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Preventing recurrence of postpartum depression by regulating sleep

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Abstract

Introduction—Women are at a high risk of recurrence of depression in the postpartum period. Given the circumscribed duration of the risk period and knowledge of its triggers, postpartum depression should be easily preventable. However, prophylactic drug studies have reported contradictory findings partly due to the heterogeneity of the disorder. Currently, there are no studies on the efficacy of psychotherapy in the prevention of postpartum depression in women with major depressive or bipolar disorder.

Areas Covered: This review evaluates the results of controlled medication and psychotherapeutic studies in the prevention of depression in women with major depressive disorder or bipolar disorder; it further suggests that the management of sleep loss/insomnia may be an effective strategy in the prevention of postpartum depression.

Expert opinion—A thorough understanding of the clinical course of the antecedent mood disorder and historical treatment response is necessary before the implementation of strategies for the prevention of postpartum depression. Targeting disturbed and/or insufficient sleep – a common and early transdiagnostic symptom of peripartum psychiatric disorders - may be a more effective intervention for the prevention of postpartum depression and psychiatric comorbidities in some individuals than the traditional approach of antidepressant use.

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V Sharma reports participation with AMOSO (Academic Medical Organization of Southwestern Ontario). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Keywords

antidepressants; depression; insomnia; mood stabilizers; postpartum; prevention; sleep

1. Introduction

Postpartum depression is the most common psychiatric complication of childbirth. Globally, approximately 17 % of women have depression[1], however, the prevalence estimates vary greatly by country, cut-off score on the screening tool, and diagnostic characterization. Although symptoms emerge most commonly following delivery, one large population study found that 33.4% of women experienced the onset of their depressive episode during pregnancy and 26.5% had depression before the index pregnancy[2]. Most mothers with postpartum depression have pre-existing psychiatric illnesses including major depressive disorder, bipolar I disorder, or bipolar II disorder[3]. Despite drug treatment during pregnancy, nearly 20% of women with bipolar I disorder, 29% with bipolar II disorder, and 16% with major depressive disorder have an episode of depression during the first 6 months after delivery[4]. Common risk factors for postpartum depression include premenstrual syndrome, violent experiences, unintended pregnancy, and antenatal anxiety and/or depression[5], [6].

Given the deleterious effects of postpartum depression for mothers and infants, there has been a concerted effort to screen for depression during and after pregnancy[7]–[9]. The American College of Obstetricians and Gynecologists[10] recommends screening for depression and anxiety at the initial prenatal visit, later in pregnancy, and at postpartum visits using a standardized, validated tool such as the Edinburgh Postnatal Depression Scale (EPDS)[11]. Similarly, the US Preventive Services Task Force (USPSTF) 2019 statement on Interventions to Prevent Perinatal Depression recommends that all pregnant and postpartum persons should be assessed for clinical risk factors (personal or history of depression, history of physical or sexual abuse, unplanned or unwanted pregnancy, current stressful life events, pre gestational or gestational diabetes, and other complications during pregnancy such as preterm delivery or pregnancy loss) and social vulnerabilities (low socioeconomic status, lack of social or financial support, and adolescent parenthood)[12]. Based on their systematic review, the USPSTF also recommends counseling including cognitive-behavioral therapy or interpersonal psychotherapy for women at risk of developing perinatal depression. Because their review excluded studies targeting clinical populations, the Task Force did not make specific recommendations for the prevention of postpartum depression in women with pre-existing psychiatric illness, yielding a gap in treatment guidelines for those at highest risk, i.e., individuals with major depressive disorder, bipolar I disorder, or bipolar II disorder.

A recent study that critically appraised systematic reviews of interventions for postpartum depression concluded that antidepressants and telemedicine were the most effective preventative interventions based on reviews of the highest methodological quality[13]. However, authors of an earlier Cochrane review found that evidence supporting the effectiveness of antidepressants for the prevention of postpartum depression was inconclusive[14]. Given the conflicting information, it is essential to examine the reasons for

discordant research findings and explore clinical opportunities for the effective prevention of postpartum depression and its common psychiatric comorbidities. In this review, we examine the potential sources of the clinical heterogeneity of postpartum depression and discuss how these factors may contribute to treatment challenges. We then review the extant pharmacological data on the prevention of major depression after delivery and propose a personalized approach based on a thorough understanding of the clinical course of the underlying mood disorder and past treatment response. Given that insufficient/disrupted sleep is a transdiagnostic symptom that is ubiquitous during and after pregnancy[15], we contend that the management of sleep loss/insomnia may be an effective strategy for the prevention of a major depressive episode in women with major depressive disorder or bipolar disorder. Finally, we outline knowledge gaps and offer suggestions for future research.

2. Heterogeneity of postpartum depression

Despite fundamental controversies about its diagnostic status, the term postpartum depression continues to be used by professionals as well as the lay public to refer to an episode of depression after delivery[16]. The diagnostic status of postpartum depression has been intensely debated since 1858 when Louis-Victor Marcé published his monograph, *Treatise on Insanity in Pregnant, Postpartum, and Lactating Women*[17]. Marcé argued that symptoms of puerperal illness are *many* and *varied* and each symptom could be found in non-puerperal cases, but puerperal syndrome was different from non-puerperal illnesses. The Diagnostic and Statistical Manual of Mental Disorders (5^{th} ed.; DSM-5) acknowledges the heightened risk of recurrence of depression during and after pregnancy by allowing the use of the peripartum specifier but does not consider postpartum depression a distinct clinical entity[18]

Several factors including polarity (unipolar or bipolar)[19], [20], the timing of onset (before, during, or after pregnancy)[2], [21], the latency of onset (early vs. late)[22] and type of occurrence (first onset vs. recurrent)[23], as well as comorbid disorders (both physical and psychiatric)[2], [20], may contribute to the clinical heterogeneity of postpartum depression[21], [24]. Mandelli et al. retrospectively evaluated the association between postpartum depression and mood disorders[25]. Compared to women without a history of postpartum depression, those with such a history were younger, had earlier illness onset, and were more likely to have a family history of bipolar disorder. A history of postpartum depression among women with bipolar II disorder, bipolar I disorder, and major depressive disorder was present in 50%, 27.5%, and 21.6% respectively (p=0.004), suggesting that bipolar disorders confer greater risk than unipolar depression. The postpartum period is the most common time of occurrence; however, most depression cases (60%) begin during or before pregnancy[2]. Recurrences of postpartum depression in multiparous women tend to cluster after delivery, but women remain at risk of recurrence for approximately 7 months postpartum[22]. The first onset of depression after delivery is less common, but its clinical significance lies in its association with bipolar disorder. Depending on the diagnostic criteria used, 15–50% of women whose first depressive episode occurs postpartum eventually develop bipolar disorder[23]. Studies thus far have emphasized the role of pregnancy and childbirth in the onset of depression, however, there is emerging evidence that the abrupt

cessation of breastfeeding may increase the risk of depression[26], highlighting the potential role of alternate factors in triggering depression in the perinatal period. For example, changes in the neurohormonal milieu because of hormonal perturbations following the abrupt cessation of breastfeeding and resumption of menstruation may alter γ-aminobutyric acid (GABA) receptors such that the neurosteroid allopregnanolone may contribute to, rather than improve, symptoms of depression in susceptible women[27]. Longitudinal studies are needed to clarify the relationship between breastfeeding and postpartum depression, as depression follows the cessation of exclusive breastfeeding and resumption of menstruation in some women[26], [27].

The exceptionally high incidence of psychiatric comorbidity, particularly anxiety disorders and obsessive-compulsive disorder, further adds to the heterogeneity of postpartum depression[2], [16]. For instance, a large population-based study in which postpartum depression was confirmed with diagnostic interviews found that 51.8% of those with postpartum depression also met the criteria for a comorbid anxiety disorder[2]. Additionally, new onset obsessive-compulsive disorder is more than twice as likely to occur in the perinatal period compared with other times in adulthood[28]. Similarly, women with a history of premenstrual dysphoric disorder appear to be at a particularly high risk of postpartum depression[29]. Post-traumatic stress disorder (PTSD) is another clinical entity that is common in pregnancy, is linked to sleep dysregulation, and has significant overlap with postpartum depression[30]. Furthermore, recent evidence indicates a bidirectional relationship between trauma and disturbed sleep, i.e., PTSD confers an increased risk for insomnia and depression, and insomnia during pregnancy is associated with higher rates of childbirth-related PTSD[31]. Thus, psychiatric comorbidity is a rule rather than an exception among women with postpartum depression. Overlapping diagnoses can make the diagnosis and treatment of postpartum depression more challenging[21]. Notably, sleep and circadian dysregulation are well-documented features of both anxiety disorders[32] and obsessive-compulsive disorder[33].

Taken together, this evidence highlights the heterogeneity of postpartum depression, which in turn suggests differing etiology and perhaps different treatment approaches[24].

3. Prevention of postpartum depression in women with pre-existing mood disorder

Recurrence of depression after delivery should be preventable because at-risk women can be identified, the nature and timing of the trigger are known, and the risk period is short (usually 7 months in women with unipolar depression)[22]. Antidepressants are commonly prescribed for the prevention of postpartum depression; however, the prophylactic effect of antidepressants has been assessed in only two controlled trials[34], [35]. Both studies used the same methodology and neither provided convincing evidence that antidepressants were superior to placebo. Importantly, both excluded those with a history of psychosis, bipolar disorder, other current Axis 1 disorders (except generalized anxiety and panic disorder), and antisocial or borderline personality disorder, potentially limiting the generalizability of the findings and omitting those at the highest risk. Women with a history of postpartum

depression who were free of depression in pregnancy were randomized to an antidepressant (nortriptyline or sertraline) or placebo. The treatment period in both studies was 17 weeks. In the nortriptyline study, 23% (6/26) of women who took the drug and 24% (6/25) of women who took a placebo had a recurrence of postpartum depression (RR 0.96, 95% CI 0.36 to 2.59)[35]. In the smaller sertraline study, 7% (1/14) of women who took the drug had a recurrence of postpartum depression compared with 50% (4/8) of women who took a placebo (RR 0.14, 95% CI 0.02 to 1.07). Even though women with bipolar disorder or psychosis were excluded, two participants (one case in each study) developed hypo/mania.

Another study found that antidepressant use in the third trimester of pregnancy was ineffective in preventing postpartum depression in women with a history of major depressive disorder who were currently euthymic[36]. Notably, the Hamilton Depression Rating Scale score specifically on work activities, early insomnia, and suicidality items significantly predicted postpartum depression. Similar results were reported by Pope et al. who compared rates of postpartum recurrence among women with major depressive disorder who were treated with antidepressants (monotherapy or combination therapy), to women receiving no psychotropic medication[37]. Due to the limited evidence, a Cochrane review did not make any specific recommendations about the prophylactic use of antidepressants[14].

A paucity of evidence exists for the efficacy of mood-stabilizing drugs in the prevention of postpartum depression in women with bipolar I or II disorder [19]. A single-blind, non-randomized study by Wisner found valproate was not significantly more effective than monitoring alone in preventing postpartum mood in women with bipolar disorder[38]. Prevention of depression in women with bipolar disorder is particularly important for several reasons: 1) bipolar depression tends to be more severe than its unipolar counterpart in the postpartum period[2], 2) the risk of psychiatric hospitalization is exponentially high in the first few weeks after delivery[39], and 3) the absence of data on the prophylactic use of mood stabilizers may contribute to the inappropriate use of antidepressants which in turn may increase the risk of psychiatric hospitalization due to the induction of manic/mixed episodes[19], [40]. Finally, antidepressant monotherapy may also endanger the safety of the mother and her baby[41]. Lithium is commonly recommended for postpartum prophylaxis of postpartum mood episodes[42], however, there are no randomized controlled trials in women with bipolar disorder.

Currently, there are no psychotherapeutic studies on the prevention of postpartum depression in women with major depressive or bipolar disorder.

4. Dysregulated sleep: a final common pathway

The association of sleep dysregulation with serious postpartum mental illness has been recognized since antiquity. Hippocrates described the tragic case of a woman with psychosis who experienced insomnia on postpartum day 1 with progressive worsening of sleep loss and the emergence of psychotic symptoms[43]. In 1896, Savage described the sleep disturbance of puerperium as “miserable sleeplessness”[44]. A few years later Jones observed that “the almost universal early symptom in puerperal cases is loss of sleep. For this reason, early attention should be given to sleeplessness”[45]. More recently,

studies have implicated sleep loss in the causation of puerperal psychosis and bipolar mood episodes[16], [46]. Literature is emerging on the relationship between disturbed sleep and the heterogeneous symptoms observed in peripartum psychopathology[15]. Sleep disturbance is also common among women experiencing mood changes associated with various reproductive events including menstruation[47]. Since premenstrual dysphoric disorder is a major risk factor for postpartum depression, it is possible that sleep disturbance may underlie the association of menstrual periods and childbirth with the occurrence of mood symptoms.

Sleep changes are ubiquitous in pregnancy and postpartum, and multiple studies have demonstrated links between disturbed sleep and peripartum depression[15], [21], [48]–[57]. A systematic review and meta-analysis of studies published in the last decade confirmed the association of poor sleep with perinatal depression (OR 1.49, 95% CI 1.19 to 1.79)[58]. Thus, perinatal sleep changes may predict the development of depression more than changes in hormones. However, perinatal sleep dysregulation can take many forms – ranging from a clinical diagnosis of insomnia to insufficient sleep duration, to aberrant sleep timing – yet few studies have specified different phenotypes of perinatal sleep loss. A recent study[55] distinguished between individuals who experienced perinatal sleep disturbance due to insufficient opportunity to obtain adequate sleep, and those who faced the same challenges and reported the inability to initiate or maintain sleep, thereby meeting DSM-5 criteria for insomnia disorder. The percentages of the sample (n=163) that had perinatal sleep disturbance versus insomnia disorder were 37.3% versus 19.8% in the 3rd trimester and 40.4% versus 10.6% at 6 months postpartum. Both sleep disturbance phenotypes were associated with greater depressive symptoms, but those who met the criteria for insomnia disorder also had significantly higher anxiety.

Differences in the methods used to characterize sleep (e.g., self-reports, clinical interviews, objective measurements) likely contribute to mixed findings about associations between sleep dysregulation and postpartum depression and anxiety. In Lawson et al.'s 2015 systematic review of 31 studies examining associations between disturbed sleep and mood disorders, the strongest and most consistent relationships were observed between subjectively reported sleep disturbance and postpartum depression, with more variable findings for links between sleep dysregulation and anxiety or psychosis[54]. A population-based prospective study from Norway found that mid-pregnancy insomnia was significantly associated with concurrent depression but not postpartum depression[59]. The same study also found an association between mid-pregnancy insomnia with current and postpartum generalized anxiety and obsessive-compulsive symptoms. Data from the FinnBrain Birth Cohort Study found a sleep latency of ≥ 20 minutes, insomnia in late pregnancy, and anxiety during early pregnancy, predicted depressive symptoms postpartum[60]. Another Norwegian study found that insomnia in pregnancy may be a marker of postpartum depression[61].

Longitudinal studies have reported that sleep quality changes from the second to the third trimester[62]. A prospective study using both objective and subjective measures of sleep found that antenatal sleep duration significantly predicted class membership to the high and moderate comorbidity classes. Additionally, mothers with higher wakefulness sleep onset (WASO) in the postpartum period were more likely to have moderate symptoms. Kalmbach

and colleagues found that cognitive arousal while trying to fall asleep may worsen insomnia that in turn aggravates the cognitive arousal[63].

Details of prospective studies of peripartum sleep in women with major depressive disorder are outlined in Table 1[36], [51], [56], [64]–[67]. These studies highlight the importance of assessing sleep loss/insomnia among women who are at risk of developing recurrences of depression during or after pregnancy. Poor sleep after delivery may perpetuate depression or anxiety thus creating a vicious cycle. Since insomnia and sleep loss may cause the hyperactivation of stress and inflammatory systems, these sleep conditions may favor anxiety and depression through the hyperactivation of the stress system causing a state of allostatic overload[68]. Also, insomnia and insomnia-related cognitive arousal may fuel perinatal depressive cognition[68], [69].

4.1 Targeting insomnia to prevent postpartum depression

A few studies have tested whether insomnia treatment during pregnancy can improve sleep and prevent postpartum depression. Manber and colleagues enrolled pregnant women (n=179) who met diagnostic criteria for insomnia to receive individual cognitive behavioral therapy for insomnia (CBT-I) or a control treatment (pseudo-desensitization therapy for insomnia) and found that women in the CBT-I group reported significantly greater reductions in insomnia (large effect size for a decrease in Insomnia Severity Index) and depressive symptoms (small effect size for a decrease in EPDS)[70]. A more scalable intervention – digitally delivered cognitive behavioral therapy for insomnia (dCBT-I) has also been tested with promising results. Felder et al (2020) [71] randomized women up to 28 weeks gestation (N = 208) with insomnia to 6 weekly sessions of dCBT-I or standard care and found that the dCBT-I participants had higher rates of insomnia remission and lower rates of insomnia caseness at 6 months postpartum as well as fewer postpartum depressive and anxiety symptoms. Two other studies of perinatal dCBT-I also demonstrated improvements in subjective sleep disturbances but did not show differences in mood symptoms between participants treated with dCBT-I and controls[72], [73]. Of note, all studies excluded women at the highest risk for postpartum depression, namely those with bipolar disorder or significant depressive symptoms at enrollment. Currently, there are no studies on the effectiveness of CBT-I in the prevention of postpartum recurrence in women with major depressive disorder or bipolar disorder.

Medication trials for the treatment of peripartum insomnia are uncommon. A double-blind, placebo-controlled study found that treatment of insomnia with trazodone or diphenhydramine during the third trimester was significantly associated with a reduction in depressive symptoms postpartum[74]. Considering the emerging evidence of the association of sleep loss with thoughts of suicide, addressing insomnia is also important from a safety point of view[75], [76]. Moreover, antidepressants without the concurrent use of mood stabilizers might increase the risk of mixed episodes and consequently the safety of the newborn.

Taken together, the literature although sparse, suggests that targeting insomnia/sleep loss may be effective in the prevention of postpartum depression in some women[77]. Moreover,

emphasizing the potential role of sleep dysregulation in the etiology, phenomenology, and treatment of postpartum depression may reduce stigma-related barriers to care.

4.2 Challenges and barriers to uptake of sleep intervention

Several factors such as nausea, gastroesophageal reflux disease, nocturia, physical discomfort, and restless legs contribute to insomnia in pregnancy. Similarly, increased stressors, childcare for a new infant, and hormone level changes can cause insomnia/sleep loss. Sleep reactivity-the degree to which a stressor disrupts sleep- may affect vulnerability to mood and anxiety disorders[78]. For a thorough review of the neurobiology of insomnia please refer to reviews by Palagini et al., 2014; Harvey et al, 2014[79]; and Kalmbach et al., 2018[78]. Insomnia is a common symptom as well as a prodrome of various psychiatric disorders. Thus, determining whether the sleep change is a harbinger of peripartum depression is problematic. Variability in the timing of the onset of postpartum depression makes it difficult to ascertain the optimal time for the introduction of sleep intervention. Some women are extremely anxious about trying medication for insomnia due to the fear that they won't be able to wake up to provide childcare. This is especially a concern for mothers who do not have nocturnal support. While others are concerned about the passage of medication in breast milk. The inability to access CBT-I due to the lack of funds may also be an issue for some women.

5. Expert opinion

5.1 Personalized risk estimation

Since many women have an onset of depression during or before index pregnancy[2], early identification of at-risk women in pregnancy is necessary to implement strategies[75]. Screening instruments including the EPDS assess the risk of recurrence based on current or recent (usually 1–2 weeks) symptoms. This means currently pregnant euthymic women who are at risk of postpartum depression due to a history of a mood disorder will have a negative screen on the screening tool. Moreover, screening women for depression alone will omit those who are at risk of postpartum depression due to a history of hypo/mania. Risk-based screening should incorporate questions about personal and family history of major depressive disorder[80], bipolar disorder, and puerperal psychosis along with current symptoms, significant life events, and perceived social support available after delivery[74]. Women should also be assessed for a history of premenstrual dysphoric disorder [81] and other comorbid psychiatric disorders particularly anxiety. Screening for hypo/manic symptoms after delivery is also important because these symptoms precede depression in some cases[82]. There is preliminary evidence that prevention of hypo/manic episodes may also prevent the ensuing depression[82].

Although the EPDS has a sleep question, this item links sleep difficulties to unhappiness and does not specify the severity or duration of sleep loss. Women at risk of postpartum depression should be assessed for insomnia/sleep loss. Screening for insomnia may also identify women at risk of developing other psychiatric disorders that commonly accompany postpartum depression.

Sleep difficulties, including insufficient sleep and insomnia, can be identified easily during routine checkups, and further assessed using valid, reliable tools such as the Insomnia Symptom Questionnaire[83]. Screening for insomnia may also identify women at risk of developing other psychiatric disorders such as anxiety disorders or obsessive-compulsive disorder as well as other sleep problems that increase maternal morbidity and mortality, e.g., sleep-disordered breathing[84]. Women meeting the diagnostic criteria for insomnia disorder should be referred for further evaluation and management. At-risk women (e.g., those with a mood disorder) should be assessed for prodromal/early symptoms of depression - especially sleep loss during and after pregnancy. The use of a mood diary may facilitate prospective data on changes in sleep, mood, and anxiety. Information about the relationship between cognition, sleep, and mood as well as sleep hygiene practices should be incorporated into psychoeducation for the prevention of postpartum depression.

5.2 Intervention

Personalized risk assessment and treatment history should guide the choice of intervention strategies during and/or after pregnancy to minimize the risk of postpartum depression. A nationwide study from Japan found that maternal short sleep and late bedtime prior to and during pregnancy increased the risk of offspring's sleeping disturbances[85]. Sharing nocturnal caregiving tasks between parents allows the mother to have more uninterrupted sleep, which may contribute to greater consolidation of infant and toddler sleep[86].

Controlled drug trials thus far have addressed a specific sub-population of women at risk of postpartum recurrence of depression, i.e., those with a history of postpartum depression. Given the heterogeneity of the condition, a one-size-fits-all approach is unlikely to be effective in preventing all cases of postpartum depression. While some women may benefit from antidepressants or mood stabilizers, targeting disturbed and/or insufficient sleep may be a more effective intervention for the prevention of postpartum depression and possibly common comorbidities. The use of drugs such as trazodone or diphenhydramine in the third trimester may be effective in the prevention of postpartum depression in some women. Management of sleep loss, whether from insomnia or insufficient opportunity to sleep may also be effective in the prevention of common psychiatric comorbidities that accompany postpartum depression. There is preliminary evidence that quetiapine and olanzapine are effective in the prevention of mood episodes in women with bipolar I or II disorder[87]. A study by Bilszta found that mood stabilizers but not antidepressants or antipsychotics were effective in preventing postpartum recurrence of psychosis[88]. As these medications pass through breast milk, mothers who plan to breastfeed should be provided information about the levels of medication in breast milk and infant blood, and the potential adverse effects in the baby. Alternatives to the medications including App-based interventions including an automated psychosocial component to prevent postpartum depression should also be discussed with the patient[89], [90]

The joint position paper by the European Insomnia Network, the Italian Marcè Society, and international experts recommended that CBT-I should be the preferred treatment for insomnia during and after pregnancy[75]. Even though there are no studies on CBT-I in the prevention of postpartum depression, patients might benefit from a discussion of

strategies including cognitive restructuring, stimulus control, and relaxation training to manage insomnia. According to the National Institute for Health and Clinical Excellence (NICE) guidelines on the pharmacological treatment of antenatal and postnatal mental health medication should only be considered in cases of lack of response to non-pharmacological interventions or for severe cases of insomnia when there are no alternate safe strategies available[91].

5.3 Future research

Further high-quality research is needed due to the paucity of drug and psychotherapeutic studies in the prevention of unipolar or bipolar postpartum depression. Following Wisner and colleagues' pilot study of sertraline nearly 20 years ago, there have not been any controlled trials of antidepressants in the prevention of postpartum depression[34]. Brexanolone, the only FDA-approved drug for the treatment of postpartum depression has not been studied in the prevention of depression in women with major depressive disorder or bipolar disorder[92]. Extant literature on the topic, albeit limited, has focused exclusively on women with a history of postpartum depression[93]. Research is needed on the prevention of recurrence and the first occurrence of a major depressive episode in the postpartum period. However, conducting drug studies on women at risk of postpartum depression is challenging due to difficulties with recruitment and retention[94].

A more nuanced characterization of sleep dysregulation and testing putative mechanisms of links with mood dysfunction would advance this area of research. For instance, there is emerging evidence that worry and rumination while trying to fall asleep may cause nocturnal cognitive arousal, which in turn causes insomnia and elevated depressive symptoms[69]. Given that sleep dysregulation is a common symptom as well as a trigger of postpartum depression, studies of alternate drugs (such as positive allosteric modulators of γ-aminobutyric acid-A receptors) and interventions that target maternal sleep disturbance including CBT-I and alternate drugs, are needed. Future research must include a detailed characterization of sleep including assessments. It is important to develop a risk assessment tool that incorporates clinical, psychosocial and lifestyle factors and test it in high-risk populations.

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Article Highlights:

- Sleep and circadian dysregulation are well-documented features as well as risk factors of postpartum depression.
- Targeting insomnia/sleep loss may be effective in the prevention of postpartum depression in some women.
- Emphasizing sleep dysregulation in diagnosis and treatment may reduce stigma-related barriers to care.
- There is a paucity of pharmacological and psychotherapeutic studies on the prevention of postpartum depression in women with major depressive disorder or bipolar disorder.
- It is essential to examine the reasons for discordant research findings and explore clinical opportunities for the effective prevention of postpartum depression and its common psychiatric comorbidities.
- Personalized risk assessment and treatment history could guide the choice of preventative strategies.
- Challenges and barriers to the uptake of sleep intervention should be acknowledged.

Table 1

Peripartum Sleep Changes in Women with Major Depressive Disorder

Author	N	Type	Monitoring Period	Diagnostic Criteria	Depression Measure	Current Mood Status	Study Findings
Field et al., 2007	253 (83 depressed and 170 non-depressed)	Prospective	2nd trimester	DSM-IV	CES-D score ≥ 16	Not currently depressed or currently depressed	More sleep disturbances and higher depression, anxiety and anger scores
Okun et al., 2009	51	Prospective	36 weeks' gestation till 20 weeks postpartum	SADS	HDRS score ≥ 15 and clinician interview	Not currently depressed	Self-reported sleep quality did not predict recurrence but predicted timing of recurrence
Okun et al., 2011	56	Prospective	36 weeks' gestation till 17 weeks postpartum	DSM-IV*	HDRS score ≥ 15 and clinician interview	Not currently depressed	Diminished sleep quality during the first several weeks postpartum was associated with an increased risk for recurrence of PPMD
Okun et al., 2011	240 (59 depressed and 181 non-depressed)	Prospective	20 weeks' gestation	DSM-IV	SIGH-ADS	Not currently depressed or currently depressed	At 20- and 30-weeks sleep was more disturbed in the depressed group. At 36 weeks, sleep was disturbed regardless of mood status or AD use. In the control group, disturbed sleep, in conjunction with AD use was associated with higher depression scores
Sharkey et al., 2013	12	Prospective	3rd trimester	DSM-IV		Not currently depressed	Large circadian phase shifts and associations between circadian measures and depressed mood
Suri et al., 2017	300	Prospective	60 days before and 60 days after delivery	DSM-5	HDRS	Euthymic	3rd trimester total HDRS scores significantly predicted PPD ($P < .0001$); specifically, scores on 3 HDRS items alone (work activities, early insomnia, and suicidality) significantly predicted PPD
Okun et al., 2018	116	Prospective	20–26 weeks gestation and 6 months postpartum	DSM-5	PHQ-9 ≥ 10, EPDS ≥ 11, and clinical interview	Currently depressed	Poor sleep quality was significantly associated with depression and anxiety symptoms in the postpartum period

Abbreviations: AD – Antidepressant, CES-D – Centre for Epidemiologic Studies Depression Scale, DSM – Diagnostic and Statistical Manual of Mental Disorders, EPDS – Edinburgh Postnatal Depression Scale, HDRS – Hamilton Depression Rating Scale, SADS – Social Avoidance and Distress Scale, SIGH-ADS – Structured Interview Guide for the Hamilton Rating Scale with Atypical Depression Supplement, PHQ-9 – Patient Health Questionnaire, PPD – Postpartum Depression, PPMD – Postpartum Major Depression