

# A Narrative Review-Postpartum Depression: Risk Factors, Emerging Biomarkers, Screening Approaches, and Interventions

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## Abstract

**Purpose:** To synthesize recent advances in understanding postpartum depression (PPD), focusing on emerging biomarkers, screening approaches, and interventions across diverse populations. The review aimed to evaluate the complex interplay of sociodemographic, obstetric, and biological risk factors while assessing the effectiveness of various prevention and treatment strategies.

**Methods:** A narrative review of peer-reviewed literature was conducted to synthesize emerging evidence on biomarkers, screening approaches and treatment strategies for Postpartum Depression (PPD). Relevant studies were identified and analyzed to provide an integrative overview of current evidence

**Results:** Emerging biomarkers showed promise for early PPD detection, with evidence linking maternal microbiome changes to both PPD and infant neurodevelopment. Novel screening methods complemented traditional tools, potentially improving detection rates. New interventions, including zuranolone and online cognitive behavioral therapy, demonstrated significant efficacy in reducing PPD symptoms. Integrated care models combining mental health services with obstetric and pediatric care showed promise in addressing the complex needs of affected women and families.

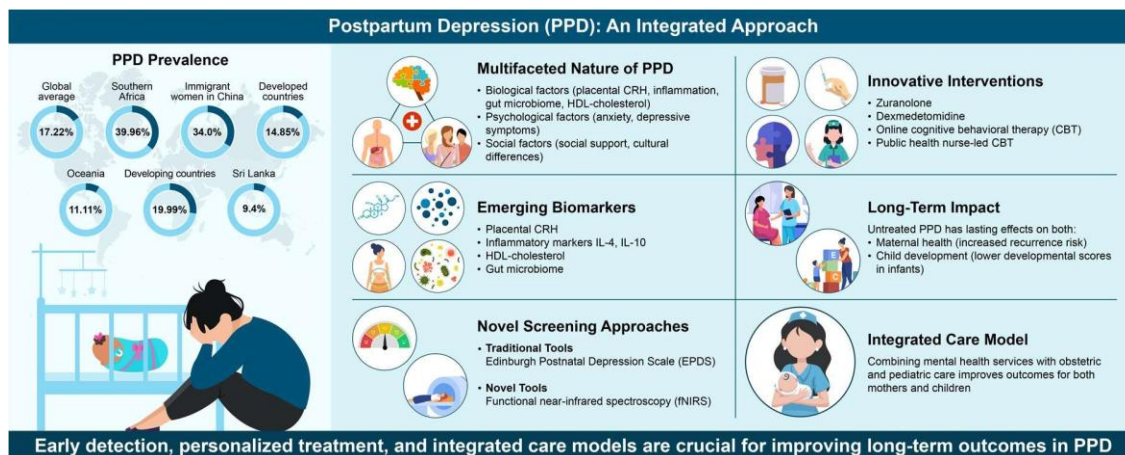
**Conclusion:** The multifaceted nature of PPD necessitates a comprehensive approach to prevention, screening, and treatment. Implementation of universal screening in prenatal and postpartum care settings, utilizing culturally adapted tools, alongside personalized treatment strategies incorporating novel pharmacological options and technology-assisted psychological interventions, can significantly improve outcomes for women at risk for or experiencing PPD.

## Key Words:

Postpartum Depression, Maternal Mental Health, Perinatal Screening, Biomarkers.

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## Graphical Abstract



## Introduction

Postpartum depression (PPD) is a significant mental health disorder that affects women following childbirth, with far-reaching consequences for maternal health, infant development, and family

functioning. Despite its impact, PPD often remains underdiagnosed and undertreated, particularly in diverse and underserved populations. The global prevalence and risk factors for PPD across different regions and populations are summarized in Table 1. The complex etiology of PPD, involving interplay

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between biological, psychological, and social factors, presents challenges for effective prevention, screening, and treatment. This complexity

necessitates a comprehensive, culturally sensitive approach to address PPD across diverse populations and healthcare settings.

**Table 1:** Postpartum Depression: Global Prevalence and Risk Factors

Region/Population	Prevalence (%)	Key Risk Factors
Global average [2]	17.22	Low education level, financial problems, lack of social support
Southern Africa [2]	39.96	Exposure to violence, unplanned pregnancy
Oceania [2]	11.11	Not specified in the study
Developed countries [2]	14.85	Prior history of depression
Developing countries [2]	19.99	Financial hardship, lack of partner support
Immigrant women in China [37]	34.00	Recent immigration (<2 years), insufficient family income, low social support
Sri Lanka [4]	9.40	Low education level, previous mental illness, maternal age 30-39 years

PPD[1] is a pervasive and debilitating mental health disorder that affects approximately one in six women following childbirth [2]. Its impact extends beyond the affected mothers, influencing infant development, family dynamics, and broader societal health outcomes [3]. Despite its prevalence and significance, PPD remains underdiagnosed and undertreated, particularly in diverse and underserved populations [4].

The etiology of PPD is multifaceted, involving a complex interplay of biological, psychological, and social factors [5]. Recent advances in neurobiology, genetics, and clinical research have shed new light on the underlying mechanisms of PPD, paving the way for novel approaches to prevention, detection, and treatment [6]. Of particular interest is the emerging evidence linking the maternal gut microbiome to both PPD and infant neurodevelopment, opening up new avenues for intervention [3].

This review synthesized recent findings on PPD across diverse populations, focusing on three key areas: emerging biomarkers and screening tools, innovative treatment strategies, and long-term consequences for maternal-child health. The review study examined promising biological markers, including placental corticotropin-releasing hormone [5,7] and inflammatory indicators [8], alongside novel screening technologies such as functional near-infrared spectroscopy [9]. The review also evaluated the efficacy of new interventions, ranging from online cognitive behavioral therapy [10] to pharmacological treatments such as zuranolone [11]. Finally, the long-term impacts of PPD on maternal health, child development, and family functioning were explored, emphasizing the critical importance of early detection and intervention in mitigating these effects [3].

## Methodology

For this narrative review we synthesized the literature on Postpartum Depression that was published between January 2000 to January 2026. Relevant articles were identified through searches of PubMed/Medline using MeSH terms and keywords including “perinatal mental health”, “postpartum depression”, “screening” “biomarkers”, “treatment” and “intervention”, “gut microbiome”, “risk factors”. Emphasis was placed on peer-reviewed English-language articles including randomized controlled trials (RCTs), systematic reviews, meta-analyses, prospective cohort studies, and cross-sectional studies reporting original data on PPD diagnosis, emerging biomarkers, prevalence, screening tools/strategies or intervention approaches. The aim of this review was to provide integrative and conceptually informed synthesis of current evidence rather than an exhaustive systematic synthesis.

## Discussion/Observations

### Pathophysiology

PPD arises from a complex interplay of biological, psychological, and social factors. Pronounced hormonal fluctuations following childbirth, particularly the rapid decline in estrogen and progesterone levels, have long been implicated in PPD pathophysiology [5]. Recent research has focused on the role of the hypothalamic-pituitary-adrenal (HPA) axis, with elevated levels of placental corticotropin-releasing hormone (pCRH) during pregnancy associated with increased PPD risk [5]. However, Meltzer-Brody et al. found no significant association between mid-pregnancy pCRH levels and PPD risk in their study [7], underscoring the complexity of hormonal influences and the need for further research to clarify the role of pCRH as a biomarker.

Emerging evidence suggests that inflammatory processes may contribute to the development of

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PPD. Ono et al. reported lower levels of anti-inflammatory cytokines, particularly IL-4 and IL-10, in women who developed PPD [8], aligning with the broader understanding of the role of inflammation in depression.

The gut-brain axis has emerged as a promising area of investigation in PPD [12,13]. Zhou et al. found alterations in the gut microbiota of infants whose mothers had PPD symptoms, suggesting a potential link between maternal mental health and the infant gut microbiome [3]. While the exact mechanisms remain unclear, this finding opens up new avenues for understanding PPD's biological underpinnings.

Genetic factors also contribute to susceptibility to PPD. Pinheiro et al. identified an interaction between the serotonin transporter gene polymorphism (5-HTTLPR) and stressful life events in predicting PPD risk [6]. Epigenetic changes, are an active area of PPD research, though findings are still preliminary [14-16].

Neuroimaging studies have provided insights into PPD-associated brain changes. Xu et al. reported increased activity in the left inferior occipital gyrus and decreased activity in the right anterior cingulate cortex in women with PPD, suggesting alterations in emotional processing and regulation networks [17].

## Clinical Presentation

PPD typically manifests within the first few weeks to months after childbirth, although onset may occur at any time within the first year postpartum. While sharing features with major depressive disorder, PPD is distinguished by its timing and unique maternal characteristics.

Core symptoms of PPD include persistent sadness, anhedonia, and feelings of worthlessness or excessive guilt. These symptoms often exceed the transient "baby blues" experienced by many women shortly after delivery [18].

Women with PPD may experience significant anxiety, often centered on the infant's health and their caregiving abilities. Intrusive thoughts about harming the infant, while distressing, are relatively common and rarely lead to action. However, they may contribute to avoidance behaviors and impaired maternal-infant bonding [18].

Sleep disturbances beyond those expected with infant care are common. Affected women may struggle with sleep initiation even when the infant is asleep or experience early morning awakening with an inability to return to sleep [11].

Physical symptoms may include changes in appetite, excessive fatigue, and psychomotor agitation or retardation. Some women report difficulty

concentrating or making decisions, which can interfere with daily functioning and infant care [10].

In severe cases, suicidal ideation or, rarely, thoughts of infanticide may occur. It is crucial to distinguish PPD from postpartum psychosis, a rare but severe condition characterized by delusions, hallucinations, and grossly disorganized behavior [18].

The presentation of PPD can vary across cultures. Røysted-Solås et al. noted that in some cultures somatic symptoms may be more prominent than mood symptoms [4]. Cultural factors may also influence how women express their distress and their willingness to seek help for mental health concerns.

## Assessment and Diagnosis

Accurate and timely diagnosis of PPD is crucial for effective management. The assessment process typically involves screening, clinical evaluation, and, when necessary, additional diagnostic tests.

PPD screening is recommended at various points during the perinatal period. The Edinburgh Postnatal Depression Scale (EPDS) [19] remains the most widely used and validated screening tool. Røysted-Solås et al. reported a 9.4% prevalence in Sri Lanka using a cut-off score of  $\geq 9$ , while Kale et al. found a 4.8% prevalence in Mumbai, India, using a cut-off of  $>13$  [4,20]. Cut-off scores may vary across populations, highlighting the importance of cultural adaptation and validation.

The Patient Health Questionnaire-9 (PHQ-9) [21] and the Beck Depression Inventory (BDI) [22] are also used for PPD screening, although less frequently than the EPDS. Kim et al. found that prepartum depression scores on both the EPDS and BDI were strong predictors of PPD, correctly identifying depressed mothers (96.7%) and non-depressed mothers (76.9%) at 24 weeks of pregnancy [23].

Clinical evaluation should assess mood, anxiety symptoms, suicidal ideation, and thoughts of infant harm and functional impairment, particularly concerning infant care and bonding. A thorough history should cover previous psychiatric disorders, as Guintivano et al. reported that 53.2% of women with PPD had a history of major depressive disorder [24].

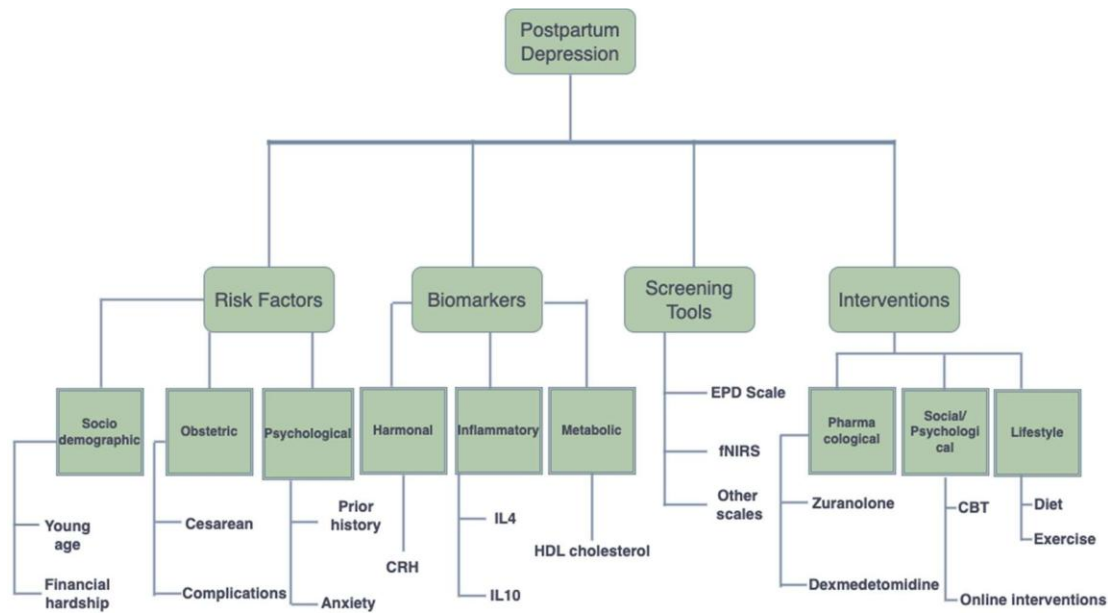
Differential diagnosis is essential, as PPD can be mistaken for other postpartum mood disorders. Wisner et al. found that 22.6% of women who screened positive for PPD had bipolar disorder [18], emphasizing the need for comprehensive screening for bipolar disorder, particularly in women with a personal or family history of bipolar disorder or those with atypical presentation or treatment resistance.

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Emerging technologies show promise in enhancing PPD assessment. Song et al. investigated the use of functional near-infrared spectroscopy (fNIRS) as an objective method for early detection of PPD [9]. They found that fNIRS might be more sensitive in detecting PPD risk compared to the EPDS, reporting PPD prevalence rates of 18.3% and 16.5% using two different fNIRS criteria, compared to 11.0% using EPDS ( $\geq 11$ ).

Laboratory tests may help rule out medical conditions mimicking PPD symptoms, such as thyroid dysfunction or anemia. Research on potential biomarkers is ongoing. Pillai et al. found an association between PPD and lower levels of High-Density Lipoprotein cholesterol (HDL-c), suggesting potential metabolic markers for PPD risk [25]. An integrated model of PPD risk factors,

biomarkers, screening tools, and interventions is presented in Figure 1. Vitamin deficiencies have also been associated with PPD risk. Dhiman et al. reported that low levels of vitamin B<sub>12</sub> were associated with an increased risk of PPD [26]; women with PPD had lower serum levels of total, free, and bioavailable vitamin B<sub>12</sub> than non-depressed women. Lin et al. investigated the relationship between postpartum nutritional status and PPD in Taiwanese women [27]. While not directly measuring gut metabolites, they found that women with PPD had significantly lower plasma riboflavin levels (by 13.9%) and displayed a higher ratio of n-6 to n-3 fatty acids. These nutritional imbalances may potentially influence both gut-microbiome composition and metabolomic profiles, although direct causal relationships were not established.



**Figure 1: Integrated Model of Postpartum Depression: Risk Factors, Biomarkers, Screening Tools, and Interventions**

## Treatment

Traditional antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), have long been the mainstay of pharmacological treatment for PPD [28]. Treatment typically involves a combination of psychotherapy, pharmacotherapy, and supportive interventions. The choice of treatment should be individualized based on symptom severity, patient preference, and other factors such as breastfeeding status.

Psychotherapy, particularly cognitive behavioral therapy (CBT), has shown significant efficacy in treating PPD. Van Lieshout et al. conducted a randomized clinical trial evaluating the

effectiveness of adding a one-day online CBT workshop to the usual PPD treatment care [10]. The study demonstrated significant reductions in PPD symptoms (EPDS scores decreased from 16.47 to 11.65,  $p < 0.001$ ) and anxiety symptoms (GAD-7 scores decreased from 12.41 to 7.97,  $p < 0.001$ ) in the intervention group. Participants receiving CBT had higher odds of experiencing clinically significant improvements in PPD symptoms (OR 4.15, 95% CI 2.66-6.46) and anxiety symptoms (OR 3.09, 95% CI 1.99-4.81).

In a subsequent study, Van Lieshout et al. explored the effectiveness of public health nurse-delivered group CBT for PPD [29]. This randomized

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controlled trial found that nurses with minimal psychiatric training could deliver group CBT effectively, leading to significant improvements in depression, worry, and mother-infant relationships. The intervention group showed greater reduction in EPDS scores ( $B = -5.35, p < 0.01$ ) and higher odds of clinically significant improvement ( $OR = 3.44, 95\% CI: 1.49-7.94$ ) immediately post-treatment.

Pharmacological treatment, particularly with SSRIs, remains a mainstay of PPD management, especially for moderate-to-severe cases. However, concerns about potential side effects and impact on breastfeeding have led to research into alternative pharmacological approaches.

Deligiannidis et al. reported that zuranolone, a neuroactive steroid, improved both depressive and anxiety symptoms, as well as insomnia and patient-reported functional health outcomes, in women with PPD [11]. The study found higher rates of concurrent remission of depressive and anxiety symptoms with zuranolone compared to placebo at day 15 (40.5% vs. 19.2%,  $p=0.007$ ) and day 45 (52.1% vs. 23.2%,  $p<0.001$ ). The FDA's approval of Zuruvae (zuranolone) in August 2023 marked a significant milestone in PPD treatment, representing the first oral medication specifically indicated for the condition [30]. The approval of zuranolone offers a more accessible treatment option for women with PPD, potentially improving treatment adherence and outcomes. Clinical trials demonstrated significant improvement in depressive symptoms compared to placebo, with effects maintained four weeks after the last dose. The phase 3 CORAL study evaluated the efficacy and safety of zuranolone 50 mg co-initiated with standard-of-care antidepressant therapy (zuranolone +ADT) versus placebo+ADT in adults with major depressive disorder (MDD) [31]. Zuranolone+ADT

demonstrated significantly greater improvement in depressive symptoms at Day 3 compared to placebo+ADT. The safety profile was consistent with previous studies, with most treatment-emergent adverse events being mild or moderate. These results suggest zuranolone may provide rapid improvement when co-initiated with standard antidepressants in patients with MDD.

Another innovative approach involves the use of dexmedetomidine, an  $\alpha_2$ -adrenergic receptor agonist. Zhou et al. conducted a randomized clinical trial examining the efficacy of dexmedetomidine for PPD prevention in women with prenatal depression [32]. They found that dexmedetomidine administration in the early postpartum period reduced the incidence of PPD significantly. The positive PPD screening incidence at 7 days postpartum was 12.6% in the dexmedetomidine group compared to 32.1% in the control group ( $RR 0.39, 95\% CI 0.25-0.62, p < .001$ ).

Non-pharmacological interventions, such as exercise and nutritional approaches, are gaining attention. Papadopoulou et al. found that higher adherence to the Mediterranean diet was associated with a more than two-fold lower probability of PPD, suggesting potential dietary interventions for PPD prevention and management [33]. A summary of emerging biomarkers and novel interventions for PPD is presented in Table 2. Social-support interventions play a crucial role in PPD management. Wang et al. found that a lack of social support was associated with a significantly higher prevalence of PPD (32.03% vs. 15.15% with support) [2], underscoring the potential value of interventions aimed at enhancing social support for postpartum women, such as support groups or home visiting programs.

**Table 2:** Emerging Biomarkers and Novel Interventions for Postpartum Depression

Category	Biomarker/ Intervention	Key Findings	Potential Impact
Hormonal Biomarker [5]	Placental CRH	Elevated pCRH at 25 weeks gestation predicted PPD symptoms	Early risk identification
Inflammatory Biomarker [8]	IL-4, IL-10	Lower levels associated with PPD	Potential screening tool
Metabolic Biomarker [25]	HDL-cholesterol	Lower levels in women with PPD	Indicator for severe PPD symptoms
Gut Microbiome [3]	Infant gut microbiota diversity	Higher diversity in infants of mothers with PPD	Link between maternal PPD and infant development
Pharmacological Intervention [11]	Zuranolone	Improved depressive and anxiety symptoms	Rapid-acting treatment for PPD
Pharmacological Intervention [32]	Dexmedetomidine	Reduced PPD incidence in high-risk women	Potential preventive treatment
Psychological Intervention [10]	Online CBT workshop	Significant reduction in PPD symptoms	Accessible, scalable intervention

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Category	Biomarker/ Intervention	Key Findings	Potential Impact
Psychological Intervention [29]	Public health nurse-led CBT	Effective in reducing PPD symptoms	Integration into public health services
Technological Screening [9]	fNIRS	More sensitive than EPDS in detecting PPD risk	Objective screening method

Inpatient treatment may be necessary for women with severe PPD, suicidal ideation, or psychotic symptoms. Electroconvulsive therapy (ECT) can be considered for severe treatment-resistant cases, particularly when rapid improvement is needed [34].

Treatment decisions should consider potential risks and benefits, particularly for breastfeeding mothers. Close monitoring and follow-up are essential, with treatment-plan adjustments based on response and tolerability.

### Prognosis

The prognosis for PPD is generally favorable with appropriate treatment, but outcomes vary widely depending on several factors. Timely diagnosis and intervention are crucial for optimal outcomes.

With effective treatment, many women experience significant symptom improvement within 6 to 12 weeks. Van Lieshout et al. reported that women receiving online CBT showed substantial improvements in depressive symptoms, with effects maintained at 12-week follow-up. However, some women may experience a more protracted course, with symptoms persisting for months or years without adequate treatment [10].

Recurrent risk in subsequent pregnancies is a significant concern. Rich-Edwards et al. found that a history of depression was a strong predictor of both antenatal and postpartum depressive symptoms, suggesting that women with a history of PPD may be at increased risk in future pregnancies [35].

Long-term consequences of PPD can be significant if left untreated. Zhou et al. demonstrated potential impact of maternal PPD on infant neurodevelopment, finding that infants of mothers with PPD symptoms had significantly lower developmental scores[3]. It is important to consider child outcomes in assessing the overall prognosis of PPD.

Factors associated with better prognosis include early detection and treatment, strong social support, and absence of comorbid psychiatric disorders. Conversely, factors such as severe symptoms, comorbid anxiety or bipolar disorder, and inadequate social support may be associated with poorer outcomes [36].

While acute symptoms may resolve with treatment, some women experience residual symptoms or

vulnerability to future depressive episodes. Ongoing monitoring and support, particularly during subsequent pregnancies, are crucial for optimizing long-term outcomes for both mothers and their children.

### Conclusions

PPD presents a significant global health challenge with far-reaching consequences for maternal health, child development, and family functioning. This review underscored the complex, multifaceted nature of PPD, highlighting the need for comprehensive, culturally sensitive approaches to prevention, detection, and treatment. The integration of emerging biomarkers, novel screening technologies, and innovative interventions offers promising avenues for improving outcomes. Focusing on personalized, integrated care models that combine mental health services with obstetric and pediatric care is essential. Leveraging these advances and addressing the diverse needs of affected populations, clinicians and researchers can substantially mitigate the burden of PPD and its long-term impacts on mothers, children, and families.

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**SS:** Conceptualization, methodology, investigation, data collection and analysis, writing - original draft preparation.

**SM:** Methodology, data analysis, validation, writing - review and editing, visualization.

## Abbreviations

PPD: Postpartum Depression; pCRH: Placental corticotropin-releasing hormone; HPC: hypothalamic-pituitary-adrenal; EPDS: The Edinburgh Postnatal Depression Scale; PHQ-9: Patient Health Questionnaire-9; BDI: Beck Depression Inventory; fNIRS: Functional near-infrared spectroscopy; HDL-c: High-Density Lipoprotein cholesterol; SSRIs: Selective serotonin reuptake inhibitors; CBT: Cognitive behavioral therapy; MDD: Major depressive disorder; ECT: Electroconvulsive therapy.

## Disclaimer

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