https://doi.org/10.1037/abn0000640

77. Low J, Bishop A, Pilkington PD (2022) The longitudinal effects of paternal perinatal depression on internalizing symptoms and externalizing behavior of their children: a systematic review and meta-analysis. Ment Health Prev 26: 200230. https://doi.org/10.1016/j.mhp.2022.200230

78. Stolper H, van der Vegt M, van Doesum K, Steketee M (2024) The integrated family approach in mental health care services: a study of risk factors. Int J Environ Res Public Health 21: 640. https://doi.org/10.3390/ijerph21050640

79. Gupta N, Gupta M, Madabushi JS, Zubiar F (2023) Integrating psychosocial risks with emerging evidence for borderline personality disorders in adolescence: an update for clinicians. Cureus 15: e39815. https://doi.org/10.7759/cureus.40295

80. Tung I, Hipwell AE, Grosse P, Battaglia L, Cannova E, et al. (2024) Prenatal stress and externalizing behaviors in childhood and adolescence: a systematic review and meta-analysis. Psychol Bull 150: 107. https://doi.org/10.1037/bul0000407

81. Prom MC, Denduluri A, Philpotts LL, Rondon MB, Borba CP, et al. (2022) A systematic review of interventions that integrate perinatal mental health care into routine maternal care in low- and middle-income countries. Front Psychiatry 13: 859341. https://doi.org/10.3389/fpsyt.2022.859341

82. Blackmore R, Boyle JA, Gray KM, Willey S, Highet N, et al. (2022) Introducing and integrating perinatal mental health screening: development of an equity-informed evidence-based approach. Health Expect 25: 2287–2298. https://doi.org/10.1111/hex.13526

83. Griffen A, McIntyre L, Belsito JZ, Burkhard J, Davis W, et al. (2021) Perinatal mental health care in the United States: an overview of policies and programs. Health Aff 40: 1543–1550. https://doi.org/10.1377/hlthaff.2021.00796

84. Mazza M, Caroppo E, Marano G, Chieffo D, Moccia L, et al. (2021) Caring for mothers: a narrative review on interpersonal violence and peripartum mental health. Int J Environ Res Public Health 18: 5281. https://doi.org/10.3390/ijerph18105281

85. Webb R, Uddin N, Ford E, Easter A, Shakespeare J, et al. (2021) Barriers and facilitators to implementing perinatal mental health care in health and social care settings: a systematic review. Lancet Psychiatry 8: 521–534. https://doi.org/10.1016/s2215-0366(20)30467-3

86. Masters GA, Yuan Y, Li NC, Straus J, Moore Simas TA, et al. (2023) Improving front-line clinician capacity to address depression and bipolar disorder among perinatal individuals: a longitudinal analysis of the Massachusetts Child Psychiatry Access Program (MCPAP) for Moms. Arch Womens Ment Health 26: 401–410. https://doi.org/10.1007/s00737-023-01324-1

87. Bell K, Ashby BD, Scott SM, Poleshuck E (2024) Integrating mental health care in ambulatory obstetrical practices: strategies and models. Clin Obstet Gynecol 67: 154–168. https://doi.org/10.1097/grf.0000000000000841

88. Shuffrey LC, Thomason ME, Brito NH (2022) Improving perinatal maternal mental health starts with addressing structural inequities. JAMA Psychiatry 79: 387–388. https://doi.org/10.1001/jamapsychiatry.2022.0097

89. Zimmermann M, Peacock-Chambers E, Merton C, Pasciak K, Thompson A, et al. (2023) Equitable reach: patient and professional recommendations for interventions to prevent perinatal depression and anxiety. Gen Hosp Psychiatry 85: 95–103. https://doi.org/10.1016/j.genhosppsych.2023.10.003

90. Modak A, Ronghe V, Gomase KP, Mahakalkar MG, Taksande V, et al. (2023) A comprehensive review of motherhood and mental health: postpartum mood disorders in focus. Cureus 15: e37985. https://doi.org/10.7759/cureus.46209

91. Withers M, Trop J, Bayalag M, Schriger SH, Ganbold S, et al. (2023) "They should

ask about our feelings": mongolian women's experiences of postpartum depression. Transcult Psychiatry 60: 1005–1016. https://doi.org/10.1177/13634615231187256

92. Gabriel AS, Allen TD, Devers CE, Eby LT, Gilson LL, et al. (2023) A call to action: taking the untenable out of women professors' pregnancy, postpartum, and caregiving demands. Ind Organ Psychol 16: 187–210. https://doi.org/10.1017/iop.2022.111

93. Waters L, Cameron K, Nelson-Coffey SK, Crone DL, Kern ML, et al. (2022) Collective wellbeing and posttraumatic growth during COVID-19: how positive psychology can help families, schools, workplaces and marginalized communities. J Posit Psychol 17: 761–789. https://doi.org/10.1080/17439760.2021.1940251

94. Islam A, Begum F, Williams A, Basri R, Ara R, et al. (2023) Midwife-led pandemic telemedicine services for maternal health and gender-based violence screening in Bangladesh: an implementation research case study. Reprod Health 20: 1-13. https://doi.org/10.1186/s12978-023-01674-0

95. Dadi AF, Miller ER, Azale T, Mwanri L (2021) "We do not know how to screen and provide treatment": a qualitative study of barriers and enablers of implementing perinatal depression health services in Ethiopia. Int J Ment Health Syst 15: 41. https://doi.org/10.1186/s13033-021-00466-y

96. Chan AW, Reid C, Skeffington P, Marriott R (2021) A systematic review of EPDS cultural suitability with Indigenous mothers: a global perspective. Arch Womens Ment Health 24: 353–365. https://doi.org/10.1007/s00737-020-01084-2

97. Dagher RK, Bruckheim HE, Colpe LJ, Edwards E, White DB (2021) Perinatal depression: Challenges and opportunities. J Womens Health 30: 154–159. https://doi.org/10.1089/jwh.2020.8862

98. Singla DR, Savel K, Dennis CL, Kim J, Silver RK, et al. (2022) Scaling up mental healthcare for perinatal populations: is telemedicine the answer? Curr Psychiatry Rep 24: 881-887. https://doi.org/10.1007/s11920-022-01389-2

99. Iturralde E, Hsiao CA, Nkemere L, Kubo A, Sterling SA, et al. (2021) Engagement in perinatal depression treatment: a qualitative study of barriers across and within racial/ethnic groups. BMC Pregnancy Childbirth 21: 11. https://doi.org/10.1186/s12884-021-03969-1

100. Li L, Yue SW, Xu J, Qiao J, Redding SR, et al. (2023) Effectiveness of internet-based psychological interventions for treating perinatal depression: a systematic review and meta-analysis. J Clin Nurs 32: 3087–3101. https://doi.org/10.1111/jocn.16399

101. Ameyaw EK, Baatiema L (2025) Mobile health (mHealth) across maternity care continuum. In Liamputtong P (ed) Handbook of Concepts in Health, Health Behavior and Environmental Health. Singapore: Springer Nature, Singapore, pp 1–21.