Adverse childhood experiences and postpartum depression in bipolar disorder

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Abstract

Background
Women are particularly vulnerable to recurrence of bipolar disorder (BD) following childbirth. Risk of postpartum psychosis (PP) is especially high, but postpartum depression (PPD) is also common. Adverse childhood experiences (ACEs) have not been associated with PP, but have been associated with PPD in non-bipolar samples. The relationship between ACEs and PPD within BD remains to be investigated. Here, we examined this association in a large, well-defined sample of women with BD.

Methods
Participants were 575 parous women with DSM-IV BD. Lifetime psychopathology, including perinatal, was assessed via semi-structured interview and case-notes. ACEs, assessed via self-report and case-notes, were compared between women with lifetime PPD (n=368) and those without a lifetime history of perinatal mood episodes (n=207).

Results
In univariate analysis exposure to 3 or more ACEs, and to childhood abuse specifically, was significantly associated with PPD (p=0.026 and 0.041 respectively), but this did not remain significant after adjusting for lifetime number of episodes of depression and parity. *Post-hoc* analysis revealed more frequent episodes of depression to be associated with both a history of 3 or more ACEs and of childhood abuse.

Limitations
Limited range of ACEs assessed and potential recall bias.

Conclusions
Increased frequency of ACEs and particularly childhood abuse was associated with more frequent lifetime episodes of depression, but not specifically episodes with postpartum onset. Understanding factors that mediate the pathway between ACEs and PPD in BD has implications for risk prediction of PPD.

Introduction

Women with bipolar disorder (BD) are particularly vulnerable to recurrence of mood episodes in relation to childbirth (Di Florio et al., 2013; Wesseloo et al., 2016). While postpartum psychoses occur in 1-2 in every 1000 deliveries in the general population (VanderKruik et al., 2017), risk is dramatically elevated among women with BD, with almost one in five deliveries being affected (17%; Wesseloo et al., 2016). Postpartum non-psychotic depression (PPD) is also common in BD (Sharma et al., 2017). Depending on the methodology of the study, estimates indicate that PPD follows between 19-60% of deliveries within this population (Di Florio et al., 2015; Mandelli et al., 2016; Viguera et al., 2011). Severe postpartum mood disorders are associated with adverse consequences for the mother, baby and wider family; placing the mother at increased risk of suicide (Gressier et al., 2017) and the infant at risk of developmental impairment (Hoffman et al., 2017).

Although PPD is a common occurrence among women with BD, predictors of these episodes within this high-risk group are poorly understood. Studies which have examined potential risk factors for PPD have primarily been conducted in general population samples (Gaillard et al., 2014; Guintivano et al., 2018; Leigh and Milgrom, 2008; Meltzer-Brody et al., 2018; Robertson-Blackmore et al., 2013) and/or among women with a history of major depressive disorder (Kettunen and Hintikka, 2017; Tian et al., 2012). Antenatal depression, lifetime history of depression, poor social support, marital difficulties, increased parity and adverse life events have been implicated among the strongest risk factors for episodes of PPD (Howard et al., 2014).

Adverse childhood experiences (ACEs) have also been associated with peripartum depression (Tebeka et al., 2016) and specifically PPD (Guintivano et al., 2018; Kettunen and Hintikka, 2017; Meltzer-Brody et al., 2018; Plaza et al., 2012) in non-bipolar samples of women. This is in contrast to episodes of postpartum psychoses, for which there is little indication that ACEs influence risk of these episodes both in general population samples (Dowlatshahi and Paykel, 1990; Meltzer-Brody et

al., 2018) and as we have reported previously, specifically among women who have BD (Perry et al., 2016). Within the general population (Guintivano et al., 2018; Meltzer-Brody et al., 2018), and among those with a lifetime history of abuse (Garabedian et al., 2011), exposure to an increased number of ACEs has been demonstrated to have a cumulative effect on risk of PPD. Moreover, compared to parous women who do not experience PPD, women who present with clinically impairing PPD have been shown to be significantly more likely to report a history of childhood abuse (Guintivano et al., 2018; Kettunen and Hintikka, 2017; Plaza et al., 2012). However, this finding has not been observed in all studies (De Venter et al., 2015; Robertson-Blackmore et al., 2013).

ACEs have been shown to increase lifetime risk of BD (Rowland and Marwaha, 2018) and also to adversely influence the overall course of BD. compared to individuals with BD who do not have a history of any ACEs, those who have experienced ACEs are significantly more likely to have an earlier age at onset of BD, more frequent episodes of mood illness, greater affective instability, increased suicidality, persecutory auditory hallucinations and greater psychiatric comorbidity (Garno et al., 2005; Janiri et al., 2014; Marwaha et al., 2015; Post et al., 2015; Sala et al., 2014; Upthegrove et al., 2015).

Despite indication that ACEs are associated with PPD in non-bipolar samples and that ACEs adversely influence the course of BD, the relationship between ACEs and PPD within BD remains to be investigated. Research in this area is of importance, given that bipolar PPD may be distinct from other forms of depression following childbirth (Sharma et al., 2017). For these reasons, here, we address the question of whether over and above their impact on risk of BD, ACEs are associated with PPD in women with BD.

Methods

Participants

Women were recruited as part of a large, on-going programme of research investigating genetic and non-genetic determinants of mood disorders (Bipolar Disorder Research Network, BDRN; www.bdrn.org). Participants were recruited systematically through UK National Health Service (NHS) Community Mental Health Teams or lithium clinics, and non-systematically via the BDRN website and the patient support charity, Bipolar UK. The research has UK NHS Research Ethics Committee approval and Research and Development approval in all participating NHS Trusts/Health Boards (MREC/97/7/01).

BDRN inclusion criteria specify that participants must: a) be aged 18 years or over; b) have the ability to provide written, informed consent; c) have an age of illness onset before 65 years, and d) be of UK white ethnicity due to a focus of the research programme on investigating genetic determinants of mood disorder. Participants are excluded if they have only experienced affective illness as a result of substance abuse, medication or, secondary to physical illness.

Psychiatric assessments

Detailed lifetime psychopathology was assessed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN, Wing et al., 1990), a semi-structured interview administered by trained research psychiatrists or psychologists. Where available, psychiatric case notes were also screened. Best-estimate main lifetime diagnosis according to DSM-IV criteria was made along with ratings of perinatal psychiatric history (type and onset of the lifetime most impairing perinatal mood episode) and lifetime clinical variables. In cases of ambiguity, at least two members of the research team made clinical and diagnostic ratings blind to each other's ratings and consensus was agreed through discussion. Mean kappa statistics were 0.85 for DSM–IV diagnosis, 0.97 for the lifetime most impairing perinatal mood episode, and between 0.81 and 0.99 for other key clinical categorical

variables. Mean intra-class correlation coefficients were between 0.91 and 0.97 for key clinical continuous variables.

Measurement of adverse childhood experiences

History of ACEs was obtained using the BDRN Childhood Life Events Questionnaire (CLEQ, see Perry et al., 2016). The CLEQ was administered verbally to all participants following the SCAN interview once rapport had been established. Participants were asked if they had experienced one or more childhood experiences before the age of 16 years, which are listed below. Due to the sensitive nature of such events, we chose to not specifically ask about experiences of childhood abuse. Instead, participants were given the opportunity to disclose additional events by being asked "Are there any other significant life events you experienced as a child?" Case notes were also reviewed for any mention of ACEs including abuse.

Participants also completed the self-report Brief Life Events Questionnaire (BLEQ) asking about severe life events based on the list proposed by Brugha et al. (1985). An open question was added to the questionnaire, which asked participants "Do you think that there is anything that has happened to you during your life which has contributed to you becoming unwell?" Answers were examined for evidence of any ACEs, including abuse.

These sources of information were combined to code the presence or absence of the following types of ACE occurring before the age of 16 years for each participant: (1) Any abuse (sexual and/or physical and/or emotional), (2) sexual abuse, (3) physical abuse, (4) emotional abuse, (5) death of a parent, (6) death of a sibling, (7) death of a close friend, (8) divorce and/or separation of parents and (9) serious physical illness requiring hospitalisation.

Sample

Rates of postpartum recurrence in the BDRN sample have been reported previously (Di Florio et al., 2013). During the period in which data on ACEs were collected, 1579 parous women with BD were recruited to BDRN. For this study, analyses were restricted only to women who experienced the onset of BD before at least one pregnancy (n=1091). Of these, 748 women (68.6%) experienced a lifetime recurrence of BD within six months of delivery, of which 368 (49.2%) experienced a lifetime most impairing episode of non-psychotic depression with onset within 6 weeks of delivery (PPD group). Onset criterion for PPD was restricted to the first 6 weeks following childbirth to be consistent with both DSM-5 and ICD-11 definitions of the postpartum period. As we have previously examined the role of ACEs in the occurrence of postpartum psychosis, women with a lifetime history of mania, hypomania or affective psychosis within six months of any delivery were excluded from this analysis.

To ensure the comparison group comprised only women without any history of mood symptoms or episodes with onset during the perinatal period, women were excluded if they had a lifetime history of a) mood disorder with onset during pregnancy (n=112) or b) significant mood symptoms with onset within 6 weeks of delivery that did not meet full clinical criteria for an episode (n=24). The final comparison group of women (no perinatal mood episode group, No PME) therefore comprised 207 parous women with BD who had no lifetime history of any affective or psychotic episode/symptoms during pregnancy or within 6 months following delivery. A six-month cut-off was used to define the postpartum period to further ensure that this group did not include any women who may have experienced episodes of mood illness related to childbirth.

Statistical analysis

Data were analysed using SPSS version 24. The number of ACEs (defined categorically as history of 0, 1 or more, 2 or more and 3 or more ACEs, where any type of childhood abuse was included only

once) and the prevalence of each individual ACE was compared between the PPD and No PME groups using chi-squared tests. To further investigate whether ACEs increase vulnerability to episodes of depression more generally (potentially acting as a non-specific trigger of episodes of depression with onset during the postpartum period), associations between ACEs and PPD were assessed in binary logistic regression models adjusted for lifetime number of episodes of depression (mean per illness year). Lifetime number of deliveries was also controlled for, given that lifetime risk of PPD is likely to increase with increased parity. P-values of <0.05 were considered significant.

Results

The demographic and clinical characteristics of the sample are described in Table I. The median age of participants at interview was 47 years (range 19-85). The majority of the sample had during their lifetime married or lived as married (96.7%), were educated below degree level (66.8%) and were recruited to the study non-systematically (67.7%). 60.3% had a lifetime DSM-IV diagnosis of BD-I and the median age at onset of BD (defined as age of first impairing mood episode) was 18 years (range 5-37). Participants had experienced, on average, 0.27 (range 0.02-7.16) lifetime episodes of mania per illness year and 0.41 (range 0-10.01) lifetime episodes of depression per illness year. The median age at first pregnancy was 24 years (range 13-40) and the median number of deliveries was 2 (range 1-7).

(INSERT TABLE I)

More than half of all participants experienced at least one ACE (61.2%, n=352/575). As shown in Table II, in unadjusted analyses we observed a threshold relationship between the number of ACEs experienced and the occurrence of PPD. Compared to women with no PME, those with PPD were significantly more likely to have experienced 3 or more ACEs (4.3% and 9.0% respectively; p=0.026, OR 2.40, 95% CI 1.10-5.24) but not fewer than 3 ACEs. The association between 3+ ACEs and PPD

was no longer significant after controlling for lifetime mean number of episodes of depression per illness year and parity (p=0.183, OR 1.82, 95% CI 0.75-4.37).

(INSERT TABLE II)

The results of between group analyses by type of ACE are presented in Table III. In unadjusted comparisons, women in the PPD group were significantly more likely to report a history of any childhood abuse compared to women in the No PME group (27.4% and 19.8% respectively, p=0.041, OR=1.53, 95% CI 1.02-2.31). However, similar to our findings in relation to the number of ACEs, after adjusting for lifetime number of episodes of depression and parity, the association between history of any childhood abuse and PPD was not significant (p=0.442, OR 1.21, 95% CI 0.75-1.91). No significant associations were found between the prevalence of any other ACE and the occurrence of PPD in unadjusted or adjusted comparisons.

Post-hoc analyses revealed that history of any abuse during childhood and history of 3 or more ACEs were both significantly associated with an increased mean number of episodes of depression per illness year (both p<0.001) but not parity (p=0.104 and 0.764 respectively).

(INSERT TABLE III)

Discussion

This study is the first to examine the relationship between ACEs and PPD in women who have BD. We did not find a direct association between ACEs and PPD in our sample. In univariate analyses, we found a history of 3 or more ACEs and specifically of childhood abuse (of any type) to be associated with PPD. However, these relationships did not remain significant after adjusting for lifetime number of episodes of depression (mean per illness year) and lifetime number of deliveries. Childhood abuse

and the occurrence of 3 or more ACEs were both found to be associated with an increased lifetime frequency of episodes of depression, which suggests that although ACEs are associated with lifetime number of depressive episodes in women who have BD they are not specifically associated with those with postpartum onset.

Despite several studies reporting a direct association between ACEs and PPD (Guintivano et al., 2018; Kettunen and Hintikka, 2017; Meltzer-Brody et al., 2018; Plaza et al., 2012), our findings are consistent with others that have also demonstrated no direct relationship between these factors (De Venter et al., 2015; Robertson-Blackmore et al., 2013). In a community sample of parous women, De Venter et al. (2015) found that a history of childhood abuse was not associated with symptoms of depression at 12 or 24 weeks postpartum. Rather, history of depression prior to pregnancy and symptoms of depression during pregnancy emerged as significant predictors of PPD. Robertson-Blackmore et al. (2013) reported childhood sexual abuse to be significantly associated with antenatal depression, but not PPD.

In contrast to the previous studies that have reported a significant association between ACEs and PPD, we further attempted to distinguish between the influence of ACEs on susceptibility to depression more generally (i.e. episodes occurring at any time) and depression occurring specifically within the postpartum period. The mechanism through which the frequency of episodes of depression may mediate the pathway between ACEs and PPD is unclear. However, it is plausible that ACEs increase vulnerability to episodes of depression more generally, some of which occur in the postpartum period but are not triggered specifically in relation to childbirth. To examine this hypothesis further, factors mediating possible pathways between ACEs and PPD in BD require investigation in larger samples.

Alternatively, it is possible that we did not find evidence of a direct relationship between ACEs and PPD within our sample for several other reasons. Namely, our findings may instead reflect differences in the underlying aetiology of PPD across mood disorders. Previous literature has only examined the occurrence of PPD within the general population or within the context of major depressive disorder. As highlighted previously, emerging evidence indicates bipolar PPD to be distinct from other forms of PPD (Sharma et al., 2017). Therefore, it is possible that ACEs differentially influence risk of PPD in women with a lifetime diagnosis of major depressive disorder compared to women with BD. Furthermore, methodological differences between studies may also account for differences in findings. For example, we defined PPD according to standardised diagnostic criteria, while the majority of studies have defined PPD based on symptom scores of depression assessed using brief screening measures (Guintivano et al., 2018; Meltzer-Brody et al., 2018; Plaza et al., 2012). Finally, the types of ACEs assessed also differed between studies. For example, in a recent population study, out of home care during childhood was identified as one of the strongest risk factors for PPD (Meltzer-Brody et al., 2018), a factor not assessed within our study.

The findings of our study are subject to limitations. First, we assessed a limited range of specified ACEs. The role that other ACEs (such as out of home care) may play in the occurrence of PPD among women with BD remains unclear. Secondly, ACEs may be under or over-estimated within our sample. As ACEs were assessed via self-report during a face-to-face interview, history of particularly traumatic events such as childhood abuse may not have been disclosed. Similarly, the retrospective nature of the study may have increased the likelihood of recall bias. However, to address these limitations, we also reviewed responses within self-report questionnaires and psychiatric case-notes for any mention of ACEs. Thirdly, the demographic characteristics of our sample suggest our findings may have limited generalisability to the wider BD population. For example, the median age of onset of BD (18 years) and age at first pregnancy (24 years) in our sample is younger than previously

reported (Rowland and Marwaha, 2018; Viguera et al., 2011 respectively) and parity of women in our sample is slightly higher than has been reported in other BD populations (Power et al., 2013). However, these discrepancies are likely explained by methodological differences between studies. We defined age at onset of BD as the age at onset of first impairment, which is usually younger than age at diagnosis of BD. The younger age at first pregnancy in our sample likely reflects generational differences in the age at which women have children. The median age of women in our sample was 47 years which may account for them having children earlier than more recent generations of women of childbearing age. The age at which women in the UK give birth to their first child has steadily increased over time (Office for National Statistics, 2018). Parity is increased in our sample because we restricted analysis to parous women only – women without children were excluded from this study.

In conclusion, we found evidence to indicate that history of three or more ACEs, and in particular childhood abuse, is associated with increased frequency of lifetime depressive episodes, but not specifically PPD. To investigate these findings further, future research should aim to longitudinally examine factors that potentially mediate the pathway between ACEs and PPD in larger samples of women with BD. Such research would have important implications for risk prediction of PPD among women with BD and also for understanding the aetiology of mood disorders related and unrelated to childbirth.

Table I. Demographics, lifetime clinical characteristics and perinatal history of the sample

	Total sample (n=575)
Age at interview (years)	
Median (IQR)	47 (16)
Range	19-85
Marital history (%, n)	
Married/lived as married	96.7 (535)
Never married/never lived as married	3.3 (18)
Education (%, n)	
Degree level or higher	33.2 (185)
Below degree level	66.8 (372)
Method of recruitment (%, n)	
Systematic	32.3 (183)
Non-systematic	67.7 (384)
DSM-IV diagnosis (%, n)	
BD-I	60.3 (347)
BD-II	39.7 (228)
Age at onset of BD (years)	
Median (IQR)	18 (7)
Range	5-37
Mean number of episodes of mania per illness year	
Median (IQR)	0.27 (0.42)
Range	0.02-7.16
Mean number of episodes of depression per illness year	
Median (IQR)	0.41 (0.59)
Range	0.00-10.01
Age at first pregnancy (years)	
Median (IQR)	24 (7)
Range	13-40
Number of deliveries	
Median (IQR)	2 (2)
Range	1-7

Ns differ due to missing data. BD: bipolar disorder. BD-I: bipolar I disorder. BD-II: bipolar II disorder

Table II. Number of adverse childhood experiences according to perinatal psychiatric history

Number of ACEs % (n)	PPD (n=368)	No PME (n=207)	Unadjusted		Adjusted [a]	
			p value	OR (95% CI)	p value	OR (95% CI)
0 (reference group)	36.7 (135)	42.5 (88)	-	-	-	-
1 or more	63.3 (233)	57.5 (119)	0.169	1.28 (0.91-1.81)	0.446	1.16 (0.79-1.69)
2 or more	25.3 (93)	22.2 (46)	0.222	1.31 (0.85-2.05)	0.873	1.04 (0.63-1.72)
3 or more	9.0 (33)	4.3 (9)	0.026*	2.40 (1.10-5.24)	0.183	1.82 (0.75-4.37)

PPD: Lifetime history of non-psychotic postpartum depression with onset within 6 weeks of delivery, No PME: No lifetime history of perinatal mood episodes during pregnancy or within 6 months postpartum, [a] adjusted for lifetime mean number of episodes of depression per illness year and lifetime number of deliveries. * <0.05

Table III. Prevalence of each type of adverse childhood experience according to perinatal psychiatric history

	PPD (n=368)	No PME (n=207)	Unadjusted		Adjusted[a]	
			p value	OR (95% CI)	p value	OR (95% CI)
Death of a parent (%, n)						
Present	7.3 (27)	8.2 (17)	0.705	0.89 (0.47-1.67)	0.483	0.791 (0.41-1.53)
Absent	92.7 (341)	91.8 (190)				
Death of a sibling (%, n)						
Present	4.3 (16)	2.9 (6)	0.385	1.52 (0.59-3.95)	0.279	1.89 (0.60-6.01)
Absent	95.7 (352)	97.1 (201)				
Death of a close friend (%, n)						
Present	12.8 (47)	10.6 (22)	0.448	1.23 (0.72-2.11)	0.547	1.20 (0.66-2.20)
Absent	87.2 (321)	89.4 (185)				
Divorce/separation (%, n)						
Present	22.6 (83)	19.8 (41)	0.442	1.18 (0.78-1.80)	0.667	1.11 (0.70 -1.76)
Absent	77.4 (285)	80.2 (166)				
Serious physical Illness (%, n)						
Present	24.7 (91)	22.7 (47)	0.586	1.12 (0.75-1.67)	0.593	1.13 (0.73-1.75)
Absent	75.3 (277)	77.3 (160)				
Any abuse[b] (%, n)						
Present	27.4 (101)	19.8 (41)	0.041*	1.53 (1.02-2.31)	0.442	1.21 (0.75-1.91)
Absent	72.6 (267)	80.2 (166)				
Emotional abuse (%, n)						
Present	5.4 (20)	5.3 (11)	0.951	1.02 (0.48-2.18)	0.550	0.78 (0.34-1.78)
Absent	94.6 (348)	94.7 (196)				
Physical abuse (%, n)						
Present	12.5 (46)	9.2 (19)	0.23	1.41 (0.81-2.48)	0.710	1.13 (0.60-2.14)
Absent	87.5 (322)	90.8 (188)				
Sexual abuse (%, n)						
Present	18.2 (67)	14.5 (30)	0.254	1.31 (0.83-2.10)	0.772	1.10 (0.64-1.84)
Absent	81.8 (301)	85.5 (177)				

PPD: Lifetime history of non-psychotic postpartum depression with onset within 6 weeks of delivery, No PME: No lifetime history of perinatal mood episodes during pregnancy or within 6 months postpartum, [a] adjusted for lifetime mean number of episodes of depression per illness year and lifetime number of deliveries, [b]Including emotional, physical or sexual abuse. * <0.05

Brugha, T., Bebbington, P., Tennant, C., Hurry, J., 1985. The List of Threatening Experiences: a subset of 12 life event categories with considerable long-term contextual threat. Psychol. Med. 15, 189–194. https://doi.org/10.1017/S003329170002105X

De Venter, M., Smets, J., Raes, F., Wouters, K., Franck, E., Hanssens, M., Jacquemyn, Y., Sabbe, B.G.C.C., Van Den Eede, F., Venter, M. De, Smets, J., Raes, F., Wouters, K., Franck, E., Hanssens, M., Jacquemyn, Y., Sabbe, B.G.C.C., Van Den Eede, F., De Venter, M., Smets, J., Raes, F., Wouters, K., Franck, E., Hanssens, M., Jacquemyn, Y., Sabbe, B.G.C.C., Van Den Eede, F., 2015. Impact of childhood trauma on postpartum depression: a prospective study. Arch. Womens. Ment. Health 19, 337–342. https://doi.org/10.1007/s00737-015-0550-z

Di Florio, A., Forty, L., Gordon-Smith, K., Heron, J., Jones, L., Craddock, N., Jones, I., 2013. Perinatal episodes across the mood disorder spectrum. JAMA psychiatry 70, 168–75.

Di Florio, A., Jones, L., Forty, L., Gordon-Smith, K., Craddock, N., Jones, I., 2015. Bipolar disorder , miscarriage , and termination. Bipolar Disord. 17, 102–105. https://doi.org/10.1111/bdi.12217

Dowlatshahi, D., Paykel, E.S., 1990. Life events and social stress in puerperal psychoses: absence of effect. Psychol. Med. 20, 655–662. https://doi.org/10.1017/S0033291700017177

Gaillard, A., Le Strat, Y., Mandelbrot, L., Keïta, H., Dubertret, C., 2014. Predictors of postpartum depression: Prospective study of 264 women followed during pregnancy and postpartum. Psychiatry Res. 215, 341–346. https://doi.org/10.1016/j.psychres.2013.10.003

Garabedian, M.J., Lain, K.Y., Hansen, W.F., Garcia, L.S., Williams, C.M., Crofford, L.J., 2011. Violence Against Women and Postpartum Depression. J. Women's Heal. 20, 447–453. https://doi.org/10.1089/jwh.2010.1960

Garno, J.L., Goldberg, J.F., Ramirez, P.M., Ritzler, B.A., 2005. Impact of childhood abuse on the clinical course of bipolar disorder. Br. J. Psychiatry 186, 121–125. https://doi.org/10.1192/bjp.186.2.121

Gressier, F., Guillard, V., Cazas, O., Falissard, B., Glangeaud-Freudenthal, N.M.-C., Sutter-Dallay, A.-L., 2017. Risk factors for suicide attempt in pregnancy and the post-partum period in women with serious mental illnesses. J. Psychiatr. Res. 84, 284–291. https://doi.org/10.1016/j.jpsychires.2016.10.009

Guintivano, J., Sullivan, P.F., Stuebe, A.M., Penders, T., Thorp, J., Rubinow, D.R., Meltzer-Brody, S., 2018. Adverse life events, psychiatric history, and biological predictors of postpartum depression in an ethnically diverse sample of postpartum women. Psychol. Med. 48, 1190–1200. https://doi.org/10.1017/S0033291717002641

Hoffman, C., Dunn, D.M., Njoroge, W.F.M., 2017. Impact of Postpartum Mental Illness Upon Infant Development. Curr. Psychiatry Rep. 19, 1–6. https://doi.org/10.1007/s11920-017-0857-8

Howard, L.M., Molyneaux, E., Dennis, C.L., Rochat, T., Stein, A., Milgrom, J., 2014. Non-psychotic mental disorders in the perinatal period. Lancet 384, 1775–1788. https://doi.org/10.1016/S0140-6736(14)61276-9

Janiri, D., Sani, G., Danese, E., Simonetti, A., Ambrosi, E., Angeletti, G., Erbuto, D., Caltagirone, C., Girardi, P., Spalletta, G., 2014. Childhood traumatic experiences of patients with bipolar disorder type I and type II. J. Affect. Disord. 175, 92–97. https://doi.org/10.1016/j.jad.2014.12.055

Kettunen, P., Hintikka, J., 2017. Psychosocial risk factors and treatment of new onset and recurrent depression during the post-partum period. Nord. J. Psychiatry 71, 355–361. https://doi.org/10.1080/08039488.2017.1300324

Leigh, B., Milgrom, J., 2008. Risk factors for antenatal depression, postnatal depression and parenting stress. BMC Psychiatry 8, 24. https://doi.org/10.1186/1471-244X-8-24

Mandelli, L., Souery, D., Bartova, L., Kasper, S., Montgomery, S., Zohar, J., Mendlewicz, J., Serretti, A., 2016. Bipolar II disorder as a risk factor for postpartum depression. J. Affect. Disord. 204, 54–58. https://doi.org/10.1016/j.jad.2016.06.025

Marwaha, S., Gordon-Smith, K., Broome, M., Briley, P.M., Perry, A., Forty, L., Craddock, N., Jones, I., Jones, L., 2015. Affective instability, childhood trauma and major affective disorders. J. Affect. Disord. 190, 764–771. https://doi.org/10.1016/j.jad.2015.11.024

Meltzer-Brody, S., Larsen, J.T., Petersen, L., Guintivano, J., Florio, A. Di, Miller, W.C., Sullivan, P.F., Munk-Olsen, T., 2018. Adverse life events increase risk for postpartum psychiatric episodes: A population-based epidemiologic study. Depress. Anxiety 35, 160–167. https://doi.org/10.1002/da.22697

Office for National Statistics, 2018. Childbearing for Women Born in Different Years, England and Wales: 2017.

Perry, A., Gordon-Smith, K., Di Florio, A., Forty, L., Craddock, N., Jones, L., Jones, I., 2016. Adverse childhood life events and postpartum psychosis in bipolar disorder. J. Affect. Disord. 205, 69–72. https://doi.org/10.1016/j.jad.2016.06.061

Plaza, A., Garcia-Esteve, L., Torres, A., Ascaso, C., Gelabert, E., Luisa Imaz, M., Navarro, P., Valdés, M., Martín-Santos, R., 2012. Childhood physical abuse as a common risk factor for depression and thyroid dysfunction in the earlier postpartum. Psychiatry Res. 200, 329–35. https://doi.org/10.1016/j.psychres.2012.06.032

Post, R.M., Altshuler, L.L., Kupka, R., Mcelroy, S.L., Frye, M.A., Rowe, M., Leverich, G.S., Grunze, H., Suppes, T., Keck, P.E., Nolen, W.A., 2015. Verbal abuse, like physical and sexual abuse, in childhood is associated with an earlier onset and more difficult course of bipolar disorder. Bipolar Disord. 17, 323–330. https://doi.org/10.1111/bdi.12268

Power, R.A., Kyaga, S., Uher, R., MacCabe, J.H., Langstrom, N., Landen, M., McGuffin, P., Lewis, C.M., Lichtenstein, P., Svensson, A.C., 2013. Fecundity of Patients With Schizophrenia, Autism, Bipolar Disorder, Depression, Anorexia Nervosa, or Substance Abuse vs Their Unaffected Siblings. JAMA Psychiatry 70, 22–30. https://doi.org/10.1001/jamapsychiatry.2013.268

Robertson-Blackmore, E., Putnam, F.W., Rubinow, D.R., Matthieu, M., Hunn, J.E., Putnam, K.T., Moynihan, J.A., O'Connor, T.G., 2013. Antecedent trauma exposure and risk of depression in the perinatal period. J. Clin. Psychiatry 74, e942-8. https://doi.org/10.4088/JCP.13m08364

Rowland, T.A., Marwaha, S., 2018. Epidemiology and risk factors for bipolar disorder. Ther. Adv. Psychopharmacol. 8, 251–269. https://doi.org/10.1177/2045125318769235

Sala, R., Goldstein, B.I., Wang, S., Blanco, C., 2014. Childhood maltreatment and the course of bipolar disorders among adults: epidemiologic evidence of dose-response effects. J. Affect. Disord. 165, 74–80. https://doi.org/10.1016/j.jad.2014.04.035

Sharma, V., Doobay, M., Baczynski, C., 2017. Bipolar postpartum depression: An update and recommendations. J. Affect. Disord. 219, 105–111. https://doi.org/10.1016/j.jad.2017.05.014

Tebeka, S., Le Strat, Y., Dubertret, C., 2016. Developmental trajectories of pregnant and postpartum depression in an epidemiologic survey. J. Affect. Disord. 203, 62–68. https://doi.org/10.1016/j.jad.2016.05.058

Tian, T., Li, Yihan, Xie, D., Shen, Y., Ren, J., Wu, W., Guan, C., Zhang, Z., Zhang, D., Gao, C., Zhang, X.,

Wu, J., Deng, H., Wang, G., Zhang, Y., Shao, Y., Rong, H., Gan, Z., Sun, Y., Hu, B., Pan, J., Li, Yi, Sun, S., Song, L., Fan, X., Li, Yi, Zhao, X., Yang, B., Lv, L., Chen, Yunchun, Wang, X., Ning, Y., Shi, S., Chen, Yiping, Kendler, K.S., Flint, J., Tian, H., 2012. Clinical features and risk factors for post-partum depression in a large cohort of Chinese women with recurrent major depressive disorder. J. Affect. Disord. 136, 983–987. https://doi.org/https://doi.org/10.1016/j.jad.2011.06.047

Upthegrove, R., Chard, C., Jones, L., Gordon-Smith, K., Forty, L., Jones, I., Craddock, N., 2015. Adverse childhood events and psychosis in bipolar affective disorder. Br. J. Psychiatry 206, 191–197. https://doi.org/10.1192/bjp.bp.114.152611

VanderKruik, R., Barreix, M., Chou, D., Allen, T., Say, L., Cohen, L.S., Barbour, K., Cecatti, J.G., Cottler, S., Fawole, O., Firoz, T., Gadama, L., Ghérissi, A., Gyte, G., Hindin, M., Jayathilaka, A., Kalamar, A., Kone, Y., Lange, I., Magee, L.A., Mathur, A., Binns, A.M.C., Morgan, M., Munjanja, S., Gichuhi, G.N., Petzold, M., Sullivan, E., Taulo, F., Tunçalp, Ö., von Dadelszen, P., 2017. The global prevalence of postpartum psychosis: A systematic review. BMC Psychiatry 17, 1–9. https://doi.org/10.1186/s12888-017-1427-7

Viguera, A.C., Tondo, L., Koukopoulos, A.E., Reginaldi, D., Lepri, B., Baldessarini, R.J., 2011. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am. J. Psychiatry 168, 1179–85. https://doi.org/10.1176/appi.ajp.2011.11010148

Wesseloo, R., Kamperman, A.M., Munk-Olsen, T., Pop, V.J.M., Kushner, S.A., Bergink, V., 2016. Risk of Postpartum Relapse in Bipolar Disorder and Postpartum Psychosis: A Systematic Review and Meta-Analysis. Am. J. Psychiatry 173, 117–127. https://doi.org/10.1176/appi.ajp.2015.15010124

Wing, J.K., Babor, T., Brugha, T., Burke, J., Cooper, J.E., Giel, R., Jablenski, A., Regier, D., Sartorius, N., 1990. SCAN: Schedules for Clinical Assessment in Neuropsychiatry. Arch. Gen. Psychiatry. https://doi.org/10.1001/archpsyc.1990.01810180089012