

## Postpartum Depression Effects, Risk Factors and Interventions: A Review

Tiffany Field\*

University of Miami, Miller School of Medicine, Fielding Graduate University, Santa Barbara, CA 93105, USA

\*Corresponding author: Field T, University of Miami, Miller School of Medicine, Fielding Graduate University, Santa Barbara, USA, Tel: 8003401099; E-mail: tfield@med.miami.edu

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### Abstract

This review involved a literature search on postpartum depression effects, risk factors and interventions on Pubmed and PsycInfo. Empirical studies, systematic reviews and meta-analyses published in the years 2014-2016 are briefly summarized here. The approximate 10 - 20% postpartum depression prevalence rate and the effects on the mother such as altered connectivity in brain regions, effects on the father (17% depressed) and on the social, behavioural and cognitive problems of the offspring have led to screening mandates that have been effective. In this recent literature, risk factors for postpartum depression have included socio-demographic factors such as low income and social support, being an immigrant, and experiencing a deployment during delivery. Mothers' early childhood experiences including disorganized attachment, maltreatment and childhood sexual abuse are also risk factors. The most frequently published risk factors in the 2014-16 time period have been prenatal depression, sleep disturbances, elevated cortisol and low levels of oxytocin. With respect to interventions, antidepressants have been rarely studied in contrast to cognitive behavioural therapy, interpersonal therapy, and mother-infant psychotherapy and biochemical interventions including oxytocin. Given the ethical problem of random assignment once treatments are known to be effective, very few randomized controlled trials appear in the literature, and the screening/diagnostic problems have limited the number of prospective longitudinal studies.

**Keywords:** Postpartum depression; Risk factors; Behavioural therapy; Depression; Review

### Introduction

This narrative review involved a literature search on postpartum depression effects, risk factors and interventions found in the years 2014-2016 on PubMed and PsycInfo. Postpartum depression has also been labelled postnatal depression. In this literature search, 210 papers appeared under the term postpartum depression while only 123 appeared under the term postnatal depression. For the selection process, the inclusion criteria were empirical studies, systematic reviews and meta-analyses published on depression effects, risk factors and interventions. Exclusion criteria included non-English papers, case studies, under-powered samples, and non-peer reviewed papers. Following these screening criteria, 101 publications were selected for the review here. Meta-analyses could not be performed because of the limited number of studies with similar research protocols, measures and randomized controlled trials.

To briefly outline this review, the approximate 10 - 20% prevalence rate and the effects on the mothers such as altered connectivity in brain regions, on the fathers (17% depressed) and on the social, behavioural and cognitive problems of the offspring have led to screening mandates that have been effective. In this recent literature, risk factors for postpartum depression have included socio-demographic factors such as low income and social support, being an immigrant, and experiencing a deployment during delivery. Mothers' early childhood experiences including disorganized attachment, maltreatment and childhood sexual abuse have also been risk factors. The most frequently studied risk factors have been prenatal depression, sleep disturbances, elevated cortisol and low of oxytocin levels.

With respect to interventions, antidepressants have been rarely studied in contrast to cognitive behaviour therapy, interpersonal therapy, and mother-infant psychotherapy and biochemical interventions including oxytocin. Given the ethical problem of random assignment once treatments are known to be effective, very few randomized controlled trials appear in the literature, and the screening/diagnostic problems have limited the number of prospective longitudinal studies.

### Prevalence and Timing of Depression

Postpartum depression, defined as a psychological mood disorder, has been characterized as having many symptoms including obsessive-compulsive behaviours, anxiety, paranoid ideation, depressed mood, diminished pleasure/interest, and psychomotor agitation/retardation [1]. It has occurred in some studies within 4-6 weeks of giving birth and has continued for at least 2 weeks (up to 84%) [1-3]. The early occurrence has been only 11% as opposed to 17% experiencing postpartum depression three months after delivery [4].

In at least one study on a large representative U.S. sample (N=11,256), the depressive symptoms in women of childbearing age did not differ during the postpartum period as compared to pregnancy [5,6]. The neurobiological profiles also seem to be similar. In an overview of fMRI studies on women with postpartum depression, the findings from eleven studies appeared to replicate the findings of fMRIs on major depression, suggesting that postpartum depression did not have a distinct neurobiological profile [7]. However, the samples were small and lacked direct comparison with major depression individuals. The authors suggested that a neuroimaging signature for postpartum depression might be found if a greater variety of magnetic resonance imaging techniques were used on larger samples.

Based on the Edinburgh Postnatal Depression Scale, the prevalence of this diagnosis has ranged from 16% in the United States to 21% in Italy and 15% when averaged across women in Western countries. In the US study, 24% of the postpartum depressed women indicated having thought about suicide and 7% had these thoughts quite frequently [7-9].

Paternal postpartum depression during the first 3 months following birth has ranged from 5% in Sweden to 6% in Italy Epifano, et al. [8] to 10% in France to 17% in Japan and to 21% in Finland [10-13]. Maternal and paternal postpartum depression was significantly correlated in at least two of these studies [10,13]. However, paternal depression was also associated with male hormone changes during the postpartum period as noted in the review of the French studies [11]. In at least one other study, only the fathers' history of depression symptoms during pregnancy was associated with their postpartum depression symptoms [12]. In the review of the French literature, paternal postpartum depression was shown to have negative effects on infant development independently of maternal postpartum depression [11].

The variability in these timing and prevalence data may relate to cross-cultural differences. The inconsistent findings may also derive from differences in the data collection and analyses methods including concept analysis Lee, et al. [14], item response theory, an online quantitative cross-sectional survey design Teaford, et al. [7], a regional longitudinal study Suto, et al. [12] and an interpretative phenomenological analysis [9].

### Postpartum Depression Effects on the Mothers and Offspring

The effects of postpartum depression on the mothers include sleep problems and less brain connectivity in the amygdala (Table 1). Most of the studies have focused on the negative effects on the offspring including sleep problems, behaviour problems and lower cognitive performance.

Effects	Measures	Authors
<b>Mothers</b>		
<duration sleep	sleep diary and actigraphy	Sharkey et al. [15]
<connectivity in amygdala	fMRIs	Wonch et al. [16]
<b>Offspring</b>		
<duration sleep and >feeding @2-6 wks	sleep diaries	Sharkey et al. [15]
>negative perception M-I relationship @ 3 mos.	self-report	Tikotzky [17]
<cognitive scores @ 4 mos.	Bayley scales	Smith-Neilsen et al. [18]
<imitation @ 13 mos.	observations	Perra et al. [19]
>externalizing @ 18 mos.	observations	Oh et al. [21]
<accurate labeling facial @ 3 yrs.	observations	Meiser et al. [22]

<cognitive performance @ 3 yrs.	IQ tests	Mirhosseini et al. [24]
	total and verbal IQ	Sui et al. [25]
>cortisol reactivity @ 22 yrs.	social threat	Barry et al. [26]

**Table 1:** Postpartum depression effects on mothers and their offspring's.

### Effects on the mothers

Although the effects of postpartum depression on the mothers are rarely studied except for the depression symptoms, at least one research group has reported disturbed sleep patterns [15]. In that study, the mothers completed sleep diaries and wore wrist actigraphs. Shorter duration maternal sleep was associated with higher depression scores and with shorter infant sleep.

Postpartum depressed mothers' connectivity and brain responses were assessed by fMRIs while viewing smiling pictures of their own and other infants as well as positive non-infant stimuli [17]. As in previous studies on depressed individuals, the postpartum depressed mothers showed decreased brain connectivity in the amygdala which has been implicated in the processing of social and emotional stimuli. Although this is compelling evidence that less activation occurs in a social-emotional part of the brain, it is not clear how this information can be used clinically. That is, fMRI's are too expensive for screening, and parts of the brain cannot be manipulated therapeutically. As in other studies showing the similarity between fMRIs of postpartum and major depression Fiorelli, et al. [6], these data also suggest a commonality between postpartum and non-postpartum depression.

### Effects on the offspring

Recent research on postpartum depression effects on infants and children include sleep and feeding disturbances at 2-6 weeks, mother-infant relationships at 3 months, Bayley cognitive scores at 4 and 13 months, imitation at 13 months, internalizing behaviours at 18 months, labelling facial emotional expressions at preschool age, cognitive performance at preschool age, IQ scores of children, and cortisol reactivity at 22 years of age. These long-term effects raise the possibility that the mothers are chronically depressed, not just postpartum depressed.

In a small sample (N=30) 2-6 week-old infants of postpartum depressed mothers had disturbed sleep and more frequent feeding [15]. Shorter duration maternal sleep was correlated with shorter duration infant sleep. It is not clear whether the more frequent feeding accounted for the shorter duration sleep for both the infants and mothers. Unfortunately the sample was too small to conduct mediation or structural equations analyses to determine mediating variables. In a larger sample (N=80) on 3-18-month-old infants, postpartum depression was related to negative maternal perceptions of the mother-infant relationship [17]. But more disturbed maternal sleep was also related to negative perceptions of the relationship, again suggesting maternal sleep as a mediating variable for postpartum depression effects on their infants.

In a study on four and 13-month-olds, infants were given Bayley developmental tests [18]. At four months the infants of postpartum depressed mothers had inferior cognitive scores but at 13 months when 79% of the postpartum depressed mothers were no longer

depressed, the infants no longer had inferior cognitive scores, suggesting that the early effects on cognitive function were not long-lasting.

In an imitation study, 13-month-old infants of postpartum depressed mothers were less likely to imitate modelled actions (a 72% reduction in likelihood) than infants of non-depressed mothers [19]. This may relate to less experience with reciprocal imitation during their early interactions with their depressed mothers [20].

At 18 months, the offspring of postpartum depressed mothers were noted to have more externalizing problems [21]. However, in this study, both depression and posttraumatic stress disorder were comorbid in the mothers, suggesting a greater risk factor for the infants.

Preschool age children of postpartum depressed mothers have been less likely to correctly label facial emotional expressions than preschoolers of non-depressed mothers [22]. However, the same children were successful at recognizing facial expressions of basic emotions. Surprisingly, this finding was not related to current mental health of the mother. These effects were potentially confounded by both depressed and anxiety disorder mothers being grouped together for the data analyses given that these syndromes have different effects. Also, as in other studies, some of the mothers may have had comorbid depression and anxiety which is very common and the comorbidity likely has more serious effects than depression alone [23].

In a literature review, inferior cognitive performance was noted in children of postpartum depressed mothers [24]. These adverse effects were mediated by the mothers' interpersonal behaviour and by infant gender, with male children showing more severe effects. In a meta-analysis based on 974 cases included in 7 studies, the children (two years and older) of postpartum depressed mothers showed a lower full scale IQ than the children of non-depressed mothers [25,26]. Lower verbal IQs were also reported in these studies.

In a study on the biological sensitivity to social stress in 22-year-old offspring of postpartum depressed parents, those adult offspring showed greater cortisol reactivity in response to a social-evaluative threat [27]. This finding was surprising, especially since the group differences could not be explained by concurrent depressive or anxiety symptoms in the participants or by elevated basal cortisol levels at 13 years.

Surprisingly very few developmental follow-up studies have appeared in the recent literature on postpartum depression, especially as compared to the recent literature on prenatal depression effects. The earlier postpartum depression effects literature may have been sufficiently compelling for researchers to shift their inquiries to screening, risk factors and interventions. These issues have dominated the more recent literature. The postpartum depression effects on mothers, fathers and offspring briefly summarized here as well as many other effects noted in the earlier literature have highlighted the importance of screening and referrals for treatment.

## Screening

The U.S. Preventive Services Task Force recently recommended that all women be screened for depression during pregnancy and the postpartum period. State-level mental health policies have mandated depression screening in at least 13 states including Massachusetts, New Jersey, Illinois and West Virginia [27]. This systematic review on state policies suggests that the screening alone has had a limited impact, but

when combined with patient education mandates including home visits with a mental health component, they have been more effective.

The Edinburgh Postnatal Depression Scale (EPDS) is the most commonly used screening tool and its validation and reliability have been the focus of hundreds of recent publications. It has also been validated in several countries, and screening for prenatal depression is recommended in a number of countries.

In a validation study from Portugal, telephone interviews were used for screening [28]. In this cross-sectional study, telephone interviews were administered to 1083 women and 24% of them had an EPDS score greater than 10. After the telephone interview, 199 participants were interviewed face-to-face on the Structured Clinical Interview for DSM-IV (SCID). The correlation between the self-reported EPDS and the EPDS by telephone was 0.69. Scores greater than 10 showed a sensitivity of 72%, a specificity of 72% and a positive predictive value of 68%. The authors concluded that administering the EPDS by telephone was a cost-effective alternative.

In a systematic review of studies that had screened at well-baby care clinics, six studies were included, and of those, four studies showed improvement in detection, referral and/or treatment rates [29]. The small number of studies that met criteria for this review, however, highlights the need for additional studies on the benefits of screening in well-baby care settings.

In an attempt to educate physicians on the need for screening, an educational session was given about postpartum depression and a modification of the electronic medical record (EMR) was made for providers' screening for postpartum depression [30]. Following the EMR change, a chart review was conducted from three time periods: time one was before the educational session, time two was after the educational but before the EMR change and time three was after the screening and the EMR change. Documented screening increased from 0% at time one to 2% at time 2 to 74% at time 3. Thus, the combination of provider education and screening questions integrated into the EMR enhanced the screening rates among physicians.

Screening efforts have almost exclusively relied on the EPDS as a screening measure. It is not clear how or why this has happened as other screening instruments such as the Beck Depression Inventory and the Centre for Epidemiological Studies-Depression scales were used in earlier studies on postpartum depression. Although it is a self-report measure with all the associated limitations of self-report measures, it has been apparently valid when compared to clinical interview measures based on the DSM-IV and reliable when given repeatedly. As screening becomes more common and electronic programs are used more frequently, as, for example, in the phone interviews noted above, additional risk factors may be used to formulate risk profiles for postpartum depression. Although many independent risk factors have been identified, profile analyses or even regression analyses have not been conducted to determine the relative variance in postpartum depression that can be explained by the different risk factors summarized below.

## Risk Factors

Approximately half the papers found in this literature search relate to risk factors for postpartum depression (Table 2). These risk factors can be organized in several categories including: demographics; immigration; cross-cultural; early childhood factors for the mother including disorganized attachment, childhood maltreatment and

sexual abuse; prenatal depression; obstetric factors including delivery mode, obstetric complications, deployment during delivery; breast-feeding; sleep disturbances; miscellaneous factors including body image, partner violence, and substance use; multiple factors as revealed by reviews and meta-analyses; and biochemical risk factors including hormones and immune measures. Most of these have been identified in retrospective, cross-sectional studies and surveys.

Risk factors	Authors
<b>Demographic</b>	
<income and social support	Pope et al. [31]
ethnicity	Liu et al. [32]
<socioeconomic status and non-U.S. born	Liu et al. [33]
rural residence	Mollard et al. [35]
non-western cultures	Eavagoron
immigrant status	Falah-Hassani et al. [37]
<b>Mothers' childhood risk factors</b>	
disorganized attachment	Nonnemacher et al. [40]
anxious attachment	Warfa et al. [41]
maltreatment	Morelen et al. [42]
sexual abuse	Wasu
Prenatal depression	
fathers' prenatal depression	Paulson et al. [46]
mothers' prenatal depression	Batmaz et al. [44], Chojenta et al. [45], Kettunen et al. [1], Underwood et al. [47]
<b>Obstetric factors</b>	
vaginal delivery preference but Caesarean delivery	Houston et al. [49]
pregnancy complications	Collaborators [50]
deployment	Levine et al. [51]
<b>Miscellaneous risk factors</b>	
prenatal sleep disturbances	Tham et al. [52]
postpartum sleep disturbances	Bhati et al. [53]
body image dissatisfaction	Hain et al. [54], Silveira et al. [55]
intimate partner violence	Kothari et al. [56], Tsai et al. [57]
multiple risk factors (child attachment and abuse, prenatal depression, social support)	Tebeka et al. [58], Kruse et al. [59], Lara et al. [60], Iliadis et al. [61]
<b>Biochemical factors</b>	
>hematocrit 3rd trimester	Roomruangwong et al. [62]
>corticotropin-releasing hormone	Hahn-Holbrook [63]
<cortisol 1st and 2nd trimester	Scheyer et al. [64]
>cortisol at 36 wks. Gestation	Iliadis et al. [61]

>day 14 cortisol and interleukin 8/10 ratios	Corwin et al. [66]
<oxytocin	Jobst et al., Moura et al. [68]
>cortisol and < oxytocin	Cox et al. [69]
>testosterone	Aswathi et al.
>c-reactive protein	Roomruangwong et al. [72]
>c-reactive protein and >interleukin-6	Liu et al. [74]
<magnesium	Edalati-Fard et al. [73]
>leptin	
<brain-derived neurotrophic factor	Gao, et al. [76]

**Table 2:** Risk factors for postpartum depression.

### Demographic Factors

In the studies included in this recent review, several demographic risk factors have been surveyed including income, social support, ethnicity, education, unemployment, rural location, culture, and immigrant status. Surprisingly, age of the mother and marital status have rarely appeared as risk factors in these studies.

In a large Canadian survey (N=6421) the EPDS and demographic data were collected [31]. Following this survey, logistic regression analysis revealed that lower income and lower social support were associated with postpartum depression, although breast-feeding duration was not. In a similar US survey on 2423 women from various ethnic groups, risk factors as well as postpartum depression and the presence of depressed mood and anhedonia varied across the different ethnic groups [32]. Socioeconomic status and being non-US born were risk factors for these groups. In another report on the same database, these authors noted that African-Americans and Hispanics who endorsed high relational and high financial stress were more likely to have high depressed mood and anhedonia scores while high physical stress was associated with high depressed mood among Asian Pacific islanders [33].

Although many have reported postpartum risk factors at 6 weeks, in a study on Mexican women, the risk factors were reported at 6 months at which time the prevalence of postpartum depression was 9% as opposed to 11% at six weeks [34]. At the six-month period women with depression versus those without depression were younger, had fewer years of schooling, and were un-partnered, unemployed and poorer. A limitation of the study is that the attrition was high (25%) and the non-completers were younger; less educated and reported more depressive symptoms, suggesting that the prevalence may have been underestimated.

Rural women apparently have a higher risk of postpartum depression based on a review of 11 studies conducted in US rural populations [35]. The review suggested that although screening and prevention programs may be feasible for rural women, those women seem to rely on social networks and may view mental health care as stigmatic and therefore are not responsive to screening and prevention efforts.

Culture is another risk factor. Following a systematic electronic search and a review of 106 papers that met criteria, significant cross-cultural differences were noted in the prevalence of postpartum depression, as might be expected [36]. Both the prevalence and the

somatization of depressive symptoms were more frequent in non-Western cultures. Fewer mental health services and less effective postpartum practices were also factors in their analyses.

Immigrant status is another factor that has been identified in several studies. First, with regard to prevalence, immigrant women were twice more likely (20 vs. 10%) to experience depressive symptoms postpartum than non-immigrant women in a meta-analysis of the literature including 24 studies on 13,749 women [37]. The risk factors among immigrant women included shorter length of residence in the new country, less social support, inferior marital adjustment and insufficient household income. In a literature review on 26 studies comparing immigrant women in industrialized countries with Arab women in their own countries, the prevalence of postpartum depression among immigrant women ranged from 11 to 60% while the range among Arab women was 10 to 37% [38]. The risk factors identified included lack of social support, stressful life events, low income and intimate partner violence.

In still another systematic review, 15 studies were identified on South Asian women who had migrated to high income countries [39]. Although the postpartum depression prevalence in this group was extremely varied (2-52%), most estimates have ranged from 5-20%. The most common risks were social factors including social isolation, the quality of relationships with partners, barriers to health care, lack of English language proficiency and lack of attention to mental health and cultural factors by healthcare providers.

Several limitations have been noted about this literature including limited recruitment strategies, lack of representativeness of the samples, variability of inclusion and exclusion criteria, different assessment measures, some of which had not been formally validated and inadequate data analysis strategies including the lack of subgroup analyses. Further, the authors were typically researchers from the countries they were studying, suggesting potential biases toward their countries of origin.

## Mothers' Childhood Risk Factors for Postpartum Depression

Several childhood risk factors have been noted for postpartum depressed mothers including disorganized attachment, most particularly anxious attachment, maltreatment and sexual abuse. These links are tenuous at best as they depend on long-term memory as self-reported data rather than data from prospective longitudinal studies. Further, the outcome measures such as bonding are based on self-report, non-standardized measures. Nonetheless, they are suggestive of historical risk factors that should be considered when formulating risk profiles for postpartum depression.

Regarding early disorganized attachments, an exploratory analysis in one study suggested that postpartum depression had a medium-sized mediation effect on the relationship between disorganized attachment style in childhood and bonding to offspring as an adult [40]. In this study, the mediating variable, postpartum depression, was assessed by a more standardized measure (the Structured Clinical Interview), than the outcome variable, bonding (Postpartum Bonding Questionnaire) or the predictor variable, disorganized attachment style (Attachment Style Interview), highlighting the exploratory nature of this study.

In a systematic review on early attachment styles, only 20 of 353 papers from several databases met inclusion criteria, representing a

total of 2,306 participants [41]. The authors found that insecure attachment was a risk factor for postpartum depression, with the anxious attachment style being more frequently associated with postpartum depression symptoms than avoidant or dismissive styles of attachment. They also highlighted the importance of this research by noting that the cost of caring for women with postpartum depression in the UK was approximately 35.7 million pounds per year.

With regard to childhood maltreatment, an observational study on mothers who had experienced childhood maltreatment included videotaping the mothers and their infants interacting with each other [42]. In the data analysis of this study, the severity of child maltreatment predicted depression and posttraumatic stress disorder symptoms, and those maternal symptoms, in turn, predicted positive and negative behaviours of the mothers during their interactions with their infants.

Entering childhood sexual abuse and postpartum depression as search words in another review of the literature yielded only seven eligible studies [43]. Although the findings suggested consistent relationships between childhood sexual abuse and prenatal depression, the relationships between childhood sexual abuse and postpartum depression were inconsistent.

## Prenatal Depression

Prenatal depression was the most frequently studied risk factor for postpartum depression in the current literature search [1,44-47]. In a sample of 80 couples, prenatal depression persisted from 28 weeks gestation through 6 months for 75% of mothers and 86% of fathers [46]. Prenatal depression in fathers predicted worsening depression across the first six months postpartum for mothers but not vice versa. In a small sample study, prenatal Beck Depression Inventory scores were significantly correlated with EPDS postpartum depression scores [44]. In a larger sample study (N=5219 women in Australia), more risk factors explained a significant amount of the variance on postpartum depression including emotional distress during labor, postnatal anxiety, and breastfeeding for less than six months [45]. Breastfeeding for 6 months was a protective factor in at least one other recent study in which breastfeeding not only contributed to lower postpartum depression scores but also to lower postpartum weight [48].

In other studies, incidence data suggested that "pure" postpartum depression was rare, with only 4% having experienced depression exclusively during the postpartum period [1]. In this study, 42% of postpartum depressed women had experienced prenatal depression. In a review of 16 longitudinal studies (selected from 523 studies) on 35,419 women, 39% of those who experienced antenatal (prenatal) depression continued to be depressed during the postpartum period, and on average, 47% of those who had postnatal depression had also experienced prenatal depression [47]. This review also suggested that depression rates were higher during pregnancy than during the first year following childbirth.

Data from these studies combine to suggest that prenatal depression is one of the most common predictors of postpartum depression. However, as in the postpartum period studies, screening has rarely been conducted on large clinical samples. The conclusions are limited to samples of women who are fortunate to have been in prenatal depression studies. And, even in those research samples, follow-up assessments have rarely been conducted to locate the women who had been prenatally depressed and to ensure their referrals for therapy. With the incidence of prenatal depression being so high, and given the

strong associations between prenatal and postnatal depression it would seem that the obstetric community or at least the women themselves would seek referrals.

## Obstetric Factors

Research on obstetric factors in the recent literature has focused on delivery mode, obstetric complications and deployment during delivery. In a longitudinal study on delivery mode preferences, most of the women preferred vaginal delivery (92%) [49]. A stronger preference for vaginal delivery was associated with elevated depression scores for those who ultimately experienced caesarean deliveries but not for those who had vaginal deliveries. This association was no longer significant at 6-8 months post-delivery. Given that at least a third of the sample had experienced a previous caesarean delivery, it is not clear how this variable affected the relationships between delivery preference, delivery experience and depression.

In another study by 33 collaborators on 17,912 records representing 19 institutions in 7 countries, poor mood, anxiety and prenatal depression as well as pregnancy complications were associated with postpartum depression [50]. To determine deployment effects, deployment status before, during or after delivery and postpartum depression were entered into a logistic regression model in a study on 161,454 births [51]. A significant relationship was noted only for those pregnancies in which deployment occurred during pregnancy with a return after delivery. An interaction effect was also noted between pre-existing depression and deployment during delivery.

## Miscellaneous Risk Factors

A few risk factors that appeared in the recent literature but did not seem to fit in the above categories are discussed here including sleep disturbances, body image and partner violence. Although sleep disturbances are often comorbid with depression, only 2 papers on that topic were found on prenatal sleep disturbances as a risk factor in this recent literature search. In one study, the EPDS was completed along with the Pittsburgh Sleep Quality Index during pregnancy and again at 3 months postpartum [52]. Although prenatal depression symptoms were the strongest predictor of postpartum depression, sleep disturbances during pregnancy were independently associated with postpartum depression. In a systematic review of the literature on postpartum sleep disturbance and postpartum depression, several databases were searched including PubMed, Medline, PsychInfo and Cochrane [53]. The effect size for the relationship between postpartum sleep disturbance and depression across 13 studies ranged between 0.4 and 1.7. However, as the authors pointed out, the samples were predominantly well- educated and middle-class and the measurement of sleep differed across studies, introducing potential bias.

Body image dissatisfaction has been implicated as a risk factor in a prospective study from six weeks antepartum to 6 and 12 weeks postpartum [54]. In this study, significant concerns about one's appearance (called dysfunctional consciousness in this study), was a risk factor for postpartum depression. Resilience as a protective factor weakened the effect of dysfunctional consciousness on postpartum depression. In a critical review of the literature based on a PubMed search, 19 studies on body image dissatisfaction and postpartum depression was identified [55]. Body image was consistently but weakly related to postpartum depression in the body image to postpartum depression direction rather than the reverse.

Intimate partner violence has also been associated with postpartum depression in a cross-sectional telephone-survey of 301 postpartum women 2 months after delivery [56]. In that study 10% screened positive for postpartum depression while as many as 21% screened positive for current or previous adult emotional or physical abuse by a partner. Intimate partner violence outweighed the influence of poverty on postpartum depression. In another study, a secondary analysis was conducted on longitudinal data collected from 1,238 postpartum women [57]. A one standard deviation increase in intimate partner violence intensity was associated with a 12% relative increase in postpartum depression scores on the EPDS over the same time period.

## Multiple Risk Factors

Unlike most of the univariate studies already reviewed, multivariate studies have included multiple variables in their surveys/interviews and in their data analyses. These include a large National Epidemiologic Study on a sample of 1,085 women with postpartum depression who were interviewed on multiple measures [58]. The women reported higher rates of sexual abuse in childhood, family history of depression, substance use disorder, bipolar disorder, a history of suicide attempts, stressful life events in the last year and pregnancy complications. This study was limited by not separating those women who had postpartum depression from those who had prenatal depression that continued into the postpartum period, a problem with many of the postpartum depression studies.

In a structural equations modelling study the authors tested a relational theory that a low sense of belonging, loneliness and delayed or impaired bonding predicted postpartum depression [59]. The model explained 35% of the variance in postpartum depression with loneliness and impaired bonding as the strongest predictors. Additional predictors were a low sense of belonging, less social support from a partner and healthcare practitioner and a lower sense of competence about parenting. This study raises the question of whether impaired bonding is a risk for postpartum depression rather than the reverse relationship.

In a study on 210 Mexican mothers interviewed at 6 weeks and 6 months postpartum, univariate logistic regressions were conducted [60]. These suggested that social support, marital satisfaction, life events, a history of psychopathology, anxiety symptoms, depressive symptoms, the traditional female role, previous miscarriages/termination of pregnancy and unplanned/unwanted pregnancy were significant predictors for postpartum depression at both assessment periods. Demographic variables including age, education, marital status and income were only significant at the first time period.

In a study on 1,037 non-depressed Swedish women, those who reported high levels of neuroticism in late pregnancy had a fourfold increased risk for developing postpartum depression [61]. Major depression, somatic and psychic trait anxiety was also associated with an increased risk of developing postpartum depression. In a Korean study on 186 pregnant women, parenting stress, antepartum depression and postpartum family support explained 75% of the variance on postpartum depression [2].

These multivariate studies from several different countries combined with the previously discussed univariate studies suggest that a profile of risk factors for postpartum depression could be formulated based on profile, mediator, regression or structural equations analyses. The psychological factors that consistently appear include childhood attachment and abuse problems, prenatal depression, and social

support. Surprisingly, very few data analyses have yielded significant demographic risk factors such as age, education and income of the mother or pregnancy and delivery complications. Occasional unique variables have occurred in these studies such as unwanted delivery method and late pregnancy neuroticism which may have been variables of particular interest to the investigators rather than being reflective of postpartum depressed women's reports. The profile would necessarily include hormonal risk factors which are discussed in the next section.

## Biochemical Risk Factors

Not surprisingly, increasing numbers of studies have revealed biochemical risk factors for postpartum depression. Of these, the most frequently researched include elevated cortisol and low oxytocin levels. Others include elevated haematocrit, testosterone, C-reactive protein, interleukin-6 (a pro-inflammatory cytokine), leptin, and brain-derived neurotrophic factor (BDNF), as well as lower zinc and magnesium and an interaction between hypothalamic-pituitary-adrenal dysregulation and inflammatory processes.

In one of the recent studies on biomarkers predictive of postpartum depression, the incidence of depression based on the EPDS decreased from the end of term (24%) to 2-3 days post-delivery (8%) to 4-6 weeks post-delivery (5%) [62]. After the effects of prenatal depression on postpartum depression at times 2 and 3, increased haematocrit in the third trimester was a significant biomarker of postpartum depression at time 3.

In a study on whether placental corticotropin-releasing hormone (the precursor of cortisol) mediated the association between prenatal family support and postpartum depression in 210 women, prenatal family support predicted fewer postpartum depression symptoms [63]. In contrast, increased placental corticotropin-releasing hormone predicted more depressive symptoms postpartum but also mediated the relationship between family support and postpartum depression.

Different timing of prenatal saliva cortisol was predictive of postpartum depression in a sample of 100 women [64]. Higher postpartum depression scores at 3 months occurred in women with lower cortisol levels when awakening during the first and second trimester, a lower average daily cortisol during the second trimester and a flatter diurnal cortisol pattern during the second and third trimester and at 3 months postpartum. These data are suggestive of chronic depression, although this many assays across pregnancy would not be cost-effective for screening.

In a simpler study from Sweden, 365 pregnant women completed the EPDS at 36 weeks gestation and again at 6 weeks postpartum and provided saliva samples for cortisol assays [65]. In a logistic regression model a positive association was shown between cortisol levels and postpartum depressive symptoms which remained significant after controlling for history of depression, partner support, breastfeeding, stressful life events and sleep problems as potential confounders.

In a more complex study on bidirectional psychoneuroimmune interactions during the early postpartum period, 152 women completed the EPDS and provided saliva samples during the third trimester and days 7 and 14 following birth [66]. In a multiple logistic regression model, family history of depression, day 14 cortisol and day 14 interleukin 8/10 ratios were significant predictors of postpartum depression. One unit increase in cortisol and the interleukin ratio

resulted in an approximately 2-fold increase in postpartum depression and correctly classified 84% of the women.

Reduced oxytocin has been researched more than other biomarkers for postpartum depression in this review of the recent literature. Although oxytocin typically has positive effects, it was noted to have negative effects when administered during childbirth labour in at least one study from France [67]. Another group of investigators followed the course of the natural production of oxytocin in 100 women during pregnancy (35 and 38 weeks gestation) and again at 2 days, 7 weeks and 6 months postpartum [68]. Oxytocin levels increased from the 38th week gestation to 2 days post-delivery in the non-depressed women, whereas they decreased in women with postpartum depression. Breastfeeding problems were also associated with postpartum depression which would not be surprising given that oxytocin levels may mediate the breastfeeding problems. Others have suggested that the co-occurrence of breastfeeding and postpartum depression may be mediated by abnormal oxytocin signalling [69]. In this sample of 52 pregnant women, those with postpartum depression symptoms showed elevated cortisol and lower oxytocin levels during breastfeeding. Based on a literature search of Pubmed, PsychINFO, Web of Science and Science Direct, 6 oxytocin studies were identified that included 620 pregnant women [70]. Oxytocin levels were assessed during pregnancy and after delivery, and higher oxytocin levels were associated with fewer postpartum depression symptoms.

High levels of testosterone have also been associated with postpartum depression based on the EPDS at 24-26 hours post-delivery in at least one study [71]. In the same study, estradiol and progesterone levels did not differentiate postpartum depressed from non-depressed a woman who was surprising given the frequently noted associations between testosterone, progesterone and estradiol. Testosterone levels predicted the development of postpartum depression with 79% sensitivity, 63% specificity, 68% positive and 74% negative predictive value with area under the curve being 0.71.

Other biochemical risk factors include elevated C-reactive protein and lower zinc levels assayed at the end of pregnancy that then predicted postpartum depression [72]. In a study by another group, however, zinc was not significantly related to EPDS scores, while magnesium was significantly inversely related to EPDS scores [73]. And, in a study by a third group, elevated C-reactive protein was again associated with postpartum depression, although the assays this time were conducted early in the postpartum period [74]. In this study another inflammatory biomarker, interleukin-6, was also associated with postpartum depression.

Leptin levels were predictive of postpartum depression measured by the EPDS in another study with a sensitivity of 89% and a specificity of 73% and area under the curve at 0.87 [75]. Brain-derived neurotrophic factor (BDNF) has also been studied as a predictor of postpartum depression [76]. In this study on 340 women seen at 3 months postpartum, serum BDNF levels were lower in the women with higher EPDS scores. The optimal cut off value of BDNF had a sensitivity of 83% and a specificity of 73% with the area under the curve at 0.81.

In a systematic review of research on bio-psychosocial risk factors for postpartum depression from 2000 to 2013, 214 publications on 151,651 women met inclusion criteria [77]. The biological and psychosocial literatures were distinct, and very few studies provided integrative analyses. The strongest biological factors were hypothalamic-pituitary-adrenal (HPAC) dysregulation, inflammatory processes and genetic vulnerabilities. The strongest psychosocial

predictors were severe life events, relationship quality and support from the partner and mother.

Although HPAC dysregulation and inflammatory processes as well as social support were predictor variables in the literature just reviewed, the genetic vulnerability factors were rarely found in the current literature. An earlier literature review on the genetics involved in postpartum depression suggested that genes typically related to major depression have also been related to postpartum depression including those involved in the metabolism of serotonin, brain-derived neurotrophic factor and tryptophan [78]. Methodologically speaking, this review is consistent with that of Yim, et al. [77], in finding a very distinct biological and psychosocial literature with very few integrative analyses.

The many developmental effects of postpartum depression on mothers, fathers and their offspring would alone argue for the development of intervention strategies. The countless risk factors that have been identified suggest that profiles of risk factors might be formulated to identify those needing intervention and interventions may be tailored to those risk profiles. So, for example, a depressed mother who has a history of child maltreatment may be referred to a psychodynamic therapy while a depressed mother with a low level of oxytocin may respond to intranasal oxytocin therapy.

## Intervention Studies

The intervention studies identified from this review can be grouped as follows: pharmacotherapy, cognitive behaviour therapy (including phone and internet delivery), interpersonal (including by phone), peer support by volunteers (including text messaging and telephone support), self-help on the internet, expressive writing, mother-infant interaction coaching, massage and intranasal oxytocin therapy. A demonstration of the need for treatment was shown in a study on 78 women who were diagnosed with depression in the first trimester of pregnancy and who were referred or not referred to a psychiatric centre [79]. The 29% of women who received treatment did not experience postpartum depression. In contrast, 92% of the women in the untreated group experienced postpartum depression.

## Pharmacotherapy

In a qualitative systematic review of randomized clinical trials comparing SSRIs to placebo and/or other treatments, six randomized clinical trials comprising 595 women met inclusion criteria [80]. The treatment comparison groups included psychodynamic therapy, cognitive behaviour therapy, a tricyclic antidepressant and a placebo group. In all studies higher response and remission rates were noted for those treated with SSRIs. Limitations of these randomized clinical trials were that no drug-free control groups were included, the women in the trials were not a representative sample, attrition was high and long-term efficacy and tolerability were assessed in only two trials.

In a Cochrane database review 6 trials with 596 participants were included from the UK, the US and Israel [81]. Meta-analyses were conducted on 4 studies comparing SSRIs with placebo. In two of these both the experimental and placebo groups also received psychotherapy. Women randomized to the SSRIs again had higher rates of response or remission. However, the studies were limited by the absence of no-drug control groups and missing adverse effects data as well as high rates of attrition leading to a risk for bias. Notably missing are data on breastfeeding inasmuch as that practice is typically the reason given for avoiding antidepressants.

## Cognitive Behaviour Therapy (CBT)

CBT has also been notably effective for women with postpartum depression. For example, in one study two groups of mothers were recruited at 2 days postpartum including one high risk group (high EPDS score) and one low risk group (low EPDS score) [82]. The high risk group went through CBT and the low risk group did not. At 12 months the low risk group who did not have CBT had higher EPDS scores.

In a comparison between cognitive behaviour therapy, sertraline (an SSRI) and sertraline combined with cognitive behaviour therapy, cognitive behaviour therapy was the more effective treatment when assessed at a 24-week follow-up [83]. These results are not only surprising but they also are inconsistent with those from several other studies, raising questions about the study's validity. Self-selection factors may have led to a confounding of group differences.

**Telephone-based CBT:** Has also been effective in at least one study from Hong Kong [84]. In that study, 397 women with a high EPDS score on the second day postpartum were randomly assigned to a telephone-based CBT or standard care group. At 6 weeks the CBT group had lower EPDS scores which were sustained at 6 months.

**Internet-based CBT:** Like telephone-based CBT has reduced postpartum depression. In this randomized controlled trial, women who were diagnosed with depression based on the Structured Clinical Interview for DSM-IV were assigned to an internet CBT treatment group or a treatment as usual group [85]. At the end of the 3 month period, 79% of the internet CBT group no longer met diagnostic criteria for depression as opposed to 18% of the treatment as usual group. These studies were limited to their comparisons with treatment as usual groups.

**Interpersonal therapy (IPT):** IPT, like CBT, has been effective with postpartum depression, although again most of the comparisons have been made with treatment as usual groups. In one study, for example, 205 pregnant women were randomized to either an interpersonal therapy group or a treatment as usual group [86]. At 6 months the overall depression rate in the interpersonal therapy group was lower (16%) than in the control group (31%). As the authors suggested, it is unclear if these results would generalize to a sample that was more heterogeneous on socio-economic, cultural and marital status. And, again the comparison was made with a treatment as usual group rather than a cohort or treatment comparison group.

In a telephone-administered interpersonal psychotherapy by nurse-midwives' study, the treatment group received up to eight 50-minute telephone sessions and the control group was referred to mental health professionals [87]. At eight and 12 weeks, depression was significantly lower among women in the telephone group. In a review on interpersonal psychotherapy effects on postpartum depression, four clinical trials met criteria including three trials with group interventions and one that required the presence of a partner [88]. The evidence from this review suggested that IPT given as a monotherapy or in combination with antidepressants can decrease postpartum depression and lengthen the time in remission.

In a qualitative review of therapies for preventing postpartum depression, eight RCTs on biological interventions were identified and 37 RCTs on psychological interventions [89]. Of those 45 studies, 20 showed positive effects of the intervention and 25 showed no effect. Among the biological studies the most effective treatments were antidepressants and nutrients and among the psychological studies

interpersonal therapy was the most effective. These studies, however, differed in their screening, sampling, measures and interventions, making these results difficult to interpret. In a meta-analysis on 14 psychological interventions, the effects of the different types of therapy did not differ (seven using cognitive behaviour therapy, two on interpersonal therapy, two on counselling and three on other interventions) [90]. All of the interventions resulted in reduced depression, lower stress and anxiety and improved relationships.

Peer support interventions. Social support by other mother volunteers and by health volunteers has also been effective. Telephone support from health volunteers, for example, in one study led to a greater decrease in depression than for a control group after 6 months [91]. Text message support has also been effective for reducing postpartum depression [92]. In this study, text messages were sent 4 times per week for 6 months. Even a fully-automated self-help internet intervention has lowered depression symptoms [93]. This intervention had greater effects on mothers with high versus low levels of depression symptoms. Although the results from these studies were positive, a narrative review of peer support intervention studies suggested mixed findings [94]. This conclusion was not surprising given that each of the 6 studies reviewed had different selection criteria for volunteers and different type interventions that varied in length, nature of support, frequency and mode of delivery (Table 3).

Intervention	Authors
SSRIs	De Crescenzo et al. [80], Molyneaux et al. [81]
Cognitive Behavior Therapy (CBT)	Carta et al. [82], Milgrom et al. [85]
Telephone-based CBT	Ngai et al. [84]
Internet-based CBT	Milgrom et al. [85]
Interpersonal therapy (IPT)	Zlotnick et al. [86], Miniati et al. [88]
Telephone-based IPT	Posmontier et al. [87]
<b>Peer support groups</b>	
Telephone support by Health volunteers	Shamshiri et al. [91]
Text messaging	Broom et al. [92]
Self-help internet	Barrera et al. [93]
<b>Mother-infant interactions</b>	
Perinatal Dyadic Psychotherapy	Goodman et al. [95]
Group therapy	De Camps-Meschino et al. [96]
Expressive writing	Blasio et al. [97]
Massage therapy	Choi et al. [98]
Oxytocin	Mah et al. [100], Mah [101]

**Table 3:** Postpartum depression interventions.

### Mother-Infant Interventions

Several studies have documented the negative impact of postpartum depression on mother-infant interactions [20]. Both individual and group therapies have been effective in facilitating mother-infant

interactions. One of the therapies, called Perinatal Dyadic Psychotherapy (PDP) was effective in a study in which 6-week-old infants were randomly assigned to PDP or usual care plus monitoring by phone [95]. The PDP was comprised of 8 home visits by nurses focused on supportive, relationship-based and developmentally-based infant-oriented components. Although depression significantly decreased, surprisingly the groups did not differ post-intervention or at a 3-month follow-up on postpartum depression or mother-infant interactions, suggesting that depression monitoring by phone was equally positive and more cost-effective.

Another research group assessed the effects of a group therapy on maternal-infant interactions [96]. They claimed to have developed this new therapy that they conducted for 12 weeks for infant's 6-12-months-old that effectively reduced postpartum depression. Unlike many other research groups, they also measured recruitment and retention rates, missed sessions and reasons for not participating.

Two other forms of therapy emerged from this literature search including expressive writing and massage therapy. In the expressive writing study, postpartum depressed women were randomized to either expressive writing or neutral writing conditions [97]. Three months later the depressive symptoms were lower in the women who performed the expressive writing task versus the neutral writing task, suggesting that this can be a low-cost intervention for postpartum depression. In the massage therapy study, foot reflexology was provided once a day for three days in Korea [98]. This protocol resulted not only in decreased depression for the massage group but also decreased urinary cortisol levels. It is not clear, however, whether this was a randomized controlled trial and the data were analysed separately by group rather than by repeated measures by group interaction ANOVAs.

In a review of 19 intervention studies targeting the mother-infant relationship, positive effects were noted on several infant and child behaviours including temperament and internalizing/externalizing behaviours [99]. However, as the authors noted, the measures across studies were so variable that it was difficult to compare the effect sizes of the different studies.

**Oxytocin:** Oxytocin has become a popular treatment of choice for postpartum depression. At least two studies on the use of oxytocin were identified in this recent literature. In one study within- subjects randomized controlled – blind assignments were made to assess the effects of intranasal oxytocin or placebo on mother-infant caregiving [100]. In the oxytocin condition the postpartum depressed mothers were more likely to rate infant crying more urgent and elected a harsher caregiving strategy in response to the cries. In contrast, the oxytocin did not affect the mother's interaction with her own infant. In a systematic review on the relationships between oxytocin, postpartum depression and parenting, the postpartum depressed mothers were noted to interact less sensitively with their infants [101]. The findings of this review suggested that oxytocin effects on postpartum depression were inconsistent with even some data suggesting that oxytocin had a negative effect on mood.

### Limitations and Future Directions

The recent literature on postpartum depression has focused primarily on assessing the validity and reliability of the EPDS (not reviewed here), and the risk factors and interventions for postpartum depression, as opposed to the earlier literature that was primarily focused on developmental consequences of postpartum depression.

The primary problem with the risk factor studies is that they have focused either on single risk factors such as early childhood maltreatment or low oxytocin levels in the case of the biochemical studies or they combine many risk factors and report the prevalence of those. It would seem that a multivariable – multivariate analysis approach would yield more information on the relative importance of the different risk factors. Regression, mediation, structural equations or profile analyses could hierarchize or at least profile the risk factors that could then supplement the EPDS for screening purposes. Another effective approach would be to have investigators follow meta-analyses guidelines for developing their RCT protocols. In that way multiple investigators would be using similar randomization strategies (which need to be more fully described) and assessment measures so that studies would be sufficiently standardized to yield more robust results in the meta-analyses. If that happened, there would be more than one percent of the studies in the literature that met inclusion criteria for those meta-analyses.

For the intervention studies, many of the samples were small which could conceivably result in false negative findings and the rejection of effective treatments. Others failed to adequately describe the randomization process and although many used randomized controlled trials, dropout rates were not addressed as well as retention rates, reasons for not participating and missed sessions, all of which would be important factors for assessing an intervention. These would also be necessary for replicating protocols. Further, methods to ensure treatment fidelity were typically not given. Variety of assessment measures has been compounded by heterogeneity of inclusion criteria. Participants in most of the studies have been recruited on the basis of the EPDS and only a few studies have used the Structured Clinical Interview for recruitment. Further, many of the participants have likely experienced the more serious condition of comorbid depression and anxiety, although anxiety and the comorbidity were rarely assessed. Other factors that were highly variable included the parity of the mother, the type, severity and timing of the postpartum depression as well as the age of the infant which would all seem to significantly impact the intervention process. In contrast, the samples have been homogeneous on marital/partner relationships, and many were also homogeneous on ethnicity and socioeconomic status, raising the question of generalizability of the data. Further, the treatment efforts have focused on intervention rather than prevention. Prevention programs need to be designed and women screened for these programs during both the prenatal and postpartum periods.

Finally, replications are needed. An inherent problem in our research and publication system is that unique findings are more likely to be published. Thus, investigators focus on unique variables, for example, the recent focus on oxytocin as both a risk factor and an intervention before having documented conclusive data on the older cortisol pet variable. Researchers are reluctant to replicate and funding agencies are less likely to fund and journals less likely to publish replications. This inherent problem affects the progress of this research, not unlike other bodies of research. Nonetheless, the size and extent of this recent research has contributed to the adoption of screening and the development of interventions by many that promise to reduce the problems associated with postpartum depression for parents, children and clinicians alike.

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