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Prevalence of Bipolar Disorder in Perinatal Women:

A Systematic Review and Meta-Analysis

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Abstract

Objective: To estimate overall prevalence of bipolar disorder (BD) and the prevalence and timing of bipolar-spectrum mood episodes in perinatal women.

Data Sources: Databases (PubMed, Scopus, PsycINFO, CINAHL, Cochrane, ClincalTrials.gov) were searched from inception to March 2020.

Study Selection: Included studies were original research in English that had (1) populations of perinatal participants (pregnant or within 12 months postpartum), aged ≥ 18 years, and (2) a

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Author contributions: The authors all had full access to the data and participated in formulating the research questions. G.A.M. designed and conducted the literature review with guidance from N.B. and C.M.U.; study selection was carried about by G.A.M. and J.H.; data extraction and assessment were done by G.A.M., J.H., and L.X.; analyses were conducted by G.A.M. under the supervision of N.B. All co-authors contributed to the manuscript composition and interpretation. G.A.M. and N.B. had final responsibility for the decision to submit.

Relevant financial relationships: **Dr Moore Simas** is a consultant as the Obstetric Engagement Liaison for MCPAP for Moms and as such has received a stipend from the Massachusetts Department of Mental Health via Beacon Health Options. She has served on ad hoc advisory boards and as a speaker for Sage Therapeutics, was a consultant for Sage Therapeutics and Ovia, and has received honoraria from Miller Medical Communications. Dr Moore Simas is the co-chair of the American College of Obstetricians and Gynecologists' Maternal Mental Health Expert Work Group. **Dr Byatt** is the statewide Medical Director of the Massachusetts Child Psychiatry Access Program (MCPAP) for Moms and thus has received salary and/or funding support from Massachusetts Department of Mental Health. She has served on ad hoc advisory boards and as a speaker for Sage Therapeutics, was a consultant for Sage Therapeutics and Ovia Health, and has received honoraria from Miller Medical Communications, WebMD/Medscape, and Mathematica. Dr Byatt is also a member of the American College of Obstetricians and Gynecologists' Maternal Mental Health Expert Work Group. **Ms Masters**, **Ms Hugunin**, **Dr Xu**, **Dr Ulbricht**, and **Dr Ko** have no conflicts of interest to report.

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Additional information: The data that support the findings of this study are available from the corresponding author (G.A.M.) upon reasonable request. This work was prepared while Dr Ulbricht was employed at the University of Massachusetts Medical School.

Supplementary material: Available at Psychiatrist.com.

screening/diagnostic tool for BD. Search terms described the population (eg, *perinatal*), illness (eg, *bipolar disorder*), and detection (eg, *screen*, *identify*).

Data Extraction: Study design data, rates, and timing of positive screens/diagnoses and mood episodes were extracted by 3 independent reviewers. Pooled prevalences were estimated using random-effects meta-analyses.

Results: Twenty-two articles were included in qualitative review and 12 in the meta-analysis. In women with no known psychiatric illness preceding the perinatal period, pooled prevalence of BD was 2.6% (95% CI, 1.2%–4.5%) and prevalence of bipolar-spectrum mood episodes (including depressed, hypomanic/manic, mixed) during pregnancy and the postpartum period was 20.1% (95% CI, 16.0%–24.5%). In women with a prior BD diagnosis, 54.9% (95% CI, 39.2%–70.2%) were found to have at least one bipolar-spectrum mood episode occurrence in the perinatal period.

Conclusions: Our review suggests that the perinatal period is associated with high rates of bipolar-spectrum mood episodes and that pregnant and postpartum women represent a special risk population. This review may help to inform clinical care recommendations, thus helping to identify those who may have bipolar disorder to connect them with needed care.

Bipolar disorder (BD) is a serious mental illness with significant health ramifications for patients, their families, providers, and the health care system.[1–4] In the general population, prevalence estimates of bipolar-spectrum disorders are 2%–3%.[5] Perinatal women (those pregnant or within 1-year postpartum) may be at increased risk for bipolar-spectrum mood episodes.[6–11] The reasons for increased bipolar-spectrum mood episode occurrence during the perinatal period are multifactorial and include (1) overlap between peak reproductive years and BD onset, (2) hormonal and physiological changes accompanying pregnancy, and (3) stress related to childbirth and parenting.[6–8,12,13]

BD is a risk factor for perinatal suicide, postpartum psychosis, and infanticide.[11–18] Despite the association between untreated or inadequately treated perinatal BD and poor neurodevelopmental and psychosocial outcomes in offspring,[11–17] detection, diagnosis, and effective treatment remain elusive. For example, BD may be misdiagnosed as unipolar depression and treated with unopposed antidepressant medications, potentially precipitating mania and/or suicidality.[19–21] Prior systematic reviews[6,12] demonstrate increased risk of bipolar-spectrum mood episode recurrence in perinatal women with preexisting BD and poor outcomes with lack of treatment. However, to date, no systematic reviews have estimated the overall prevalence of BD or bipolar-spectrum mood episodes in perinatal women without a known BD diagnosis preceding the perinatal period.

In this review, we systematically evaluated the studies measuring rates of BD during pregnancy and the postpartum period. The goal of this review was to examine (1) the prevalence of BD in perinatal women and (2) the prevalence and timing of bipolar-spectrum mood episodes in the perinatal time period. The synthesis of these data could help to inform clinical care and screening recommendations specific to BD.

METHOD

Data Sources and Search Strategy

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we conducted a literature review of the following databases: PubMed, Scopus, PsycINFO, CINAHL, Cochrane, and ClincalTrials.gov. Search terms included keywords describing the population (eg, perinatal, pregnancy, postpartum), illness of interest (eg, bipolar disorder), and screening processes (eg, screen, identify). A complete description of our search strategy may be found in Supplementary Appendix 1. Articles were limited to those published in peer-reviewed journals that were available in English through March 2020. Additional articles were identified via the reference sections of eligible articles. Our study protocol was registered with Prospero (#CRD42020172166). The University of Massachusetts Chan Medical School Institutional Review Board determined this study to not require human subject research review.

Study Selection

The initial search, as defined by the aforementioned criteria, yielded 4,052 records. After removing duplicates, two independent reviewers (G.A.M., J.H.) reviewed titles and abstracts to assess first-pass eligibility, excluding 2,786. Supplementary Appendix 2 illustrates the full PRISMA study identification, screening, eligibility, and inclusion process. Independent reviewers (G.A.M., J.H., L.X.) reviewed the 177 full-text articles for final study eligibility. Any inconsistencies between the reviewers were resolved through discussion and consensus. Eligibility criteria included the following: (1) study population of perinatal people (pregnant or within 12 months postpartum), aged ≥ 18 years; (2) use of screening/diagnostic tool(s) validated in the perinatal population to detect BD; and (3) accessible article and relevant data. Articles were also included if they included populations with preexisting psychiatric diagnoses (eg, unipolar depression, anxiety disorders, BD), as long as a screening/diagnostic tool to detect BD was used as a part of the study, and/or if the population were on psychotropic medications before, during, or after pregnancy. Articles were excluded if (1) participants were recruited based on an unrelated medical condition that secondarily assessed psychiatric symptoms, (2) screening/diagnostic assessment was conducted outside of the perinatal period, and (3) BD prevalence was not reported. After final review and consensus, 22 articles were included in the qualitative review and 12 in the meta-analyses (see Supplementary Appendix 2 for details). Full details, including study population specifics, tools used, prior diagnoses, and treatments, are available in Supplementary Appendix 3.

Data Extraction

Data extraction began on June 8, 2020. Eligible articles were extracted by 3 independent reviewers (G.A.M., J.H., L.X.), with inconsistencies resolved through consensus. Extracted data were entered into REDCap.[22,23] Articles were examined for key study elements, including (1) study design and population, (2) screening/diagnostic tools, and (3) rates and timing of positive BD screens, diagnoses, mood symptoms, and/or episodes.

Quality Assessment

Study quality was assessed using a modified version of the Downs and Black checklist,[24] which evaluates study design in 5 areas: (1) reporting, or design specifics; (2) external validity; (3) bias; (4) confounding; and (5) power. We modified the checklist to exclude items that were not applicable or were not able to be assessed, as has been done previously (Supplementary Appendix 4).[25,26]

Study quality was assessed and recorded during data extraction, with inconsistencies resolved through consensus. For each study, an overall quality percentage score was calculated (total points awarded divided by total points possible). Quality scores were used to examine overall trends in extant study quality and to conduct subanalyses.

Data Reporting

We differentiated the study populations into two categories for analyses: (1) participants with no known psychiatric illness preceding the perinatal period (henceforth referred to as “no psychiatric history preceding the perinatal period”) and (2) participants with BD, based on diagnostic interview, or probable BD, based on a validated screening tool to detect bipolar disorder (eg, the Mood Disorder Questionnaire [MDQ]), preceding the perinatal period (henceforth referred to as “BD preceding the perinatal period”). Some studies also examined participants with a history of any mood disorder, including a history of either bipolar or unipolar depression. The heterogeneity of these groups was too high for these studies to be included in the meta-analyses and thus they were included only in the qualitative review. Of note, most articles did not ask about gender and instead made assumptions, based on pregnant or postpartum status. Therefore, we refer to participants in these studies as women, acknowledging that people who do not identify as women can also be childbearing persons.

We examined rates of BD prevalence and timing of bipolar-spectrum mood episodes across study populations. In studies that reported more than one prevalence value (eg, used more than one scoring methodology), the rates were reported separately. BD was measured as either an overall prevalence or mood episode occurrence/recurrence. *Prevalence of BD* was operationalized as women identified via diagnostic or screening tools that measure bipolar-spectrum mood episodes, past or current (eg, the MDQ) over all women screened across included studies. *BD mood episode occurrence/recurrence* was operationalized as women experiencing a “current” bipolar-spectrum mood episode occurring during the perinatal period, as determined by either (1) diagnostic interview (eg, current mood episode on the Structured Clinical Interview for the *DSM-IV* [SCID]) or (2) symptoms occurring concurrently that correspond with established thresholds on validated instruments (eg, 10+ score on the Edinburgh Postnatal Depression Scale [EPDS][27] or 8+ score on the Highs scale[28]). Mood episodes were reported both collectively and by subgroup (hypomanic/manic, depressive, mixed). Symptom clusters reported in studies that were “subthreshold,” or not meeting aforementioned criteria, were not included.

Meta-Analysis

Pooled estimates and 95% confidence intervals (CIs) were calculated for the following: (1) overall BD prevalence and bipolar-spectrum mood episode occurrence in women with no psychiatric illness preceding the perinatal period and (2) bipolar-spectrum mood episode occurrence during the perinatal period among women with BD. When more than one rate was available in a study (eg, by use of different scoring methods), the more conservative value was used in analyses. Pooled prevalence and 95% CIs were calculated following methodology previously published by Barendregt et al,[29] in which the inverse variance method and double arcsine transformation were used, and resultant values were transformed back to the original proportion format for presentation and interpretation. We used random-effects models to calculate pooled prevalence rates because the studies included varied by design and quality. A fixed-effects model was also run as a sensitivity analysis. Meta-analyses were conducted using MetaXL version 5.3 (EpiGear International).

RESULTS

Description of Studies

A total of 22 observational studies met inclusion criteria (Supplementary Appendix 2). Most were conducted in obstetric settings (63.6%)[30–39,41–44] and detected BD using diagnostic instruments (77.3%),[30,32,35,37–50] including the SCID (68.2%),[30,32,37–48,50] the Mini-International Neuropsychiatric Interview (MINI, 9.1%),[35,47] and the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV, 4.5%).[49] Less than a third (31.8%) used the MDQ screening instrument to identify potential BD.[30,31,33,34,36,40,51] Studies consisted of women who were pregnant (13.6%),[34,42,48] postpartum (40.9%),[30,31,33,35,37,40,43,44,51] or both (45.5%).[32,36,38,39,41,45–47,49],50 Eleven studies examined the prevalence of BD in women with no psychiatric history preceding the perinatal period.[30–37,43,49,51] Most studies did not distinguish between sex and gender and appeared to assume gender identity or expression.

Quality Assessment

The mean quality rating was 73.7% (range, 45.5%–92.9%) (Supplementary Appendix 3). The main study design limitations included (1) insufficient reporting of potential or actual adverse events (eg, suicidality was reported without description of study plan to address and/or follow-up), (2) limited or no description of participants lost to follow-up and/or the effects on results, and (3) inadequate description of the confounders and/or adjustment for said variables in analyses.

Prevalence of BD in Women With No Psychiatric History Preceding Perinatal Period

In the studies that used the MDQ to screen for BD in women with no psychiatric history preceding the perinatal period (studies = 6), prevalence ranged from 3.3% to 25.5% (Table 1).[30,31,33,34,36,51] Studies that used diagnostic tools estimated rates from 0% to 2.9%.[32,35,37,43,49]

Most studies examined rates in the postpartum period only or across both pregnancy and postpartum; only 2 studies[32,34] examined rates in pregnancy alone (Table 2).

Among studies that evaluated rates of BD in women with no psychiatric history preceding the perinatal period (studies = 11, people = 6,325),[30–37,43,49,51] no statistically significant differences were observed in the random- or fixed-effects models; therefore, only the random-effects output is reported. Prevalence of BD was 2.6% (95% CI, 1.2%–4.5%; Table 3, Figure 1). When restricted to studies with higher quality scores (≥ 70%, studies = 6, people = 4,218), the prevalence was 4.5% (95% CI, 2.9%–6.4%). The heterogeneity of prevalence estimates was high (I^2 = 92%, I^2 = 81% in higher quality). In studies that used the MDQ (studies = 6, people = 2,848), [30,31,33,34,36,51] the pooled prevalence was 4.8% (95% CI, 3.1%–6.9%). When restricted to studies using the MDQ with higher quality scores (studies = 5, people = 2,694), prevalence was 4.9% (95% CI, 2.9%–7.4%). In studies that used diagnostic interviews to diagnose BD (studies = 5, people = 3,477),[32,35,37,43,49] the pooled prevalence was 0.7% (95% CI, 0.0%–2.3%). Four of the 5 studies in this group were of poorer quality; thus, pooled prevalence based on quality could not be calculated.

Bipolar-Spectrum Mood Episode Occurrence

Sixteen studies reported on bipolar-spectrum mood episode occurrence among pregnant and postpartum women, including depressive, manic/hypomanic, and/or mixed episodes. [30–39,41,44–46,50,51] Measurement tools and methodologies varied greatly; the most common tools used to measure mood episodes were the EPDS and the SCID mood modules. All studies that examined mood episodes looked at depressive episodes and some also looked at hypomanic (4 studies), manic (3 studies), or mixed episodes (2 studies) (Table 1). Five studies examined occurrence of depressive episodes among women with BD as compared to individuals with unipolar depression. [30,31,33,36,46]

Bipolar-Spectrum Mood Episodes in Women With No Psychiatric History Preceding the Perinatal Period

Among women with no psychiatric history preceding the perinatal period, the rate of bipolar-spectrum mood episodes was higher than the overall rate of BD.[37,38,51] For example, Pingo et al[37] found that 31.6% of women (n = 57) screened positive for hypomania and 17.5% for a mixed episode during the perinatal period, while 0% had a BD diagnosis via SCID. The pooled prevalence rate of mood episodes (studies = 10, people = 4,473) occurring during the perinatal time period was 20.1% (95% CI, 16.0%–24.5%) (Table 3, Figure 2). When restricted to studies with higher quality scores (studies = 6, people = 3,520), the prevalence was 16.1% (95% CI, 12.4%–20.1%). The estimate in pregnant women (studies = 2, people = 744) was 22.0%; the prevalence in postpartum women (studies = 8, people = 3,754) was 18.0%.

Bipolar-Spectrum Mood Episodes in Women With BD Preceding the Perinatal Period

In women with BD preceding the perinatal period (studies = 7, people = 2,814), 54.9% (95% CI, 39.2%–70.2%) had at least one bipolar-spectrum mood episode occurrence in the perinatal period. All studies included in this estimate had quality ratings above 70%. The prevalence of episodes was 51.4% in pregnant women (study = 1, people = 53) versus 54.8% in postpartum women (studies = 6, people = 2,240).

Comparing Depressive Episodes Rates in Women With and Without BD

Eight studies compared rates of depressive episodes in women with and without BD (people = 4,238); in 6 of 8 studies, depressive episodes were higher in women with BD than in those without.[30–33,36,39,44,46] When prevalence rates were compared (studies = 3, people = 2,287), women with probable BD (via positive MDQ) were 6.5 times (95% CI, 2.0%–20.8%) more likely to have a depressive episode than those without probable BD (via negative MDQ).[30,33,36]

DISCUSSION

Bipolar disorder is exacerbated during pregnancy and the postpartum period and is associated with adverse outcomes.[6,12] Estimating the prevalence of BD and bipolar-spectrum mood episodes occurring in the perinatal period is critical to inform guidelines to adequately detect, assess, and treat BD. We found that, in women both with and without known psychiatric illness preceding the perinatal period, bipolar-spectrum mood episode occurrence in the perinatal period exceeded expected estimates.[5,52,53] Our review and analyses of the limited extant literature on this group suggest that pregnant and postpartum women are at greater risk for bipolar-spectrum mood episodes during the perinatal period than previously thought.

Though our meta-analyses estimated that the rate of BD in women with no psychiatric history preceding perinatal period was 2.6%, our pooled prevalence rates also estimated that 20.1% of these people were estimated to have had manic/hypomanic, mixed, or depressive episodes in the perinatal period. This discrepancy may well represent women with index episodes occurring for the first time during the perinatal period who will go on to have lifelong illness. In fact, this is expected; in addition to the psychosocial and physiologic stresses that occur in the perinatal period that may trigger mood episodes, peak fertility and birthing years overlap with the established age at onset range for BD. Additionally, it is to be expected that at least some of the women who were found to have a mood episode during the perinatal period, though had no diagnosis previously, were misdiagnosed or never diagnosed. Further, as our estimates include at least some data based on screening tools, some of these mood episodes are expected to be false-positives (likely at least 2% based on MDQ specificity).[54]

Still, the prevalence of BD in the general population and women outside of the perinatal period is not 20% but rather around 2%–3%.[5] It is well-known that as many as 1 in 7 women will experience a depressive episode in the perinatal period,[55,56] many of whom will not meet criteria for another psychiatric illness before or after that time. Though surely some of these BD-spectrum episodes represent women who already had undiagnosed BD or who will go on to have lifelong illness, we may also be seeing women with episodes more circumscribed to the perinatal period itself. Prior studies[57,58] have documented and discussed this phenomenon; however, it is considerably less understood than discrete depressive episodes in this period. Further, just as depressive episodes can occur as part of various psychiatric disorders, BD symptoms may occur as part of other psychiatric illnesses (eg, attention-deficit/hyperactivity disorder, borderline personality disorder). It is important that future work examine how detection and management of BD and related symptoms may

need to be tailored for the perinatal population and its unique risk factors, challenges, and illness manifestations.

We also found that women with a known BD diagnosis preceding the perinatal period had a heightened risk of bipolar-spectrum mood episode occurrence/recurrence in pregnancy and the postpartum period. When compared with women with unipolar depression in our data, women with BD preceding the perinatal period had a substantially higher risk for depressive episode occurrence. This phenomenon has implications for treatment and monitoring of patients with known BD. If borne out in other studies, it also could be potentially useful in distinguishing between unipolar and bipolar depression.

The American College of Obstetricians and Gynecologists' Council on Patient Safety in Women's Health Care and other organizations recommend that obstetric and other front-line providers screen for BD in the perinatal period prior to initiating pharmacotherapy for depression.[59,60] Wisner et al[44] found that 1 in 5 perinatal women with symptoms of depression (via EPDS) were likely to have BD. Given our findings that bipolar-spectrum mood episodes are more common in the perinatal time period and occur in both pregnancy and postpartum, strategies to improve screening and treatment may consider expanding to include universal screening for BD as part of their clinical guidance and workflow adaptations, alongside existing recommendations to universally screen for depression.[60–63] There are brief validated tools that can be administered alongside those for depression in prenatal and postpartum visits.[64,65] Further, algorithms exist to help providers use screening tool results to inform subsequent assessment and treatment planning.[66] Some clinical settings are starting to employ these. However, we also recognize that recommendations for increases in screening need to be considered in the larger clinical context, including feasibility, resources, and provider capacity to respond to a screen.[67] As processes are put in obstetric practice to conduct universal depression screening, including BD in these protocols may be indicated and become more tenable.

In addition, screening for and detecting undiagnosed BD among women presenting with depressive symptoms before starting treatment is important because antidepressant monotherapy can precipitate mania and/or suicidality.[19,20] Women with undetected BD or BD that is misdiagnosed as unipolar depression may be prescribed unopposed antidepressants preceding pregnancy, putting them at higher risk for a BD episode during the perinatal period. Conversely, women with BD on preexisting or newly prescribed mood stabilizers should be at decreased risk of a BD episode. This is an important area that merits further exploration. While a subset of our studies included women on psychotropic mediations, it was beyond the scope of this study to examine the protective or promoting effects of medications on the rate of BD mood episodes.

Our review also suggests that future recommendations may consider screening for BD and/or relevant symptoms more than once during pregnancy or postpartum. For example, screening in the first trimester may detect preexisting BD, while screening later in the postpartum period may detect new onset illness. This suggestion is supported by our finding of high pooled prevalences of episodes in both pregnancy and the postpartum period, indicating that mood onset can occur anytime in the perinatal period. Further, individual

studies like that of Sharma et al[47] support this notion of screening more than once. They followed incident BD diagnoses that were diagnostic conversions from major depression. Of women previously diagnosed with unipolar depression, they found that 6.5% (n = 146) converted to BD in the perinatal period.

Further work is needed to establish the ideal time(s) to screen for BD and bipolar-spectrum mood episodes. The vast majority of the studies included in our meta-analyses enumerated episodes across the entire perinatal period or only postpartum. While there are nuanced differences seen among individual studies between pregnancy and the postpartum period, our meta-analyses yielded quite similar rates between pregnancy and postpartum. The limited studies in our review examining episode occurrence in pregnancy only indicated that this time period is critical to consider for illness onset/recurrence. More studies need to examine women that are currently pregnant to estimate differences in risk between pregnancy and the postpartum period. Further, our findings have implications for women of child-bearing age outside of the perinatal period. Future studies assessing prevalence of BD in people of child-bearing age who are not pregnant or postpartum in parallel to those who are pregnant or postpartum are necessary to help elucidate some of the risks specific to the perinatal period itself.

Our work provides a synthesis of the extant research describing aggregate overall and current mood episode prevalence rates of BD in perinatal women. It also indicates that significant gaps in the literature remain and further studies specific to BD in the perinatal period are necessary to make estimates more robust. Many studies that otherwise met all inclusion criteria and may have yielded useful information to contribute to prevalence estimates were excluded. For example, we excluded 25 because they did not address BD, despite an ability to do so (eg, used the SCID but reported data only on depression and anxiety). It appears that examining BD in the perinatal period has not been prioritized in studies in the ways that perinatal depression or anxiety have been.[9] Bipolar-spectrum mood episodes other than depression need to be examined more thoroughly to provide more robust estimates in the perinatal time period.

Future work can help to address the specific design limitations seen in many studies in this review, such as including greater efforts to understand the characteristics of participants lost to follow-up and exploring and including confounders that may be pertinent risk factors for BD, including substance use and family history. Additionally, prospective efforts should strive to be more inclusive of other perinatal people, or those that do not identify as women, to estimate rates in other perinatal populations. Most studies included did not make mention the gender identities of their participants.

This review has many strengths, including its novel contribution to the field on an understudied area. It encompasses a comprehensive reference search. Data review and extraction were completed using multiple reviewers for scientific rigor. Limitations of this review include its small sample size and heterogeneity across studies, such that the pooled prevalence rates should be interpreted with caution. As aforementioned, pooled prevalences were estimated from diagnostic and screening tools, the latter of which likely inflated

estimates. We were unable to include articles that were not written in English, though articles from many disparate geographic areas were included.

CONCLUSION

Perinatal mental health conditions, including BD, are now cited as one of the leading obstetric complications in the US and are a preventable cause of maternal mortality.[59,68] This review suggests that recognizing the potential for BD and BD-spectrum mood episodes in the perinatal period is important, given the prevalence estimates in this population and the associated morbidity and mortality of untreated illness. It also emphasizes the need for more population-based and prospective studies to corroborate our findings and draw further conclusions to build on this study and elucidate the extent to which BD affects the perinatal population. This review may inform clinical care and screening recommendations, such that all perinatal women are screened for BD at least once. Such screening may improve the identification of women at risk and connect them to the best clinical care possible.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Points

- Perinatal mental health conditions, including bipolar disorder (BD), are now cited as one of the leading obstetric complications in the US and are a preventable cause of maternal mortality. However, there are no current studies that aggregate BD rates from multiple data sources.
- In perinatal women, particularly those who present with symptoms of depression, providers should consider screening for BD. Rates of BD-spectrum mood episodes may be higher than in the general population and than previously estimated.
- Providers should always screen for BD before initiating antidepressant pharmacotherapy.

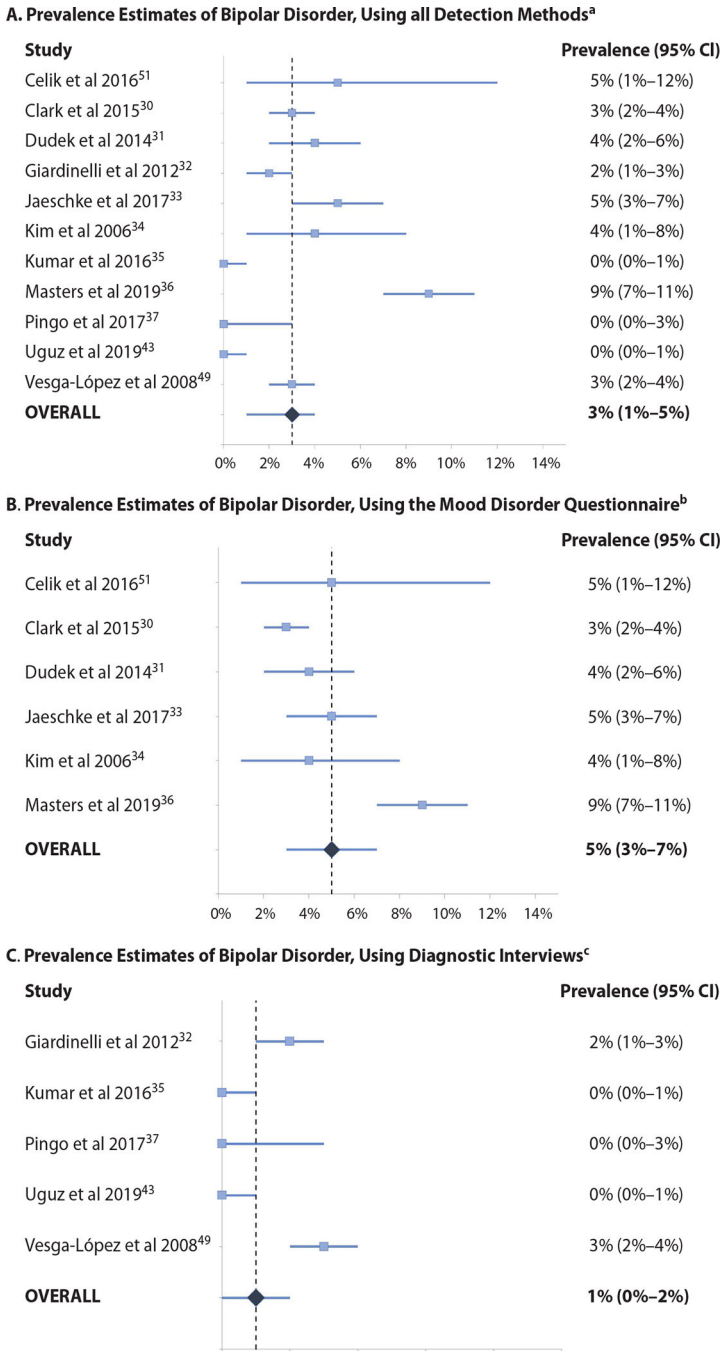

Figure 1. Forest Plots Demonstrating Estimates of the Overall Prevalence of Bipolar Disorder in Women Without Known Psychiatric Illness Preceding the Perinatal Period

[a]Forest plot of studies included in pooled prevalence calculations ($P = .00$). Heterogeneity score (I^2) was found to be 92%.

[b]Forest plot of studies that used the Mood Disorder Questionnaire to estimate rates of BD and pooled prevalence estimate ($P = .00$). Heterogeneity score (I^2) was 78%.

[c]Forest plot of studies that used a diagnostic interview to estimate rates of BD and pooled prevalence estimate ($P = .00$). Heterogeneity score (I^2) was 90%.

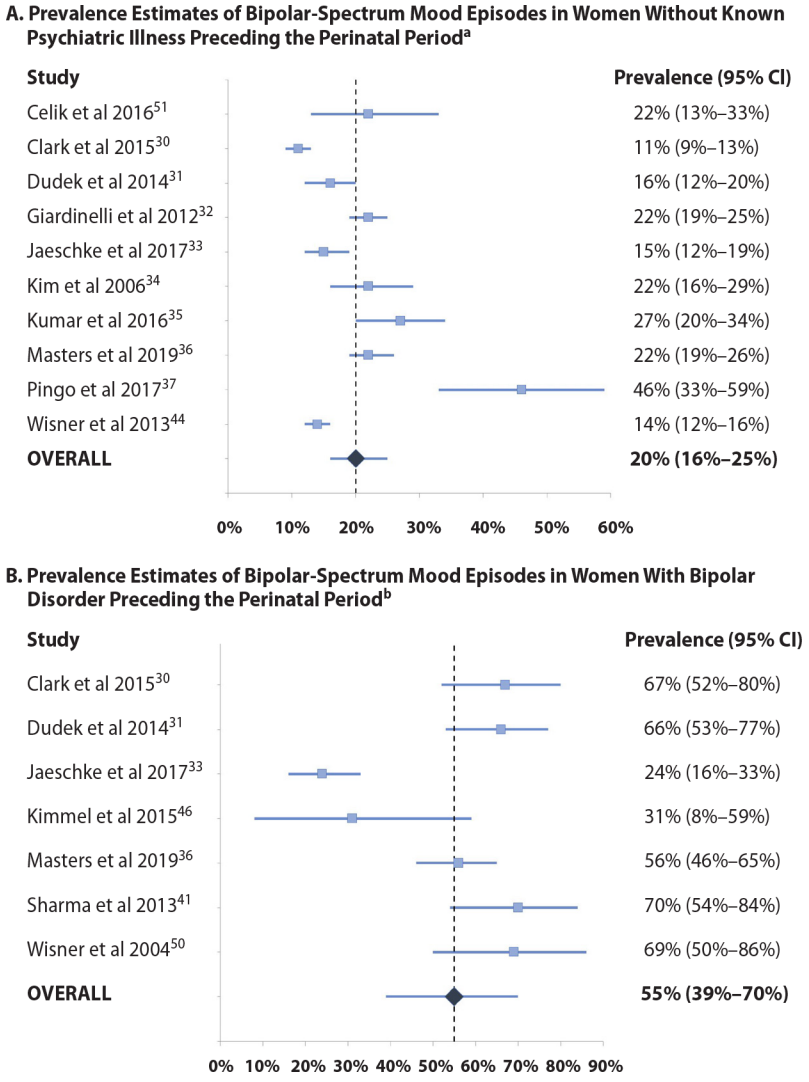

Figure 2. Forest Plots Demonstrating Estimates of the Occurrence of Bipolar-Spectrum Mood Episodes in the Perinatal Period

[a]Forest plot of BD and pooled prevalence estimate ($P = .00$). Heterogeneity score (I^2) was 91%.

[b]Forest plot of BD and pooled prevalence estimate ($P = .00$). Heterogeneity score (I^2) was 89%.

Table 1.

Prevalence of Bipolar Disorder and Bipolar-Spectrum Mood Episodes in the Perinatal Period[a]

	Perinatal Status			Overall Rates of Bipolar Disorder		Rates of Mood Episodes That Occur in the Perinatal Period			
Article Identifier	**Pregnant**	**Postpartum**	**Population**	**Rates**	**Notes on Study Calculation of Overall Rates**	**Manic Rates**	**Depressive Rates**	**Mixed Rates**	**Notes on Study Calculation of Episode Rates**
Celik et al 2016[51] (n = 63)		X	All	4.8%–17.5%	MDQ original scoring (7 + 2) method[b] used (4.8%) and alternate MDQ scoring (7+ only)[c] used (17.5%)	No rates; see Notes for scores	22.2%–42.9%	NA	mHCL-32 used to measure manic symptoms (27.0% had 13+ symptoms but validated criteria are higher; therefore, does meet criteria for potential manic/hypomanic episode); EPDS used to measure depressive episodes (42.9% positive); BDS used to measure depressive episodes (22.2% positive)
Clark et al 2015[30] (n = 1,279)		X	All	3.3%	MDQ original scoring (7 + 2) method[b] used (3.3%) in all participants; for those that screened positive on EPDS and/or MDQ, SCID was used (37.0%)	NA	11.1%	NA	EPDS used to measure depressive episodes (11.0% positive in all participants, 66.7% in those MDQ+; 91.2% in those with BD per SCID)
			MDQ+	100%[d]		NA	66.7%	NA	
Driscoll et al 2017[45] (n = 159)	X	X	BD only	100%[e]	SCID used	No rates; see Notes for scores	No rates; see Notes for scores	NA	Scales were used to measure differences between women who continued or discontinued psychiatric medications in pregnancy/PP. SIGH-ADS and HDRS used to measured depression at points in pregnancy—the mean scores were similar across groups and of mild/moderate severity; SIGH-ADS and HDRS scores tended to be lower PP for all groups. MRS used to measure mania—similar, low scores across all groups in pregnancy and PP
Dudek et al 2014[31] (n = 344)		X	All	3.8%–25.5%	MDQ original scoring (7+2) method[b] used (3.8%), alternate MDQ scoring (7+ only)[c] used (25.5%), and alternate MDQ scoring (8+ only)[f] used (15.1%)	NA	16.0%	NA	EPDS used to measure depressive episodes (16.0% positive in all, 65.6% positive in MDQ+ using 7+ only scoring, 72.1% positive in MDQ+ using 8+ only scoring)
			MDQ+	100%[d]		NA	65.6%–72.1%	NA	
Giardinelli et al 2012[32] (n = 590)	X		All	1.5%	SCID used	NA	21.9%	NA	EPDS used to measure depressive symptoms in pregnancy and postpartum, but neither rates, scores, nor associations with bipolar disorder reported; in pregnancy, overall 12%
		X				NA	13.2%	NA	

Article Identifier	Perinatal Status: Pregnant	Perinatal Status: Postpartum	Overall Rates of Bipolar Disorder: Population	Overall Rates of Bipolar Disorder: Rates	Overall Rates of Bipolar Disorder: Notes on Study Calculation of Overall Rates	Rates of Mood Episodes That Occur in the Perinatal Period: Manic Rates	Rates of Mood Episodes That Occur in the Perinatal Period: Depressive Rates	Rates of Mood Episodes That Occur in the Perinatal Period: Mixed Rates	Rates of Mood Episodes That Occur in the Perinatal Period: Notes on Study Calculation of Episode Rates
									scored 10–12,10% > 13; postpartum, 7.6% scored 10–12,5.6% > 13.
Jaeschke et al 2017[33] (n = 434)		X	All	4.6%–23.7%	MDQ original scoring (7+2) method[b] used (4.6%) and alternate MDQ scoring (7+ only)[c] used (23.7%)	NA	15.2%	NA	EPDS used to measure depressive episodes (15.2% positive overall; 24.3% positive in those MDQ+; 12.4% in those MDQ−)
			MDQ+	100%[d]		NA	24.3%	NA	
Kim et al 2006[34] (n = 154)	X		All	3.9%	MDQ original scoring (7+2) method[b] used	NA	22.1%	NA	PRIME-MD PHQ used to measure depressive episodes (14.3% screened positive for minor depression, 7.8% for major depression)
Kimmel et al 2015[46] (n = 93)	X	X	BD/MDD	32.3%[e]	SCID used	NA	16.2%–44.0%	NA	SCID used to measure current depressive episodes (30.8% developed postpartum depression in BD;44.0% developed postpartum depression in MDD, 39.5% overall); Overall, 25% remained well all through perinatal period; 25% were depressed in pregnancy but recovered and were well postpartum; 33.9% were depressed all perinatal period; 16.2% were well in pregnancy but developed PPD.
		X	BD	100%		NA	30.8%	NA	
Kumar et al 2016[35] (n = 152)		X	All	0%	MINI used	NA	27.0%	NA	MINI used to diagnose depressive episodes (27.0% with depressive disorder NOS)
Masters et al 2019[36] (n = 574)	X	X	All	8.7%–18.8%	MDQ original scoring (7+2) method[b] used (8.7%) and alternate MDQ scoring (7+ only)[c] used (18.8%)	NA	22.5%	NA	EPDS used to measure depressive episodes (22.5% positive overall; 55.6% positive in those MDQ+)
			MDQ+	100%[d]		NA	55.6%	NA	
Pingo et al 2017[37] (n = 57)		X	All	0%	SCI D used	31.6%	15.8%–45.6%	17.5%	Highs scale used to measure hypomanic episodes at 3 days PP (31.6%); EPDS used to measure depressive episodes at 3 days pp (15.8% positive) and 6 weeks PP (45.6%); 17.5% positive on both highs and EPDS at 3 days PP to measured mixed episodes
Pope et al 2013[38] (n = 147)	X	X	MDD/BDII	36.1%[e]	SCI D used	No rates; see Notes for scores	NA	NA	YMRS used to measure hypomanic symptoms (40.8% score > 3, but validated criteria cutoff is higher; therefore, does meet criteria for potential manic/hypomanic episode)

	Perinatal Status			Overall Rates of Bipolar Disorder		Rates of Mood Episodes That Occur in the Perinatal Period			
Article Identifier	**Pregnant**	**Postpartum**	**Population**	**Rates**	**Notes on Study Calculation of Overall Rates**	**Manic Rates**	**Depressive Rates**	**Mixed Rates**	**Notes on Study Calculation of Episode Rates**
Robakis et al 2015[39] (n = 98)	X	X	Combined	8.2%[e,g]	SCI D used	NA	No rates, see notes for scores	NA	EPDS was used to measure depressive symptoms: mean postnatal EPDS scores were 5.81 for women with no mood disorder history, 6.86 for women with history of unipolar depression, and 12.25 for women with history of bipolar disorder, respectively
Sharma and Xie 2011[40] (n = 125)		X	MDD/BD	45.6%–48.0%[e]	MDQ original scoring (7+2) method[b] used (45.6%) and alternate MDQ scoring (8+ only)[f] used (48.0%); SCID used (45.6%)	NA	NA	NA	NA
Sharma et al 2013[41] (n = 53)	X		BDII	100%[e]	SCID used	8.1%	43.2%	NA	SCID used to measure hypomanic and depressive episodes; 51% had a mood episode while pregnant; 70.3% had a mood episode postpartum; 8.11% had 1+ hypomanic episodes in pregnancy and 43.24% had 1+ depressive episodes in pregnancy; 27.03% had 1+ hypomanic episodes in pregnancy and 43.24% and 1+ depressive episodes in pregnancy
		X				27.0%	43.2%	NA	
Sharma et al 2014[47] (n = 146)	X		MDD/BDII	37.0%	SCID used at start (37.0%) and MINI at end (41.1%) to see conversion rate to BD	NA	NA	NA	NA
		X		41.1%		NA	NA	NA	
Sit et al 2014[42] (n = 192)	X		Combined	26.0%[e,g]	SCID used	NA	NA	NA	NA
Solé et al 2019[48] (n = 200)	X		Combined	50.0%[e,g]	SCID used	NA	NA	NA	NA
Uguz et al 2019[43] (n = 1,154)		X	All	0.2%	SCID used	NA	NA	NA	NA
Vesga-López et al 2008[49] (n = 1,524)	X	X	All	2.9%	AUDADIS-IV used	NA	NA	NA	NA
Wisner et al 2004[50] (n = 37)	X		BD	100%	SCI D used	NA	NA	NA	Episodes compared between medicated (VLP) and non-medicated groups; hypomanic/manic episode postpartum (6.7% in VLP vs 9.1% in
		X		100%[e]		7.7%	50.0%	11.5%	

Article Identifier	Perinatal Status		Overall Rates of Bipolar Disorder			Rates of Mood Episodes That Occur in the Perinatal Period			
	Pregnant	Postpartum	Population	Rates	Notes on Study Calculation of Overall Rates	Manic Rates	Depressive Rates	Mixed Rates	Notes on Study Calculation of Episode Rates
									non-medicated); mixed episode PP (6.7% in VLP vs 18.2% in non-medicated); depressive episode PP (53.3% in VLP vs 45.5% non-medicated); any episode PP (66.7% in VLP vs 72.7% non-medicated)
Wisner et al 2013[44] (n = 826)		X	All	NA	SCID used (22.6% in those with postpartum depression)	NA	14.0%	NA	EPDS used (14.0% overall, 100% in those with postpartum depression); higher
			PPD	22.6%		NA	100% See Notes for association	NA	EPDS cut points more predictive of BD than MDD or others

[a] Table 1 presents prevalence of BD and bipolar-spectrum mood episodes by study in this review. Perinatal status indicates when the sampling was done—during pregnancy only, postpartum only, or both. Population describes the group of women in the denominator of the reported rates; all indicates that there were no pertinent exclusion criteria and the sample ostensibly represents the "general" perinatal population; MDQ+ is reporting rates for the subset of the sample that had a positive MDQ score (and thus probably have BD); BD only is reporting rates only in women with BD preceding the perinatal period. Rates or rate ranges are reported both for prevalence of BD and by mood episode type. Finally, Notes elaborate more on the specifics of how rate measurements were conducted.

[b] Original scoring (7 + 2) method = screen is considered positive if individuals report at least 7 of 13 symptoms associated with bipolar disorder and that these co-occurred and caused a significant impairment to their life.

[c] Alternative scoring (7+ only) method = screen is considered positive if individuals report at least 7 of 13 symptoms associated with bipolar disorder, without any supplementary questions.

[d] Examining symptoms within the participants that were MDQ+ only.

[e] Studies not included in lifetime prevalence calculation summaries because diagnoses/symptoms were part of inclusion criteria/were confirmatory rather than diagnostic.

[f] Alternative scoring (8+ only) method = screen is considered positive if individuals report at least 8 of 13 symptoms associated with bipolar disorder, without any supplementary questions.

[g] Combined = includes participants with mood disorders and asymptomatic participants as controls.

Abbreviations: AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV,* BD = bipolar disorder, BDS = Beck Depression Scale, EPDS = Edinburgh Postnatal Depression Scale, GA = gestational age, HDRS = Hamilton Depression Rating Scale, MDD = major depressive disorder, MDQ = Mood Disorder Questionnaire, mHCL-32 = Modified hypomania Checklist, MINI = Mini-International Neuropsychiatric Interview, MRS = Mania Rating Scale, NA = not applicable, NOS = not otherwise specified, PP = postpartum, PPD = postpartum depression, PPH = postpartum hypomania, PRIME-MD PHQ=Primary Care Evaluation of Mental Disorders Patient Health Questionnaire, SCID = Structured Clinical Interview for *DSM-IV,* SI = suicidal ideation, SIGH-ADS = Structured Interview Guide for the Hamilton Depression Rating Scale–Atypical Depression Supplement, VLP = valproate, YMRS = Young Mania Rating Scale.

Table 2.

Summary of Overall Prevalence Rates of Bipolar Disorder and Bipolar-Spectrum Mood Episode Occurrence From Included Studies, Stratified by Perinatal Stage

	Prevalence Rates		Current Episode or Symptom Occurrence		
Category	**MDQ**	**Diagnostic**	**Depressive Episodes**	**Hypomanic/Manic Episodes**	**Mixed Episodes**
Women without known psychiatric illness preceding the perinatal period					
Pregnant women only (studies = 2)	3.3%–25.5%	0.0%–2.9%	21.9%–22.1%	…	…
Postpartum women only (studies = 9)			11.1%–45.6%	31.6%	17.5%
All perinatal women (studies = 12)			11.1%–45.6%	31.6%	17.5%
Women with bipolar disorder preceding the perinatal period					
Pregnant women only (studies = 4)	100%	100%	43.2%	8.1%	…
Postpartum women only (studies = 7)			24.3%–72.1%	7.7%–27.0%	11.5%
All perinatal women (studies = 8)			24.3%–72.1%	7.7%–27.0%	11.5%

Abbreviations: AUDADIS-IV = Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV,* Diagnostic = includes the Structured Clinical Interview for *DSM-IV,* MDQ = Mood Disorder Questionnaire, MINI = Mini-International Neuropsychiatric Interview.

Table 3.

Results of Meta-Analyses[a]

Studies Included		Pooled Prevalence (%)	95% CI	Heterogeneity Index
Pooled Prevalence of Overall Bipolar Disorder in Women Without Known Psychiatric Illness Preceding the Perinatal Period, as Identified by Positive Screens and/or Diagnostic Interviews				
All studies using Mood Disorder Questionnaire (studies = 6, n = 2,848)[30,31,33,34,36,51]		4.8	3.1–6.9	78%
All studies using diagnostic interview (studies = 5, n = 3,477)[32,35,37,43,49]		0.7	0.0–2.3	90%
All studies that estimate prevalence of bipolar disorder in women without known psychiatric illness preceding the perinatal period (studies = 11, n = 6,325)[30–37,43,49,51]		**2.6**	**1.2–4.5**	**92%**
Population	**Studies included**	**Pooled Prevalence (%)**	**95% CI**	**Heterogeneity Index**
Pooled prevalence of any type of bipolar-spectrum mood episode in the perinatal population				
Women without known psychiatric illness preceding the perinatal period	Episodes in pregnancy (studies = 2, n = 744)[32,34]	22.0	19.0–25.0	
	Episodes postpartum (studies = 8, n = 3,754)[30–33,35,37,44,51]	18.0	14.1–22.2	
	Any episodes in perinatal period (studies = 10, n = 4,473)[30–37,44,51]	**20.1**	**16.0–24.5**	**91%**
Women with bipolar disorder preceding the perinatal period	Episodes in pregnancy (studies = 1, people=53)[41]	51.4		
	Episodes postpartum (studies = 6, n = 2,240)[30,31,33,41,46,50]	54.8	34.6–74.3	
	Any episodes in perinatal period (studies = 7, n = 2814)[30,31,33,36,41,46,50]	**54.9**	**39.2–70.2**	**89%**

[a]Heterogeneity index = degree of heterogeneity across studies that impacts meta-analytic estimates. Diagnostic interviews included in the estimate above include the Structured Clinical Interview for the *DSM-IV*, the Mini-International Neuropsychiatric Interview, and the Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV*.