Key Topics in Perinatal Mental Health

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Preface

We are delighted to write this preface to *Key Topics in Perinatal Mental Health*, this multidisciplinary book on all things related to mothers' mental health edited together, friends and colleagues.

When we first discussed the idea of this book, we were immediately overwhelmed by the scale of representing the breadth and depth of themes in the broader perinatal mental health context: from clinical psychiatry to biology to cultural factors; from public health to pharmacovigilance to psychotherapy. We are so grateful to the many colleagues who have accepted our invitation to write a chapter for this book, allowing to represent such complexity.

Across more than 30 chapters, we read state-of-the-art discussions generated in societal and geographical contexts as varied as Italy, the United Kingdom, Spain and India.

We start with a diagnosis-based series of chapters that discuss all relevant mental disorders, from the management of established diagnoses in the context of the perinatal period (for example, depression, bipolar disorder and anxiety disorders) to perinatal-specific disorders and symptoms (for example, intrusive thoughts of infant-related harm, puerperal psychosis and mother–infant bonding disorders). We also have an important contribution on perinatal affective disorders in fathers, highlighting the importance on men's mental health in the perinatal period.

Having discussed the clinical disorders, we move into the sphere of prevention, screening and public health in general. We describe initiatives across the world, including specific experiences that cover aspects as diverse as teratology services and services for migrant women, and ranging from volunteer association to state-funded public services.

The final section describes the research landscape. Again, the diversity of topics and approaches is staggering: from biomarkers to domestic violence, from motherhood in adolescence to cancer and pregnancy. Not unexpectedly, we also discuss the implications of the COVID-19 pandemic in the perinatal period.

While this preface can only scratch the surface of such an exhaustive and comprehensive book, we want to emphasise the passion and the empathy that emanate from all contributions.

The passion that brings together clinicians, mental health practitioners and researchers from such a variety of backgrounds, united by the notion of helping not only a mother in difficulties but also her developing offspring, and thus contributing to improving mental health of the next generation.

And the compassion for some of the most vulnerable people in our society: women and children whose suffering does not originate in an individual vacuum but instead often represents the society's failure to look after those in the direst need.

Milan, Italy — Mauro Percudani
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Contents

Part I

Perinatal Psychopathology, Beyond Postpartum Depression

Depression in Pregnancy: Biological, Clinical, and Psychosocial Effects

1

Rebecca H. Bind, Kristi Sawyer, and Carmine Pariante

1.1 Introduction

Major Depressive Disorder (MDD) is a common psychiatric disorder that is one of the biggest contributors to disability worldwide [1]. It affects millions of people globally and can be recurrent and chronic [2]. The core symptoms of MDD can alter mood, affect, sleep, appetite, cognition, and psychomotor activity [3] and can lead to decreased quality of life, comorbid diseases, substance use, and burden on health-care services [2]. Furthermore, according to the Organisation for Economic Co-operation and Development, mental illness including depression costs the UK alone almost £100 billion every year.

MDD can occur at any point in life, including during a woman's perinatal period, that is, during and/or after pregnancy. When MDD is experienced during pregnancy, it is referred to as antenatal MDD. Antenatal MDD may occur as either a continuation of symptoms that began prior to conception or as an episode that specifically began during the pregnancy. It can occur both in women with and without a history of depression and affects up to 20% of pregnant women [4].

When MDD is experienced following childbirth, it is referred to as postnatal MDD. Postnatal MDD is thought to be the most frequently reported complication related to childbirth [5]. With regard to mental illness during the perinatal period, postnatal MDD has been much more widely studied than antenatal MDD and has been found to affect not only mother, but also her baby, and not only in the short term, but also potentially in the long term. Of note, though, is that a significant risk

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factor for postnatal MDD is antenatal MDD. Furthermore, it is thought that up to 39% of women with postnatal MDD experience a continuation of symptoms from the antenatal period [6], and thus it is important to consider the effects that antenatal depression may also have. This chapter will discuss the maternal and offspring biological, clinical, and psychosocial outcomes in the context of women who are depressed in pregnancy.

1.2 Background on Antenatal MDD

In order to understand the effects that antenatal MDD may have on both mothers and their offspring, it is first important to discuss the aetiology, epidemiology, classification and clinical features, and treatment options for women experiencing depression in pregnancy. These concepts will be discussed below.

1.2.1 Aetiology of Antenatal MDD

While the aetiology of MDD is still not fully disentangled, it is thought that it primarily occurs as a result of genotype, environmental stress [7], epigenetics, or an interaction between genes and environment [8]. Population-based twin studies have identified that genes are responsible for about 40% of depression, while the rest is likely due to environmental triggers [9]. Furthermore, with regard to heritability of depression, women are found to be more susceptible than men (42% of depression vs 29%, respectively) [10], suggesting there is a hormonal component and rendering the perinatal period sensitive.

With regard to environmental stress, it is thought that those who develop MDD in the face of environmental triggers are genetically predisposed to handle stress differently [7]. For example, some who develop MDD have overactive hypothalamic–pituitary–adrenal (HPA) axes [7], a hormonal pathway that is set in utero, and can be influenced by maternal cortisol activity during pregnancy [11]. Additionally, other pathophysiological mechanisms have been identified, including inflammation, vitamin D levels, and neurotrophic growth [12]. Finally, it is thought that epigenetic changes may contribute to risk for MDD as a result of environmental, hormonal, or stochastic factors leading to intergenerational predisposition for disease [8, 13].

While there is not a plethora of research investigating the specific aetiology of antenatal MDD, it is thought that a combination of social and biological factors may underpin the emergence of symptoms during a period when hormones are already rapidly changing [4]. Notable risk factors include a history of maternal childhood maltreatment, a history of MDD, low socio-economic status (SES), young age, lower education, and lack of social support [14]; and, furthermore, biological factors such as HPA axis changes and inflammation [11].

1.2.2 Epidemiology of Antenatal MDD

According to the World Health Organization (WHO), MDD is classified as the greatest contributor to disability globally, and affects upwards of 300 million people, or about 4.5% of the global population [1]. Additionally, it negatively impacts the individual not only on a psychological and physical level, but also on a financial and social level [15]. The greatest risk factors for depression have been identified as poverty, unemployment, childhood history of abuse, stressful life events, illness, and substance use [1]. Furthermore, MDD is often associated with morbidity and mortality [16]. Epidemiological studies indicate that MDD typically begins earlier in life and has a propensity to reoccur [15]. Moreover, twice as many women experience MDD as men, largely due to the fact that women go through hormonal changes at various points in life, particularly during the perinatal period [17].

In fact, up to 20% of women in high-income countries experience an episode of MDD during their antenatal period, with rates even higher in middle- and low-income countries [4]. Studies have been mixed as to which trimester poses the greatest risk for depression: Some have found that the first trimester has the highest prevalence [18], while others have found that the second and third trimesters have a higher prevalence [19]. Furthermore, women who experience depression during pregnancy are at heightened risk for the depression to continue into the postnatal period [4] and 20% of new mothers meet criteria for postnatal MDD [20].

1.2.3 Classification and Clinical Features of Perinatal MDD

The main two symptoms of MDD, classified by the *Diagnostic and Statistical Manual, Fifth Edition* (DSM-V) are depressed/irritable mood as well as decreased interest or pleasure in everyday activities [21]. Additionally, further symptoms may include changes in weight or appetite, sleep patterns, activity level, energy level, feelings about oneself including guilt or worthlessness, and concentration abilities. Furthermore, it has been found that women with higher depressive symptoms during pregnancy are less likely to engage in self-care and have poorer health and functionality during their pregnancies [22]. Finally, these changes may be accompanied by thoughts of, or plans for, suicide.

In order for a diagnosis of MDD to be made, five of the aforementioned symptoms, including the main two, must be met, and must have been present for most of the day, nearly every day, for at least a 2-week period. Furthermore, the symptoms must cause significant distress and/or impairment in everyday function. Finally, it is important to disentangle whether the symptoms are that of depression, or stem from something else, such as physical illness, substance use, or bereavement. An episode of MDD can be categorised as mild, moderate, or severe (with or without psychotic features), according to the person's severity of symptoms, and can occur as a single-episode MDD, recurrent episodes of MDD, or chronic MDD.

1.2.4 Treatment for Antenatal MDD

Treatment options for MDD include pharmacological, psychological, and physical interventions [23]. Pharmacological treatments are most commonly antidepressants [ADs] (selective serotonin reuptake inhibitors [SSRIs], serotonin noradrenalin reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], and monoamine oxidase inhibitors [MAOIs]) or mood stabilisers (lithium or sodium valproate). Psychological treatments recommended are cognitive behavioural therapy (CBT) or psychotherapy. And, finally, physical treatments utilised are electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), or vagal nerve stimulation (VNS). The recommended treatment for mild depression is typically psychological therapy, alongside exercise and lifestyle changes, while the gold standard for moderate to severe depression is antidepressant therapy. In treatment-resistant patients, the addition of mood stabilisers may be recommended, or a second AD. And finally, if all above fails, physical interventions may be recommended.

As women with antenatal MDD are pregnant and psychotropic medication can cross into the placenta, though, treatment of symptoms may not follow the same protocol as with MDD outside the pregnancy period. With regard to antidepressants, patients must decide with their healthcare practitioner whether the benefit of taking medication during pregnancy for symptom relief outweighs the cost of any potential effect on the developing foetus [24]. If women do not opt for antidepressant treatment, non-drug alternatives are available, including psychotherapy [25], exercise [26], and non-traditional medicine [27]; however, there is a paucity of literature to support whether these interventions are as effective as drug therapy. Surprisingly, one study identified that 86% of pregnant women with depression in their sample were not receiving any treatment for their symptoms [28], highlighting the need for more widespread mental health screening during the perinatal period.

1.2.5 Summary

Overall, MDD is a global health problem, and of particular concern with regard to the perinatal period and beyond. Despite the paucity of evidence about the aetiology of MDD during the perinatal period, the identification and treatment as soon as possible is of the utmost importance, given its potential to affect both mother and baby, both in the immediate as well as in the long term, as well as the social and economic burden placed upon society by lack of identification and treatment. As such, in this chapter we will discuss the biological, clinical, and psychosocial effects of depression in pregnancy on not only mothers, but on their offspring as well.

1.3 Biological Effects of Depression in Pregnancy

Depression across all life stages is associated with marked alterations in a number of biological systems, including the HPA axis, immune system, and other endocrine systems. This is also true of the perinatal period, which is further complicated by the profound biological changes associated with healthy pregnancy and the postpartum period. Pregnancy is a period in which biological communication between mother and baby is essential, therefore it is perhaps not surprising that biological changes in the mother are 'transmitted' to the developing foetus and can be measured in the offspring postnatally. This section reviews evidence for such biological changes in both the mother and offspring in the context of maternal perinatal depression.

1.3.1 Effects on the Mother

The biological aetiology of depression during pregnancy is complex and displays considerable heterogeneity. This may, in part, be due to the use of antidepressant medications during pregnancy, which may mitigate some of the biological changes associated with antenatal depression.

1.3.1.1 In Pregnancy

One of the most well-studied biological systems in the context of depression, the hypothalamic–pituitary–adrenal (HPA) axis, has shown inconsistent trends in association with antenatal depression. Indeed, a systematic review [29] reported that only half of studies found higher cortisol levels in those experiencing antenatal depression, when compared with pregnant controls, while a handful of studies reported the opposite effect. A further review concluded that the majority of papers do not show an association between antenatal depression and cortisol levels [30]; however, of those that do, differences were most often found in the second and third trimesters. When investigating diurnal cortisol levels, the most common pattern found, where there is one, is that women suffering antenatal depression show a blunted cortisol awakening response, but higher overall levels throughout the day, which remain elevated in the evening [11, 31, 32].

More recently, a role for the maternal immune system has been suggested. Studies often find that, when compared with healthy pregnant women, women suffering antenatal depression show higher levels of peripheral cytokines such as interleukins-6 and -10, tumour necrosis factor alpha and vascular endothelial growth factor [11, 33]. Furthermore, women reporting higher levels of depressive symptoms may also show an exaggerated inflammatory responses to the immune challenge of vaccination [34].

1.3.1.2 In the Postpartum

Depression in the postpartum is often a continuation of antenatal symptoms; however specific biological predictors of postnatal mood have also been proposed. The drastic changes in sex hormones post-birth are often associated with the precipitation of mood symptoms [35]. More specifically, it seems that rather than having differing sex hormone levels, women at greater risk of postnatal depression show enhanced sensitivity to normal pregnancy–related fluctuations in sex hormones levels. Research has shown that if non-pregnant, euthymic women with a history of postnatal depression are administered oestradiol and progesterone that mimic pregnancy levels, then these hormones are withdrawn at similar magnitudes to that experienced after childbirth, 60% of those with a history of postnatal depression develop mood symptoms, while none without a history of postnatal depression experience such symptoms [36].

Oxytocin, the neuropeptide associated with childbirth, maternal attachment, and lactation [37], has also been shown to be associated with postnatal depressive symptoms. Interestingly, antenatal depressive symptoms, although not associated with concurrent oxytocin levels, were negatively associated with oxytocin levels 3 months post-birth [38]. Furthermore, lower oxytocin levels during pregnancy are associated with the development of postnatal depression in the early postnatal period [39]. This relationship between oxytocin levels and depressive symptoms is particularly important, as antenatal oxytocin levels are associated with maternal care [40], and may therefore be associated with the quality of the mother–child relationship formed. Indeed, there is some evidence that mother–child synchrony in oxytocin levels exists post-birth [41, 42], and may underpin successful bonding and attachment.

1.3.2 Effects on the Offspring

The ‘Fetal Origins of Mental Health’ discussed by O’Donnell and Meaney in their ‘Developmental Origins of Health and Disease Hypothesis’ [43] suggests that the quality of foetal growth and development, as well as the in utero environment in which a foetus develops may predict an offspring’s risk of non-communicable chronic illnesses, including mental health disorders, by programming the growing foetus in a manner which predisposes to later psychopathology [44]. As such, the effect of antenatal depression on the foetus in utero is of particular interest in the context of the intergenerational transmission of psychopathology, in which the offspring of antenatally depressed mothers are more likely to develop mental health problems themselves later in life [45].

1.3.2.1 HPA Axis

The most well-studied foetal programming mechanism in the context of mental health disorders is the HPA axis. It is likely that the foetuses of antenatally depressed

mothers are exposed to elevated cortisol levels in utero, both because, as discussed above, maternal circulating cortisol levels are higher, but also due to the downregulation of the enzyme 11-beta-hydroxysteroid dehydrogenase type 2 in the placenta, resulting in a reduced metabolism of cortisol into its less active form, cortisone, and thus more active cortisol reaching the developing foetus [46]. Indeed, various studies have reported associations between maternal cortisol levels during pregnancy and offspring neonatal cortisol levels and cortisol reactivity to stressors [47–52]. This association has been shown to persist into infancy [11, 53], and perhaps even into childhood, although the literature is mixed at this stage [54–56]. Taken with the associations reported between HPA axis functioning and mental health disorders, this could be an important mechanism to target in order to improve offspring mental health outcomes.

1.3.2.2 Brain Development

Antenatal depression has been associated with slower foetal growth, particularly of the head [57, 58]. This is important, given the suggestion that foetal head circumference can be used as a proxy for brain size, and therefore development [59]. Indeed, there is some evidence that maternal antenatal depression may influence foetal brain development. For example, antenatal depressive symptoms have been associated with neonatal right hippocampal morphology [60] and right amygdala volume [61]. Interestingly, in infants born to antenatally depressed mothers, a pattern of greater functional connectivity of the amygdala was observed, which was consistent with patterns observed in adolescents and adults with major depressive disorder [62]. Finally, in childhood, evidence of sex-specific effects has been reported, such that antenatal depressive symptoms were associated with larger volume and functional connectivity of the amygdala in girls, but not in boys [63, 64].

1.3.3 Section Summary

Maternal depression in the perinatal period is often associated with alterations in cortisol levels and immune functioning, although results show some inconsistency. Furthermore, women experiencing depression show altered functioning and sensitivity of the oxytocin and reproductive hormone systems, which are particularly relevant in the postpartum period. These alterations, along with others, both biological and psychosocial, are likely to underlie alterations observed in the offspring of depressed mothers. From a biological viewpoint, these include alterations in the HPA axis and in physical growth and brain development. It is important that these are studied in further detail, including with reference to sex-specific effects, in order that the chain of transmission of biological risk factors for mental health disorders from mother to child can be broken.

1.4 Clinical Effects of Depression in Pregnancy

Depression in pregnancy carries clinical implications not just for mothers, but also for their babies: Women who experience antenatal depression are at risk to have a continuation of their depression beyond pregnancy, potentially creating long-lasting difficulties with mental health and increased need for clinical and health services. Furthermore, research suggests that offspring of antenatally depressed women are at risk to experience mental health difficulties themselves throughout the course of their lives. This section will discuss the literature on the clinical implications of depression in pregnancy on both mothers and their offspring.

1.4.1 Effects on Mother

Studies find that women who are depressed in pregnancy are at greater risk for subsequent depressive episodes: It is thought that up to 39% of women with postnatal MDD experience a continuation of symptoms from the antenatal period [6], and, furthermore, that 25% of mothers who experience antenatal depression will go on to experience MDD beyond their infant's first year of life [20]. Finally, those who experience MDD during the perinatal period are much more likely to experience subsequent depressive episodes across the first 5 years of their children's lives [65, 66]. Unfortunately, one grave consequence of perinatal MDD is suicide, and it is in fact found to be the leading cause of maternal death in the postnatal period [67].

It is thus imperative to identify and treat maternal antenatal depression, as it can profoundly impact both mother and developing child. As mentioned above, women who do not receive treatment for their mood are at risk of entering into a chronic depressive state [68], which has deleterious effects on not only their mental health, but also on physical health.

1.4.2 Effects on Offspring

With regard to the developing infant, research has begun to identify effects of antenatal MDD on offspring at many stages of development. For example, a few studies have found that neonates born to mothers who were depressed in pregnancy had less optimal neonatal behaviour [11, 69]. Furthermore, as infants exposed to antenatal MDD develop into children and adolescents, they are at greater risk for psychopathology, including depression [70] and behavioural problems [71]. And finally, when the reach adulthood, they continue to be at greater risk for psychopathology [72].

Increasing attention has been given recently to the possibility for mothers who experience depression antenatally to transmit this vulnerability during pregnancy, thereby rendering their offspring susceptible to developing psychopathology themselves. While much of the literature on the effects of antenatal MDD on offspring

mental health previously focused on psychopathology emergence in adolescence through to adulthood, and have assessed maternal depression retrospectively, recent literature has investigated psychopathology earlier on, in childhood.

In a recent study, Barker et al. [73] reported that the presence of antenatal depressive symptoms in mothers was associated with an increased likelihood for externalising problems, encompassing conduct, and oppositional disorders as well as attention-deficit hyperactivity disorder in their children. Interestingly, the authors also found that antenatal anxiety symptoms were associated with internalising problems, including anxiety and depression, indicating that different types of psychopathology in pregnancy may manifest differently in offspring. And, furthermore, they found sex differences, whereby girls of depressed mothers were more likely to develop internalising disorders.

In a subsequent study, Plant et al. [74] found a significant association between maternal childhood maltreatment (CM) and child psychopathology—both internalising and externalising disorders—at 10 years which persisted to 13 years, and was directly mediated by antenatal MDD, and further compounded by postnatal MDD. The findings of this study are important, as they underline the importance of maternal CM in the relationship between antenatal MDD and child mental health problems. The authors posited that their findings are indicative of a pathway, whereby a mother who has been maltreated in her childhood is at increased susceptibility to becoming depressed in pregnancy, and through foetal programming effects, due to her own HPA axis dysregulation, may induce HPA axis changes in her foetus, rendering her offspring vulnerable to becoming emotionally labile due to a maladaptive stress response [75].

Many studies have identified an association between antenatal depression and offspring psychopathology all the way through to adulthood [70, 72, 76]. These findings indicate that the effects of antenatal depression on offspring outcomes are long lasting, stressing the importance of intervention during pregnancy in order to prevent ongoing, enduring mental health problems in offspring. Additionally, it is important to note that many of the studies that have examined the relationship between antenatal MDD and offspring psychopathology have found that the intergenerational transmission of psychopathology is in fact present independently of postnatal MDD, and thus antenatal symptomology may carry biological consequences over and above the effects of the postnatal environment.

1.4.2.1 Biological Mechanisms Underpinning Intergenerational Transmission of Psychopathology

In a review that summarised literature on the relationship between maternal antenatal stress/depression and child psychopathology, the authors identified the most likely mechanistic candidates involved [77]: Firstly, they discussed the maternal HPA axis as one possibility; as mentioned above, it believed that depression during pregnancy elevates circulating cortisol levels, and given that cortisol can cross the placental barrier, elevated cortisol levels in the mother passes into the developing

foetus and impacts foetal development [78]. One consequence of heightened maternal cortisol during pregnancy is increased offspring cortisol in the postnatal period [11], and thus a dysregulated stress response system may predispose offspring to future victimisation and psychopathology.

Another putative mechanism they identified is changes in uterine blood flow: Stress during pregnancy activates adrenaline hormones, which can induce constriction of blood vessels and thereby reduce oxygen to the foetus, potentially leading to neurodevelopmental problems and subsequent psychopathology in offspring [79]. Furthermore, studies have identified that psychiatric problems during pregnancy are associated with altered foetal behaviour, possibly due to sympathetic nervous system activation [80]. Finally, another recognised mechanism is inflammation as a result of stress during pregnancy: Animal studies have found that inflammation during pregnancy is associated with altered foetal neurodevelopment, thus increasing vulnerability to psychopathology later in life [77].

In a subsequent review, Sawyer et al. [45] identified that genetics also plays a large role in the intergenerational transmission of psychopathology, given that the heritability of MDD is 40% in women and 30% in men [10], and thus genetic predisposition cannot be discounted as a possible mechanism. However, one study attempted to disentangle whether this transmission is more due to genetic profiling or to foetal environment exposure, and followed women who had gone through in vitro fertilisation and become pregnant with a child that they were either related or unrelated to [81]. Interestingly, the authors found differences in heritability, whereby offspring, both related and unrelated, to mothers stressed in pregnancy were more likely to develop internalising disorders, while only related offspring to stressed mothers were more likely to develop behavioural disorders, suggesting that different disorders may have different aetiologies.

1.4.3 Section Summary

Maternal depression during pregnancy puts women at great risk of continuing to remain unwell into the postnatal period and beyond into their children's early years unless they are identified and treated. Furthermore, offspring of antenatally depressed mothers are more likely to develop psychopathology themselves, beginning as early as childhood through adulthood.

1.5 Psychosocial Effects of Depression in Pregnancy

Antenatal depression has psychosocial implications on both mothers and their infants. Mothers experiencing depression in pregnancy may experience difficulties with self-care, relationships, stress, and coping. Furthermore, women are at risk for difficulties interacting with their infants in the postpartum period. This section will discuss the literature on the psychosocial effects of depression in pregnancy on mothers and their infants.

1.5.1 Effects on Mother

Women experiencing antenatal depression are less likely to feel supported, both socially and medically [82]. With regard to medical care, depressed women typically do not access adequate health care services and are also less likely to engage in proper self-care. This unfortunately puts expectant mothers and their babies at risk for adverse birth outcomes, and thus it is important to identify women who are not taking adequate self-care. Furthermore, antenatally depressed women report feeling a lack of social support from family, friends, and partners, and subsequently experience low self-esteem [14]. It is thought that lack of social support is associated with depression as women are without adequate practical and emotional support, thereby hindering their abilities to cope and lowering their threshold for stress associated with parenting [83]. Moreover, pregnant women who perceive low social support are less likely to engage in self-care, highlighting the importance of partner and peer support for pregnant women's emotional and physical well-being.

Studies show that antenatal depression not only impacts the mother who is suffering, but also her network around her. For example, research has found that partners of women experiencing depression are profoundly impacted [84], and in fact are at risk of becoming depressed themselves [85]. Furthermore, presence of maternal depression may inadvertently place added pressure on her partner to compensate with regard to home and childcare duties [86]. And, moreover, studies have found strong correlations between maternal depression and marital conflict [87], and that this discord may in fact be one mediator in the relationship between maternal depression and adverse outcomes in children [88].

One of the most commonly identified psychosocial effects of antenatal depression is difficulty coping with stress. In fact, women who are depressed during pregnancy are more likely to experience parenting stress once giving birth [14]. More specifically, it has been found that depression during the third trimester is associated with increased parenting stress at both 3 months and 6 months postpartum, and that usage of antidepressants in pregnancy does not buffer against this effect [89]. One suggested mechanism behind this finding is that via foetal programming, antenatal depression is associated with increased infant difficult behaviour, which may in turn drive maternal stress. Studies suggest that increased parenting stress can strain the mother–offspring relationship [90], which will be discussed below.

1.5.2 Effects on the Dyad

As mentioned above, women who are depressed in pregnancy are at risk of increased stress, which may affect their developing relationship with their offspring. As such, studies have found that women who are depressed during their pregnancies are at risk to have greater difficulty in bonding with their unborn babies [91]. For example, women who exhibit heightened depressive symptoms during pregnancy are also

more likely to ruminate and excessively worry, two phenomena that are predictive of difficulties with foetal bonding [92], that is, the act of a mother emotionally connecting with her unborn baby and preparing for motherhood [93]. Furthermore, additional studies have found that women who are clinically depressed in pregnancy display reduced maternal–foetal attachment in the second and third trimesters [94], measured as 'a woman's own reflections on pregnancy and motherhood, her enjoyment of pregnancy, excitement about motherhood, and hopefulness for the future.' It is thus unsurprising that depression, which manifests as withdrawal and disconnectedness, can render a woman unable to connect with, and care for, her foetus.

It is important to identify difficulties in foetal attachment, as it is a known predictor of maternal sensitivity and the quality of the mother–infant relationship in the postpartum period [95], and thus it is thought that women who are antenatally depressed and are having difficulties bonding with their unborn baby will be at heightened risk for suboptimal mother–infant interactions postnatally and reduced sensitivity. In fact, studies confirm that antenatal depression is associated with disruptions in the mother–infant relationship in the postpartum, independently of postnatal depression. In one study, mother–infant interaction was assessed in the context of both antenatal and postnatal depression, in an effort to elucidate whether there was a difference in dyadic interaction based on timing of maternal symptoms [96]. The authors found that women who exhibited high levels of depression during mid pregnancy, but not postnatally, were less responsive toward their infants than women with no antenatal depression. Interestingly, they also found that women who did not experience antenatal depression and who experienced only postnatal depression early in the postpartum, did not have altered responsiveness, but that women whose postnatal depression persisted into the late postpartum did exhibit less responsiveness. Overall, this study's findings are important, as they show that mother–infant interaction is affected by antenatal depression independently of postnatal depression, and that postnatal depression only affects the interaction if its occurrence coincides with the timing of the interaction.

Another study investigated the continuity of maternal sensitivity across the first 2 years of life [97] and found that 80% of mothers who scored in the low range of sensitivity throughout the 2 years, had reported symptoms of antenatal depression. Indeed studies have shown that the association between postnatal depression and less optimal mother–infant interaction may be attributable to a continuation of impaired foetal attachment (that is, in pregnancy) into the postnatal period [98], and that mothers' unresponsiveness may actually begin during pregnancy, not postnatally [96], and furthermore, that foetal attachment has been found to be highly predictive of postnatal bonding [98, 99]. As the early mother–infant interaction is highly predictive of infant attachment status after 12 months [100], and early attachment has long been associated with subsequent offspring outcomes [101], it is thus important to identify mothers at risk of difficulties in their interactions and provide support and guidance.

1.5.3 Section Summary

Women who are depressed during pregnancy are less likely to feel emotionally and physically supported, engage in adequate self-care, and are more likely to experience relationship difficulties and stress. Furthermore, antenatal depression puts women at risk of not properly bonding with their foetus, and in turn creates difficulties in establishing an optimal relationship with their babies in the postpartum.

1.6 Conclusion

Perinatal mental health problems are one of the leading causes of maternal mortality, and, as mentioned above, suicide is the leading cause of death for women suffering from mental illness during the perinatal period [67]; however, with proper identification and treatment, symptoms can be alleviated and deleterious outcomes for both mother and infant can be prevented. As of 2014, it was estimated that perinatal mental illness costs the UK at least £8 billion per each year's cohort of births, with 72% of these costs allocated towards the children and 28% towards the mothers. With regard to perinatal depression specifically, each dyad is thought to cost a total of £74,000. Additionally, it has been found that partners of women experiencing perinatal depression are at risk of becoming unwell themselves [102], making the relationship more likely to end. Because of the great cost burden on society stemming from mental illness during the perinatal period, it has become imperative to better identify and treat women as soon as possible, including more widespread mental health assessments, mother and baby units, and parent–infant interventions. Indeed, there has been an incredible public interest in perinatal mental health, with women voluntarily sharing the experience of their suffering in public outlets [103].

Economically, it was projected in 2017 that untreated mood and anxiety disorders among new mothers will cost the US$14.2 billion for all births in that year alone [104]. This figure estimated the cost burden of not treating a mother's mental health, spanning from pregnancy until her child reaches the age of 5, and anticipated that roughly $7.5 billion of the costs for mothers and their babies born in 2017 would occur in the perinatal period, while the remaining $6.7 billion of the costs would occur in the proceeding 4 years of the child's life. Taken all together, maternal mental health should be treated with high priority, as it not only impacts a mother's biological, clinical, and psychosocial outcomes, but it impacts those of her baby as well.

References

1. WHO. Depression and other common mental disorders: global health estimates. Geneva: World Health Organization; 2017.
2. Culpepper L. Understanding the burden of depression. J Clin Psychiatry. 2011;72 https://doi.org/10.4088/JCP.10126tx1c.

3. Fava M, Kendler KS. Major depressive disorder. Neuron. 2000;28:335–41. https://doi.org/10.1016/S0896-6273(00)00112-4.
4. Biaggi A, Conroy S, Pawlby S, Pariante CM. Identifying the women at risk of antenatal anxiety and depression: a systematic review. J Affect Disord. 2016;191:62–77. https://doi.org/10.1016/j.jad.2015.11.014.
5. Wisner KL, Parry BL, Piontek CM. Postpartum depression. N Engl J Med. 2002;347(3):194–9.
6. Underwood L, Waldie K, D'Souza S, Peterson ER, Morton S. A review of longitudinal studies on antenatal and postnatal depression. Arch Womens Ment Health. 2016;19:711–20. https://doi.org/10.1007/s00737-016-0629-1.
7. Goldberg D. The aetiology of depression. Psychol Med. 2006;36(10):1341–7. https://doi.org/10.1017/S0033291706007665.
8. Mill J, Petronis A. Molecular studies of major depressive disorder: the epigenetic perspective. Mol Psychiatry. 2007;12:799–814. https://doi.org/10.1038/sj.mp.4001992.
9. Kendler KS, Prescott CA. A population-based twin study of lifetime major depression in men and women. Arch Gen Psychiatry. 1999;56(1):39–44. https://doi.org/10.1001/archpsyc.56.1.39.
10. Kendler KS, Gatz M, Gardner CO, Pedersen NL. A Swedish national twin study of lifetime major depression. Am J Psychiatr. 2006;163(1):109–14. https://doi.org/10.1176/appi.ajp.163.1.109.
11. Osborne S, Biaggi A, Chua TE, Du Preez A, Hazelgrove K, Nikkheslat N, et al. Antenatal depression programs cortisol stress reactivity in offspring through increased maternal inflammation and cortisol in pregnancy: the psychiatry research and motherhood - depression (PRAM-D) study. Psychoneuroendocrinology. 2018;98:211–21. https://doi.org/10.1016/j.psyneuen.2018.06.017.
12. Verduijn J, Milaneschi Y, Schoevers RA, Van Hemert AM, Beekman ATF, Penninx BWJH. Pathophysiology of major depressive disorder: mechanisms involved in etiology are not associated with clinical progression. Transl Psychiatry. 2015;5(9):e649. https://doi.org/10.1038/tp.2015.137.
13. Nestler EJ. Epigenetic mechanisms of depression. JAMA Psychiatry. 2014;71:454–6. https://doi.org/10.1001/jamapsychiatry.2013.4291.
14. Leigh B, Milgrom J. Risk factors for antenatal depression, postnatal depression and parenting stress. BMC Psychiatry. 2008;8(1):24. https://doi.org/10.1186/1471-244X-8-24.
15. McKeever A, Agius M, Mohr P. A review of the epidemiology of major depressive disorder and of its consequences for society and the individual. Psychiatr Danub. 2017;29(Suppl 3):222–31.
16. Hasin DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of major depressive disorder: results from the national epidemiologic survey on alcoholism and related conditions. Arch Gen Psychiatry. 2005;62(10):1097–106.
17. Desai HD, Jann MW. Women's health series major depression in women: A review of the literature. J Am Pharmac Assoc (1996). 2000;40(4):525–37.
18. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol. 2005;106(5):1071–83.
19. Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR. Prevalence of depression during pregnancy: systematic review. Obstet Gynecol. 2004;103(4):698–709.
20. Falana SD, Carrington JM. Postpartum depression: are you listening? Nurs Clin N Am. 2019;54:561–7. https://doi.org/10.1016/j.cnur.2019.07.006.
21. Association, A. P. (2013). Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub.
22. Orr ST, Blazer DG, James SA, Reiter JP. Depressive symptoms and indicators of maternal health status during pregnancy. J Women's Health. 2007;16(4):535–42. https://doi.org/10.1089/jwh.2006.0116.
23. Taylor DM, Barnes TRE, Young AH. The Maudsley prescribing guidelines in psychiatry. John Wiley & Sons; 2018.

24. Koren G, Nordeng H. Antidepressant use during pregnancy: the benefit-risk ratio. Am J Obstet Gynecol. 2012;207:157–63. https://doi.org/10.1016/j.ajog.2012.02.009.
25. Dennis C-L, Ross LE, Grigoriadis S. Psychosocial and psychological interventions for treating antenatal depression. Cochrane Database Syst Rev. 2007; https://doi.org/10.1002/14651858.CD006309.pub2.
26. Daley A, Foster L, Long G, Palmer C, Robinson O, Walmsley H, Ward R. The effectiveness of exercise for the prevention and treatment of antenatal depression: systematic review with meta-analysis. BJOG Int J Obstet Gynaecol. 2015;122(1):57–62. https://doi.org/10.1111/1471-0528.12909.
27. Dennis C-L, Dowswell T. Interventions (other than pharmacological, psychosocial or psychological) for treating antenatal depression. Cochrane Database Syst Rev. 2013; https://doi.org/10.1002/14651858.CD006795.pub3.
28. Marcus SM, Flynn HA, Blow FC, Barry KL. Depressive symptoms among pregnant women screened in obstetrics settings. J Women's Health. 2003;12(4):373–80.
29. Seth S, Lewis AJ, Galbally M. Perinatal maternal depression and cortisol function in pregnancy and the postpartum period: a systematic literature review. BMC Pregnancy Childbirth. 2016;16(1):1–9. https://doi.org/10.1186/s12884-016-0915-y.
30. Orta OR, Gelaye B, Bain PA, Williams MA. The association between maternal cortisol and depression during pregnancy, a systematic review. Arch Womens Ment Health. 2018;21(1):43–53. https://doi.org/10.1007/s00737-017-0777-y.
31. Nazzari S, Fearon P, Rice F, Ciceri F, Molteni M, Frigerio A. The biological underpinnings of perinatal depressive symptoms: A multi-systems approach. J Affect Disord. 2020;274:1004–12. https://doi.org/10.1016/j.jad.2020.05.023.
32. O'Connor TG, Tang W, Gilchrist MA, Moynihan JA, Pressman EK, Blackmore ER. Diurnal cortisol patterns and psychiatric symptoms in pregnancy: short-term longitudinal study. Biol Psychol. 2014b;96(1):35–41. https://doi.org/10.1016/j.biopsycho.2013.11.002.
33. Azar R, Mercer D. Mild depressive symptoms are associated with elevated C-reactive protein and proinflammatory cytokine levels during early to midgestation: a prospective pilot study. J Women's Health. 2013;22(4):385–9. https://doi.org/10.1089/jwh.2012.3785.
34. Christian LM, Franco A, Iams JD, Sheridan J, Glaser R. Depressive symptoms predict exaggerated inflammatory responses to an in vivo immune challenge among pregnant women. Brain Behav Immun. 2010;24:49–53.
35. Bloch M, Daly RC, Rubinow DR. Endocrine factors in the etiology of postpartum depression. Compr Psychiatry. 2003;44(3):234–46. https://doi.org/10.1016/S0010-440X(03)00034-8.
36. Bloch M, Schmidt PJ, Danaceau M, Murphy J, Nieman L, Rubinow DR. Effects of gonadal steroids in women with a history of postpartum depression. Am J Psychiatr. 2000;157(6):924–30. https://doi.org/10.1176/appi.ajp.157.6.924.
37. Alves E, Fielder A, Ghabriel N, Sawyer M, Buisman-Pijlman FTA. Early social environment affects the endogenous oxytocin system: a review and future directions. Front Endocrinol. 2015;6:32. https://doi.org/10.3389/fendo.2015.00032.
38. Eapen V, Dadds M, Barnett B, Kohlhoff J, Khan F, Radom N, Silove DM. Separation anxiety, attachment and inter-personal representations: disentangling the role of oxytocin in the perinatal period. PLoS One. 2014;9(9):e107745. https://doi.org/10.1371/journal.pone.0107745.
39. Skrundz M, Bolten M, Nast I, Hellhammer DH, Meinlschmidt G. Plasma oxytocin concentration during pregnancy is associated with development of postpartum depression. Neuropsychopharmacology. 2011;36(9):1886–93. https://doi.org/10.1038/npp.2011.74.
40. Kim S, Fonagy P, Koos O, Dorsett K, Strathearn L. Maternal oxytocin response predicts mother-to-infant gaze. Brain Res. 2014;1580:133–42. https://doi.org/10.1016/j.brainres.2013.10.050.

41. Feldman R, Gordon I, Influs M, Gutbir T, Ebstein RP. Parental oxytocin and Early caregiving jointly shape children's oxytocin response and social reciprocity. Neuropsychopharmacology. 2013;38(7):1154–62. https://doi.org/10.1038/npp.2013.22.
42. Pratt M, Apter-Levi Y, Vakart A, Feldman M, Fishman R, Feldman T, et al. Maternal depression and child oxytocin response; moderation by maternal oxytocin and relational behavior. Depress Anxiety. 2015;32(9):635–46. https://doi.org/10.1002/da.22392.
43. O'Donnell KJ, Meaney MJ. Fetal origins of mental health: the developmental origins of health and disease hypothesis. Am J Psychiatr. 2017;174(4):319–28. https://doi.org/10.1176/appi.ajp.2016.16020138.
44. Entringer S, Buss C, Wadhwa PD. Prenatal stress, development, health and disease risk: A psychobiological perspective-2015 Curt Richter award paper. Psychoneuroendocrinology. 2015;62:366–75. https://doi.org/10.1016/j.psyneuen.2015.08.019.
45. Sawyer KM, Zunszain PA, Dazzan P, Pariante CM. Intergenerational transmission of depression: clinical observations and molecular mechanisms. Mol Psychiatry. 2018;1 https://doi.org/10.1038/s41380-018-0265-4.
46. Seth S, Lewis AJ, Saffery R, Lappas M, Galbally M. Maternal prenatal mental health and placental 11β-HSD2 gene expression: initial findings from the mercy pregnancy and emotional wellbeing study. Int J Mol Sci. 2015;16(11):27482–96. https://doi.org/10.3390/ijms161126034.
47. Davis EP, Glynn LM, Waffarn F, Sandman CA. Prenatal maternal stress programs infant stress regulation. J Child Psychol Psychiatry Allied Discip. 2011;52(2):119–29. https://doi.org/10.1111/j.1469-7610.2010.02314.x.
48. Diego MA, Field T, Hernandez-Reif M, Cullen C, Schanberg S, Kuhn C. Prepartum, postpartum, and chronic depression effects on newborns. Psychiatry. 2004;67(1):63–80. https://doi.org/10.1521/psyc.67.1.63.31251.
49. Field T, Diego M, Dieter J, Hernandez-Reif M, Schanberg S, Kuhn C, et al. Prenatal depression effects on the fetus and the newborn. Infant Behav Dev. 2004a;27(2):216–29. https://doi.org/10.1016/J.INFBEH.2003.09.010.
50. Lundy BL, Jones NA, Field T, Nearing G, Davalos M, Pietro PA, et al. Prenatal depression effects on neonates. Infant Behav Dev. 1999;22(1):119–29. https://doi.org/10.1016/S0163-6383(99)80009-5.
51. Nazzari S, Fearon P, Rice F, Dottori N, Ciceri F, Molteni M, Frigerio A. Beyond the HPA-axis: exploring maternal prenatal influences on birth outcomes and stress reactivity. Psychoneuroendocrinology. 2019;101:253–62. https://doi.org/10.1016/j.psyneuen.2018.11.018.
52. Romero-Gonzalez B, Caparros-Gonzalez RA, Gonzalez-Perez R, Delgado-Puertas P, Peralta-Ramirez MI. Newborn infants' hair cortisol levels reflect chronic maternal stress during pregnancy. PLoS One. 2018;13(7) https://doi.org/10.1371/journal.pone.0200279.
53. Fernandes M, Stein A, Srinivasan K, Menezes G, Ramchandani PG. Foetal exposure to maternal depression predicts cortisol responses in infants: findings from rural South India. Child Care Health Dev. 2015;41(5):677–86. https://doi.org/10.1111/cch.12186.
54. Laurent HK, Leve LD, Neiderhiser JM, Natsuaki MN, Shaw DS, Harold GT, Reiss D. Effects of prenatal and postnatal parent depressive symptoms on adopted child HPA regulation: independent and moderated influences. Dev Psychol. 2013;49(5):876–86. https://doi.org/10.1037/a0028800.
55. Stonawski V, Frey S, Golub Y, Rohleder N, Kriebel J, Goecke TW, et al. Associations of prenatal depressive symptoms with DNA methylation of HPA axis-related genes and diurnal cortisol profiles in primary school-aged children. Dev Psychopathol. 2019;31(2):419–31. https://doi.org/10.1017/S0954579418000056.
56. Swales DA, Winiarski DA, Smith AK, Stowe ZN, Newport DJ, Brennan PA. Maternal depression and cortisol in pregnancy predict offspring emotional reactivity in the preschool period. Dev Psychobiol. 2018;60(5):557–66. https://doi.org/10.1002/dev.21631.

57. El Marroun H, Jaddoe VWV, Hudziak JJ, Roza SJ, Steegers EAP, Hofman A, et al. Maternal use of selective serotonin reuptake inhibitors, fetal growth, and risk of adverse birth outcomes. Arch Gen Psychiatry. 2012;69(7):706–14. https://doi.org/10.1001/archgenpsychiatry.2011.2333.
58. Henrichs J, Schenk JJ, Roza SJ, Van Den Berg MP, Schmidt HG, Steegers EAP, et al. Maternal psychological distress and fetal growth trajectories: the generation R study. Psychol Med. 2010;40(4):633–43. https://doi.org/10.1017/S0033291709990894.
59. Cooke RWI, Lucas A, Yudkin PLN, Pryse-Davies J. Head circumference as an index of brain weight in the fetus and newborn. Early Hum Dev. 1977;1(2):145–9. https://doi.org/10.1016/0378-3782(77)90015-9.
60. Wang C, Shen M, Guillaume B, Chong YS, Chen H, Fortier MV, et al. FKBP5 moderates the association between antenatal maternal depressive symptoms and neonatal brain morphology. Neuropsychopharmacology. 2018;43(3):564–70. https://doi.org/10.1038/npp.2017.232.
61. Qiu A, Shen M, Buss C, Chong YS, Kwek K, Saw SM, et al. Effects of antenatal maternal depressive symptoms and socio-economic status on neonatal brain development are modulated by genetic risk. Cereb Cortex. 2017;27(5):3080–92. https://doi.org/10.1093/cercor/bhx065.
62. Qiu A, Anh TT, Li Y, Chen H, Rifkin-Graboi A, Broekman BFP, et al. Prenatal maternal depression alters amygdala functional connectivity in 6-month-old infants. Transl Psychiatry. 2015;5(2):e508. https://doi.org/10.1038/tp.2015.3.
63. Soe NN, Wen DJ, Poh JS, Chong Y-S, Broekman BF, Chen H, et al. Perinatal maternal depressive symptoms alter amygdala functional connectivity in girls. Hum Brain Mapp. 2018;39(2):680–90. https://doi.org/10.1002/hbm.23873.
64. Wen DJ, Poh JS, Ni SN, Chong YS, Chen H, Kwek K, et al. Influences of prenatal and postnatal maternal depression on amygdala volume and microstructure in young children. Transl Psychiatry. 2017;7(4):e1103. https://doi.org/10.1038/tp.2017.74.
65. Cooper PJ, Murray L. Course and recurrence of postnatal depression: evidence for the specificity of the diagnostic concept. Br J Psychiatry. 1995;166(2):191–5.
66. O'Hara MW, Neunaber DJ, Zekoski EM. Prospective study of postpartum depression: prevalence, course, and predictive factors. J Abnorm Psychol. 1984;93(2):158.
67. Bauer A, Parsonage M, Knapp M, Iemmi V, Adelaja B Costs of perinatal mental health problems. 2014
68. Wachs TD, Black MM, Engle PL. Maternal depression: a global threat to children's health, development, and behavior and to human rights. Child Dev Perspect. 2009;3(1):51–9.
69. Field T, Diego M, Hernandez-Reif M, Vera Y, Gil K, Schanberg S, et al. Prenatal maternal biochemistry predicts neonatal biochemistry. Int J Neurosci. 2004b;114(8):933–45. https://doi.org/10.1080/00207450490461305.
70. Pawlby S, Hay DF, Sharp D, Waters CS, O'Keane V. Antenatal depression predicts depression in adolescent offspring: prospective longitudinal community-based study. J Affect Disord. 2009;113(3):236–43.
71. O'Connor TG, Heron J, Glover V. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. J Am Acad Child Adolesc Psychiatry. 2002;41(12):1470–7.
72. Plant DT, Pariante CM, Sharp D, Pawlby S. Maternal depression during pregnancy and offspring depression in adulthood: role of child maltreatment. Br J Psychiatry. 2015;207(3):213–20. https://doi.org/10.1192/bjp.bp.114.156620.
73. Barker ED, Jaffee SR, Uher R, Maughan B. The contribution of prenatal and postnatal maternal anxiety and depression to child maladjustment. Depress Anxiety. 2011;28(8):696–702.
74. Plant DT, Jones FW, Pariante CM, Pawlby S. Association between maternal childhood trauma and offspring childhood psychopathology: mediation analysis from the ALSPAC cohort. Br J Psychiatry. 2017;211(3):144–50. https://doi.org/10.1192/bjp.bp.117.198721.
75. Talge NM, Neal C, Glover V, Early Stress, Translational Research and Prevention Science Network: Fetal and Neonatal Experience on Child and Adolescent Mental Health. Antenatal

maternal stress and long-term effects on child neurodevelopment: how and why? J Child Psychol Psychiatry. 2007;48(3–4):245–61.
76. O'Donnell KJ, Glover V, Barker ED, O'Connor TG. The persisting effect of maternal mood in pregnancy on childhood psychopathology. Dev Psychopathol. 2014;26(2):393–403.
77. O'Connor TG, Monk C, Fitelson EM. Practitioner review: maternal mood in pregnancy and child development–implications for child psychology and psychiatry. J Child Psychol Psychiatry. 2014a;55(2):99–111.
78. Sarkar P, Bergman K, O'Connor TG, Glover V. Maternal antenatal anxiety and amniotic fluid cortisol and testosterone: possible implications for foetal programming. J Neuroendocrinol. 2008;20(4):489–96.
79. Fisk NM, Glover V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. BMJ. 1999;318(7177):153–7.
80. Monk C, Fifer WP, Myers MM, Bagiella E, Duong JK, Chen IS, et al. Effects of maternal breathing rate, psychiatric status, and cortisol on fetal heart rate. Dev Psychobiol. 2011;53(3):221–33.
81. Rice F, Harold GT, Boivin J, Van den Bree M, Hay DF, Thapar A. The links between prenatal stress and offspring development and psychopathology: disentangling environmental and inherited influences. Psychol Med. 2010;40(2):335–45.
82. Evans EC, Bullock LFC. Optimism and other psychosocial influences on antenatal depression: a systematic review. Nurs Health Sci. 2012;14(3):352–61.
83. Agostini F, Neri E, Salvatori P, Dellabartola S, Bozicevic L, Monti F. Antenatal depressive symptoms associated with specific life events and sources of social support among Italian women. Matern Child Health J. 2015;19(5):1131–41.
84. Burke L. The impact of maternal depression on familial relationships. Int Rev Psychiatry. 2003;15(3):243–55.
85. Goodman JH. Influences of maternal postpartum depression on fathers and on father–infant interaction. Infant Mental Health J. 2008;29(6):624–43.
86. Chang JJ, Halpern CT, Kaufman JS. Maternal depressive symptoms, father's involvement, and the trajectories of child problem behaviors in a US national sample. Arch Pediatr Adolesc Med. 2007;161(7):697–703.
87. Johnson SL, Jacob T. Marital interactions of depressed men and women. J Consult Clin Psychol. 1997;65(1):15.
88. Hanington L, Heron J, Stein A, Ramchandani P. Parental depression and child outcomes–is marital conflict the missing link? Child Care Health Dev. 2012;38(4):520–9.
89. Misri S, Kendrick K, Oberlander TF, Norris S, Tomfohr L, Zhang H, Grunau RE. Antenatal depression and anxiety affect postpartum parenting stress: a longitudinal, prospective study. Can J Psychiatry. 2010;55(4):222–8.
90. Teti DM, Nakagawa M, Das R, Wirth O. Security of attachment between preschoolers and their mothers: relations among social interaction, parenting stress, and mother's sorts of the attachment Q-set. Dev Psychol. 1991;27(3):440.
91. Misri S, Kendrick K. Perinatal depression, fetal bonding, and mother-child attachment: a review of the literature. Curr Pediatr Rev. 2008;4(2):66–70.
92. Schmidt D, Seehagen S, Vocks S, Schneider S, Teismann T. Predictive importance of antenatal depressive rumination and worrying for maternal–Foetal attachment and maternal well-being. Cogn Ther Res. 2016;40(4):565–76.
93. Mercer RT. Becoming a mother versus maternal role attainment. J Nurs Scholarsh. 2004;36(3):226–32.
94. McFarland J, Salisbury AL, Battle CL, Hawes K, Halloran K, Lester BM. Major depressive disorder during pregnancy and emotional attachment to the fetus. Arch Womens Ment Health. 2011;14(5):425.
95. Petri E, Palagini L, Bacci O, Borri C, Teristi V, Corezzi C, et al. Maternal–foetal attachment independently predicts the quality of maternal–infant bonding and post-partum psychopathology. J Matern Fetal Neonatal Med. 2018;31(23):3153–9. https://doi.org/10.1080/14767058.2017.1365130.

96. Pearson RM, Melotti R, Heron J, Joinson C, Stein A, Ramchandani PG, et al. Disruption to the development of maternal responsiveness? The impact of prenatal depression on mother–infant interactions. Infant Behav Dev. 2012;35(4):613–26.
97. Kemppinen K, Kumpulainen K, Raita-Hasu J, Moilanen I, Ebeling H. The continuity of maternal sensitivity from infancy to toddler age. J Reprod Infant Psychol. 2006;24(3):199–212.
98. Dubber S, Reck C, Müller M, Gawlik S. Postpartum bonding: the role of perinatal depression, anxiety and maternal–fetal bonding during pregnancy. Arch Womens Ment Health. 2015;18(2):187–95.
99. Rossen L, Hutchinson D, Wilson J, Burns L, Olsson CA, Allsop S et al. Predictors of postnatal mother-infant bonding: the role of antenatal bonding, maternal substance use and mental health. Arch Womens Ment Health. 2016;19(4):609–22.
100. Crittenden PM. CARE-index manual. Miami: Family Relations Institute; 2003.
101. DeKlyen M, Greenberg MT. Attachment and psychopathology in childhood*;* 2008)
102. Burgess A. Fathers' roles in perinatal mental health: causes, interactions and effects. New Digest. 2011;53:24–9.
103. Gladwell H. 2021. Six months after giving birth, I finally sought help for my postnatal depression. Inspire the Mind, November 4, 2020, https://bit.ly/3ssgkM6.
104. Luca DL, Garlow N, Staatz C, Margiotta C, Zivin K. Societal costs of untreated perinatal mood and anxiety disorders in the United States. Mathematica Policy Research; 2019

Postpartum Depression

2

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2.1 Introduction

Pregnancy, childbirth, and postpartum are periods of high vulnerability to the development or relapse of perinatal mental disorders. Many women may present postpartum "maternity blues" or "baby blues," a transient mood disturbance related to hormonal changes that occur after childbirth. Nevertheless, for some women this mood disturbance can persist and be more severe, developing a postpartum depression (PPD), one of the most common complications of childbearing [1]. Postpartum depression (PPD) is a significant public health problem associated with increased morbidity for both infants and mothers. The symptoms can range from mild to severe and an appropriate detection and treatment are imperative.

In this chapter we will conduct a brief review of the most relevant aspects of PPD.

2.1.1 Epidemiology of Postpartum Depression

Epidemiological data of postpartum depression are from studies conducted in countries across the world, and different incidence and prevalence values are reported between countries. The most recent systematic review and meta-analysis [2] found that the incidence of postpartum depression was 12% (95% CI 0.04–0.20) while the

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overall prevalence of depression was 17% (95% CI 0.15–0.20) among healthy mothers without a prior history of depression. Prevalence was similar regardless of the type of diagnostic tool used; however, there were statistical differences in the prevalence between different geographical regions. There was no statistical difference in prevalence between different screening time points, but an increasing prevalence was observed beyond 6 months postpartum.

In low-income and middle-income countries (LAMIC) antepartum and postpartum depression is highly prevalent affecting about one in four and one in five women, respectively. Specifically, postpartum depression prevalence was estimated in 19.7% (16.9–22.8%) [3]. We must consider that these numbers may be an underestimate with the lower reports resulting from mental health stigma, cultural norms, and myths in relationship with maternity.

Data on whether there is an increased risk of depression in postpartum period than in another times in life are scarce. American study compared prevalence of psychiatric disorders in a pregnant women sample with nonpregnant women of childbearing age sample and found that pregnancy per se was not associated with an increased risk of new onset or recurrence of mental disorders; however, the risk of major depressive disorder was significantly higher in postpartum women (9.3%) than in nonpregnant women (8.1%) (OR 1.59, 95% CI = 1.15–2.20) [4]. Also, a study found that primiparous women had an increased risk of incident hospital admission through the first 3 months after childbirth, especially for women with affective disorders (bipolar and unipolar) [5].

The onset of postnatal depression is variable, and is not always in the first weeks following the birth; moreover, the perinatal vulnerability to depression begins before delivery and extends beyond 6 weeks postpartum. In a study of women with postpartum depression, 11.5% reported prenatal onset, 22.0% late postpartum onset (>6 weeks), and 66.5% early postpartum symptom onset (<6 weeks). Those reporting pregnancy onsets were more likely to be unmarried, and those with a late postpartum onset were less likely to report a history of postpartum depression [6].

2.2 Causes of PPD.

The exact causes of PPD are unknown, but it is considered that there are different vulnerabilities that can precipitate it and included within the general stress-vulnerability model. This model considers giving birth as a neurohormonal and immunological stress factor, and the transition to motherhood as a psychosocial stress factor. Both factors demand an adaptive effort in order to respond to the demands of motherhood. The depression may be a result of the different types of bio-psycho-social vulnerabilities [7]:

(a) *Genetic vulnerability*. For depression occurring in the early postpartum period (onset in the first 8 weeks), symptom severity, heritability, and epigenetic data suggest that PPD may be distinct to major depressive disorder occurring outside

of the perinatal period, whereas depression occurring in the later postpartum period may be more similar [8]. In one of the more recent studies of heritability of PPD, the authors investigated the relative importance of genetic and environmental influences on perinatal depression, and the genetic overlap between perinatal depression and nonperinatal depression in a sample of twins and a sample of sisters [9]. The heritability of perinatal depression was estimated at 54% and 44%, respectively, in separate samples, and the heritability of nonperinatal depression at 32%. The authors suggest that perinatal depression constitutes a subset of depression that could be prioritized and future genetic studies using genomic methods will require international collaborations to include a large number of patients.

Moreover we must considered mechanisms like epigenetic modifications. Epigenetic alterations have been demonstrated in two genes; TTC9B and HP1BP3 DNA methylation at early antenatal time points showed moderate evidence for association to the change in estradiol and allopregnanolone over the course of pregnancy, that may be important for mediating hormonal sensitivity [10]. Specifically, antenatal TTC9B and HP1BP3 gene DNA methylation is prospectively predictive of postpartum depression (PPD) with ~80% accuracy [10, 11].

Other genes like serotonin transporter gen (5-htt) have been implicated to greater vulnerability for depressive symptoms after childbirth with controversial results [12, 13].

(b) *Neurohormonal vulnerability.* The sudden decrease in estrogens during birth and the immediate postnatal period bring about a sharp decrease in brain neurotransmitters, which contribute to the presence of the depressive symptoms in the postnatal period. One experimental study [14] investigated the possible role of changes in gonadal steroid levels in postpartum depression by simulating two hormonal conditions related to pregnancy and parturition in euthymic women with and without a history of postpartum depression. Overall, 63% of women with a history of PPD and none of the women in the comparison group developed significant mood symptoms during the withdrawal period suggesting that women with a history of postpartum depression are differentially sensitive to mood-destabilizing effects of gonadal steroids. Author's hypotheses that gonadal steroids function as major neuromodulators, profoundly altering the activity of central nervous system neurotransmitter systems implicated in mood regulation and mood disorders (serotonin, norepinephrine, MAO, GABA, BDNF). Latest studies have shown that peripartum changes in allopregnanolone, a major progesterone metabolite, may play a critical role in PPD through gamma aminobutyric acid (GABA) receptors [15]. Allopregnanolone is a positive allosteric modulator of synaptic and extrasynaptic γ-aminobutyric acid type A (GABAA). The failure of GABAA receptors to adapt to the rapid fluctuations in allopregnanolone levels at childbirth is hypothesized to be a trigger for postpartum depression [16]. Postpartum period is characterized by an accelerated immune response mediated by pro-inflammatory and anti-inflammatory changes that may play a role in the vulnerability

to mood disorders during the peripartum period. However, few studies have directly investigated the role of the immune system in postpartum depression with controversial results [17].

(c) *Cognitive vulnerability*. The impact of perinatal experiences is different depending on personality traits, cognitive style, and the coping strategies used and family, social, and logistic support. Moreover, high perfectionism and particularly high concern over mistakes is a personality dimension associated with major postpartum depression [18]. Also, neuroticism has been described as a predictor for postpartum suicidal ideation [19].

(d) *Psychosocial vulnerability*. The changes in the transition and in the combining of roles together with other psychosocial factors can affect the mood during this period: physical changes and self-image, loss of occupational status, penalization of professional or working life, loneliness or social isolation, and lack of time.

2.3 Course and Recurrence of Postpartum Depression

2.3.1 Course of PPD

Available data on the course of PPD show how that this can be a chronic, non-benign disease. A review of 23 prospective studies about course of PPD (depressive symptoms or clinical diagnosis) described that about 30% of mothers from community samples, diagnosed with PPD, and 50% of mothers with PPD from clinical samples still meet criteria for depression during the first postnatal year and thereafter [20]. Recent study [21] measures the course of postpartum major depressive episode with survival analysis. Results showed that the mean time to achieve partial remission was 28.2 weeks, while the mean time to achieve total remission was 49.4 weeks, almost a year.

Various studies identified the factors associated with chronic course of postpartum depression. The most frequent reported are poor social or partner support, the onset of the episode before or during pregnancy [21] and having a previous history of treated depressive episodes [21]. Principal factors associated with chronic course of PPD are poor social or partner support, childhood sexual abuse [20], having financial problems [21], and previous psychiatric history (especially previous depressive episodes) [20, 21]. Also, onset of symptoms during pregnancy has been identified as a risk factor for most severely and chronic postpartum depression symptoms [20, 22, 23], suggesting that timing of symptom onset could be a useful indicator of prognosis of PPD, with more chronic and/or severe trajectories of postpartum depression in women with high prenatal depressive symptoms. The risk factors associated with prognosis would give us clues for an early intervention in the event of pregnancy symptoms being detected, as well as for the implementation of specific interventions for mothers with PPD at risk of becoming chronic.

2.3.2 Recurrence of PPD

Major depressive disorder is a highly recurrent illness. The risk of the recurrence of major depressive disorder progressively increases with each successive episode and decreases as the duration of recovery increases [24]. Few studies examined recurrence rates of PPD in a follow-up studies of interventions. Our team research conducted a 2-year follow-up study of a cohort of mothers with a major depressive episode in the postpartum period and found a total of 16.5% relapses/recurrences during the 2-year follow-up (6.4% relapses and 10.1% recurrences, a rate that rose to 11.3% considering only mothers who achieved complete remission). Factors that have independently shown an association with relapses/recurrences were the onset of depression before pregnancy and emotional abuse in childhood [25].

Furthermore, women who have suffered from one episode of postpartum-onset major depression experience increased risk for recurrence in the year following another birth, with a recurrence rate of 41% (a quarter in a first 2 postpartum weeks [26]). This risk is higher for women with early-onset PPD (47%) than for women with late-onset PPD (22%) [27].

2.4 Detection and Diagnosis of Postpartum Depression

There is international consensus on the need for screening of postpartum depression. NICE Guideline, one of the principal resources for perinatal mental health disorders, recommends Whooley questions at the first contact of pregnant women with primary care and the early postnatal period [28]:

1. During the past month, have you often been bothered by feeling down, depressed, or hopeless?
2. During the past month, have you often been bothered by little interest or pleasure in doing things?

A positive response to the two-item instrument had a sensitivity of 96% (95% CI 90–99%) and a specificity of 57% (95% CI 53–62%) [29]. If a woman responds positively to one of the questions, it is recommended using the Edinburgh Postnatal Depression Scale (EPDS) as part of a full assessment for perinatal depression. EPDS is the most widely researched and used screening tool for postpartum depression [30]. This brief ten-item tool has been translated and validated into more than 20 languages with different cut-off points (a cut-off score of 13 is most commonly used). In case of positive screening for depression, we must take into account that a clinical evaluation is the gold standard for determining a diagnosis.

The diagnosis of PPD is made by a clinical interview with the patient. So far, there are no imaging or laboratory tests that can help to provide a reliable diagnosis of this disorder. The last version of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) [31] classified PPD as “Major Depressive Disorder,

with peripartum onset." This specifier can be applied if onset of mood symptoms occurs during pregnancy or in the 4 weeks following delivery. This definition has caused controversy because it potentially excludes depressive episodes with later onset. In addition, the diagnostic criteria for a major depressive episode do not differ from other periods, and include at least 2 weeks of persistent low mood or anhedonia, as well as at least five of the following: depressed mood, diminished interest or pleasure, changes in appetite, a slowing down of thought and a reduction of physical movement, fatigue or loss of energy, sleep disturbance, feelings of worthlessness or guilt, diminished ability to think or concentrate, indecisiveness, thoughts of death, or suicidal ideation. This classification can lead to underdiagnosis of PPD because some of these symptoms, such as sleep disturbance and appetite disturbance, fatigue, or concentration difficulties need careful inquiry, could be underestimated in a mother with a baby. In addition, postpartum depression is characterized by the presence of prominent anxiety symptoms and restlessness that can lead to diagnostic confusion. It is also essential to assess the presence of suicidal ideation but also infanticide thoughts, and not to confuse infanticide ideas with intrusive thoughts of infant-related harm. Thoughts of harming the infant are described in 41% of depressed mothers and could cause difficulties in mother–baby relationship like fear of being alone with the infant and/or inability to care for the infant [32].

Some of the symptoms we advise should be considered are summarized in Table 2.1 [33].

Table 2.1 Symptoms to consider in women with postpartum depression

Depressive mood for most of the day	"Looking at my baby I can't stop crying." "I see a black future." "I feel I am in an endless tunnel." "I will never be like I was before"
Decrease in interest or ability to enjoy	This difficulty can include enjoying the newborn baby: "I don't feel like being with my baby or I can't be alone with it" or, on the contrary: "To be with my baby, is the only thing that soothes me"
Changes in appetite and weight	Loss of appetite and weight or on the contrary an increase in appetite with anxiety due to eating, and an increase in weight
Changes in sleep pattern	Insomnia unrelated to the waking up of the baby. There can also be excessive sleepiness during the day (hypersomnia)
Feeling of tiredness and loss of energy	
Anxiety and persistent feeling of fear and uneasiness	"I am continuously suffering." "I don't stop thinking that my baby is ill or has a serious illness"
Feelings of blame and/or uselessness	"I am not a good mother." "I don't know how to give him a bath, or change him." "I can't soothe him when he cries." "I would prefer someone to look after him"
Decrease in the ability to concentrate	There can be difficulties to make decisions as regards the nurturing and basic care of the baby. "I go periods without dressing him because I don't know if have to put on a short- or long-sleeved shirt"
Thoughts of harm baby	
Difficulties in bonding with the newborn baby	"I look at him and I feel that it is not my child, I would prefer that someone will look after him"

Postpartum depression should not be confused with the "postpartum/maternity blues," defined as low mood and mild depressive symptoms that are transient and self-limited. The depressive symptoms include sadness, crying, exhaustion, irritability, anxiety, decreased sleep, decreased concentration, and labile mood. These symptoms typically develop within 2–3 days of childbirth, peak over the next few days, and resolve by themselves within 2 weeks of their onset [34]. Postpartum blues are extremely common and are estimated to occur in about 50% or more of women within the first few weeks after delivery [1]. Postpartum blues can be distinguished from a depressive episode by the severity and persistence of the latter. For example, severe obsessional preoccupations, ideas of guilt, and suicidality are not usually present with the blues. If symptoms of "postpartum blues" persist or worsen, it is advisable to consult a specialist for to rule out postnatal depression or other perinatal mental health disorder.

Furthermore, diagnostic assessment should evaluate for a history of manic or hypomanic symptoms, as first-onset postpartum depression can indicate underlying bipolar disorder. A register-based cohort study showed that the risk of bipolar disorder among women with a nonpsychotic postpartum affective episode was higher than that in women with an affective episode outside the postpartum period [35]. Our team conducted a prospective longitudinal study with an 8-year follow-up in a cohort of women diagnosed with postpartum major depressive episode (DSM-IV-TR criteria) at 6 weeks postpartum (index episode). Approximately 12% of women diagnosed with postpartum major depressive episode meet diagnostic criteria of Bipolar Disorder Type II at 8-years of follow-up [36].

2.5 Risk Factors for Postpartum Depression

Significant risk factors for PPD include a history of depression prior to or during pregnancy, anxiety during pregnancy, poor marital relationship, stressful life events, negative attitude toward pregnancy, and lack of social support are significant contributors to postpartum depression. Factors that have shown a stronger association are as follows:

- *Previous psychiatric history*. The current greatest predictor of PPD is the assessment of psychiatric disorders both prior to and during pregnancy, specially previous depressive episodes. Women with history of depressive disorder had high risk for recurrence (43%), especially if discontinued their medication during pregnancy (68%) [37]. It's imperative to ask about previous psychiatric history and consider that women with histories of depression who are euthymic in the context of ongoing antidepressant therapy should be aware of the association of depressive relapse during pregnancy and postpartum with antidepressant discontinuation.
- *Premenstrual syndrome (PMS).* Women with this syndrome are vulnerable to present depressive symptoms due to the changes in the reproductive hormones that are produced in the postnatal period. Current evidence supports a significant

association between history of PMS and development of PPD (OR: 2.20, 95% CI: 1.81–2.68) [38].

- *Stressful life events*. During the pregnancy like, for example, an illness, death, or suffering of a loved one; a difficult or emergency delivery; unplanned pregnancy; to have contradictory feelings; or chronic stressful situations, such as a lack of social support (considered an independent predictor of PPD), financial problems, or low income [39].
- *Situations of abuse or violence*. Women who experience any violence events are at a higher risk of developing PPD (OR 2.04; 95% CI 1.72–2.41). Different types of violence events such as sexual (OR = 1.56; 95% CI: 1.35–1.81), emotional (OR = 1.75; 95% CI: 1.61–1.89), and physical violence (OR = 1.90; 95% CI: 1.36–2.67), as well as domestic (OR = 2.05; 95% CI: 1.50–2.80) or childhood violence (OR = 1.59; 95% CI: 1.34–1.88) also increased the risk of developing PPD [40].

2.6 Consequences of Postpartum Depression

Untreated maternal depression is associated with serious morbidity for the mother, the infant, the mother–baby bonding, and the family system. Recent systematic review evaluate both the infant and the maternal consequences of untreated maternal postpartum depression [41]. The main results are summarized below.

- *Impact on mother:*
  - Poor physical health (physical functioning, bodily pain, and general health perceptions).
  - More consultations to healthcare professionals or emergencies.
  - Lower scores on quality of life.
  - Greater perceived stress, more negative life events, more financial problems, and more illness among close relatives.
  - Lower levels of household functioning (household care).
  - More likely to be at risk for homelessness.
  - More relationship difficulties and therefore lower social function.
  - Poor relationship with partner.
  - More sexual dysfunction during the first year after childbirth.
  - More tobacco use.
  - Increased prevalence of suicidal ideation and thoughts of self-harm.
  - Higher risk of suicide and infanticide.
- *Impact on baby.*
  - Gained less weight (controversial results).
  - Physical health concerns and a greater proportion of childhood illnesses.
  - More diarrheal episodes per year.
  - Greater overall pain in the infants and a stronger infant pain response during routine vaccinations.
  - Febrile disease.

  - Reduced probability of receiving age-appropriate vaccinations or age-appropriate well-child visits.
  - Threefold increased risk of mortality in infants up to 6 months of age, with an approximately twofold increased risk of mortality up to 12 months of age.
  - Increased incidence of infant night-time awakenings.
  - More problematic infant sleep patterns.
  - Higher risk of sleep disorders in children whose mothers had severe and/or chronic depressive symptoms.
  - Impaired motor development in infants at different times of evaluation (6–8 months, 12 months, and 18 months of age. Some studies did not found association.
  - Significant and negative association between maternal postpartum depressive symptoms and cognitive development in children.
  - Infants of depressed mothers also had a significantly higher fear score and higher degrees of emotional disorders, including anxiety disorders.
  - Child behavioral problems at age 2 years, more mood disorders and a more difficult temperament, more internalizing of problems, lower scores on the Communication and Symbolic Behavior Scales Developmental Profile, less mature regulatory behaviors, and higher fear scores that increased behavioral inhibition.
- *Impact on mother–baby interactions.*
  - Poor mother-to-infant bonding.
  - Less closeness, warmth, and sensitivity.
  - More difficulties in their relationships with their child during the first year.
  - More negative perceptions of their relationship with their infant.
  - Chronically depressed mothers were more likely to be insecurely attached.
  - Attachment insecurity or disorganization at 14 months.
  - Discontinue breastfeeding (early interruption of exclusive breastfeeding in the first months).
  - Engage in less-healthy feeding practices with their infant.
  - Less-healthy practices with infant (place their infant in the back-to-sleep position, to use a car seat).
  - Less participation in positive enrichment activities with the child.
  - Lower perception of their competence.
  - Risk of maltreatments (for example spanking their child).

2.7 Treatment of Postpartum Depression

Treatment of PPD should include not only pharmacological and/or psychological interventions of depressive episodes, but also maternal interaction intervention and accurate assessment of potential social vulnerabilities. Likewise, the management of depression and other mental health problems during pregnancy and the postnatal period differs from at other times because of the potential impact of any difficulties and treatments on the woman and the baby. As we have previously described there

are difficulties on the one hand because of the impact of untreated depression on mother and baby, and on the other hand for the risks associated with taking psychotropic medication during pregnancy and breastfeeding.

Clinical guidelines suggest that nonpharmacological treatments such as cognitive behavioral therapy or interpersonal psychotherapy are first-line treatment for mild or moderate depression during perinatal period (pregnant or lactating mother). However, for women with severe depressive episode or women that do not respond to psychotherapy we must considered pharmacological options. Concerns related to pharmacologic treatment of PPD include exposure to medication in breast milk, the effect of treatment on the ability of the mother to care for the baby (e.g., for sedative effects), and the perceived stigma of mother. The optimal way to treat depression during pregnancy and postpartum period remains uncertain. Antidepressants, specifically selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs), are frequently used as a first-line treatment for depressive disorders. These treatments can be used in combination with psychological interventions. Recent publication in *Nature* about postpartum psychiatric disorders [42] developed an algorithm for management of postpartum psychiatric disorders and recommend:

- For mild mood and/or anxiety disorders: Psychological support interventions.
- For severe mood and/or anxiety disorders: Evidence-based psychological treatment (if available) and/or pharmacological therapy. If women are breastfeeding, they recommend the use of sertraline. If women are not breastfeeding, they recommend following evidence-based pharmacotherapeutic guidelines for the treatment of non-postpartum depression or anxiety. Sertraline is often recommended as a first-line pharmacological treatment in breastfeeding women because of its very minimal passage into breast milk. However, in patients with a prior psychiatric history we should consider previous response to other treatment, even those that have less data regarding safety during breastfeeding. Most antidepressant treatments also have minimal passage into breast milk and, therefore, can be used in women with poor response to sertraline or previous response to these drugs.

Other treatments that we must consider during perinatal period are electroconvulsive therapy, especially in case of severe depression and psychotic symptoms, and transcranial magnetic stimulation (TMS). Current evidence of randomized controlled trials showed that TMS could improve depression symptoms and cognitive function in patients with PPD.

Finally, in the latest studies, various randomized placebo-controlled studies were conducted with brexanolone for severe postpartum depression. All studies found a significant improve on depressive symptoms for group treated with allopregnanolone at hour 60 [43]. Since 2019, brexanolone become the first FDA-approved medication for the treatment of PPD. More data is needed, especially its compatibility with breastfeeding and the durability of the antidepressant effect. Recently, Sage Therapeutics has developed an allopregnanolone analog [44] that is in the clinical trial phase and may be a next oral treatment for PPD.

2.8 Conclusions

Postpartum depression is the most common perinatal mental disorder, and it can affect more than 1 in 10 women. The symptoms can be mild, but in some cases the symptoms and the evolution are serious, requiring combined interventions (psychotherapy and psychopharmacology) and even hospital admission in severe cases. The consequences of postpartum depression do not only involve maternal health but also the baby health and mother–baby relationship, which requires a multidisciplinary intervention with a holistic evaluation. We can minimize the risks with an early diagnosis and intervention. For this reason, screening for depression is recommended at all stages of the perinatal period. More research is needed on possible prevention interventions, study of course and impact, and possible therapeutic targets.

References

1. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Nonpsychotic mental disorders in the perinatal period. Lancet. 2014;384:1775–88. https://doi.org/10.1016/S0140-6736(14)61276-9.
2. Shorey S, Chee CYI, Ng ED, Chan YH, Tam WWS, Chong YS. Prevalence and incidence of postpartum depression among healthy mothers: a systematic review and meta-analysis. J Psychiatr Res. 2018;104:235–48. https://doi.org/10.1016/j.jpsychires.2018.08.001.
3. Gelaye B, Rondon MB, Araya R, Williams MA. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. Lancet Psychiatry. 2016;3(10):973–82. https://doi.org/10.1016/S2215-0366(16)30284-X.
4. Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry. 2008;65(7):805–15. https://doi.org/10.1001/archpsyc.65.7.805.
5. Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB. New parents and mental disorders: a population-based register study. JAMA. 2006;296(21):2582–9. https://doi.org/10.1001/jama.296.21.2582.
6. Stowe ZN, Hostetter AL, Newport DJ. The onset of postpartum depression: implications for clinical screening in obstetrical and primary care. Am J Obstet Gynecol. 2005;192(2):522–6. https://doi.org/10.1016/j.ajog.2004.07.054.
7. Manual de Psiquiatria Perinatal. Guía para el manejo de los trastornos mentales durante el embarazo, posparto y lactancia. Capítulo 1. Epidemiología de los Trastornos Mentales Perinatales. 1.3.1. Depresión Posparto. 2016. Ll Garcia-Esteve y M Valdés. Ed Panamericana. ISBN 9788491100447.
8. Batt MM, Duffy KA, Novick AM, Metcalf CA, Epperson CN. Is postpartum depression different from depression occurring outside of the perinatal period? A review of the evidence. Focus (Am Psychiatr Publ). 2020;18(2):106–19. https://doi.org/10.1176/appi.focus.20190045. Epub 2020 Apr 23. PMID: 33162848
9. Corwin EJ, Kohen R, Jarrett M, Stafford B. The heritability of postpartum depression. Biol Res Nurs. 2010 Jul;12(1):73–83. https://doi.org/10.1177/1099800410362112.
10. Osborne L, Clive M, Kimmel M, Gispen F, Guintivano J, Brown T, Cox O, Judy J, Meilman S, Braier A, Beckmann MW, Kornhuber J, Fasching PA, Goes F, Payne JL, Binder EB, Kaminsky Z. Replication of epigenetic postpartum depression biomarkers and variation with hormone levels. Neuropsychopharmacology. 2016 May;41(6):1648–58. https://doi.org/10.1038/npp.2015.333.

11. Payne JL, Osborne LM, Cox O, Kelly J, Meilman S, Jones I, Grenier W, Clark K, Ross E, McGinn R, Wadhwa PD, Entringer S, Dunlop AL, Knight AK, Smith AK, Buss C, Kaminsky ZA. DNA methylation biomarkers prospectively predict both antenatal and postpartum depression. Psychiatry Res. 2020;285:112711. https://doi.org/10.1016/j.psychres.2019.112711. Epub 2019 Nov 27. PMID: 31843207; PMCID: PMC7702696
12. Sanjuan J, Martin-Santos R, Garcia-Esteve L, Carot JM, Guillamat R, Gutierrez-Zotes A, Gornemann I, Canellas F, Baca-Garcia E, Jover M, Navines R, Valles V, Vilella E, de Diego Y, Castro JA, Ivorra JL, Gelabert E, Guitart M, Labad A, Mayoral F, Roca M, Gratacos M, Costas J, van Os J, de Frutos R. Mood changes after delivery: role of the serotonin transporter gene. Br J Psychiatry. 2008;193(5):383–8. https://doi.org/10.1192/bjp.bp.107.045427.
13. Binder EB, Newport DJ, Zach EB, Smith AK, Deveau TC, Altshuler LL, Cohen LS, Stowe ZN, Cubells JF. A serotonin transporter gene polymorphism predicts peripartum depressive symptoms in an at-risk psychiatric cohort. J Psychiatr Res. 2010 Jul;44(10):640–6. https://doi.org/10.1016/j.jpsychires.2009.12.001.
14. Bloch M, Schmidt PJ, Danaceau M, Murphy J, Nieman L, Rubinow DR. Effects of gonadal steroids in women with a history of postpartum depression. Am J Psychiatry. 2000;157(6):924–30. https://doi.org/10.1176/appi.ajp.157.6.924.
15. Stewart DE, Vigod SN. Postpartum depression: pathophysiology, treatment, and emerging therapeutics. Annu Rev Med. 2019;27:183–96. https://doi.org/10.1146/annurev-med-041217-011106.
16. Meltzer-Brody S, Kanes SJ. Allopregnanolone in postpartum depression: role in pathophysiology and treatment. Neurobiol Stress. 2020;12:100212. https://doi.org/10.1016/j.ynstr.2020.100212. PMID: 32435663; PMCID: PMC7231991
17. Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019;52:165–80. https://doi.org/10.1016/j.yfrne.2018.12.001. Epub 2018 Dec 12. PMID: 30552910; PMCID: PMC6370514
18. Gelabert E, Subirà S, García-Esteve L, Navarro P, Plaza A, Cuyàs E, Navinés R, Gratacòs M, Valdés M, Martín-Santos R. Perfectionism dimensions in major postpartum depression. J Affect Disord. 2012;136(1–2):17–25. https://doi.org/10.1016/j.jad.2011.08.030. Epub 2011 Sep 17
19. Gelabert E, Gutierrez-Zotes A, Navines R, Labad J, Puyané M, Donadon MF, Guillamat R, Mayoral F, Jover M, Canellas F, Gratacós M, Guitart M, Gornemann I, Roca M, Costas J, Ivorra JL, Subirà S, de Diego Y, Osorio FL, Garcia-Esteve L, Sanjuan J, Vilella E, Martin-Santos R. The role of personality dimensions, depressive symptoms and other psychosocial variables in predicting postpartum suicidal ideation: a cohort study. Arch Womens Ment Health. 2020;23(4):585–93. https://doi.org/10.1007/s00737-019-01007-w. Epub 2019 Dec 4
20. Vliegen N, Casalin S, Luyten P. The course of postpartum depression: a review of longitudinal studies. Harv Rev Psychiatry. 2014;22(1):1–22. https://doi.org/10.1097/HRP.0000000000000013.
21. Torres A, Gelabert E, Roca A, Navarro P, Plaza A, Subirà S, Martin-Santos R, Ascaso C, Garcia-Esteve L. Course of a major postpartum depressive episode: a prospective 2 years naturalistic follow-up study. J Affect Disord. 2019 Feb;15(245):965–70. https://doi.org/10.1016/j.jad.2018.11.062.
22. Postpartum Depression: Action Towards Causes and Treatment (PACT) Consortium. Heterogeneity of postpartum depression: a latent class analysis. Lancet Psychiatry. 2015;2:59–67. https://doi.org/10.1016/S2215-0366(14)00055-8.
23. Luoma I, Korhonen M, Salmelin RK, Helminen M, Tamminen T. Long-term trajectories of maternal depressive symptoms and their antenatal predictors. J Affect Disord. 2015;170:30–8. https://doi.org/10.1016/j.jad.2014.08.017.
24. Solomon DA, Keller MB, Leon AC, et al. Multiple recurrences of major depressive disorder. Am J Psychiatry. 2000;157(2):229–33. https://doi.org/10.1176/appi.ajp.157.2.229.
25. Torres A, Gelabert E, Roca A, Navarro P, Plaza A, Subirà S, Martin-Santos R, Ascaso C, Garcia-Esteve L. Course of a major postpartum depressive episode: a prospective 2 years natu-

ralistic follow-up study. J Affect Disord. 2019 Feb;15(245):965–70. https://doi.org/10.1016/j.jad.2018.11.062.
26. Wisner KL, Perel JM, Peindl KS, Hanusa BH. Timing of depression recurrence in the first year after birth. J Affect Disord. 2004 Mar;78(3):249–52. https://doi.org/10.1016/S0165-0327(02)00305-1.
27. Stowe ZN, Hostetter AL, Newport DJ. The onset of postpartum depression: implications for clinical screening in obstetrical and primary care. Am J Obstet Gynecol. 2005 Feb;192(2):522–6. https://doi.org/10.1016/j.ajog.2004.07.054.
28. National Institute for Health and Care Excellence (NICE). Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline [CG192]. Published date: 17 December 2014 Last updated: 11 February 2020.
29. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression. Two questions are as good as many. J Gen Intern Med. 1997;12(7):439–45. https://doi.org/10.1046/j.1525-1497.1997.00076.x. PMID: 9229283; PMCID: PMC1497134
30. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987 Jun;150(782–6) https://doi.org/10.1192/bjp.150.6.782.
31. American Psychiatric Association. Depressive disorders. Diagnosis and statistical manual of mental disorders. 5th ed; 2013. https://doi.org/10.1176/appi.books.9780890425596.807874.
32. Jennings KD, Ross S, Popper S, Elmore M. Thoughts of harming infants in depressed and nondepressed mothers. J Affect Disord. 1999 Jul;54(1–2):21–8. https://doi.org/10.1016/s0165-0327(98)00185-2.
33. www.clinicbarcelona.org/en/assistance/diseases/postnatal-depression.
34. Balaram K, Marwaha R. Postpartum blues. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2021.
35. Liu X, Agerbo E, Li J, Meltzer-Brody S, Bergink V, MunkOlsen T. Depression and anxiety in the postpartum period and risk of bipolar disorder: a Danish nationwide register-based cohort study. J Clin Psychiatry. 2017;78(5):e469–76.
36. Roca A, Gonzalez A, Gelabert E, Torres A, Solé E, Sureda B, Navarro P, Andrés S, Imaz ML, Martin-Santos R, Garcia-Esteve L. Postpartum depression and risk of bipolar disorder: an 8-year follow-up study. Eur Neuropsychopharmacol. 2019;29(1):S503–4. https://doi.org/10.1016/j.euroneuro.2018.11.750.
37. Cohen LS, Altshuler LL, Harlow BL, Nonacs R, Newport DJ, Viguera AC, Suri R, Burt VK, Hendrick V, Reminick AM, Loughead A, Vitonis AF, Stowe ZN. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006;295(5):499–507. https://doi.org/10.1001/jama.295.5.499. Erratum in: JAMA 2006 Jul 12;296(2):170
38. Cao S, Jones M, Tooth L, Mishra GD. History of premenstrual syndrome and development of postpartum depression: a systematic review and meta-analysis. J Psychiatr Res. 2020;121:82–90. https://doi.org/10.1016/j.jpsychires.2019.11.010. Epub 2019 Nov 17
39. Norhayati MN, Hazlina NH, Asrenee AR, Emilin WM. Magnitude and risk factors for postpartum symptoms: a literature review. J Affect Disord. 2015;175:34–52. https://doi.org/10.1016/j.jad.2014.12.041. Epub 2014 Dec 31
40. Zhang S, Wang L, Yang T, Chen L, Qiu X, Wang T, Chen L, Zhao L, Ye Z, Zheng Z, Qin J. Maternal violence experiences and risk of postpartum depression: a meta-analysis of cohort studies. Eur Psychiatry. 2019;55:90–101. https://doi.org/10.1016/j.eurpsy.2018.10.005. Epub 2018 Nov 13
41. Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O. Consequences of maternal postpartum depression: a systematic review of maternal and infant outcomes. Women's Health (Lond Engl). 2019;15:1745506519844044. https://doi.org/10.1177/1745506519844044.
42. Meltzer-Brody S, Howard LM, Bergink V, Vigod S, Jones I, Munk-Olsen T, Honikman S, Milgrom J. Postpartum psychiatric disorders. Nat Rev Dis Primers. 2018 Apr;26(4):18022. https://doi.org/10.1038/nrdp.2018.22.

43. Frieder A, Fersh M, Hainline R, Deligiannidis KM. Pharmacotherapy of postpartum depression: current approaches and novel drug development. CNS Drugs. 2019;33(3):265–82. https://doi.org/10.1007/s40263-019-00605-7. PMID: 30790145; PMCID: PMC6424603
44. Martinez Botella G, Salituro FG, Harrison BL, Beresis RT, Bai Z, Blanco MJ, et al. Neuroactive steroids. 2. 3alpha-hydroxy-3beta-methyl-21-(4-cyano-lH-pyrazol-1′-yl)-19-nor-5betapregnan-20-one (SAGE-217): a clinical next generation neuroactive steroid positive allosteric modulator of the (gamma-aminobutyric acid)A receptor. J Med Chem. 2017;60(18):7810–9. https://doi.org/10.1021/acs.jmedchem.7b00846.

Bipolar Disorders

3

Verinder Sharma

3.1 Introduction

Bipolar disorder is a common disabling illness that usually begins in late adolescence or young adulthood [1, 2]. The disorder is commonly subdivided into bipolar I, bipolar II, and subthreshold bipolar disorder. Bipolar I disorder is equally common in men and women; however, bipolar II disorder appears more common in women. According to the World Mental Health Survey Initiative, bipolar disorder has a lifetime prevalence of 2.4%, of which more than half of the cases have a diagnosis of subthreshold bipolar disorder [3]. There are gender differences in the manifestation of bipolar disorder as women are more likely to have rapid cycling, mixed episodes, and suicide attempts. Women with bipolar disorder are also more likely to have comorbid thyroid disease, bulimia, and post-traumatic stress disorder [4]. Recently published large sample studies on bipolar disorder have found overrepresentation of women, suggesting a change in the prevalence of the disorder in two genders [5].

The illness course in women is impacted by reproductive events, particularly childbirth, leading to clustering of mood episodes during the reproductive life cycle [6]. The postpartum period is associated with increased risk of first onset of hypo/mania as well as depression [7–9]. Women with preexisting bipolar disorder are at risk of recurrence of hypo/manic, depressive, and mixed episodes in spite of the prophylactic use of psychotropic drugs [10]. Pregnancy, on the other hand, is thought to have a variable effect on the course of the disorder. The effect of pregnancy on the illness course in untreated women has not been studied prospectively; however, data from retrospective studies and population-based cohort studies have

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suggested that pregnancy may have a positive effect [11]. Thus, management of bipolar disorder during and after pregnancy requires understanding of the course of treated and untreated illness, as well as risks associated with the use of psychotropic drugs for the mother and the fetus or neonate. Peripartum management of bipolar disorder is further complicated by diagnostic challenges, paucity of controlled pharmacologic or psychotherapeutic data, and concerns about the safety of psychotropic drugs during lactation.

In this chapter, I review the screening, and diagnostic assessment of bipolar disorder followed by a discussion of its management prior to, during, and after pregnancy. Due to the lack of data on the role of psychotherapy, treatment discussion mainly focuses on pharmacotherapy. In order to avoid duplication, topics such as safety of drug use during pregnancy, the postpartum period, and lactation are not discussed in detail. Similarly, discussion of the diagnosis and treatment of puerperal psychosis is omitted.

3.2 Screening and Diagnostic Evaluation

Women are commonly screened for depression during and after pregnancy. The American College of Obstetricians and Gynecologists recommends screening at least once during the perinatal period for depression using a standardized, validated tool [12]. There are several compelling reasons that women should be screened for hypo/manic symptoms during pregnancy and the postpartum period [13]. A study of 10,000 women who underwent screening using the Edinburgh Postnatal Depression Scale (EPDS) between 4 and 6 weeks postpartum found that nearly 23% had bipolar disorder [14]. Several studies using the Highs scale have reported that 9.6–46.1% of women have hypomanic symptoms in the postpartum period [15, 16]. Some of these women have bipolar disorder because the hypomanic symptoms are followed by episodes of depression. Symptoms of hypo/mania are particularly common among women referred to perinatal clinics for postpartum depression. In one study, more than half of the women referred with a diagnosis of postpartum depression met the DSM-IV criteria for bipolar disorder—bipolar disorder not otherwise specified (29%), bipolar II disorder (23%), and bipolar I disorder (2%) [17]. Some women experience a change in diagnosis from major depressive disorder to bipolar disorder due to the first onset of hypo/mania in the postpartum period [8, 9]. Screening for bipolar disorder is necessary to prevent psychiatric hospitalization in the first few weeks after delivery [18]. Also, failure to detect and diagnose maternal bipolar disorder may lead to inappropriate treatment and increase the risk of harm to self or the newborn [19].

Reluctance to seek mental health treatment and a denial or rejection of bipolar diagnosis further contribute to diagnostic delay. The lack of awareness among clinicians of the common occurrence of hypo/manic symptoms may affect receipt of accurate diagnosis. Some delay is unavoidable because a diagnosis of bipolar disorder requires presence of hypo/mania; however, proper screening and diagnosis may mitigate risks associated with inappropriate treatment. For example, women at risk of developing bipolar disorder due to a history of bipolar disorder or puerperal

psychosis in a first-degree family member can be identified and monitored for emergence of hypo/manic symptoms. Clinical features such as younger age at illness onset, de novo depression after childbirth, onset of depression immediately after delivery, atypical symptoms of depression, current psychotic symptoms, mixed features, and history of bipolar disorder in first-degree family members should alert clinicians to consider bipolar disorder a differential diagnosis in women presenting with a depressive episode after delivery [20].

According to the Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines, all women with depressive symptoms should be screened for bipolar disorder during pregnancy and the postpartum period. Validated screening tools such as the Mood Disorder Questionnaire (MDQ) alone or in conjunction with the EPDS are useful [21, 22]. The MDQ is the most studied screening tool for bipolar disorder in the peripartum population. A positive screen requires endorsement of 7 or more of the 13 items, occurrence of items during the same period of time, and "moderate" or "serious" problem as a result of the endorsed items. An alternate scoring method (endorsement of seven or more items only) is more appropriate for bipolar II, or otherwise specified bipolar and related disorder because patients with these diagnostic subtypes are unlikely to say "yes" to question 3 of the MDQ. The Highs scale is another tool that has also been studied in the postpartum population [23]. Unlike the MDQ that assesses lifetime occurrence of hypo/manic symptoms, the Highs scale focuses on these symptoms in the postpartum period.

A positive screen for bipolar disorder should be followed by clinical assessment to confirm or exclude a diagnosis of bipolar disorder. A positive screen may also occur in cases of major depressive disorder with mixed features.

Women should also be screened and evaluated for psychiatric disorders that commonly co-occur with bipolar disorder such as anxiety disorders, obsessive–compulsive disorder, and substance use disorder. Simple screening questions for obsessive–compulsive disorder are "*Do you have unpleasant thoughts, urges, or images that repeatedly enter your mind? "Do you feel driven to perform certain behaviors or mental acts over and over again?*" The Generalized Anxiety 7-item (GAD-7) scale is a validated tool to screen for anxiety symptoms [15]. Clinical evaluation should include questions about family history because women with a history of bipolar disorder in the family are at a high risk of switching from major depressive disorder to bipolar disorder in the postpartum period. A population-based study from Denmark found increased relative risk of postpartum psychiatric disorders in first-time mothers who had a family history of bipolar disorder (hazard ratio = 2.86, 95% CI = 1.88–4.35) [24].

3.3 Preconception Care and Counselling

Since 50% of pregnancies are unplanned in women with bipolar disorder, it is important to consider the safety of medication use during pregnancy when prescribing mood stabilizers for women of reproductive age [25]. Valproic acid should not

be used in women of reproductive age because first trimester use of the drug has been associated with increased risk of neural tube defects, lower IQ, and autism spectrum disorders [26]. Moreover, valproic acid is not effective in preventing postpartum mood episodes in women with bipolar disorder [27]. Drugs such as topiramate, lamotrigine, or carbamazepine can affect pharmacokinetics of birth control drugs and thereby cause contraceptive failure [28].

The goal of preconception counselling is to improve pregnancy outcomes through risk assessment, psychoeducation, health promotion, and intervention. Women with bipolar disorder should be offered counselling at least 3 months prior to considering pregnancy or immediately upon discovery of pregnancy [29]. An important task of preconception counseling is confirmation of diagnosis of bipolar disorder and its subtype. A thorough psychiatric evaluation should be carried out to clarify the illness course including the frequency, severity, duration, and dominant polarity of mood episodes as well as duration of euthymic intervals, psychiatric and physical comorbidities, and hospitalizations. Risk assessment should identify women at high risk of suicide due to the personal history of serious attempts, or family history of completed suicide. Medication history including patterns of response to psychotropic medications, time to relapse following discontinuation of medications, and time to respond with reintroduction of medications should be obtained.

Women should be informed of the effect of pregnancy and postpartum on the course of bipolar disorder, as well as the effect of untreated bipolar disorder on pregnancy outcomes, and risk–benefit analysis of medication use. Decisions about whether or not to start, continue, discontinue, or modify medication should be made collaboratively with the patient and involvement of a partner or family member, if possible. Some women may require discontinuation of typical antipsychotics and risperidone in order to increase the likelihood of conception, as these medications often increase serum prolactin levels and thus interfere with ovulation. Modifiable risk factors such as obesity, tobacco use, and poor diet quality should be addressed [29]. Women dependent on alcohol or drugs should be advised to cease use of these substances, and when necessary should be referred to detoxification services. Preconception counselling should provide an opportunity to shore up social supports.

Reasons for seeking preconception counselling are varied. Due to the potential risk of genetic transmission of bipolar disorder to offspring, women with or without psychiatric illness may seek counseling to decide whether or not to pursue pregnancy. As childbirth is associated with increased risk of first onset of depression, mania, or puerperal psychosis, even women with no history of psychiatric illness should be offered follow-up during and after pregnancy. Sometimes women are referred because they wish to have a medication-free pregnancy. Women who have been clinically stable for 4–6 months, and are at low risk for recurrence can have their mood stabilizer tapered off prior to pregnancy [29]. Medication-free pregnancy may not be an option for those who have severe and frequent mood episodes, mania-preponderant illness, or history of frequent psychiatric hospitalizations, serious suicide attempts, and substance use disorder. Women taking valproate should be

recommended to switch to a different psychotropic drug. An opportunity to discuss the effectiveness of current medication in managing/preventing peripartum recurrences is another common reason for preconception counselling. The risk of mood instability following changes to the drug regimen has to be carefully weighed against the risk associated with the continuation of medications. Every effort should be made to simplify the drug regimen and preference given to mood stabilizing drugs. Antidepressants should be avoided particularly in women with bipolar I disorder.

3.4 Treatment During Pregnancy

3.4.1 General Considerations

Depression is the most common presentation of bipolar disorder during pregnancy. Several studies have found higher rates of depression in the first trimester compared to other trimesters. Abrupt discontinuation of psychotropic drugs, particularly antidepressants, may cause withdrawal symptoms and also increase the risk of recurrence of mood episodes. Abrupt cessation of alcohol use or drugs upon discovery of pregnancy can produce withdrawal symptoms including anxiety, depression, and insomnia. Sleep disturbance due to severe nausea and vomiting that normally peaks in the first trimester may contribute to depression. Thus, it is important to clarify whether mood changes are symptoms of bipolar disorder or are due to withdrawal from medications/substances. Bipolar mood episodes in pregnancy are usually recurrences in the context of preexisting illness; however, hypo/mania can also have first onset during pregnancy. It is unclear how commonly bipolar disorder has first onset during pregnancy.

Similar to valproic acid, carbamazepine is a teratogen and should be avoided. Also, carbamazepine is a strong inducer of hepatic enzymes and may lower the levels of coadministered drugs and necessitate dose increases [30]. According the National Institute for Health and Care Excellence (NICE) guidelines, lithium should be avoided during the first trimester unless antipsychotic medications have been ineffective, and a discussion about the risks and benefits of lithium has taken place with the patient [31]. Polypharmacy ($\geq$2 psychotropic drugs) for bipolar disorder is common during pregnancy. Use of antidepressants may increase the likelihood of polypharmacy as additional psychotropic drugs are needed to manage emerging symptoms of hypo/mania. Concomitant use of mood stabilizers may not be sufficient to prevent antidepressant-led mood instability. Moreover, polypharmacy may increase the risk of adverse outcomes for the mother and her fetus [32, 33]. If possible, an attempt should be made to simplify the drug regimen by gradually tapering antidepressants and benzodiazepines. Thus, preference should be given to continuation/optimization of drugs with broad spectrum of efficacy in the management of bipolar disorder. Decisions about medication use should be made on a case-by-case basis in collaboration with the patient. Drugs selected for acute treatment of mood episodes in pregnancy should ideally be effective in the prevention of mood or

psychotic episodes in the postpartum period. For women who plan to breastfeed, safety of medication during lactation is an important consideration.

Therapeutic monitoring of drugs, particularly with a narrow therapeutic range such as lithium, is necessary during the perinatal period. A study by Wesseloo et al. found serum lithium levels decreased during the first and second trimesters followed by a gradual return to preconception levels starting in the third trimester [34, 35]. They recommended close monitoring of serum lithium levels until 34 weeks of pregnancy, followed by weekly measurements until delivery and then twice weekly for the first 2 weeks postpartum. At our clinic we recommend a flexible monitoring schedule guided by serum levels rather adherence to a rigid monitoring protocol.

Since sleep loss is a symptom as well as a trigger of mood episodes especially hypo/mania, use of a drug such as quetiapine may produce quicker results than optimization of a drug like lithium. Due to increased clearance during pregnancy, lamotrigine doses may need adjustment to maintain therapeutic concentration [36]. Similarly, doses of atypical antipsychotic drugs may need adjustments due to the induction of cytochrome P450 system. In the postpartum period, the doses of these medications may require readjustment to avoid toxicity and/or improve tolerability.

3.4.2 Acute Treatment

Working in collaboration with the patient, a comprehensive and individualized treatment plan should be developed. The key goals of acute treatment should be to achieve full remission and limit the duration and consequences of mood episodes. Currently, there are no data on the acute treatment of bipolar depression during pregnancy. In general first-line options for bipolar I depression include quetiapine, lithium, lamotrigine, and lurasidone. Lamotrigine is not associated with weight gain and is less likely to cause sedation. Lamotrigine is generally well tolerated; however, it is associated with an uncommon (>0.1%) but potentially serious skin rash. Due to the slow titration of lamotrigine, it may take a few weeks before patients experience improvement of their depression. Lamotrigine is effective in preventing mood episodes during pregnancy [37]. A small study using the Danish registries did not find a significant difference in the risk of psychiatric hospitalization rates among women treated with lamotrigine versus those who took lithium during pregnancy (7.3% versus 15.3% respectively, adjusted OR 0.83; 95% CI 0.22–3.14) [34]. A recent systematic review and meta-analysis concluded that in utero exposure to lamotrigine was associated with significantly lower rates of congenital malformations (OR 1.15; 95% CI 0.62–2.16 and OR 1.25; 95% CI 0.89–1.74, respectively) compared to disease-matched controls and healthy controls. Adverse pregnancy outcomes in the lamotrigine group were not significantly increased compared to the general population group [38]. A recent meta-analysis found that in utero exposure to lithium was not associated with statistically significant increased risks for pregnancy or delivery outcomes. Lithium was associated with a significantly increased

risk (27.5% vs. 14.3%) for neonatal hospitalization within 4 weeks postpartum [39]. First-trimester exposure to lithium was specifically associated with an increased risk of major malformations, but not major cardiac malformations. These findings align with accumulating evidence that the absolute risk of malformations is much smaller than reported in earlier studies [40].

Quetiapine is the most commonly prescribed neuroleptic in the USA [41], however, there are no data on its use in the acute treatment of bipolar mood episodes in pregnancy. The drug is generally well-tolerated but some women find it difficult to fulfill childcare responsibilities due to excessive sedation. In higher doses it may cause postural hypotension and dizziness that could be problematic, particularly in the perinatal period [42]. Quetiapine use during pregnancy is associated with increased risk of gestational diabetes. The pooled risk ratio for major malformations in infants exposed to quetiapine in the National Pregnancy Registry for Atypical Antipsychotics at Massachusetts General Hospital was estimated at 1.03 (95% CI = 0.89–1.19) [43], suggesting no increased risk of malformations with first trimester exposure to quetiapine compared with the general public. A recent clinically focused review of second-generation antipsychotics reached a similar conclusion that in utero exposure to quetiapine is not associated with increased risk of major congenital malformations. Similarly, the available data overall do not suggest a clinically important increased risk for other pregnancy outcomes such as miscarriage, stillbirth, and small for gestational age [44].

A systematic review reported on use of electroconvulsive therapy (ECT) in 169 pregnant women with depression, bipolar disorder or psychotic depression [45]. Most women were in their second trimester of pregnancy. The mean number of ECT's was 9.4. Adverse events including fetal heart rate reduction, uterine contractions, and premature labor were reported for 29% of women. The overall child mortality rate was 7.1%; therefore ECT should be recommended as a last resort treatment.

3.4.3 Maintenance Treatment

The goals of maintenance treatment should be to prevent recurrence of mood episodes, manage comorbidities, minimize residual symptoms, promote medication adherence, reduce risk of self-harm, and improve functioning during pregnancy. Regular follow-up visits should be scheduled and frequency of visits increased if needed. More frequent visits are necessary in the third trimester to identify and manage prodromal/early symptoms of 'postpartum' mood or psychotic episodes. Psychoeducation about the illness and its management including strategies to promote sleep opportunities should be an integral part of the overall treatment plan. Regular tracking of mood and sleep should be encouraged to detect early symptoms of mood episodes.

Maintenance treatment planning requires an understanding of the impact of pregnancy on the course of bipolar disorder. Most of the research evidence in this

regard comes from studies of discontinuation of mood stabilizing medications that have shown a very high risk of illness recurrence during pregnancy. However, there is evidence from non-clinical samples, retrospective studies and studies of hospitalization rates that pregnancy may have a protective effect [11]. Prospective longitudinal studies controlling for diagnostic subtypes, illness course and current treatment are needed to clarify the effect of pregnancy on the course of bipolar disorder [46].

A prospective observational study of women who continued or discontinued their mood stabilizers, found that 71% had at least one recurrence during pregnancy [47]. Among women who discontinued the mood stabilizer the recurrence risk was twofold greater, the time to recurrence more than fourfold shorter and the proportion of time being ill during pregnancy was five times greater compared to those who stayed on the treatment. Interestingly, 33.3% of participants who maintained treatment had a recurrence of hypo/mania versus 19.4% of those who discontinued treatment suggesting that the unopposed use of antidepressants may have increased the risk of hypo/manic episodes. The researchers found a diagnosis of bipolar II disorder, and use of antidepressants predicted risk of recurrence. Women who discontinued the medications were more likely to be taking multiple psychotropic medications, had a longer duration of illness, were more likely to have illness onset before age 15 and had significantly higher rates of rapid cycling. They were also more likely to be taking antidepressant medications (66.1% vs.18.5%) and have a diagnosis of bipolar II disorder.

Another study by Viguera et al. found preponderance of hypo/manic and mixed states compared to depression during pregnancy in women with bipolar I disorder (13.13% vs. 8.88%) [10]**.** These results highlight the challenges clinicians encounter in managing bipolar depression during pregnancy. This is especially the case for bipolar II disorder due to the paucity of treatment data relative to bipolar I disorder. Quetiapine is the only first-line recommended drug. Lithium, lamotrigine, sertraline, and venlafaxine are second-line recommended drugs. The role of antidepressants in the treatment of bipolar II disorder remains controversial due to concerns about the risk of switching, cycling, and induction of mixed states.

Different clinical scenarios are encountered when assessing women during pregnancy. Some women present with a history of bipolar disorder while others have a history of undiagnosed or misdiagnosed bipolar disorder. For some women, first onset of hypo/mania during pregnancy may be the beginning of bipolar disorder. Women taking a mood stabilizer or an atypical antipsychotic drug whose mood is stable should continue with the same drug (s) after delivery. Women with recurrences despite maintenance treatment should be evaluated for potential contributing factors including antidepressant treatment, substance use, and dose of mood stabilizing medication, treatment adherence, and hypothyroidism. Changes should be made to the drug regimen accordingly. Some women wish to have a medication-free pregnancy but are agreeable to take medication in the postpartum period. Psychoeducation, regular symptom monitoring, sleep optimization, and assessment immediately after delivery should be the treatment strategy for these women.

3.5 Postpartum Period

3.5.1 General Considerations

Women with bipolar disorder are at a greater risk of occurrence of hypo/mania in the postpartum period than during pregnancy [48]. However, similar to pregnancy, the depressive/mixed episodes are the dominant polarity. Viguera et al. found 52% of women with bipolar I or II disorder despite treatment had illness episodes during the first 6 months postpartum [10]. A retrospective study of women who were medication-free during their pregnancies found 75% had at least one postpartum episode. Of these, nearly 60% had depression, 16% had hypo/mania and the rest mixed episodes [49]. A systematic review and meta-analysis by Wesseloo et al. reported a relapse risk of 35% (95% CI = 29, 41) in the postpartum period [50]. The relapse rate was significantly higher among women with bipolar disorder who were free of medications during pregnancy (66%, 95% CI = 57, 75) compared to those who were treated with psychotropic drugs (23%, 95% CI = 14, 37). The authors concluded that continuation of pharmacotherapy during pregnancy was effective in reducing the postpartum risk of recurrence in women with bipolar disorder or postpartum psychosis.

The postpartum period is also associated with an increased risk of first onset of hypo/mania. A prospective study by Sharma et al. found that 6.5% of women with major depressive disorder experienced a DSM-IV defined episode of hypomania during the first 6 months [9]. Another study reported that nearly 35% of women with a diagnosis of major depressive disorder had an episode of hypo/mania (defined as a score of ≥6 on the Altman Self-Rated Mania scale) during the first 3 months postpartum. Similarly, women with first onset of other psychiatric disorders are at an increased risk of developing bipolar disorder [18]. In spite of the common occurrence of hypo/manic symptoms in the postpartum period, misdiagnosis of bipolar disorder as major depressive disorder appears common. Failure to obtain history of hypo/manic symptoms may result in underdiagnosis of bipolar disorder. Misdiagnosis of bipolar disorder as unipolar postpartum depression among women attending specialized perinatal clinics is particularly high. From the aforementioned discussion, it is clear that all women with a major depressive episode should be screened for bipolar disorder. Women with psychiatric disorders who have postpartum onset are at a particularly high risk of developing bipolar disorder and should be monitored for emergence of hypo/manic symptoms during follow-up.

Abrupt cessation of exclusive breastfeeding has been associated with onset of mixed mania [51, 52]. Some women also experience worsening/recurrence of mood symptoms upon resumption of menstrual periods.

3.5.2 Acute Treatment

Drug treatment of bipolar postpartum depression has been largely overlooked [53]. The Polish Psychiatric Association recommends quetiapine alone or in

combination with an antidepressant for depression [54]. A retrospective study of quetiapine in 18 patients found 83% were "very much" or "much" improved when assessed using the Global Impression Scale [55]. The quetiapine median dose was 75 mg daily (12.5–500 mg). A study of extended release quetiapine in a median dose of 137.5 mg daily was also effective but only 15 of 26 participants completed the study [56]. It is unclear whether the concomitant use of quetiapine is protective against antidepressant-induced emergence of hypo/mania. Lamotrigine, lurasidone, or lithium are other options for acute treatment of bipolar postpartum depression. Factors to consider while selecting a suitable drug include effectiveness and tolerability of previously tried medications, suicide safety assessment, and nature of current psychiatric comorbidity. Since all psychotropic drugs are excreted in breast milk to varying degrees, decisions about the use of drugs should be made after a thoughtful analysis of potential risks and benefits. Postpartum hypo/manic episodes should be treated in the same manner as non-postpartum episodes [29].

3.5.3 Prophylactic Treatment

The prophylactic treatment should aim to (1) prevent recurrences of mood episodes, (2) prevent hypo/mania in women at risk of developing bipolar disorder, (3) reduce the risk of psychiatric hospitalization after delivery, (4) prevent harm to the mother and her baby, and (5) minimize the risk of recurrence of mood episodes beyond the postpartum period. The DSM-5 peripartum onset specifier is a reminder that postpartum episodes can begin during pregnancy. Approximately 60% of cases of postpartum depression begin during or prior to pregnancy [14]. Similarly, puerperal psychosis (generally considered a manifestation of bipolar disorder) can have a prepartum onset as evidenced by symptoms such as feeling euphoric, decreased sleep requirement, feeling active or energetic, or talking more or feeling very chatty [57]. It is, therefore, important that preventative strategies should focus on identification and treatment of mood/psychotic symptoms in late pregnancy. Sometimes it is difficult to distinguish between early times of recurrence and normative changes in sleep, energy, or mood during pregnancy. Prospective charting of symptoms using a mood diary or an app may help early detection of these symptoms. Assertive monitoring is also crucial for identification and management of modifiable risk factors such as sleep loss or the use of antidepressants.

Decisions about pharmacotherapy for prevention of postpartum episodes should be made on a case-by-case basis, taking into consideration the illness course and treatment history [58]. Particular attention should be paid to parity, diagnostic subtype, dominant polarity, sequence of mood episodes (e.g., depression–hypo/mania–euthymic interval [DMI type or the MDI type]), suicide risk assessment, and drug safety [59]. Interestingly, there are no placebo-controlled randomized trials of mood stabilizers in the prevention of postpartum mood episodes in the context of bipolar disorder. A single-blind, nonrandomized trial found valproate plus monitoring was not significantly more effective than monitoring alone for the prevention of

postpartum recurrences. A small prospective study of olanzapine used adjunctively was effective for prevention of postpartum psychosis and bipolar mood episodes [60]. Lithium is generally recommended for prevention of mania or puerperal psychosis; however, there is no evidence that the drug is effective for prevention of depressive episodes. In the absence of controlled data, a personalized, targeted approach guided by a thorough knowledge of the illness course, and treatment history should be applied. For example, lithium may be a better choice in patients with mania-preponderant illness while lamotrigine could be effective in depression-preponderant illness such as bipolar II disorder [61]. Some researchers recommend starting lithium immediately after delivery for prevention of psychosis or mania. Due to its slower onset of action compared to atypical antipsychotics, lithium may not be effective in the prevention of manic episodes occurring immediately after delivery. Antidepressants are commonly prescribed for postpartum depression; however, there are no data on their effectiveness in the prevention of depressive episodes in women with bipolar disorder.

3.5.4 Primary Prevention and Early Intervention

The postpartum period provides a remarkable opportunity for primary and secondary prevention of bipolar disorder for several reasons [62]. First, mood symptoms/episodes are common after delivery and may herald bipolar disorder. Second, women are routinely under the care of health professionals in the peripartum period and are screened for depression. Third, at-risk women including those with major depressive disorder, subthreshold mood episodes, or common psychiatric comorbidities, and a family history of bipolar disorder can be identified. And finally, putative risk factors such as sleep loss, substance use, or antidepressant therapy can be addressed. The relatively short duration of the risk period makes it easier to carry out preventative strategies. Close monitoring and early intervention via a variety of behavioral and pharmacological treatments might reduce the risk of first onset of hypo/mania in the postpartum period.

3.6 Conclusion

Both pregnancy and the postpartum period can affect the course of bipolar disorder. Studies of mood stabilizer discontinuation have found a high risk of recurrence during pregnancy; however, there is some evidence that pregnancy may have a positive effect on the course of bipolar disorder. Illness risk, including recurrences as well as first onset of bipolar mood episodes, is greater after delivery than during pregnancy. The peripartum management of the disorder involves balancing the risks associated with medication exposure versus the risks associated with untreated maternal illness. Due to its association with first onset of hypo/mania or psychosis, childbirth provides a unique opportunity for prevention or early intervention in women at risk of developing bipolar disorder.

References

1. Bauer M, Glenn T, Alda M, Andreassen OA, Angelopoulos E, Ardau R, Baethge C, Bauer R, Bellivier F, Belmaker RH, Berk M, Bjella TD, Bossini L, Bersudsky Y, Cheung EYW, Conell J, Del Zompo M, Dodd S, Etain B, et al. Influence of birth cohort on age of onset cluster analysis in bipolar I disorder. Eur Psychiatry. 2015;30(1):99–105. https://doi.org/10.1016/j.eurpsy.2014.10.005.
2. Ferrari AJ, Stockings E, Khoo JP, Erskine HE, Degenhardt L, Vos T, Whiteford HA. The prevalence and burden of bipolar disorder: findings from the global burden of disease study 2013. Bipolar Disord. 2016;18(5):440–50. https://doi.org/10.1111/bdi.12423.
3. Merikangas KR, Jin R, He J-P, Kessler RC, Lee S, Sampson NA, Viana MC, Andrade LH, Hu C, Karam EG, Ladea M, Medina-Mora ME, Ono Y, Posada-Villa J, Sagar R, Wells JE, Zarkov Z. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. Arch Gen Psychiatry. 2011;68(3):241. https://doi.org/10.1001/archgenpsychiatry.2011.12.
4. Baldassano CF, Marangell LB, Gyulai L, Nassir Ghaemi S, Joffe H, Kim DR, Sagduyu K, Truman CJ, Wisniewski SR, Sachs GS, Cohen LS. Gender differences in bipolar disorder: retrospective data from the first 500 STEP-BD participants. Bipolar Disord. 2005;7(5):465–70. https://doi.org/10.1111/j.1399-5618.2005.00237.x.
5. Dell'Osso B, Cafaro R, Ketter TA. Has bipolar disorder become a predominantly female gender related condition? Analysis of recently published large sample studies. Int J Bipolar Disord. 2021;9(1):1–7. https://doi.org/10.1186/s40345-020-00207-z.
6. Freeman MP, Smith KW, Freeman SA, McElroy SL, Kmetz GE, Wright R, Keck PE. The impact of reproductive events on the course of bipolar disorder in women. J Clin Psychiatry. 2002;63(4):284–7.
7. Azorin JM, Angst J, Gamma A, Bowden CL, Perugi G, Vieta E, Young A. Identifying features of bipolarity in patients with first-episode postpartum depression: findings from the international BRIDGE study. J Affect Disord. 2012;136(3):710–5. https://doi.org/10.1016/j.jad.2011.10.003.
8. Inglis AJ, Hippman CL, Carrion PB, Honer WG, Austin JC. Mania and depression in the perinatal period among women with a history of major depressive disorders. Arch Womens Ment Health. 2014;17(2):137–43. https://doi.org/10.1007/s00737-013-0408-1.
9. Sharma V, Xie B, Campbell MK, Penava D, Hampson E, Mazmanian D, Pope CJ. A prospective study of diagnostic conversion of major depressive disorder to bipolar disorder in pregnancy and postpartum. Bipolar Disord. 2014;16(1):16–21. https://doi.org/10.1111/bdi.12140.
10. Viguera AC, Tondo L, Koukopoulos AE, Reginaldi D, Lepri B, Baldessarini RJ. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. Am J Psychiatr. 2011;168(11):1179–85. https://doi.org/10.1176/appi.ajp.2011.11010148.
11. Sharma V, Pope CJ. Pregnancy and bipolar disorder: a systematic review. J Clin Psychiatry. 2012;73(11):1447–55. https://doi.org/10.4088/JCP.11r07499.
12. American College of Obstetricians and Gynecologists' Committee on Obstetric Practice. ACOG committee opinion no. 757: screening for perinatal depression. Obstet Gynecol. 2018;132(5):e208–12. https://doi.org/10.1097/AOG.0000000000002927.
13. Sharma V, Al-Farayedhi M, Doobay M, Baczynski C. Should all women with postpartum depression be screened for bipolar disorder? Med Hypotheses. 2018;118(March):26–8. https://doi.org/10.1016/j.mehy.2018.06.016.
14. Wisner KL, Sit DKY, McShea MC, Rizzo DM, Zoretich RA, Hughes CL, Eng HF, Luther JF, Wisniewski SR, Costantino ML, Confer AL, Moses-Kolko EL, Famy CS, Hanusa BH. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. JAMA Psychiatry. 2013;70(5):490–8. https://doi.org/10.1001/jamapsychiatry.2013.87.
15. Sharma V, Sharma P, Sharma S. Managing bipolar disorder during pregnancy and the postpartum period: a critical review of current practice. Expert Rev Neurother. 2020a;20(4):373–83. https://doi.org/10.1080/14737175.2020.1743684.

16. Sharma V, Singh P, Baczynski C, Khan M. A closer look at the nosological status of the highs (hypomanic symptoms) in the postpartum period. Archiv Women's Mental Health. 2020b;24(1) https://doi.org/10.1007/s00737-020-01023-1.
17. Sharma V, Khan M, Corpse C, Sharma P. Missed bipolarity and psychiatric comorbidity in women with postpartum depression. Bipolar Disord. 2008;10(6):742–7. https://doi.org/10.1111/j.1399-5618.2008.00606.x.
18. Munk-Olsen T, Laursen TM, Meltzer-brody S, Mortensen PB, Jones I. Psychiatric disorders with postpartum onset: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry. 2012;69(4):428–34. https://doi.org/10.1001/archgenpsychiatry.2011.157.
19. Kim J-H, Choi SS, Ha K. A closer look at depression in mothers who kill their children: is it unipolar or bipolar depression? J Clin Psychiatry. 2008;69(10):1625–31.
20. Sharma V, Doobay M, Baczynski C. Bipolar postpartum depression: an update and recommendations. J Affect Disord. 2017;219:105–11. https://doi.org/10.1016/j.jad.2017.05.014.
21. Frey BN, Simpson W, Wright L, Steiner M. Sensitivity and specificity of the mood disorder questionnaire as a screening tool for bipolar disorder during pregnancy and the postpartum period. J Clin Psychiatry. 2012;73(11):1456–61. https://doi.org/10.4088/JCP.12m07856.
22. Sharma V, Xie B. Screening for postpartum bipolar disorder: validation of the mood disorder questionnaire. J Affect Disord. 2011;131(1–3):408–11. https://doi.org/10.1016/j.jad.2010.11.026.
23. Glover V, Liddle P, Taylor A, Adams D, Sandler M. Mild hypomania (the highs) can be a feature of the first postpartum week. Association with later depression. Br J Psychiatry. 1994;164(4):517–21.
24. Bauer AE, Maegbaek ML, Liu X, Wray NR, Sullivan PF, Miller WC, Meltzer-Brody S, Munk-Olsen T. Familiality of psychiatric disorders and risk of postpartum psychiatric episodes: a population-based cohort study. Am J Psychiatr. 2018;175(8):783–91. https://doi.org/10.1176/appi.ajp.2018.17111184.
25. Rusner M, Berg M, Begley C. Bipolar disorder in pregnancy and childbirth: a systematic review of outcomes. BMC Pregnancy Childbirth. 2016;16(1) https://doi.org/10.1186/s12884-016-1127-1.
26. Veroniki AA, Rios P, Cogo E, Straus SE, Finkelstein Y, Kealey R, Reynen E, Soobiah C, Thavorn K, Hutton B, Hemmelgarn BR, Yazdi F, D'Souza J, Macdonald H, Tricco AC. Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: a systematic review and network meta-analysis. BMJ Open. 2017;7(7) https://doi.org/10.1136/bmjopen-2017-017248.
27. Wisner KL, Hanusa BH, Peindl KS, Perel JM. Prevention of postpartum episodes in women with bipolar disorder. Biol Psychiatry. 2004;56(8):592–6. https://doi.org/10.1016/j.biopsych.2004.07.022.
28. Reddy DS. Clinical pharmacokinetic interactions between antiepileptic drugs and hormonal contraceptives. Expert Rev Clin Pharmacol. 2010;3(2):183–92. https://doi.org/10.1586/ecp.10.3.
29. Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S, Alda M, MacQueen G, Milev RV, Ravindran A, O'Donovan C, McIntosh D, Lam RW, Vazquez G, Kapczinski F, et al. Canadian Network for Mood And Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord. 2018;20(2):97–170. https://doi.org/10.1111/bdi.12609.
30. Hernández-Díaz S, Smith CR, Shen A, Mittendorf R, Hauser WA, Yerby M, Holmes LB. Comparative safety of antiepileptic drugs during pregnancy. Neurology. 2012;78(21):1692–9. https://doi.org/10.1212/WNL.0b013e3182574f39.
31. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance; 2014
32. Holmes LB, Mittendorf R, Shen A, Smith CR, Hernandez-Diaz S. Fetal effects of anticonvulsant polytherapies: different risks from different drug combinations. Arch Neurol. 2011;68(10):1273–9. https://doi.org/10.1001/archneurol.2011.133.

33. Sadowski A, Todorow M, Brojeni PY, Koren G, Nulman I. Pregnancy outcomes following maternal exposure to second-generation antipsychotics given with other psychotropic drugs: a cohort study. BMJ Open. 2013;3(7):3062. https://doi.org/10.1136/bmjopen-2013-003062.
34. Wesseloo R, Liu X, Clark CT, Kushner SA, Munk-Olsen T, Bergink V. Risk of postpartum episodes in women with bipolar disorder after lamotrigine or lithium use during pregnancy: a population-based cohort study. J Affect Disord. 2017a;218(May):394–7. https://doi.org/10.1016/j.jad.2017.04.070.
35. Wesseloo R, Wierdsma AI, Van Kamp IL, Munk-Olsen T, Hoogendijk WJG, Kushner SA, Bergink V. Lithium dosing strategies during pregnancy and the postpartum period. Br J Psychiatry. 2017b;211(1):31–6.
36. Clark CT, Wisner KL. Treatment of peripartum bipolar disorder. Obstet Gynecol Clin N Am. 2018;45(3):403–17. https://doi.org/10.1016/j.ogc.2018.05.002.
37. Newport DJ, Stowe ZN, Viguera AC, Calamaras MR, Juric S, Knight B, Pennell PB, Baldessarini RJ. Lamotrigine in bipolar disorder: efficacy during pregnancy. Bipolar Disord. 2008;10(3):432–6. https://doi.org/10.1111/j.1399-5618.2007.00565.x.
38. Pariente G, Leibson T, Shulman T, Adams-Webber T, Barzilay E, Nulman I. Pregnancy outcomes following in utero exposure to lamotrigine: a systematic review and meta-analysis. CNS Drugs. 2017:1–12. https://doi.org/10.1007/s40263-017-0433-0.
39. Munk-Olsen T, Liu X, Viktorin A, Brown HK, Di Florio A, D'Onofrio BM, Gomes T, Howard LM, Khalifeh H, Krohn H, Larsson H, Lichtenstein P, Taylor CL, Van Kamp I, Wesseloo R, Meltzer-Brody S, Vigod SN, Bergink V. Maternal and infant outcomes associated with lithium use in pregnancy: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018;5(8):644–52. https://doi.org/10.1016/S2215-0366(18)30180-9.
40. Patorno E, Huybrechts KF, Hernandez-Diaz S. Response: lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;377:893–4.
41. Huybrechts KF, Hernández-Díaz S, Patorno E, Desai RJ, Mogun H, Dejene SZ, Cohen JM, Panchaud A, Cohen L, Bateman BT. Antipsychotic use in pregnancy and the risk for congenital malformations. JAMA Psychiatry. 2016;73(9):938–46. https://doi.org/10.1001/jamapsychiatry.2016.1520.
42. Park Y, Hernandez-Diaz S, Bateman BT, Cohen JM, Desai RJ, Patorno E, Glynn RJ, Cohen LS, Mogun H, Huybrechts KF. Continuation of atypical antipsychotic medication during early pregnancy and the risk of gestational diabetes. Am J Psychiatr. 2018;175(6):564–74. https://doi.org/10.1176/appi.ajp.2018.17040393.
43. Cohen LS, Góez-Mogollón L, Sosinsky AZ, Savella GM, Viguera AC, Chitayat D, Hernández-Díaz S, Freeman MP. Risk of major malformations in infants following first-trimester exposure to quetiapine. Am J Psychiatr. 2018;175(12):1225–31. https://doi.org/10.1176/appi.ajp.2018.18010098.
44. Damkier P, Videbech P. The safety of second-generation antipsychotics during pregnancy: a clinically focused review. CNS Drugs. 2018;32(4):351–66. https://doi.org/10.1007/s40263-018-0517-5.
45. Leiknes KA, Cooke MJ, Jarosch-von Schweder L, Harboe I, Høie B. Electroconvulsive therapy during pregnancy: a systematic review of case studies. Arch Womens Ment Health. 2015;18(1):1–39. https://doi.org/10.1007/s00737-013-0389-0.
46. Viguera AC, Whitfield T, Baldessarini RJ, Newport DJ, Stowe Z, Reminick A, Zurick A, Cohen LS. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. Am J Psychiatr. 2007;164(12):1817–24. https://doi.org/10.1176/appi.ajp.2007.06101639.
47. Viguera AC. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. Am J Psychiatr. 2000;157(2):179–84. https://doi.org/10.1176/appi.ajp.157.2.179.
48. Heron J, Haque S, Oyebode F, Craddock N, Jones I. A longitudinal study of hypomania and depression symptoms in pregnancy and the postpartum period. Bipolar Disord. 2009;11(4):410–7. https://doi.org/10.1111/j.1399-5618.2009.00685.x.

49. Maina G, Rosso G, Aguglia A, Bogetto F. Recurrence rates of bipolar disorder during the postpartum period: a study on 276 medication-free Italian women. Arch Womens Ment Health. 2014;17(5):367–72. https://doi.org/10.1007/s00737-013-0405-4.
50. Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJM, Kushner SA, Bergink V. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatr. 2016;173(2):117–27. https://doi.org/10.1176/appi.ajp.2015.15010124.
51. Schmidt KA, Palmer BA, Frye MA. Mixed mania associated with cessation of breastfeeding. Int J Bipolar Disord. 2016;4(1):18. https://doi.org/10.1186/s40345-016-0059-z. Epub 2016 Sep 5. PMID: 27593209; PMCID: PMC5011067
52. Sharma V. Weaning and mixed mania-A case report. J Hum Lact. 2018;34(4):745–8. https://doi.org/10.1177/0890334418777695.
53. Sharma V, Baczynski C. Is bipolar post-partum depression overlooked? Lancet Psychiatry. 2019;6(11):891–2. https://doi.org/10.1016/S2215-0366(19)30386-4.
54. Rybakowski J, Jerzy Cubała W, Ałeck PG, Rymaszewska J, Samochowiec J, Szulc A, Dudek D. Recommendations of the polish psychiatric association regarding the treatment of affective disorders in women of childbearing age. Part II: bipolar disorder. Psychiatr Pol. 2019;53(2):263–76. https://doi.org/10.12740/PP/103555.
55. Sharma V, Khan M, Sommerdyk C. Quetiapine in the acute treatment of bipolar postpartum depression: a chart review. J Clin Psychopharmacol. 2015;35(6):733–5. https://doi.org/10.1097/JCP.0000000000000415.
56. Misri S, Abizadeh J, Eng B, A., Albert, G., Ryan, D., & Swift, E. An open-label study of quetiapine extended-release in a sample of postpartum women with bipolar II depressive episode. Curr Psychopharmacol. 2015;4(1):17–26. https://doi.org/10.2174/2211556004666150604235028.
57. Heron J, McGuinness M, Blackmore ER, Craddock N, Jones I. Early postpartum symptoms in puerperal psychosis. BJOG. 2008;115(3):348–53. https://doi.org/10.1111/j.1471-0528.2007.01563.x.
58. Albertini E, Ernst CL, Tamaroff RS. Psychopharmacological decision making in bipolar disorder during pregnancy and lactation: a case-by-case approach to using current evidence. Focus. 2019;17(3):249–58. https://doi.org/10.1176/appi.focus.20190007.
59. Koukopoulos A, Reginaldi D, Tondo L, Visioli C, Baldessarini RJ. Course sequences in bipolar disorder: depressions preceding or following manias or hypomanias. J Affect Disord. 2013;151(1):105–10.
60. Sharma V, Smith A, Mazmanian D. Olanzapine in the prevention of postpartum psychosis and mood episodes in bipolar disorder. Bipolar Disord. 2006;8(4):400–4.
61. Sharma V, Sommerdyk C. Lamotrigine in the prevention of bipolar II postpartum depression. Prim Care Companion CNS Disord. 2016;18(6)
62. Sharma V, Bergink V, Berk M, Chandra PS, Munk-Olsen T, Viguera AC, Yatham LN. Childbirth and prevention of bipolar disorder: an opportunity for change. Lancet Psychiatry. 2019;6(9):786–92. https://doi.org/10.1016/S2215-0366(19)30092-6.

Anxiety Disorders

4

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4.1 Introduction

Pregnancy and the postpartum period (perinatal period), which includes the first year after birth, represent a period of major change in the life of a woman, and the process of adapting to these changes can cause substantial physical and emotional distress [1–3]. Although this period can represent a source of joy for motherhood, various physiological changes that occur may generate emotional repercussions that affect both pregnant women and the people around them [4–6]. The vulnerability for a mental disorder or the presence of a previous mental disorder increases the risk of developing perinatal mental illness, which represents a major complication of pregnancy and the postpartum period [7]. The most common mental disorders that can develop during the perinatal period are depression, anxiety, and psychosis [8, 9]; these disorders are associated with possibly serious consequences, such as suicide [10]. Several studies have related the presence of anxiety symptoms/disorders with varying results depending on methodological approaches. The pooled prevalence of anxiety symptoms during pregnancy was 22.9% in the study by Dennis [11], but according to a recent meta-analysis by Fawcett and colleagues [12], the prevalence of having at least one AD during pregnancy or the postpartum period

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was estimated to be 20.7% (range: 16.7%–25.4%) [12] with a greater prevalence in pregnancy. The prevalence differs according to the period of study: 15.2% in the prenatal period [11] and 8.5% in the postpartum period [13].

The presence of anxiety, even subclinical symptoms that could be considered a normal phenomenon during and after pregnancy, has several implications for the health of the woman and fetus/child [14]. The quality of life and daily functioning of a woman with anxiety symptoms or a disorder during the perinatal period are compromised [15]. Furthermore, previous anxiety disorders are strong predictors of developing anxiety in pregnancy, independent of other risk factors [16].

4.2 Epidemiology

The exact prevalence of anxiety symptoms or an anxiety disorder during the perinatal period varies according to the study design and population, and it remains difficult to estimate.

A recent meta-analysis [12] reported that one in five pregnant women suffer from at least one anxiety disorder (AD) during the perinatal period with a prevalence between 16.7% and 25.4% with an overall prevalence of 20.7%. One in 20 women (5.5%) meets the criteria for at least two ADs. The postpartum period is the time of greatest risk for developing ADs [12], and the prevalence is higher among postpartum women than in the general population. The estimated number of cases during the first 6 months of the postpartum period varies from 6.1% to 27.9% [11, 13].

A recent meta-analysis [11] demonstrated that the prevalence of anxiety symptoms, evaluated by a self-report questionnaire, increased differently during different periods of pregnancy: 18.2% in the first trimester, 19.1% in the second trimester, and 24.6% in the third trimester. However, it is possible to make a clinical diagnosis of at least one AD in 15.2% of women before childbirth. Overall at 1–24 weeks after childbirth, the prevalence of anxiety symptoms and ADs was 15.0% and 9.9%, respectively [11].

In a meta-analysis by Goodman and colleagues, the most common disorders in the postpartum period were generalized anxiety disorder (GAD) with an overall prevalence of 3.59% and panic disorder (PD) with an overall prevalence of 1.66% [13]. The most recent meta-analysis by Fawcett and colleagues noted that the most prevalent perinatal disorders were the following: specific phobia (4.8%), GAD (2.4%), and social phobia (2.4%) [12]. The prevalence rates of other ADs were PD (1.8%), agoraphobia (2.4%), and anxiety not otherwise specified (2.3%) [12]. The rate of ADs in low- to middle-income countries was higher than those in high-income countries [11].

Women with moderate-to-high-risk pregnancies have a higher incidence of ADs compared to women with a medically low-risk pregnancy [12, 17], and anxiety symptoms in pregnancy can increase the risk of developing postnatal depression [18].

A substantial difficulty in assessing the incidence of perinatal anxiety disorders is the scarcity of diagnostic tools and valid screening. The use of the most recent

edition of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) [19] to diagnose ADs in pregnancy poses many problems.

For mood disorders, the DSM-5 has a peripartum specifier "with the onset of peripartum" that, as discussed in various studies, fails to distinguish between "prepartum" and "postpartum" onset. This issue affects the appropriate analysis of psychopathological and clinical features of episodes [20]. There is also no specification of perinatal anxiety disorders in the DSM-5 [19]. Therefore, for example, the application of DSM-5 criteria for GAD in pregnant or postpartum women is often not possible because the DSM includes the time requirement of "at least 6 months of anxiety and excessive worry" [15]. An attempt to overcome this barrier has been made by defining perinatal GAD as meeting the criteria for GAD in the DSM-5 for a minimum of 1 month [21].

4.3 Risks Factors of Anxiety Disorders

Although risk factors for perinatal anxiety have not been widely studied similar to perinatal depression, recent literature has identified the following possible predictors [13, 22]:

- Sociodemographic and economic risk factors: low sociocultural level [23, 24], low level of education [16], young age [25, 26], unemployment [27, 28], tobacco use [29].
- Psychological and psychiatric risk factors: previous history of mental illness, especially anxiety or depression disorders, or history of psychiatric treatment during a previous pregnancy or at any time during the lifetime [28, 30, 31]; use and abuse of alcohol [32, 33]; negative cognitive styles [16, 30, 32]; trauma, either recent or in infancy [30, 34, 35]; lack of support from family or dissatisfied/poor relationship with partner [16, 28, 30]; history of abuse/neglect [36–38]; low self-esteem and perceived stress [39]; previous miscarriage or stillbirth [40]; childhood parenting experiences [41]; style of parenting (limited care and substantial control) [42, 43].
- Obstetric and pregnancy-related risk factors: unplanned or unwanted pregnancy [16, 28, 30, 32]; fear of childbirth or upcoming delivery [29]; multiparity [44, 45]; current or past pregnancy/delivery complications, history of pregnancy loss, and pregnancy terminations or stillbirth [46–48]; history of miscarriage [49]; history of episiotomies, cesarean section, or a previous negative birth experience [29, 48]; history of infertility treatments [30]; unexpected loss of pregnancy [29, 47].
- Biochemical variables: including high levels of cortisol, polyunsaturated fatty acids, and proinflammatory cytokines [16, 50]; altered level of perinatal oxytocin [51].

Limited information is available on the effect of anxiety and stress on fetal development. There is much more information about postnatal depression. The time in

utero is regarded as a critical developmental period, and some studies have shown that adverse stimuli during pregnancy can have lasting consequences for fetal and postnatal health and development through a mechanism, such as epigenetic or other biological mechanisms [52–54], including inflammatory mediators and hormones [55].

4.4 Screening for Perinatal Anxiety Disorders

The perinatal period is a complicated period that presents profound challenges for women but also for the other parent because during this period the global well-being and mental health of both parents and baby are closely connected [56, 57].

Early screening of perinatal anxiety disorders is crucial for planning assistance and treatment both to prevent and minimize the consequences for the mother and the fetus/child. This concept was confirmed by the most recent update to the National Institute for Health and Care Excellence (NICE) guidelines [58], which recommend identifying, assessing, caring for, and treating mental health problems in women before and during pregnancy and the postnatal period.

The NICE guidelines [58] suggest using the 2-item Generalized Anxiety Disorder (GAD-2) Scale to assess anxiety status, and if the woman scores 3 or more on the GAD-2 scale, the 7-item Generalized Anxiety Disorder (GAD-7) Scale should be administered [59–61].

A frequently used self-reporting tool to screen for perinatal anxiety disorders is the State-Trait Anxiety Inventory (STAI) [62], which includes 20 items for state anxiety and 20 items for trait anxiety. Each of these items corresponds to a scale of four levels of intensity. Although it investigates general anxiety symptomatology, it is useful in predicting the onset of perinatal anxiety symptomatology [63, 64].

Other instruments assess for both anxiety and depression, which are often comorbid conditions. The Hospital Anxiety and Depression Scale (HADS) [65] is frequently used and is composed of two subscales; each scale contains 10 items, with the HADS–Depression covering depression symptoms and the HADS–Anxiety covering anxiety symptoms. Specifically, the latter scale investigates anxiety in general without specific references to pregnancy. Various studies have confirmed the validity of this instrument in the perinatal period [66].

A similar instrument used in the perinatal period is the Beck Anxiety Inventory (BAI) [65]. This test is composed of 21 items that investigate physical symptoms, behaviors, thoughts, and feelings associated with states of anxiety in the preceding week. To track the specific nature of the worry, there are three instruments that are used only in the prenatal period.

A verified instrument used in Australia is the Brief Measure of Worry Severity (BMWS) [67]; this rapid administration test is composed of eight items that use a 4-point Likert scale. The questionnaire focuses on the cognitive component of anxiety that can become exacerbated in the gestational period and affect moods and general well-being. The study by Austin and collaborators highlighted the validity

of this instrument in pregnancy and its capabilities in predicting the onset of depressive disorders in the postpartum period [6].

The Penn State Worry Questionnaire (PSWQ) [68] has been used in some studies in the prenatal period [69]. This 16-item instrument measures trait anxiety, which describes the habit of worry regardless of time or situational circumstances. The items consider the critical aspects of worry that are significant from a clinical standpoint, such as intensity, its excessive nature, and the sense of uncontrollability that the person can feel.

The Pregnancy-Related Anxiety Questionnaire–Revised (PRAQ-R) [70] investigates expectant mothers' anxieties related to three different areas: fears about the baby's health, about the delivery, and their physical appearance. The abbreviated version of this test contains 10 items using a 5-point Likert scale. This instrument has proven effective in predicting significant effects on a child's development [71, 72].

The Pregnancy-related Anxiety (PrA) Scale [73] is a similar instrument that assesses anxieties about the woman's health during pregnancy, her well-being, caring for the baby, and fears about the birth and labor. This instrument is composed of 10 items using a Likert scale from 1 (not at all) to 4 (extremely). The final score ranges between 10 and 40. Several longitudinal studies have confirmed this test's predictive capability regarding short- and long-term behavioral and emotional problems [74, 75].

The Perinatal Anxiety Screening Scale (PASS) [76] is another useful instrument that studies anxiety symptoms in pregnancy and postpartum, particularly acute anxiety, general worry, specific fears, perfectionism, and social anxiety. This scale is a very accurate screening instrument because it differentiates the symptoms of various ADs but does not investigate the anxieties specific to pregnancy.

Currently, as suggested in the review by Fairbrother and colleagues [77], there is no predominant anxiety screening tool, and the commonly used scales have limitations in assessing perinatal anxiety. It is important to note that an AD diagnosis is possible only through a clinical interview performed by a psychiatrist specializing in the field of perinatal mental health. However, despite their known limitations, screening questionnaires can be valid tools for the clinician or for assisting women, as they enable them to express their feelings of distress and fears.

4.5 Clinical Characteristics and Treatment of Perinatal Anxiety Disorders

Being worried and feeling anxiety may be normal and adaptive during childbearing, but a proportion of women develop excessive levels of anxiety or pathological anxiety before and after the birth of a child [78–81]. Many women experience anxiety even at subclinical levels during the prenatal period, which could have harmful and long-term effects on mothers and children [14, 78]. Few studies have focused on the clinical presentation and treatment of postpartum anxiety disorders [82].

Anxiety symptoms in the perinatal period can be part of common ADs according to the DSM-5 [19] or abnormal states of anxiety specific to pregnancy. According to Brockington and colleagues [83], perinatal ADs show similar characteristics to classic adult ADs (panic, phobias, and GAD), but their focus changes. In pregnancy, ADs can focus particularly on fears about fetal abnormalities, fetal death, feelings of inadequacy as a mother, tokophobia (fear of childbirth), and the fear of having little support. In the postpartum period, anxiety would instead be directed at the health of the child, fear of sudden infant death, fear of having little support, and the fear of being judged [83].

Several researchers have, however, underlined the importance of distinguishing between the characteristics of ADs in general and those present in pathological anxiety specific to pregnancy. Some studies highlight that anxiety symptoms in the perinatal period are predominantly associated with worries about changes in physical appearance, fears regarding the child's health, negative expectations about maternity, or difficulties in fulfilling the maternal role [15, 84].

Several researchers have attempted to establish an AD specific to pregnancy, known as Pregnancy-related Anxiety (PrA), which would be a distinct entity. The first studies date back to the 1950s [85–87]. Both the study by Standley and colleagues and that of Levin and colleagues identified specific characteristics that included concerns about pregnancy, childbirth, and hospitalization. Subsequently, Huizink in 2004 [70] identified dimensions that also included fear about fetal abnormalities. In 2014, Huizink and colleagues reported that the presence of a GAD and anxiety specific to pregnancy exacerbate each other over time, thereby causing particularly intense levels of anxiety in future mothers [70].

Recently in a review of 38 studies, Blackmore and colleagues [87] identified three characteristics unique to anxiety in pregnancy, which were grouped into three areas: emotions (fear about childbirth or fetal abnormalities, nervousness, irritability, mood swings or distress), cognition (excessive worry about pregnancy, childbirth, and the postpartum period), and somatic symptoms (sleep disturbances, fatigue, palpitations, shortness of breath, hyperventilation, tremors, tiredness, headaches, or nausea and vomiting). Furthermore, Blackmore described nine themes specific to anxiety in pregnancy that include the health of the fetus, loss of the fetus, childbirth, health of family members and the baby, well-being of the mother, physical appearance, social and family support, and economic circumstances. It must be noted that the suggested themes are also part of a healthy and normal emotional affective reaction to an important change, and therefore, it is crucial to distinguish a normal state of anxiety from a pathological condition.

A recent review by Williams and Koleva [88] indicated that two-thirds of women profess worries about the unborn baby during pregnancy; these worries range from fears about fetal abnormalities, complications during childbirth, ability to care for the baby, and breastfeeding to concerns about body image or the relationship with their partner. However, it is only when these worries become excessive and interfere with daily life that perinatal ADs can be considered. In the study by Mudra [89], there was evidence that PrA scores, in a sample of 180 pregnant women, were overall stable, but the different dimensions (fear of giving birth, worries of bearing a

physically or mentally handicapped child, and concerns about own appearance) varied significantly over time. This finding underlines the need for differentiated evaluations of specific forms of PrA [89].

In the scientific literature, there are conflicting opinions on the appropriate treatment of ADs in the perinatal period [9, 90, 91], as well as ethical and legal implications. A few studies with limited sample sizes and poor methodological methods have attempted to evaluate pharmacological and nonpharmacological treatments. Women with ADs tend to prefer therapeutic strategies during pregnancy that include psychotherapy rather than pharmacotherapy [92]. Psychotherapy, especially cognitive–behavioral therapy (CBT) [93], is suggested as a useful approach to treat mild-to-moderate anxiety in the perinatal period although few studies have evaluated its efficacy [55, 94, 95].

A recent meta-analysis and literature review suggest positive effects of midwife-supported psychotherapy on depression and anxiety symptoms during the antenatal stage of pregnancy [96]. Another study on interpersonal psychotherapy suggests that it may be effective in reducing anxiety symptoms and worry [97]. The conclusions of the meta-analysis did not have definitive evidence of the efficacy of midwife-supported and interpersonal psychotherapy, so more studies are required to confirm this approach.

Studies on psychopharmacology during both prenatal and postpartum periods have addressed safety issues in the woman and fetus/child [98–100]. Approximately 13% of pregnant women use at least one antidepressant drug during pregnancy, mainly selective serotonin reuptake inhibitors (SSRIs) [90, 101]. Refer to Chap. 17 of this text for further discussion of drug therapy. According to the most recent update of the NICE guidelines [58], pharmacological treatment might be a valid option for anxiety disorders during pregnancy or breastfeeding if the symptoms are moderate to severe, the anxiety is comorbid with depression, or there is a high suicidal risk [90].

In the following section, the features of perinatal anxiety disorders will be described.

4.5.1 Generalized Anxiety Disorder (GAD)

The DSM-5 describes GAD as a condition characterized by excessive anxiety and worry (apprehensive expectation) occurring more days than not for at least 6 months, but the time criteria are difficult to apply to women during the perinatal period.

GAD concerns several events or activities and is accompanied by various symptoms including restlessness, fatigue, irritability, poor concentration, muscle tension, and sleep disturbance [19].

As previously reported, the prevalence of GAD in women is different according to the study methodology: Dennis reported a prevalence of 4.1% (range 1.9–6.2) [11], but Fawcett reported 2.4% (range 1.3%–3.8%) in the perinatal period [12]. The prevalence may be more common than among the general population especially in the postpartum period [102–105], and the prevalence may be higher in pregnant

women than in not-pregnant women [106]. The overall prevalence of GAD among pregnant women was 3% (range 2%–7%) and was reported as 3% (1%–12%) in the first trimester, 3% (0%–7.4%) in the second trimester, and 3% (1%–8%) in the third trimester [102].

Frequent worrying is considered a common experience in pregnant and postpartum women. Wenzel and colleagues reported that approximately one to five women displayed symptoms of subsyndromal GAD [104]. Some data seems to prove the existence of a negative influence of GAD on fetal growth [107], and the newborns of the women with GAD had significantly lower blood levels of Brain-Derived Neurotrophic Factor (BDNF) compared to control cases [108].

Women describe excessive worries that focus on pregnancy-related complications, the baby's well-being, infant safety and care, self-blame, feelings of isolation, agoraphobia, avoidance of social situations, changes in physical appearance especially weight gain, financial issues, cleanliness, breastfeeding, etc. [88, 109, 110]. Women with postpartum generalized anxiety commonly reported the presence of physical symptoms, such as disturbed sleep, palpitations, body aches, fatigue, numbness, and tingling. Cognitive symptoms are common, especially poor concentration and inability to make decisions [78].

A GAD diagnosis can be considered if worries occupy more than 50% of daily life and interfere with normal activities and functioning and/or cause significant distress [19]. GAD is also high on the diagnostic radar if the patient does not respond to reassurances about the concerns expressed, if the worries cannot be controlled, or if there is no identifiable trigger for the anxiety symptoms. In contrast to depression, women experiencing anxiety describe themselves as feeling jittery, on edge, hyperactive, and fatigued at the end of the day. They check frequently on their baby and are frequent or prompt visitors to the pediatrician or their primary physician [111].

Few studies have investigated psychosocial, psychotherapy, and psychopharmacological treatment of perinatal GAD. Regarding psychotherapy, a pilot study by Green and colleagues (2015) tested a CBT intervention in a small sample of pregnant and postpartum women ($n = 10$) who met the criteria for either GAD or social anxiety disorder (SAD) and found a significant reduction in both anxiety and depressive symptoms between pre- and post-treatment [112]. Goodman and colleagues (2014) tested a group mindfulness-based cognitive therapy intervention in a small sample of pregnant women ($n = 24$) with moderate symptoms of anxiety and worry. After treatment, there was a significant reduction in anxiety, worry, and depressive symptoms [113]. In a recent retrospective cohort study on the use of CBT in pregnant women with GAD, post-treatment levels of anxiety in treated women compared to untreated were significantly lower than those at baseline with no significant difference in gestational age or newborn birth weight [114]. In mild-to-moderate perinatal GAD, CBT is the first treatment option [15]. In moderate-to-severe cases, pharmacological treatment should be considered [15, 90] after evaluating the risks and benefits of such therapies [115–117]. SSRIs remain the first choice for pharmacological treatment, excluding paroxetine, for GAD with a response rate that varies from 30% to 50% in the perinatal period. Tricyclics are

effective in the treatment of GAD, but because of their poor safety profile, they are not recommended for pregnant women [52, 53].

According to the review by Bellantuono, the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine is also a potential treatment option during early pregnancy in women with severe GAD or women with a clear history of GAD, who are already successfully taking it for long-term maintenance treatment or have previously responded successfully to this drug treatment [31]. Venlafaxine is described as relatively safe during pregnancy in regards to malformation, but no definitive conclusions can be drawn on its safety during breastfeeding [31]. According to the Drugs and Lactation Database, venlafaxine can be used during breastfeeding, and infants, especially newborn or preterm children, should be monitored if this drug is used during lactation. Children of mothers who take venlafaxine during pregnancy should be monitored for poor neonatal adaptation syndrome [118].

4.5.2 Panic Disorder (PD)

The DSM-5 describes PD as a condition characterized by recurrent unexpected panic attacks (PAs) with at least one attack that has been followed by 1 month of persistent concern or worry about PAs or the possible consequences with a significant maladaptive change in global behavior due to PAs [19]. PAs are characterized by rapid onset of physical and psychological symptoms of anxiety [19].

Women are affected by PD more than twice as often as men, and reproductive factors may have a role in the observed trends [119, 120]. Prevalence rates of PD in the perinatal period differ between studies with an overall prevalence of 1.8% during the perinatal period according to a recent meta-analysis by Fawcett and colleagues [12] and 3% (range 2%–4%) in pregnant women in the meta-analysis by Viswasam [102]. The pooled prevalence by trimester was reported as 3% (range 2%–5%) in the first trimester and 3% (2%–6%) in the third trimester [102]. Agoraphobia, which is now distinct from PD according to the DSM-5, has an overall prevalence of 2.4% [12].

In a retrospective study, Bendelow and colleagues reported that panic manifestations improved during pregnancy but worsened in the postpartum period, and there was a high risk of new-onset panic symptoms [121]. Women with preexisting PD have an increased risk of relapse [78, 104]. In contrast to previous studies, a prospective study with a small sample size by Guler highlighted that women may experience an improvement in PD symptoms in the early postpartum period (from pregnancy to 6 weeks postnatally) [122].

Another recent prospective naturalistic study [123] suggested that the severity of panic symptoms may decrease during the postpartum period (first 6–8 weeks); half of the sample showed a decrease of at least 50% in symptom severity.

There were several limitations in the studies mentioned above including small sample sizes, and more studies are required to better understand the course of panic during and after pregnancy.

The variation in the severity of panic symptoms/disorders during pregnancy could be explained by several factors such as varying sensitivities to hormonal changes and psychosocial influences. Approximately 4–5 days after delivery, there is a precipitate drop in hormone concentrations (e.g., progesterone, estradiol, and cortisol concentrations). This major change coincides with the onset of "maternity blues" but also with an increase in new panic manifestations.

Another possible explanation for the findings is baseline respiratory abnormalities, which have been highlighted in patients with PD [124–127], but studies are required to confirm this theory in pregnant women who show significant changes in pulmonary and cardiovascular physiology [128–130].

The symptoms of PA and the subsequent behavior of individuals during the perinatal period are similar to those of classic panic [78, 131]. Mothers with PD feel more guilt and shame, which can negatively impact the course of pregnancy and a woman's self-esteem and confidence in taking care of the baby [88, 90]. PD may negatively affect gestational length and birth weight [132]. A recent study by Martini and colleagues asserted that women with PD during the perinatal period reported a shorter duration of breastfeeding, impaired bonding, more loving/affection toward their babies, and more feeding problems in their children [119].

Moreover, women with PD are more likely to display help-seeking behaviors including repeated perinatal check-ups and emergency room visits. All these factors may heavily affect the quality of life of patients, who have a high risk of isolation, and the entire family [78, 88, 133]. Given the potential for negative effects from PD, women and the fetus/child should be closely monitored during the perinatal period [123].

Few studies have investigated psychotherapy and psychopharmacological treatment in perinatal PD. Among psychotherapies, CBT is a first-line treatment in patients with PD, and its effectiveness is well established in several studies [126, 127].

A 1992 study by Robinson supports the use of psychotherapy in women with PD during the perinatal period, and the women had better control of anxiety symptoms and clinical remission of PD [134]. A Japanese case series on the use of CBT for postpartum PD reported a beneficial therapeutic effect for patients. The report suggested that therapists should prescribe tasks that patients can perform collaboratively with their children to improve adherence and clinical effects [135].

Limited data are available regarding the efficacy of anti-panic medication in pregnancy. Concerning SSRIs, a few case reports have supported the use of citalopram [136] and escitalopram [137] and demonstrated good control of anxiety symptoms and health outcomes for the child. Among tricyclic antidepressants (TCAs), nortriptyline [138] and low-dose imipramine (10–40 mg/day) [139, 140] have been suggested as possible therapies for PD during pregnancy but because of their poor safety profile, they are not recommended for pregnant women.

4.5.3 Specific Phobias (SP)

The DSM-5 describes SP as a condition characterized by marked fear or anxiety of a specific object or situation, and the symptoms are out of proportion to the actual danger and sociocultural context. The phobic object or situation is actively avoided or endured with intense fear or anxiety.

SP is a common type of AD in women during the perinatal period. Its prevalence during the perinatal period varies according to the different methods of assessment used to detect cases: 3.2%–19.9% in the review by Goodman [141] and 1.6%–3.5% in the meta-analysis by Fawcett [12]. In a recent meta-analysis by Viswasam and colleagues, the overall prevalence in pregnant woman was 6% with a range from 4% to 10%, and the prevalence by trimester was reported as 15% (range 11%–19%) in the first trimester, 9% (range 2%–38%) in the second trimester, and 4% (range 2–-8%) in the third trimester [102].

In the study by Nath and colleagues [142], the estimated prevalence of SP in the maternal population was 8.4% (range 5.8%–12.1%) with onset in childhood or adolescence and 1.5% (range 0.6%–3.7%) for pregnancy-related phobias with onset during the perinatal period.

In the study by Patel and Hollins, the most common types of pregnancy-related phobias were needle blood-injection injury (including needle phobia), tokophobia (fear of childbirth), and emetophobia (fear of vomiting) [143]. Over half of the women with SP presented with a comorbid mental disorder including Major Depressive Disorder (31%) and GAD (14.3%) [142].

Tokophobia is a specific phobia of the perinatal period that is defined as a severe fear of pregnancy and childbirth. The intensity of tokophobia can lead to pregnancy avoidance or cesarean delivery, and the onset can be primary in nulliparous women or secondary to a previous traumatic birth or perinatal depressive disorder as reported in the study by Demšar [144]. Most women attribute the fear of childbirth to fear of episiotomy, fear of having no control over the situation, fear of feeling pain, and worries for the consequences of delivery on future sexual life [144]. Tokophobia tends to appear in women with poor social support, low self-esteem, and symptoms of depression and anxiety. The partner of these women also seems to have common characteristics, such as low mood, poor quality of life, and poor relationship satisfaction [145].

Few scientific studies have addressed the role, effect, and management of SP. The impacts of particular phobias on women and their children in the perinatal period remain unclear [141, 146, 147]. Early detection may be useful to prevent potential complications (e.g., detection of medical problems through a blood test) [142].

Only a few studies with methodological limitations and small sample sizes have investigated psychological therapies, such as CBT [148, 149]. Several studies on CBT and psychoeducation with the objective to reduce the fear of childbirth were performed, but results were limited due to several limitations, and no study has specifically investigated tokophobia [142].

4.5.4 Social Anxiety Disorder (Social Phobia) (SAD)

The DSM-5 describes SAD as a disorder characterized by marked and excessive fear or anxiety of social or performance situations in which the individual is exposed to possible scrutiny, evaluation, and judgment by others [19]. Patients feel very anxious and scared about being humiliated or embarrassed, which may lead to rejection or offending others, so the social situations are avoided or endured with intense suffering [19].

SAD is a common psychiatric disorder with a worldwide prevalence of 5%–10%, and it more commonly affects women [150]. Few studies have considered the characteristics of the disorder in the perinatal period, and prevalence varies widely across studies: overall prevalence has been reported to be 2.4% (range 1.6%–3.5%) during the perinatal period [12] and 3% (range 2%–7%) in pregnant woman [102]. The prevalence by trimester was reported to be 4% (range: 3%–5%) in the first trimester, 6% (range: 0%–6.9%) in the second trimester, and 3% (range: 1%–6%) in the third trimester.

A recent prospective study [151] of Australian pregnant women reported that there were no new-onset cases of SAD or SP during pregnancy, in contrast with other ADs. All patients with SAD or SP met the diagnostic criteria during the entire pregnancy, and no women experienced remission regardless of if they received treatment.

In a sample of 180 pregnant women, Mudra and colleagues reported that women with symptoms of SAD showed higher levels of fear of childbirth and concerns about their appearance and were more likely to experience "excessive" child-related worries postpartum [89]. Two studies demonstrated that SAD increased the risk of developing postpartum depression. In a study with a sample of 500 women who were followed throughout pregnancy and until the 12th month postpartum, 20.7% of women with SAD developed depression symptoms during the first trimester and 17.2% developed minor or Major Depressive Disorder during the first month postpartum [152]. In a study with a sample of 246 mothers, the risk increased only after 10 months after delivery possibly due to several factors including returning to work and placing their children in childcare [153].

There is a lack of information on the psychological and pharmacological treatments for SAD. CBT is an effective treatment for SAD in the general population [93], but during the perinatal period, no sufficient data are available. In a sample of 10 women who met the criteria for either GAD or SAD, a CBT intervention was tested during pregnancy and in the postpartum period. There was a significant reduction in both anxiety and depressive symptoms between pre- and post-treatment, and women highly accepted and were satisfied with this treatment [112].

4.6 Consequences of Perinatal Anxiety Disorders

Several studies have shown that prenatal anxiety is associated with significant risk factors and short- and long-term consequences both in the mother and child, especially if untreated.

Women with antenatal anxiety have a high risk of preterm birth [14], spontaneous preterm delivery [14, 154], high blood pressure [155], preeclampsia [149], a cesarean delivery [155], having a child who was small for gestational age [14], lower mean birth weight [14], and smaller head circumference [14, 156].

Women with PD during pregnancy had a higher risk of polyhydramnios, anemia, and preterm deliveries with an infant who was at high risk of being small for their gestational age [157]. The same negative effect of PD in pregnancy on birth weight was also detected in women with major depression and GAD [108].

Furthermore, in the same study by Uguz [108], women with PD in pregnancy had a 1.6 times higher risk of having children with congenital abnormalities compared to women who did not suffer from PD, and the risk was 3.4 times higher for a cleft lip with/without cleft palate and 3 times higher for multiple congenital abnormalities [108].

Women with perinatal anxiety show poor adherence to medical treatment [158], worsening finances [158], disrupted mother–infant interactions [159], less bonding with their infants [119, 160], and reduced breastfeeding [161–164].

Women with anxiety during and after pregnancy show a high risk of depression, especially in the postpartum period, [81, 120, 165], or worsening comorbidities including increased risk of suicidal behavior and substance use disorders [158, 166].

Children of mothers with substantial anxiety during the perinatal period have a high risk of medical problems including allergic illnesses during infancy [167], cardio-metabolic disorders [168], or dermatological diseases [167] during adulthood. These children also have an increased risk of infant abuse, impaired child temperament [169–171], slow cognitive and social development [172, 173], and sleep problems [174]. Several studies have reported twice the risk for attention deficit hyperactivity disorder (ADHD) and an increased likelihood of anxiety symptoms or disorder [175–180] in children born from mothers with perinatal anxiety. A recent study on cerebral structure and function in children and adolescents (from birth to 17 years of age) born to mothers with anxiety in pregnancy reported alterations in cerebral structure and function in the frontal, temporal, and limbic areas [181]. A study by Uguz and colleagues reported that maternal GAD during pregnancy leads to significantly lower levels of BDNF, which could negatively impact the neurodevelopment of the fetus [108], which could influence the development of brain structure and function.

Studies that have researched the impact of maternal GAD on short- and long-term infant development have confirmed that it negatively influences both the neurodevelopment and growth of the child. Low birth weight and preterm birth associated with an anxious mother during pregnancy have also been found to be risk factors for developing GAD in later years [182]. Undiagnosed GAD in women results in less responsiveness and detached interaction toward their children, and these children tend to be more isolated and have flat and deflated moods [183].

A recent retrospective cohort study investigated the potential association between perinatal anxiety and neuropsychiatric hospitalizations in offspring. In a sample of 242,038 births, perinatal anxiety was found to be a risk factor for neuropsychiatry admissions and adverse events and long-term neuropsychiatric outcomes [155].

4.7 Untreated Perinatal Anxiety Disorders

Many of the factors described above prevent clinicians from determining whether and how to treat women with anxiety during the perinatal period. Clinicians are often faced with this difficult decision, especially regarding pharmacological treatment of psychiatric disorders in pregnancy. This problem arises from nondefinitive or inconsistent and sometimes conflicting results of studies evaluating the outcomes of psychotropic drug exposure in utero or in a baby who is breastfeeding. Clinicians have to consider both the well-being of the mother and the fetus/child. Prescribing therapy to pregnant women with ADs or during breastfeeding is a difficult task due to a lack of consensus in the literature. Ethical and legal conflicts can also make decision-making difficult.

According to the most recent update of the NICE guidelines [58], pharmacological treatment may be a valid option for ADs during pregnancy or breastfeeding if the symptoms are moderate to severe, the anxiety is comorbid with depression, or there is an increased risk of suicide. In other cases, psychotherapy, such as CBT, could be an effective therapeutic strategy even if scientific evidence is limited; several studies have methodological limitations and small sample sizes, which limit their results.

Regarding pharmacological treatment, antidepressants are considered the treatment of choice for women with ADs in the perinatal period. Safety data on antidepressant use in pregnancy are extremely limited, as pregnant women are excluded from randomized control trials for ethical reasons. Therefore, the existing evidence has been derived from either case reports or uncontrolled trials. *For more detailed information, see Chap. 17 of this book.*

It is recommended that specialists in perinatal mental health prescribe pharmacological treatments. The decision to use a pharmacological treatment in pregnant and/or breastfeeding women should always be discussed with the woman and partner so that relevant information is provided regarding the potential risks of these drugs and the consequences of untreated severe depressive/anxiety disorders. In addition, an accurate evaluation of the risk–benefit ratio should always be performed on a case-by-case basis when prescribing therapy in early pregnancy and during breastfeeding. The choice of treatment during pregnancy should be personalized, and both the severity of the symptoms and the choices of the woman and her partner should be considered. Pharmacological prescriptions should be shared and accompanied by written informed consent for medical and legal reasons to ensure a full understanding of the risks and benefits of treatment.

Our 10 general recommendations based on our expertise are as follows:

1. Try to detect anxiety symptoms/disorders early due to the risks of untreated anxiety in pregnancy.
2. Refer patients to an expert perinatal service as early as possible.
3. Based on the severity of symptoms or disorders, consider treating with non-pharmacological interventions, such as CBT.
4. If the disorder is moderate to severe, shared medical decision-making will help patients and clinicians reach the appropriate choice more easily.

5. Foster collaboration with other health figures including a gynecologist and obstetric team.
6. Psychiatrists shouldn't be afraid to prescribe an antianxiety medication in the perinatal period if necessary.
7. If medication is necessary, use the drug with the lowest known risk, use the lowest effective dose, avoid polytherapy, adjust the dosage as pregnancy progresses, reduce the dosage in the final weeks to avoid neonatal toxicity, and monitor fetal conditions during pregnancy.
8. If a woman taking psychotropic drugs finds that she is pregnant, clinicians have to consider:
   (a) The risk of stopping the medication abruptly which may trigger relapse of psychiatric disorders and the subsequent consequences for the mother and fetus.
   (b) The possibility that stopping a drug with known teratogenic risk after pregnancy is confirmed may not remove the risk of malformations.
9. Monitor the neonate for withdrawal symptoms after birth.
10. Document all decisions.

4.8 Conclusions

Perinatal anxiety is common and requires more attention and further research to clarify the best therapeutic strategy. Screening at the beginning in the first trimester for postpartum monitoring for a year following delivery is crucial for both planning treatment and mitigating potential consequences for the mother and child/fetus. Early screening would also identify potential risk factors in the perinatal period allowing for a personalized care treatment plan developed by an integrated multidisciplinary group.

References

1. Çalıkoğlu EO, Bedir B, Aydın A, Yılmaz S. An investigation of the prevalence of depression and related factors in pregnant women living in the province of Erzurum. Eur Res J. 2018;4(4):381–9.
2. Bhat NA, Hassan R, Shafiq M, Sheikh S. Sociodemographic factors: a major predictor of anxiety and depression among pregnant women. Delhi Psychiatry J. 2015;18(1)
3. O'Hara MW, Wisner KL. Perinatal mental illness: definition, description and aetiology. Best Pract Res Clin Obstet Gynaecol. 2014;28(1):3–12. https://linkinghub.elsevier.com/retrieve/pii/S1521693413001338
4. de la Fe Rodríguez-Muñoz M, Le H-N, de la Cruz IV, Crespo MEO, Méndez NI. Feasibility of screening and prevalence of prenatal depression in an obstetric setting in Spain. Eur J Obstet Gynecol Reprod Biol. 2017;215:101–5. https://linkinghub.elsevier.com/retrieve/pii/S030121151730283X
5. Gentile S, Fusco ML. Untreated perinatal paternal depression: effects on offspring. Psychiatry Res. 2017;252:325–32. https://linkinghub.elsevier.com/retrieve/pii/S0165178116309283
6. Austin M-P, Tully L, Parker G. Examining the relationship between antenatal anxiety and postnatal depression. J Affect Disord. 2007;101(1–3):169–74. https://linkinghub.elsevier.com/retrieve/pii/S0165032706004976

7. Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry. 2008;65(7):805. http://archpsyc.jamanetwork.com/article.aspx?doi=10.1001/archpsyc.65.7.805
8. Paschetta E, Berrisford G, Coccia F, Whitmore J, Wood AG, Pretlove S, et al. Perinatal psychiatric disorders: an overview. Am J Obstet Gynecol. 2014;210(6):501–509.e6. https://linkinghub.elsevier.com/retrieve/pii/S0002937813010478
9. Nillni YI, Mehralizade A, Mayer L, Milanovic S. Treatment of depression, anxiety, and trauma-related disorders during the perinatal period: a systematic review. Clin Psychol Rev. 2018;66:136–48. https://linkinghub.elsevier.com/retrieve/pii/S0272735817304075
10. Oates M. Perinatal psychiatric disorders: a leading cause of maternal morbidity and mortality. Br Med Bull. 2003;67(1):219–29. https://academic.oup.com/bmb/article/67/1/219/330390
11. Dennis CL, Falah-Hassani K, Shiri R. Prevalence of antenatal and postnatal anxiety: systematic review and meta-analysis. Br J Psychiatry. 2017;210:315–23.
12. Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The prevalence of anxiety disorders during pregnancy and the postpartum period. J Clin Psychiatry. 2019;80(4):18r12527. https://pubmed.ncbi.nlm.nih.gov/31347796
13. Goodman JH, Watson GR, Stubbs B. Anxiety disorders in postpartum women: a systematic review and meta-analysis. J Affect Disord. 2016;203
14. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Tomlinson G, Vigod SN, et al. Maternal anxiety during pregnancy and the association with adverse perinatal outcomes. J Clin Psychiatry. 2018;79(5):11–2. https://www.psychiatrist.com/JCP/article/Pages/2018/v79/17r12011.aspx
15. Misri S, Abizadeh J, Sanders S, Swift E. Perinatal generalized anxiety disorder: assessment and treatment. J Women's Heal. 2015;24(9):762–70. http://www.liebertpub.com/doi/10.1089/jwh.2014.5150
16. Martini J, Petzoldt J, Einsle F, Beesdo-Baum K, Höfler M, Wittchen H-U. Risk factors and course patterns of anxiety and depressive disorders during pregnancy and after delivery: a prospective-longitudinal study. J Affect Disord. 2015;175:385–95. https://linkinghub.elsevier.com/retrieve/pii/S0165032715000166
17. Fairbrother N, Young AH, Zhang A, Janssen P, Antony MM. The prevalence and incidence of perinatal anxiety disorders among women experiencing a medically complicated pregnancy. Arch Womens Ment Health. 2017;20(2):311–9. http://link.springer.com/10.1007/s00737-016-0704-7
18. Hutchens BF, Kearney J. Risk factors for postpartum depression: an umbrella review. J Midwifery Womens Health. 2020;65(1):96–108.
19. American Psychiatric Association, editor. Diagnostic and statistical manual of mental disorders fifth edition. American Psychiatric Association, editor. Arlington, VA: American Psychiatric Association; 2013.
20. Sharma V, Mazmanian D. The DSM-5 peripartum specifier: prospects and pitfalls. Arch Womens Ment Health. 2014;17(2):171–3. http://link.springer.com/10.1007/s00737-013-0406-3
21. Kane JB. Marriage advantages in perinatal health: evidence of marriage selection or marriage protection? J Marriage Fam. 2016;78(1):212–29. https://doi.org/10.1111/jomf.12257.
22. Lener MS, Charney DS, Feder A. Anxiety disorders. In: Simon AB, New AS, Goodman WK, editors. Psychiatry. New York: Wiley Blackwell; 2017. p. 88–102. (Mount Sinai expert guides). http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2017-19219-012&site=ehost-live.
23. Faisal-Cury A, Rossi MP. Prevalence of anxiety and depression during pregnancy in a private setting sample. Arch Womens Ment Health. 2007;10(1):25–32. https://doi.org/10.1007/s00737-006-0164-6.
24. Glazier R, Elgar F, Goel V, Holzapfel S. Stress, social support, and emotional distress in a community sample of pregnant women. J Psychosom Obstet Gynecol. 2004;25(3–4):247–55. http://www.tandfonline.com/doi/full/10.1080/01674820400024406

25. Dunkel Schetter C, Niles AN, Guardino CM, Khaled M, Kramer MS. Demographic, medical, and psychosocial predictors of pregnancy anxiety. Paediatr Perinat Epidemiol. 2016;30(5):421–9. https://doi.org/10.1111/ppe.12300.
26. Barcelona de Mendoza V, Harville E, Theall K, Buekens P, Chasan-Taber L. Effects of acculturation on prenatal anxiety among Latina women. Arch Womens Ment Health. 2016;19(4):635–44. http://link.springer.com/10.1007/s00737-016-0605-9
27. Bödecs T, Szilágyi E, Cholnoky P, Sándor J, Gonda X, Rihmer Z, et al. Prevalence and psychosocial background of anxiety and depression emerging during the first trimester of pregnancy: data from a Hungarian population-based sample. Psychiatr Danub. 2013;25(4):352–8. http://www.ncbi.nlm.nih.gov/pubmed/24247046
28. Giardinelli L, Innocenti A, Benni L, Stefanini MC, Lino G, Lunardi C, et al. Depression and anxiety in perinatal period: prevalence and risk factors in an Italian sample. Arch Womens Ment Health. 2012;15(1):21–30. https://doi.org/10.1007/s00737-011-0249-8.
29. Rubertsson C, Hellström J, Cross M, Sydsjö G. Anxiety in early pregnancy: prevalence and contributing factors. Arch Womens Ment Health. 2014;17(3):221–8. https://doi.org/10.1007/s00737-013-0409-0.
30. Bayrampour H, McDonald S, Tough S. Risk factors of transient and persistent anxiety during pregnancy. Midwifery. 2015;31(6):582–9. https://linkinghub.elsevier.com/retrieve/pii/S0266613815000662
31. Bellantuono C, Vargas M, Mandarelli G, Nardi B, Martini MG. The safety of serotonin-noradrenaline reuptake inhibitors (SNRIs) in pregnancy and breastfeeding: a comprehensive review. Hum Psychopharmacol. 2015;30(3):143–51.
32. Lee AM, Lam SK, Sze Mun Lau SM, Chong CSY, Chui HW, Fong DYT. Prevalence, course, and risk factors for antenatal anxiety and depression. Obstet Gynecol. 2007;110(5):1102–12. https://journals.lww.com/00006250-200711000-00024
33. Marcus SM, Flynn HA, Blow FC, Barry KL. Depressive symptoms among pregnant women screened in obstetrics settings. J Women's Heal. 2003;12(4):373–80. http://www.liebertpub.com/doi/10.1089/154099903765448880
34. Marchesi C, Ampollini P, Paraggio C, Giaracuni G, Ossola P, De Panfilis C, et al. Risk factors for panic disorder in pregnancy: a cohort study. J Affect Disord. 2014;156:134–8. https://www.sciencedirect.com/science/article/pii/S0165032713008422
35. Groves AK, Kagee A, Maman S, Moodley D, Rouse P. Associations between intimate partner violence and emotional distress among pregnant women in Durban. South Africa J Interpers Violence. 2012;27(7):1341–56. http://journals.sagepub.com/doi/10.1177/0886260511425247
36. Choi KW, Sikkema KJ. Childhood maltreatment and perinatal mood and anxiety disorders. Trauma Violence Abuse. 2016;17(5):427–53. http://journals.sagepub.com/doi/10.1177/1524838015584369
37. Atzl VM, Grande LA, Davis EP, Narayan AJ. Perinatal promotive and protective factors for women with histories of childhood abuse and neglect. Child Abuse Negl. 2019;91:63–77. https://pubmed.ncbi.nlm.nih.gov/30831534
38. Bayrampour H, Tomfohr L, Tough S. Trajectories of perinatal depressive and anxiety symptoms in a community cohort. J Clin Psychiatry. 2016;77(11):e1467–73.
39. Blackmore ER, Côté-Arsenault D, Tang W, Glover V, Evans J, Golding J, et al. Previous prenatal loss as a predictor of perinatal depression and anxiety. Br J Psychiatry. 2011;198(5):373–8. https://www.cambridge.org/core/product/identifier/S0007125000255116/type/journal_article
40. Glover V, O'Connor TG, O'Donnell K. Prenatal stress and the programming of the HPA axis. Neurosci Biobehav Rev. 2010;35(1):17–22. https://linkinghub.elsevier.com/retrieve/pii/S0149763409001742
41. Tyano S, Keren M, Herrman H, Cox J. Parenthood and mental health: a bridge between infant and adult psychiatry; 2010.
42. Grant K-A, Bautovich A, McMahon C, Reilly N, Leader L, Austin M-P. Parental care and control during childhood: associations with maternal perinatal mood disturbance and par-

enting stress. Arch Womens Ment Health. 2012;15(4):297–305. https://doi.org/10.1007/s00737-012-0292-0.
43. Jeong H-G, Lim J-S, Lee M-S, Kim S-H, Jung I-K, Joe S-H. The association of psychosocial factors and obstetric history with depression in pregnant women: focus on the role of emotional support. Gen Hosp Psychiatry. 2013;35(4):354–8. https://www.sciencedirect.com/science/article/pii/S0163834313000613
44. Lanzi RG, Bert SC, Jacobs BK. Depression among a sample of first-time adolescent and adult mothers. J Child Adolesc Psychiatr Nurs. 2009;22(4):194–202. https://doi.org/10.1111/j.1744-6171.2009.00199.x.
45. Redshaw M, Henderson J. From antenatal to postnatal depression: associated factors and mitigating influences. J Women's Heal. 2013;22(6):518–25. https://doi.org/10.1089/jwh.2012.4152.
46. Ali NS, Azam IS, Ali BS, Tabbusum G, Moin SS. Frequency and associated factors for anxiety and depression in pregnant women: a hospital-based cross-sectional study. Sci World J. 2012;2012:1–9. http://www.hindawi.com/journals/tswj/2012/653098/
47. Gong X, Hao J, Tao F, Zhang J, Wang H, Xu R. Pregnancy loss and anxiety and depression during subsequent pregnancies: data from the C-ABC study. Eur J Obstet Gynecol Reprod Biol. 2013;166(1):30–6. https://linkinghub.elsevier.com/retrieve/pii/S0301211512004472
48. Waqas A, Raza N, Lodhi HW, Muhammad Z, Jamal M, Rehman A. Psychosocial factors of antenatal anxiety and depression in Pakistan: is social support a mediator? Fischer G, editor. PLoS One. 2015;10(1):e0116510. https://doi.org/10.1371/journal.pone.0116510.
49. Bergner A, Beyer R, Klapp BF, Rauchfuss M. Pregnancy after early pregnancy loss: a prospective study of anxiety, depressive symptomatology and coping. J Psychosom Obstet Gynecol. 2008;29(2):105–13. http://www.tandfonline.com/doi/full/10.1080/01674820701687521
50. Glover V. Prenatal stress and its effects on the fetus and the child: possible underlying biological mechanisms. 2015. Adv Neurobiol 10:p. 269–283. http://link.springer.com/10.1007/978-1-4939-1372-5_13
51. Kroll-Desrosiers AR, Nephew BC, Babb JA, Guilarte-Walker Y, Moore Simas TA, Deligiannidis KM. Association of peripartum synthetic oxytocin administration and depressive and anxiety disorders within the first postpartum year. Depress Anxiety. 2017;34(2):137–46. https://onlinelibrary.wiley.com/doi/abs/10.1002/da.22599
52. Stonawski V, Frey S, Golub Y, Moll GH, Heinrich H, Eichler A. Af ektive Belastungen der Mutter in der Schwangerschaft und assoziierte epigenetische Veränderungen beim Kind: Eine Übersicht. Vol. 46, Zeitschrift fur Kinder- und Jugendpsychiatrie und Psychotherapie. Verlag Hans Huber AG; 2018 [cited 2021 Mar 18]. p. 155–67. https://pubmed.ncbi.nlm.nih.gov/28256157/
53. Glover V, O'Connor TG, Heron J, Golding J. Antenatal maternal anxiety is linked with atypical handedness in the child. Early Hum Dev. 2004;79(2):107–18. https://pubmed.ncbi.nlm.nih.gov/15324991/
54. Glover V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. Best Pract Res Clin Obstet Gynaecol. 2014;28(1):25–35. https://pubmed.ncbi.nlm.nih.gov/24090740/
55. Zappas MP, Becker K, Walton-Moss B. Postpartum anxiety. J Nurse Pract. 2021;17(1):60–4.
56. Cena L, Palumbo G, Mirabella F, Gigantesco A, Stefana A, Trainini A, et al. Perspectives on early screening and prompt intervention to identify and treat maternal perinatal mental health. Protocol for a prospective multicenter study in Italy. Front Psychol. 2020;11. https://www.frontiersin.org/article/10.3389/fpsyg.2020.00365/full
57. Yeaton-Massey A, Herrero T. Recognizing maternal mental health disorders: beyond postpartum depression. Curr Opin Obstet Gynecol. 2019;31(2) https://journals.lww.com/co-obgyn/Fulltext/2019/04000/Recognizing_maternal_mental_health_disorders_.6.aspx
58. NICE. Antenatal and postnatal mental health: clinical management and service guidance Clinical guideline [CG192] - Published date: 17 December 2014 - Last updated: 11 February 2020; 2020. https://www.nice.org.uk/guidance/cg192

59. Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, et al. Validation and standardization of the generalized anxiety disorder screener (GAD-7) in the general population. Med Care. 2008;46(3):266–74. https://journals.lww.com/00005650-200803000-00006
60. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10)
61. Sapra A, Bhandari P, Sharma S, Chanpura T, Lopp L. Using generalized anxiety disorder-2 (GAD-2) and GAD-7 in a primary care setting. Cureus; 2020.
62. Spielberger C, Gorsuch R, Lushene R, Vagg PR, Jacobs G. Manual for the State-Trait Anxiety Inventory (Form Y1 – Y2), vol. 4. Palo Alto, CA: Consulting Psychologists Press; 1983.
63. Grant K-A, McMahon C, Austin M-P. Maternal anxiety during the transition to parenthood: a prospective study. J Affect Disord. 2008;108(1–2):101–11. https://linkinghub.elsevier.com/retrieve/pii/S016503270700345X
64. Skouteris H, Wertheim EH, Rallis S, Milgrom J, Paxton SJ. Depression and anxiety through pregnancy and the early postpartum: an examination of prospective relationships. J Affect Disord. 2009;113(3):303–8. https://linkinghub.elsevier.com/retrieve/pii/S0165032708002401
65. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893–7. http://doi.apa.org/getdoi.cfm?doi=10.1037/0022-006X.56.6.893
66. Matthey S, Ross-Hamid C. Repeat testing on the Edinburgh depression scale and the HADS-A in pregnancy: differentiating between transient and enduring distress. J Affect Disord. 2012;141(2–3):213–21. https://linkinghub.elsevier.com/retrieve/pii/S0165032712001516
67. Gladstone GL, Parker GB, Mitchell PB, Malhi GS, Wilhelm KA, Austin M-P. A brief measure of worry severity (BMWS): personality and clinical correlates of severe worriers. J Anxiety Disord. 2005;19(8):877–92. https://linkinghub.elsevier.com/retrieve/pii/S0887618504001288
68. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn state worry questionnaire. Behav Res Ther. 1990;28(6):487–95. https://linkinghub.elsevier.com/retrieve/pii/0005796790901356
69. Murray L, Cooper P, Creswell C, Schofield E, Sack C. The effects of maternal social phobia on mother–infant interactions and infant social responsiveness. J Child Psychol Psychiatry. 2007;48(1):45–52. https://doi.org/10.1111/j.1469-7610.2006.01657.x.
70. Huizink AC, Mulder EJH, Robles de Medina PG, Visser GHA, Buitelaar JK. Is pregnancy anxiety a distinctive syndrome? Early Hum Dev. 2004;79(2):81–91. https://linkinghub.elsevier.com/retrieve/pii/S037837820400074X
71. Buss C, Davis EP, Hobel CJ, Sandman CA. Maternal pregnancy-specific anxiety is associated with child executive function at 6–9 years age. Stress. 2011;14(6):665–76. http://www.tandfonline.com/doi/full/10.3109/10253890.2011.623250
72. Van den Bergh BRH, Mulder EJH, Mennes M, Glover V. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. Neurosci Biobehav Rev. 2005;29(2):237–58. https://linkinghub.elsevier.com/retrieve/pii/S0149763404001307
73. Rini CK, Dunkel-Schetter C, Wadhwa PD, Sandman CA. Psychological adaptation and birth outcomes: the role of personal resources, stress, and sociocultural context in pregnancy. Health Psychol. 1999;18(4):333–45. http://doi.apa.org/getdoi.cfm?doi=10.1037/0278-6133.18.4.333
74. Davis EP, Sandman CA. The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. Child Dev. 2010;81(1):131–48. https://doi.org/10.1111/j.1467-8624.2009.01385.x.
75. Henrichs J, Schenk JJ, Roza SJ, van den Berg MP, Schmidt HG, Steegers EAP, et al. Maternal psychological distress and fetal growth trajectories: the generation R study. Psychol Med. 2010;40(4):633–43. https://www.cambridge.org/core/product/identifier/S0033291709990894/type/journal_article

76. Somerville S, Dedman K, Hagan R, Oxnam E, Wettinger M, Byrne S, et al. The perinatal anxiety screening scale: development and preliminary validation. Arch Womens Ment Health. 2014;17(5):443–54. http://link.springer.com/10.1007/s00737-014-0425-8
77. Fairbrother N, Corbyn B, Thordarson DS, Ma A, Surm D. Screening for perinatal anxiety disorders: room to grow. J Affect Disord. 2019;250:363–70. https://www.sciencedirect.com/science/article/pii/S0165032718323395
78. Ali E. Women's experiences with postpartum anxiety disorders: a narrative literature review. Int J Women's Health. 2018;10:237–49. https://www.dovepress.com/womens-experiences-with-postpartum-anxiety-disorders-a-narrative-liter-peer-reviewed-article-IJWH
79. Abbasi MA, Malik S, Ali K. Smoking cessation after counselling in patients presenting with acute coronary syndrome. J Ayub Med Coll Abbottabad. 2018;30(2):223–9.
80. Anniverno R, Bramante A, Mencacci C, Durbano F. Anxiety disorders in pregnancy and the postpartum period. New insights into anxiety disorders. In Tech; 2013. http://www.intechopen.com/books/new-insights-into-anxiety-disorders/anxiety-disorders-in-pregnancy-and-the-postpartum-period
81. Aris-Meijer J, Bockting C, Stolk R, Verbeek T, Beijers C, van Pampus M, et al. What if pregnancy is not seventh heaven? The influence of specific life events during pregnancy and delivery on the transition of antenatal into postpartum anxiety and depression. Int J Environ Res Public Health. 2019;16(16):2851. https://www.mdpi.com/1660-4601/16/16/2851
82. Agrati D, Browne D, Jonas W, Meaney M, Atkinson L, Steiner M, et al. Maternal anxiety from pregnancy to 2 years postpartum: transactional patterns of maternal early adversity and child temperament. Arch Womens Ment Health. 2015;18(5):693–705. http://link.springer.com/10.1007/s00737-014-0491-y
83. Brockington IF, Macdonald E, Wainscott G. Anxiety, obsessions and morbid preoccupations in pregnancy and the puerperium. Arch Womens Ment Health. 2006;9(5):253–63.
84. Pleshette N, Asch S, Chase J. A study of anxieties during pregnancy, labor, the early and late puerperium. Bull N Y Acad Med. 1956;32(6):436–55.
85. Levin JS. The factor structure of the pregnancy anxiety scale. J Health Soc Behav. 1991;32(4):368–81.
86. Standley K, Soule B, Copans SA. Dimensions of prenatal anxiety and their influence on pregnancy outcome. Am J Obstet Gynecol. 1979;135(1):22–6.
87. Blackmore ER, Gustafsson H, Gilchrist M, Wyman C, O'Connor G, T. Pregnancy-related anxiety: evidence of distinct clinical significance from a prospective longitudinal study. J Affect Disord. 2016;197:251–8. https://pubmed.ncbi.nlm.nih.gov/26999549
88. Williams KE, Koleva H. Identification and treatment of peripartum anxiety disorders. Obstet Gynecol Clin N Am. 2018;45(3):469–81. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med15&NEWS=N&AN=30092922
89. Mudra S, Göbel A, Barkmann C, Goletzke J, Hecher K, Schulte-Markwort M, et al. The longitudinal course of pregnancy-related anxiety in parous and nulliparous women and its association with symptoms of social and generalized anxiety. J Affect Disord. 2019;2020(260):111–8. https://doi.org/10.1016/j.jad.2019.08.033.
90. Perna G, Barone Y, Alciati A. Anxiety disorders. In: Perinatal psychopharmacology. Cham: Springer; 2019. p. 287–95. http://link.springer.com/10.1007/978-3-319-92919-4_17.
91. Perna G, Barone Y, Miceli W. I disturbi d'ansia in gravidanza e nel postpartum. In: Giovanni Fioriti Editore s.r.l., editor. Manuale di psichiatria perinatale; 2021.
92. Arch JJ. Cognitive behavioral therapy and pharmacotherapy for anxiety: treatment preferences and credibility among pregnant and non-pregnant women. Behav Res Ther. 2014;52(1):53–60.
93. Fordham B, Sugavanam T, Edwards K, Hemming K, Howick J, Copsey B, et al. Cognitive–behavioural therapy for a variety of conditions: an overview of systematic reviews and panoramic meta-analysis. Health Technol Assess (Rockv). 2021;25(9):1–378. https://www.journalslibrary.nihr.ac.uk/hta/hta25090

94. Maguire PN, Clark GI, Wootton BM. The efficacy of cognitive behavior therapy for the treatment of perinatal anxiety symptoms: a preliminary meta-analysis. J Anxiety Disord. 2018;60:26–34.
95. Li C, Sun X, Li Q, Sun Q, Wu B, Duan D. Role of psychotherapy on antenatal depression, anxiety, and maternal quality of life. Medicine (Baltimore). 2020;99(27):e20947. https://journals.lww.com/10.1097/MD.0000000000020947
96. Han Q, Guo M, Ren F, Duan D, Xu X. Role of midwife-supported psychotherapy on antenatal depression, anxiety and maternal health: a meta-analysis and literature review. Exp Ther Med. 2020;20(3):2599–610. http://www.spandidos-publications.com/10.3892/etm.2020.9011
97. Bright KS, Charrois EM, Mughal MK, Wajid A, McNeil D, Stuart S, et al. Interpersonal psychotherapy to reduce psychological distress in perinatal women: a systematic review. Int J Environ Res Public Health. 2020;17(22):8421. https://www.mdpi.com/1660-4601/17/22/8421
98. Viuff A-CF, Pedersen LH, Kyng K, Staunstrup NH, Børglum A, Henriksen TB. Antidepressant medication during pregnancy and epigenetic changes in umbilical cord blood: a systematic review. Clin. Epigenetics. 2016;8(1):94. http://clinicalepigeneticsjournal.biomedcentral.com/articles/10.1186/s13148-016-0262-x
99. Grigoriadis S, VonderPorten EH, Mamisashvili L, Eady A, Tomlinson G, Dennis C-L, et al. The effect of prenatal antidepressant exposure on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74(4):e309–20.
100. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Dennis C-L, Vigod SN, et al. Benzodiazepine use during pregnancy alone or in combination with an antidepressant and congenital malformations: systematic review and meta-analysis. J Clin Psychiatry. 2019;80(4)
101. Meltzer-Brody S. New insights into perinatal depression: pathogenesis and treatment during pregnancy and postpartum. Dialogues Clin Neurosci. 2011;13(1):89–100.
102. Viswasam K, Eslick GD, Starcevic V. Prevalence, onset and course of anxiety disorders during pregnancy: a systematic review and meta analysis. J Affect Disord. 2019;255:27–40. http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2019-36156-006&site=ehost-live
103. Bandelow B, Michaelis S. Epidemiology of anxiety disorders in the 21st century. Dialogues Clin Neurosci. 2015;17(3):327–35.
104. Wenzel A, Haugen EN, Jackson LC, Brendle JR. Anxiety symptoms and disorders at eight weeks postpartum. J Anxiety Disord. 2005;19(3):295–311.
105. Wenzel A, Haugen EN, Jackson LC, Robinson K. Prevalence of generalized anxiety at eight weeks postpartum. Arch Womens Ment Health. 2003;6(1):43–9.
106. Uguz F, Yakut E, Aydogan S, Bayman MG, Gezginc K. Prevalence of mood and anxiety disorders during pregnancy: a case-control study with a large sample size. Psychiatry Res. 2019;272:316–8. http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2019-11442-047&site=ehost-live
107. Uguz F, Gezginc K, Yazici F. Are major depression and generalized anxiety disorder associated with intrauterine growth restriction in pregnant women? A case-control study. Gen Hosp Psychiatry. 2011;33(6):640.e7–9. https://pubmed.ncbi.nlm.nih.gov/21749842/
108. Uguz F, Sonmez EO, Sahingoz M, Gokmen Z, Basaran M, Gezginc K, et al. Maternal generalized anxiety disorder during pregnancy and fetal brain development: a comparative study on cord blood brain-derived neurotrophic factor levels. J Psychosom Res. 2013;75(4):346–50. https://pubmed.ncbi.nlm.nih.gov/24119941/
109. Coates R, Ayers S, de Visser R. Women's experiences of postnatal distress: a qualitative study. BMC Pregnancy Childbirth. 2014;14(1):359. https://doi.org/10.1186/1471-2393-14-359.
110. Highet N, Stevenson AL, Purtell C, Coo S. Qualitative insights into women's personal experiences of perinatal depression and anxiety. Women Birth. 2014;27(3):179–84.
111. Britton JR. Maternal anxiety: course and antecedents during the early postpartum period. Depress Anxiety. 2008;25(9)
112. Green SM, Haber E, Frey BN, McCabe RE. Cognitive-behavioral group treatment for perinatal anxiety: a pilot study. Arch Womens Ment Health. 2015;18(4):631–8.

113. Goodman JH, Guarino A, Chenausky K, Klein L, Prager J, Petersen R, et al. CALM pregnancy: results of a pilot study of mindfulness-based cognitive therapy for perinatal anxiety. Arch Womens Ment Health. 2014;17(5):373–87.
114. Uguz F, Ak M. Cognitive-behavioral therapy in pregnant women with generalized anxiety disorder: a retrospective cohort study on therapeutic efficacy, gestational age and birth weight. Brazilian. J Psychiatry. 2021;43(1):61–4. https://pubmed.ncbi.nlm.nih.gov/32756804/
115. Bérard A, Iessa N, Chaabane S, Muanda FT, Boukhris T, Zhao J-P. The risk of major cardiac malformations associated with paroxetine use during the first trimester of pregnancy: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016;81(4):589–604.
116. Gentile S. SSRIs in pregnancy and lactation: emphasis on neurodevelopmental outcome. CNS Drugs. 2005;19(7):623–33.
117. Orsolini L, Bellantuono C. Serotonin reuptake inhibitors and breastfeeding: a systematic review. Hum Psychopharmacol. 2015;30(1):4–20.
118. Drugs and Lactation Database (LactMed). Venlafaxine [Updated 2021 Feb 15]. National Library of Medicine (US); 2006 [cited 2021 Mar 20]. https://www.ncbi.nlm.nih.gov/books/NBK501192/
119. Martini J, Beesdo-Baum K, Garthus-Niegel S, Wittchen H-U. The course of panic disorder during the peripartum period and the risk for adverse child development: a prospective-longitudinal study. J Affect Disord. 2020;266:722–30. http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2020-22174-094&site=ehost-live
120. Fairbrother N, Janssen P, Antony MM, Tucker E, Young AH. Perinatal anxiety disorder prevalence and incidence. J Affect Disord. 2016;200:148–55. http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=2016-28385-021&site=ehost-live
121. Hertzberg T, Wahlbeck K. The impact of pregnancy and puerperium on panic disorder: a review. J Psychosom Obstet Gynaecol. 1999;20(2):59–64.
122. Guler O, Koken GN, Emul M, Ozbulut O, Gecici O, Uguz F, et al. Course of panic disorder during the early postpartum period: a prospective analysis. Compr Psychiatry. 2008;49(1):30–4.
123. Aydogan S, Uguz F, Yakut E, Bayman MG, Gezginc K. The course and clinical correlates of panic disorder during the postpartum period: a naturalistic observational study. Braz J Psychiatry. 2020;43:6–11. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-44462020005035203&tlng=en
124. Grassi M, Caldirola D, Di Chiaro NV, Riva A, Daccò S, Pompili M, et al. Are respiratory abnormalities specific for panic disorder? A meta-analysis. Neuropsychobiology. 2014;70(1):52–60. https://www.karger.com/Article/FullText/364830
125. Grassi M, Caldirola D, Vanni G, Guerriero G, Piccinni M, Valchera A, et al. Baseline respiratory parameters in panic disorder: a meta-analysis. J Affect Disord. 2013;146(2):158–73. https://linkinghub.elsevier.com/retrieve/pii/S0165032712006052
126. Caldirola D, Perna G. Toward a personalized therapy for panic disorder: preliminary considerations from a work in progress. Neuropsychiatr Dis Treat. 2019;15:1957–70. https://www.dovepress.com/toward-a-personalized-therapy-for-panic-disorder-preliminary-considera-peer-reviewed-article-NDT
127. Perna G, Caldirola D. Is panic disorder a disorder of physical fitness? A heuristic proposal. F1000Research. 2018;7:294. https://pubmed.ncbi.nlm.nih.gov/29623195
128. Kazma JM, van den Anker J, Allegaert K, Dallmann A, Ahmadzia HK. Anatomical and physiological alterations of pregnancy. J Pharmacokinet Pharmacodyn. 2020;47(4):271–85. http://link.springer.com/10.1007/s10928-020-09677-1
129. Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. Clin Chest Med. 2011;32(1):1–13. https://linkinghub.elsevier.com/retrieve/pii/S0272523110001322
130. LoMauro A, Aliverti A. Respiratory physiology of pregnancy. Breathe. 2015;11(4):297–301. http://breathe.ersjournals.com/lookup/doi/10.1183/20734735.008615
131. Wenzel A, Gorman LL, O'Hara MW, Stuart S. The occurrence of panic and obsessive compulsive symptoms in women with postpartum dysphoria: a prospective study. Arch Womens Ment Health. 2001;4(1):5–12. https://doi.org/10.1007/s007370170002.

132. Uguz F, Sahingoz M, Sonmez EO, Karsidag C, Yuksel G, Annagur BB, et al. The effects of maternal major depression, generalized anxiety disorder, and panic disorder on birth weight and gestational age: a comparative study. J Psychosom Res. 2013;75(1):87–9.
133. Matthey S, Barnett B, Howie P, Kavanagh DJ. Diagnosing postpartum depression in mothers and fathers: whatever happened to anxiety? J Affect Disord. 2003;74(2):139–47. https://linkinghub.elsevier.com/retrieve/pii/S0165032702000125
134. Robinson L, Walker JR, Anderson D. Cognitive-behavioural treatment of panic disorder during pregnancy and lactation. Can J Psychiatr. 1992;37(9):623–6.
135. Matsumoto K, Sato K, Hamatani S, Shirayama Y, Shimizu E. Cognitive behavioral therapy for postpartum panic disorder: a case series. BMC Psychol. 2019;7(1):53. https://pubmed.ncbi.nlm.nih.gov/31439043
136. Uguz F. Low-dose mirtazapine added to selective serotonin reuptake inhibitors in pregnant women with major depression or panic disorder including symptoms of severe nausea, insomnia and decreased appetite: three cases. J Matern Neonatal Med. 2013;26(11):1066–8. http://www.tandfonline.com/doi/full/10.3109/14767058.2013.766697
137. Gentile S. Use of escitalopram during pregnancy navigating towards international guidelines and the real world. Clin Drug Investig. 2008;28(11):735–9. https://doi.org/10.2165/00044011-200828110-00006.
138. Nascimento I, Lopes FL, Valença AM, Mezzasalma MA, Nardi AE. Transtorno do pânico e gravidez. Rev Bras Psiquiatr. 2004;26(3):211–2. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-44462004000300013&lng=pt&tlng=pt
139. Uguz F, Akman C, Kaya N, Sahingoz M, Cilli AS. One year follow-up of postpartum-onset obsessive–compulsive disorder: a case series. Prog Neuro-Psychopharmacol Biol Psychiatry. 2008;32(4):1091–2. https://linkinghub.elsevier.com/retrieve/pii/S0278584608000808
140. Ware MR, DeVane CL. Imipramine treatment of panic disorder during pregnancy. J Clin Psychiatry. 1990;51(11):482–4.
141. Goodman JH, Chenausky KL, Freeman MP. Anxiety disorders during pregnancy: a systematic review. J Clin Psychiatry. 2014;75:e1153–84. https://pubmed.ncbi.nlm.nih.gov/25373126/
142. Nath S, Busuulwa P, Ryan EG, Challacombe FL, Howard LM. The characteristics and prevalence of phobias in pregnancy. Midwifery. 2020;82:102590. https://doi.org/10.1016/j.midw.2019.102590.
143. Patel RR, Hollins K. Clinical report: the joint obstetric and psychiatric management of phobic anxiety disorders in pregnancy. J Psychosom Obstet Gynecol. 2015;36(1):10–4. http://www.tandfonline.com/doi/full/10.3109/0167482X.2014.993312
144. Demšar K, Svetina M, Verdenik I, Tul N, Blickstein I, Velikonja VG. Tokophobia (fear of childbirth): prevalence and risk factors. J Perinat Med. 2018;46(2):151–4.
145. Hofberg K, Ward MR. Fear of childbirth, tocophobia, and mental health in mothers: the obstetric–psychiatric interface. Clin Obstet Gynecol. 2004;47(3):527–34. http://journals.lww.com/00003081-200409000-00006
146. Goodman JH, Chenausky KL, Freeman MP. Anxiety disorders during pregnancy. J Clin Psychiatry. 2014;75(10):e1153–84. http://www.psychiatrist.com/jcp/article/pages/2014/v75n10/v75n1018.aspx
147. Lilliecreutz C, Sydsjö G, Josefsson A. Obstetric and perinatal outcomes among women with blood- and injection phobia during pregnancy. J Affect Disord. 2011;129(1–3):289–95. https://linkinghub.elsevier.com/retrieve/pii/S0165032710005471
148. Lilliecreutz C, Josefsson A, Sydsjö G. An open trial with cognitive behavioral therapy for blood- and injection phobia in pregnant women - a group intervention program. Arch Womens Ment Health. 2010;13(3):259–65. https://pubmed.ncbi.nlm.nih.gov/19859788/
149. Stoll K, Swift EM, Fairbrother N, Nethery E, Janssen P. A systematic review of nonpharmacological prenatal interventions for pregnancy-specific anxiety and fear of childbirth. Birth. 2018;45(1):7–18. https://doi.org/10.1111/birt.12316.
150. Rose GM, Tadi P. Social anxiety disorder. StatPearls. 2021. http://www.ncbi.nlm.nih.gov/pubmed/32310350

151. Viswasam K, Berle D, Milicevic D, Starcevic V. Prevalence and onset of anxiety and related disorders throughout pregnancy: a prospective study in an Australian sample. Psychiatry Res. 2020;2021(297):113721. https://doi.org/10.1016/j.psychres.2021.113721.
152. Mauri M, Oppo A, Montagnani MS, Borri C, Banti S, Camilleri V, et al. Beyond "postpartum depressions": specific anxiety diagnoses during pregnancy predict different outcomes. J Affect Disord. 2010;127(1–3):177–84. https://doi.org/10.1016/j.jad.2010.05.015.
153. Coelho HF, Murray L, Royal-Lawson M, Cooper PJ. Antenatal anxiety disorder as a predictor of postnatal depression: a longitudinal study. J Affect Disord. 2011;129(1–3):348–53. https://doi.org/10.1016/j.jad.2010.08.002.
154. Staneva A, Bogossian F, Pritchard M, Wittkowski A. The effects of maternal depression, anxiety, and perceived stress during pregnancy on preterm birth: a systematic review. Women Birth. 2015;28(3):179–93. https://linkinghub.elsevier.com/retrieve/pii/S187151921500030X
155. Avraham L, Tamar W, Eyal S, Gali P. Perinatal outcomes and offspring long-term neuropsychiatric hospitalizations of mothers with anxiety disorder. Arch Womens Ment Health. 2020;23(5):681–8. http://link.springer.com/10.1007/s00737-020-01018-y
156. Martini J, Knappe S, Beesdo-Baum K, Lieb R, Wittchen H-U. Anxiety disorders before birth and self-perceived distress during pregnancy: associations with maternal depression and obstetric, neonatal and early childhood outcomes. Early Hum Dev. 2010;86(5):305–10.
157. Chen Y-H, Lin H-C, Lee H-C. Pregnancy outcomes among women with panic disorder — do panic attacks during pregnancy matter? J Affect Disord. 2010;120(1–3):258–62. https://linkinghub.elsevier.com/retrieve/pii/S0165032709001797
158. Kendig S, Keats JP, Hoffman MC, Kay LB, Miller ES, Moore Simas TA, et al. Consensus bundle on maternal mental health. Obstet Gynecol. 2017;129(3):422–30. https://journals.lww.com/00006250-201703000-00004
159. Stein A, Craske MG, Lehtonen A, Harvey A, Savage-McGlynn E, Davies B, et al. Maternal cognitions and mother–infant interaction in postnatal depression and generalized anxiety disorder. Vol. 121, Journal of Abnormal Psychology. Stein, Alan: Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford, United Kingdom, OX3 7JX, alan.stein@psych.ox.ac.uk: American Psychological Association; 2012. p. 795–809.
160. Tietz A, Zietlow A-L, Reck C. Maternal bonding in mothers with postpartum anxiety disorder: the crucial role of subclinical depressive symptoms and maternal avoidance behaviour. Arch Womens Ment Health. 2014;17(5):433–42. https://doi.org/10.1007/s00737-014-0423-x.
161. Dagla M, Mrvoljak-Theodoropoulou I, Karagianni D, Dagla C, Sotiropoulou D, Kontiza E, et al. Women's mental health as a factor associated with exclusive breastfeeding and breastfeeding duration: data from a longitudinal study in Greece. Children. 2021;8(2):150. https://www.mdpi.com/2227-9067/8/2/150
162. Coo S, García MI, Mira A, Valdés V. The role of perinatal anxiety and depression in breastfeeding practices. Breastfeed Med. 2020;15(8):495–500. https://www.liebertpub.com/doi/10.1089/bfm.2020.0091
163. Field T. Postnatal anxiety prevalence, predictors and effects on development: a narrative review. Infant Behav Dev. 2018;51:24–32. https://linkinghub.elsevier.com/retrieve/pii/S0163638317302357
164. Fallon V, Groves R, Halford JCG, Bennett KM, Harrold JA. Postpartum anxiety and infant-feeding outcomes. J Hum Lact. 2016;32(4):740–58. http://journals.sagepub.com/doi/10.1177/0890334416662241
165. Teissedre F, Chabol H. Postnatal depression: a study of the predictive effects of postnatal anxiety. Ir J Psychol Med. 2003;20(4):111–4. https://www.cambridge.org/core/product/identifier/S0790966700007898/type/journal_article
166. Farias DR, Pinto TDJP, Teofilo MMA, Vilela AAF, dos Santos Vaz J, Nardi AE, et al. Prevalence of psychiatric disorders in the first trimester of pregnancy and factors associated with current suicide risk. Psychiatry Res. 2013;210(3):962–8. https://linkinghub.elsevier.com/retrieve/pii/S0165178113005131
167. Andersson NW, Hansen MV, Larsen AD, Hougaard KS, Kolstad HA, Schlünssen V. Prenatal maternal stress and atopic diseases in the child: a systematic review of observational human studies. Allergy. 2016;71(1):15–26. https://onlinelibrary.wiley.com/doi/10.1111/all.12762

168. Gilles M, Otto H, Wolf IAC, Scharnholz B, Peus V, Schredl M, et al. Maternal hypothalamus-pituitary-adrenal (HPA) system activity and stress during pregnancy: effects on gestational age and infant's anthropometric measures at birth. Psychoneuroendocrinology. 2018;94:152–61. https://linkinghub.elsevier.com/retrieve/pii/S0306453017313070
169. Reck C, Müller M, Tietz A, Möhler E. Infant distress to novelty is associated with maternal anxiety disorder and especially with maternal avoidance behavior. J Anxiety Disord. 2013;27(4):404–12. https://www.sciencedirect.com/science/article/pii/S0887618513000558
170. Jover M, Colomer J, Carot JM, Larsson C, Bobes MT, Ivorra JL, et al. Maternal anxiety following delivery, early infant temperament and mother's confidence in caregiving. Span J Psychol. 2014;17
171. Field CD. A short walk through some Chinese mangroves. Wetl Aust. 2010;5(1):1. https://wetlandsaustralia.com/article/10.31646/wa.203/
172. Ali NS, Mahmud S, Khan A, Ali BS. Impact of postpartum anxiety and depression on child's mental development from two peri-urban communities of Karachi, Pakistan: a quasi-experimental study. BMC Psychiatry. 2013;13(1):274. https://doi.org/10.1186/1471-244X-13-274.
173. Barker ED, Jaffee SR, Uher R, Maughan B. The contribution of prenatal and postnatal maternal anxiety and depression to child maladjustment. Depress Anxiety. 2011;28(8):696–702. https://onlinelibrary.wiley.com/doi/abs/10.1002/da.20856
174. Clout D, Brown R. Sociodemographic, pregnancy, obstetric, and postnatal predictors of postpartum stress, anxiety and depression in new mothers. J Affect Disord. 2015;188:60–7. https://www.sciencedirect.com/science/article/pii/S0165032715305966
175. Grizenko N, Shayan YR, Polotskaia A, Ter-Stepanian M, Joober R. Relation of maternal stress during pregnancy to symptom severity and response to treatment in children with ADHD. J Psychiatry Neurosci. 2008;33(1):10–6. https://pubmed.ncbi.nlm.nih.gov/18197267
176. Grizenko N, Fortier M-E, Zadorozny C, Thakur G, Schmitz N, Duval R, et al. Maternal stress during pregnancy, ADHD symptomatology in children and genotype: gene-environment interaction. J Can Acad Child Adolesc Psychiatry. 2012;21(1):9–15. https://pubmed.ncbi.nlm.nih.gov/22299010
177. Mughal MK, Giallo R, Arnold P, Benzies K, Kehler H, Bright K, et al. Trajectories of maternal stress and anxiety from pregnancy to three years and child development at 3 years of age: findings from the all our families (AOF) pregnancy cohort. J Affect Disord. 2018;234:318–26.
178. Kingston D, Kehler H, Austin M-P, Mughal MK, Wajid A, Vermeyden L, et al. Trajectories of maternal depressive symptoms during pregnancy and the first 12 months postpartum and child externalizing and internalizing behavior at three years. PLoS One. 2018;13(4):e0195365. https://pubmed.ncbi.nlm.nih.gov/29652937
179. O'Connor TG, Heron J, Glover V. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. J Am Acad Child Adolesc Psychiatry. 2002;41(12):1470–7. https://pubmed.ncbi.nlm.nih.gov/12447034/
180. Dugan AM, Parrott JM, Redus L, Hensler JG, O'Connor JC. Low-level stress induces production of neuroprotective factors in wild-type but not BDNF +/− mice: interleukin-10 and kynurenic acid. Int J Neuropsychopharmacol. 2016;19(3):pyv089. https://academic.oup.com/ijnp/article-lookup/doi/10.1093/ijnp/pyv089
181. Adamson B, Letourneau N, Lebel C. Prenatal maternal anxiety and children's brain structure and function: a systematic review of neuroimaging studies. J Affect Disord. 2018;241:117–26. https://linkinghub.elsevier.com/retrieve/pii/S0165032718311340
182. Alder J, Fink N, Bitzer J, Hösli I, Holzgreve W. Depression and anxiety during pregnancy: a risk factor for obstetric, fetal and neonatal outcome? A critical review of the literature. J Matern Neonatal Med. 2007;20(3):189–209. https://doi.org/10.1080/14767050701209560.
183. Ruiz-Padial E, Sollers JJ, Vila J, Thayer JF. The rhythm of the heart in the blink of an eye: emotion-modulated startle magnitude covaries with heart rate variability. Psychophysiology. 2003;40(2):306–13. https://doi.org/10.1111/1469-8986.00032.

Obsessive–Compulsive Disorders

5

Gianluca Rosso and Giuseppe Maina

5.1 Obsessive–Compulsive Disorder

5.1.1 Definition and Epidemiology

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), defines obsessive–compulsive disorder (OCD) as the presence of obsessions, compulsions, or both, which must be time-consuming (e.g., more than 1 h per day) and cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. Obsessions are repetitive and persistent thoughts, images, or urges that are intrusive and unwanted and cause marked distress or anxiety. Compulsions are repetitive behaviors or mental acts that the individual feels driven to perform in order to reduce the distress and anxiety triggered by obsessions (Fig. 5.1) [1]. Common sets of obsessions and compulsions in patients with OCD include concerns about contamination together with washing or cleaning compulsions, fears of harm to oneself or others and related checking compulsions, forbidden or taboo thoughts such as intrusive aggressive, religious, or sexual thoughts together with mental rituals, and, finally, symmetry concerns and related repeating, ordering, or counting compulsions (Table 5.1) [2]. Preoccupations and rituals must be excessive or persisting, which distinguish the disorder from the occasional intrusive thoughts or repetitive behaviors, which are common in general population (e.g., double-checking that a door is locked).

The 12-month prevalence of OCD is from 1.1% to 1.8% of the population worldwide. Females are affected at a slightly higher rate than males in adulthood, although males are more commonly affected in childhood [1].

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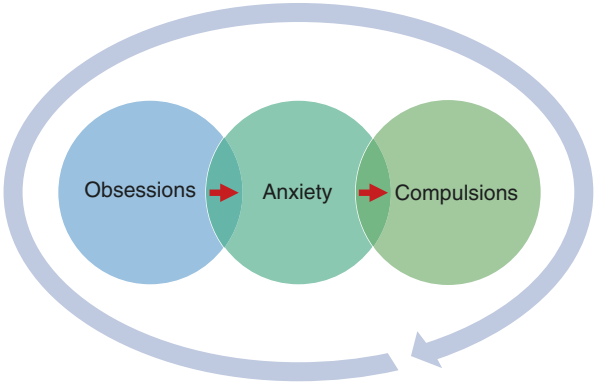

Fig. 5.1 The theoretical basis of obsessive–compulsive behavior

Table 5.1 Common obsessions and compulsions

Obsessions	Compulsions
Contamination concerns	Washing or cleaning rituals
Concerns about harm	Repetitive checking
Intrusive aggressive, sexual, or religious thoughts	Mental rituals or excessive praying
Symmetry concerns	Ordering, repeating, or counting rituals

5.1.2 Etiology

OCD is a complex psychiatric disorder with a multifaceted etiology. Experts propose a multifactorial model of inheritance where multiple genetic and biological risk factors act together with environmental stressors causing the disease onset. Several genome-wide linkage studies indicate that OCD is a polygenic disorder with many identified risk loci of small to moderate effect, including genetic variants within pathways for serotonin, dopamine, and glutamate or involved in immune and white matter pathways [3]. Biological factors (e.g., infection, altered concentrations of neurotrophic factors, pregnancy, and/or delivery) have also been suggested in OCD etiopathogenesis [3, 4]. Multiple evidence shows that exposure to pregnancy or to delivery increases the risk for OCD, with either pregnancy and delivery reported to be precipitants in 12.5% up to 40.0% of female OCD patients [5]. During pregnancy and the postpartum period, the disorder may be due to changes in the patient's natural body chemistry, including changes in hormonal levels (specifically progesterone and estrogen), or in functions of the brain [6, 7]. Besides biological causes, several environmental factors, such as experience of stressful life events (defined as a combination of major life events and subjective perception of the relevance of these events by the individual), contribute toward vulnerability to OCD [8, 9]. The most common stressful life events are emotional, financial, or health problems in the family, adverse perinatal events, starting or ending a significant relationship, moving to another city, and the death of a relative

or a friend [10]. Genetic and biological factors could be more determining in causing OCD in males. Conversely, environmental stressors, specifically adverse perinatal events and stressful or traumatic events, play a more important role in female patients [11].

5.1.3 Clinical Course

The average age at onset of OCD is 21 years, with medium onset age varying by gender (19 years for men, 22 for women) [12]. However, clinicians should investigate the age at onset of symptoms and the age when a diagnosis of OCD has been determined because these data can help predict the prognosis. This difference reflects the fact that generally OCD symptoms may appear early but the disorder may be diagnosed later when symptoms start causing clinically significant distress or impairment in social, occupational, or other important areas of functioning. The presence of significant differences in clinical profile depending on age at symptoms and disorder onset is tested; patients with early and intermediate age at symptoms onset are more likely to have an insidious mode of onset of OCD, compared to subjects with late age at symptoms onset. Furthermore, early age at disorder onset is associated with higher severity of symptoms on all OCD dimensions and with a greater disability [13]. Late-onset OCD, instead, is more likely to occur in females with long periods of subclinical obsessive–compulsive symptoms and usually shows a chronic clinical course [14].

Although OCD is generally thought to be a chronic disorder with persistent symptoms, increasing evidence shows that a subtype of OCD characterized by an episodic course may exist [15]. A chronic course implies a persistent presence of symptoms with phasic exacerbations and incomplete remissions, with significant distress and functional impairment. In the episodic course, symptoms are present only during an episode and, for the remaining time, symptoms remit for an interval of at least a month in a year, with or without treatment [16]. Some studies report differences between episodic and chronic OCD regarding sociodemographic and clinical characteristics: episodic OCD shows female preponderance, later age at onset, higher severity of obsessions and compulsions, and higher comorbidity of bipolar disorder [17].

Comorbidity is almost always present in OCD patients. With regard to general medical conditions, studies reveal high co-occurrence of OCD and physical diseases (particularly metabolic diseases): this association can be explained by the use of psychopharmacological treatments (such as second-generation antipsychotics) and the patients' severe self-neglect with the inability to perform basic activities of self-care and hygiene [18]. Concerning the association between OCD and other psychiatric diseases, recent studies confirm the higher prevalence of comorbid mood disorders, both depressive and bipolar disorders, with reciprocal influences on course and prognosis [19], but also anxiety disorders, substance use disorders,

and personality disorders, as compared to the general population [20–22]. In addition, OCD patients show a high risk of suicidality when compared to healthy controls [23]. At least one OCD patient out of ten attempts suicide during his/her lifetime, while nearly half of individuals with OCD have suicidal ideation. The most important predictors of suicidality in OCD patients are the severity of obsessions, presence of comorbid disorders (in particular substance use disorder, major depressive disorder, and personality disorder), and family history of completed suicide [24].

5.2 Obsessive–Compulsive Disorder in the Peripartum Period

Reproductive cycle events play an important role in the onset or exacerbation of OCD symptoms. Specifically, pregnancy, childbirth, and the postpartum period are clearly major life events that have been associated with an increased vulnerability for the development of OCD: an increasing number of studies show that pregnancy and postpartum may precipitate or exacerbate OCD in some women; moreover, it has been suggested that not only the perinatal period is a time of increased risk for the development of OCD, but also peripartum OCD presents distinct clinical features [25–27]. The prevalence of having at least one anxiety disorder during pregnancy or the postpartum period is estimated to be 20.7%, with a trend toward a greater prevalence in pregnancy versus the postpartum period [28]. Instead, the prevalence of OCD during pregnancy can vary depending on the gestational period. During the third trimester, a slightly higher value (3.5%) was found compared to the general population (2–3%). However, in the first and second trimesters, the prevalence of OCD is 0 and 0.5%, respectively [29]. In the postpartum period, the OCD prevalence varies from 2.4% to 11% [30]. Regarding women with preexisting OCD, 17% show worsening of symptoms during pregnancy as well as in the postpartum period [31]. Women with peripartum OCD are more likely to experience premenstrual worsening of OCD, compared to women with onset of the disease outside of the peripartum period. This suggests that some women with OCD may be differentially sensitive to reproductive cycle events. In spite of the effect of pregnancy and the postpartum period on the course of the disorder, there appears to be a lack of awareness about the common occurrence of OCD in this population.

5.2.1 Etiology

The etiopathogenesis of perinatal OCD has not been fully established. Because of the heterogeneous nature of the disease, many experts believe that perinatal OCD may be ascribed to a variety of etiologic processes and their interactions. These

include genetic, environmental, immunological, and hormonal factors. The dynamic nature of the hormonal environment has led to specific hypotheses regarding the effects of hormonal changes on peripartum OCD. Sex hormones play important roles in the central nervous system. Adrenal and gonadal steroids interact with neurotransmitters in an extremely complex balance. Steroid hormones can modulate neuronal transmission by a variety of mechanisms: they may affect the synthesis and/or release of neurotransmitters, as well as expression of receptors, membrane plasticity, and permeability [32]. Levels of estrogen, progesterone, and oxytocin vary significantly during the perinatal period. Cyclic fluctuations of gonadal hormones are not necessarily abnormal by themselves but may drive a vulnerability to OCD symptoms in some women. In fact, it is more likely to be that not all women with OCD have a vulnerability to hormonally triggered onset or exacerbation of symptoms, but instead represent a subset of them [33]. Specifically, there is growing evidence that suggest that onset or worsening of OCD symptoms during the perinatal period may be related to oxytocin fluctuations. Physiologically, oxytocin is involved in uterine contraction and lactation and in the initiation of maternal behavior; for this reason, levels of this hormone are elevated during the third trimester of pregnancy and the early postpartum period. In some recent studies, moreover, oxytocin has been reported to be more elevated in patients with OCD, compared with age and sex-matched control subjects [34]. Further work is needed in this area to be able to draw any definitive conclusions, but the potential role of oxytocin in the onset and exacerbation of OCD symptoms during the perinatal period should be considered [35]. Another area of exploration has been on fluctuations of estrogen and progesterone and their potential impacts on serotonergic transmission, which has been hypothesized to influence OCD symptoms. There has been speculation that the drop in estrogen and progesterone, which occurs after labor and delivery, may modulate the serotoninergic system, placing a subgroup of women with differential sensitivity to reproductive hormones at risk of OCD. The biological basis for this differential sensitivity remains unknown, but it has been speculated to represent the effect of genetic polymorphism in genes that regulate reproductive hormone signaling [36].

In addition to these biological processes, sleep disturbance, which is common among pregnant and postpartum women, may contribute to the development of OCD symptoms. Women's sleep is affected by pregnancy as early as the first trimester and, as pregnancy progresses, sleep quality worsens, with decreases in sleep duration and sleep efficiency. Following the birth, sleep quality continues to deteriorate, with worsened sleep efficiency and further sleep loss at night. The association between sleep disturbances and psychiatric disorders, including OCD, is recognized: circadian dysregulation causes alterations in cognitive, psychomotor, or emotional processing, which in turn could contribute to the onset of symptoms in a variety of psychiatric disorders [37]. Sleep deprivation is an important trigger for the first onset of peripartum OCD or worsening of previous OCD symptoms [38]. It is still unclear whether women

with sleep deprivation are at greater risk of developing postpartum OCD than women without sleep disturbance, but some studies speculate that neuroinflammation may be the mechanism by which sleep changes contribute to the onset or worsening of OCD [39, 40].

Furthermore, other risk factors for peripartum OCD include primiparity, personal history of depression, obsessive–compulsive and avoidant personality disorder, and family histories of mood disorders [41]. Finally, perinatal risk factors might also be associated with the subsequent development of OCD: cesarean section delivery, preterm birth, low birth weight, breech presentation, and low Apgar scores at 5 min after delivery are considered critical environmental risk factors for OCD onset or worsening of previous OCD [5].

5.2.2 Clinical Features and Course

OCD symptoms mostly occur during the third trimester of gestation and during the first 4 weeks after childbirth [7, 29]. Although the clinical presentation of peripartum OCD varies widely, obsessions are usually more frequent than compulsions [42]. Obsessions often include concerns about the well-being of the fetus or baby, and aggressive obsessions appear to be the most common: most women experience disturbing intrusive thoughts of harming fetus or newborns, accidently or intentionally (e.g., intrusive thoughts of shaking, dropping, throwing, stabbing, drowning, or suffocation babies). Secondary to obsessions, common compulsions include repetitive and ritualistic checking (e.g., repeatedly checking breathing or body of babies). Furthermore, avoidance behaviors regarding things that they fear could harm the baby are common (Table 5.2) [26, 43]. It is important to distinguish between postpartum OCD symptoms and postpartum psychosis, as both may involve ideas of harming newborns. Postpartum obsession thoughts are not associated with an increased risk of committing harm and are experienced as senseless, unwanted, and inconsistent with a person's typical personality or behavior. Conversely, postpartum psychosis typically includes psychotic symptoms, confusion, mood alteration, and agitation.

In addition to aggressive obsessions, women with pregnancy or postpartum OCD usually report contamination obsessions, with related checking and washing or cleaning compulsions, because of fear of microorganism contamination to the fetus or to the infant (Table 5.2) [36]. Perinatal OCD symptoms, especially when severe

Table 5.2 Common obsessions and compulsions in the peripartum period

Obsessions	Compulsions
Intrusive aggressive thoughts(e.g., intrusive thoughts of shaking, dropping, throwing, stabbing, drowning, or suffocation babies) *Contamination concerns*	*Repetitive checking* (e.g., repeatedly checking breathing or body of babies and avoidance of dangerous things) *Washing or cleaning rituals and repetitive checking*

or persistent, may cause severe personal distress, significant levels of anxiety, and feelings of guilt for having to spend large amounts of time dealing with obsessions and compulsions. Consequently, women may be less available to their children physically and emotionally [44]. However, the impact of peripartum OCD on the neurodevelopment of children is unknown. The disorder also affects the relationships, as family members may find it difficult to cope with the disorder for having to engage in compulsive rituals themselves or due to the need to provide constant reassurance [36, 45].

It is unclear whether OCD with pregnancy and postpartum onset is transient or persistent, but it is considered that OCD with peripartum onset tends to become chronic, especially when the disorder is not treated [41, 46].

5.2.3 Comorbidities

Psychiatric comorbidities are usually to be common in women affected by peripartum OCD. Approximately 27.5% of women have an anxiety disorder, and 70.6% have a mood disorder [45]. Between the first group of comorbidities, the most common comorbid diagnoses are generalized anxiety disorder and specific phobia [47]. Among mood disorders, major depression is the most common comorbid disorder in women with peripartum OCD, and it is associated with chronic course and poor prognosis [41, 48–50]. Furthermore, approximately 20% of women have a comorbid diagnosis of bipolar disorder [51]. Lastly, OCD with onset in the peripartum period shows higher comorbidity rates of personality disorders, specifically obsessive–compulsive, avoidant, and dependent [47].

5.2.4 Diagnosis

Symptoms of OCD should be differentiated from physiological thoughts in which women care about their children's safety, occurring in 34–65% of women after delivery [52]. These physiological thoughts of worry are usually temporary and do not interfere with normal daily functioning or childcare responsibilities. In contrast, obsessions and compulsions are clearly maladaptive and time consuming, causing distress and functional impairment [53]. Identification of peripartum OCD and its differentiation from the other common peripartum psychiatric disorders can be challenging for several reasons [54]. First, OCD symptoms may not be recognized by women as being pathological, or feelings of embarrassment and guilt may prevent women from communicating symptoms to their families or caregivers. Second, due to a general lack of awareness of peripartum OCD, clinicians may fail to elicit information about obsessions and compulsions. Due to their increased risk of developing OCD, women with prior histories of major depression, anxiety disorders, or OCD should be identified as soon as possible

during pregnancy and followed closely. Similarly, women with depression or anxiety disorders in the postpartum period should be screened for obsessive–compulsive symptoms [55]. The Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) is the most commonly used scale to evaluate the severity of symptoms and to monitor response to treatment. However, it has not been validated in women with postpartum OCD [56, 57]. The Perinatal Obsessive–Compulsive Scale (POCS) is the only one that was developed and validated in women with perinatal OCD [58]. POCS is a self-report questionnaire with a prenatal and a postpartum version. In this scale, each symptom is assessed on the severity and interference scales. The Edinburgh Postnatal Depression Scale and the State-Trait Anxiety Inventory can be used to identify and monitor contemporary symptoms of depression and anxiety, respectively [59, 60]. Moreover, women with comorbid depression should be further evaluated to determine whether depressive episodes are related to major depressive disorder or bipolar disorder.

5.2.5 Treatment

Usually, treatment of peripartum OCD can be carried out in outpatient settings. Inpatient settings may be indicated for women who are at risk for suicide, are unable to provide adequate self-care, and have a co-occurring psychiatric disorder that requires hospital treatment [61]. Most OCD treatment guidelines support the use of antidepressant drugs and cognitive behavioral approaches as first-line treatment [62–64]. The selection of treatment modality should depend on the nature and severity of OCD. In general, cognitive behavioral therapy is recommended for individuals with mild to moderate OCD and good insight into illness. Conversely, pharmacological treatment should be indicated in cases of moderate to severe OCD, comorbidity with major psychiatric disorder, risk of suicide, OCD-related sleep and eating disorders, and unresponsiveness to cognitive behavioral therapy [63–65]. Due to lack of controlled data and absence of studies on pharmacotherapy of peripartum OCD alone (i.e., without comorbid psychiatric disorders), no firm recommendations can be offered for drug treatment of peripartum OCD [66]. However, similar to treatment of OCD with onset outside peripartum period, selective serotonin reuptake inhibitors (SSRIs) are the first choice as pharmacological treatment for OCD, as abundant available data support their relative safety for embryo, fetus, and infant, while serotonin-norepinephrine reuptake inhibitors (SNRIs), clomipramine, and other antidepressants are recommended as a second- and third-line choice [67]. SSRI use in pregnancy seems to be associated with a small absolute risk of congenital heart defects and persistent pulmonary hypertension of newborns (PPHNs), as well as an absolute risk of transitory poor neonatal

adaptation syndrome but mostly of mild severity [68]. It is important to consider the risks and benefits of pharmacotherapy during pregnancy and the postpartum period. Risks to fetuses and newborns should be weighed against the potential harm of untreated obsessive and compulsive symptoms and co-occurring disorders. The choice of the right SSRI depends on individual characteristics of patients, such as nature and severity of OCD symptoms, prior treatment response, and comorbid conditions. Thus, no SSRI drug has to be avoided in particular [69]. In patients who had an inadequate response to SSRI therapy, antipsychotic treatments may be added [70, 71]. The amount of safety data regarding antipsychotic treatment, especially second-generation anti-psychotics (SGAs), during pregnancy is rapidly evolving. From a safety point of view, a substantial and reassuring amount of data overall do not suggest a clinically meaningful increased risk of congenital malformations. However, data on other pregnancy outcomes of interest (i.e., miscarriage, stillbirth, preterm birth, small for gestational age, neonatal adaption, and childhood neurodevelopment) are overall insufficient to provide confident estimates. It is imperative that clinicians consider individual disease history, clinical characteristics, treatment response, adverse reaction profile, and patient preferences, when choosing specific SGA treatment during pregnancy and peripartum period [72]. If medication is needed, monotherapy is recommended, especially at a minimum effective dose and in slow-release formulations twice or more times daily in order to minimize high peak concentrations [73]. Besides, physiological changes that occur during pregnancy induce pharmacokinetic changes (e.g., increased volume of distribution, modified cytochrome P450 activity, increased glomerular filtration rate) and may result in decreases in drug concentrations and effect [74]. Therefore, dose adjustments during pregnancy are required. Related to breastfeeding, most antidepressants are excreted in low concentrations in breast milk, and only a few reach levels considered unsafe for infants ($\geq$10% of the maternal weight-adjusted dose in breast milk). Available data do not support a formal limitation of SSRI use during breastfeeding [69, 75]. However, sertraline is one of the safest and most known medications to be used during breastfeeding, owing to its documented low levels of exposure in breastfed infants and to the very limited number of adverse events described in the literature [76].

In conclusion, based on current knowledge and due to the absence of consensus between treatment recommendations, a pragmatic-personalized risk–benefit analysis to propose pharmacological treatment before, during, and after pregnancy appears to be crucial in OCD patients [77, 78]. Personalized plans based on a shared decision-making process may help to reduce the stigma associated with the disorder, an improved pregnancy plan, and a higher awareness of risks.

Executive summary

Prevalence

- The prevalence of having at least one anxiety disorder during pregnancy or the postpartum period is estimated to be 20.7%
- The prevalence of OCD during pregnancy can vary depending on the gestational period. During the third trimester, a slightly higher value (3.5%) was found compared to the general population (2–3%). However, in the first and second trimesters, the prevalence of OCD is 0 and 0.5%, respectively. In the postpartum period, the OCD prevalence varies from 2.4% to 11%
- Also, 17% of women affected by preexisting OCD show worsening of symptoms during pregnancy and the postpartum period

Etiology

- Perinatal OCD may be ascribed to a variety of etiologic processes. These include genetic, environmental, immunological, and hormonal factors
- Cyclic fluctuations of gonadal hormones may drive a vulnerability to OCD symptoms in some women due to their potential interaction with serotonergic pathways. Moreover, the onset or worsening of OCD symptoms during the perinatal period may be related to physiological oxytocin fluctuations
- Sleep deprivation is an important trigger for the first onset or worsening of OCD. Some studies speculate that neuroinflammation may be the mechanism by which sleep disturbance contributes to OCD onset

Clinical features and course

- OCD symptoms mostly occur during the third trimester of gestation and during the first 4 weeks after childbirth
- Aggressive obsessions appear to be the most common during pregnancy and the postpartum period: Most women experience disturbing intrusive thoughts of harming fetuses or newborns. Secondary to these obsessions, common compulsions include repetitive and ritualistic checking
- Women with pregnancy or postpartum OCD usually report contamination obsessions, with related checking, washing, or cleaning compulsions
- It is unclear whether OCD with pregnancy and postpartum onset is transient or persistent, but it is considered that it tends to become chronic

Comorbidities

- Approximately 27.5% of women have an anxiety disorder, and 70.6% have a mood disorder, in particular generalized anxiety disorder, specific phobia, major depressive disorder, and bipolar disorder
- OCD with onset in the peripartum period shows higher comorbidity rates of personality disorders, specifically obsessive–compulsive, avoidant, and dependent

Diagnosis

- Due to their increased risk of developing OCD, women with prior histories of major depressive disorder, anxiety disorders, or OCD should be identified as soon as possible during pregnancy and the postpartum period
- The Yale–Brown obsessive–compulsive scale (Y-BOCS) is the most commonly used scale to evaluate the severity of symptoms and to monitor response to treatment, but it has not been validated in women with postpartum OCD
- The perinatal obsessive–compulsive scale (POCS) is the only scale that was developed and validated in women with perinatal OCD

Treatment

- Most OCD treatment guidelines support the use of antidepressant drugs and cognitive behavioral approaches as first-line treatment
- No firm recommendations can be offered for drug treatment of peripartum OCD. However, selective serotonin reuptake inhibitors (SSRIs) are the first choice due to their relative safety for the embryo, fetus, and infant
- Monotherapy is recommended at a minimum effective dose and in slow-release formulations twice or more times daily
- Most antidepressants are excreted in low concentrations in breast milk. However, available data do not support a formal limitation of SSRI use during breastfeeding

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-V. Arlington, VA: APA; 2013.
2. Stein DJ, Costa DLC, Lochner C, et al. Obsessive–compulsive disorder. Nat Rev Dis Primers. 2019;5(1):52.
3. Pauls DL, Abramovitch A, Rauch SL, et al. Obsessive–compulsive disorder: an integrative genetic and neurobiological perspective. Nat Rev Neurosci. 2014;15:410–24.
4. Maina G, Rosso G, Zanardini R, et al. Serum levels of brain-derived neurotrophic factor in drug-naïve obsessive-compulsive patients: a case-control study. J Affect Disord. 2010b;122(1–2):174–8.
5. Fernandez TV, Leckman JF. Prenatal and perinatal risk factors and the promise of birth cohort studies: origins of obsessive-compulsive disorder. JAMA Psychiatry. 2016;73(11):1117–8.
6. Diaz SF, Grus LR, Sichel DA, et al. Obsessive-compulsive disorder in pregnancy and the puerperium. Am Psychiatr Press Rev Psychiatry. 1997;16(97–11):216.
7. Maina G, Albert U, Bogetto F, et al. Recent life events and obsessive-compulsive disorder (OCD): the role of pregnancy/delivery. Psychiatry Res. 1999;89:49–58.
8. Albert U, Maina G, Bogetto F, et al. The role of recent life events in the onset of obsessive-compulsive disorder. CNS Spectr. 2000;5(12):44–50.
9. Maina G, Vaschetto P, Ziero S, et al. The post-partum as specific risk factor for the onset of obsessive-compulsive disorder: clinical- controlled study. Epidemiol Psichiatr Soc. 2001;10(2):90–5.
10. Imthon AK, Caldart CA, do Rosário MC, et al. Stressful life events and the clinical expression of obsessive-compulsive disorder (OCD): an exploratory study. J Clin Med. 2020;9(10):3371.
11. Rosso G, Albert U, Asinari GF, et al. Stressful life events and obsessive–compulsive disorder: clinical features and symptom dimensions. Psychiatry Res. 2012a;197(3):259–64.
12. Rasmussen SA, Eisen JL. The epidemiology and clinical features of obsessive-compulsive disorder. Psychiatr Clin North Am. 1992;15(4):743–58.
13. Albert U, Manchia M, Tortorella A, et al. Admixture analysis of age at symptom onset and age at disorder onset in a large sample of patients with obsessive–compulsive disorder. J Affect Disord. 2015;187:188–96.
14. Frydman I, do Brasil PE, Torres AR, et al. Late-onset obsessive-compulsive disorder: risk factors and correlates. J Psychiatr Res. 2014;49:68–74.
15. Ravizza L, Maina G, Bogetto F. Episodic and chronic obsessive-compulsive disorder. Depress Anxiety. 1997;6(4):154–8.
16. Sharma E, Math SB. Course and outcome of obsessive-compulsive disorder. Indian J Psychiatry. 2019;61:S43–50.
17. Tükel R, Oflaz SB, Özyildirım I, et al. Comparison of clinical characteristics in episodic and chronic obsessive-compulsive disorder. Depress Anxiety. 2007;24:251–5.
18. Drummond LM, Hameed AK, Ion R. Physical complications of severe enduring obsessive-compulsive disorder. World Psychiatry. 2011;10(2):154.
19. Di Salvo G, Pessina E, Aragno E, et al. Impact of comorbid obsessive-compulsive disorder on suicidality in patients with bipolar disorder. Psychiatry Res. 2020;290:113088.
20. Adam Y, Meinlschmidt G, Gloster AT, et al. Obsessive-compulsive disorder in the community: 12-month prevalence, comorbidity and impairment. Soc Psychiatry Psychiatr Epidemiol. 2012;47:339–49.
21. Maina G, Albert U, Salvi V, et al. Early-onset obsessive–compulsive disorder and personality disorders in adulthood. Psychiatry Res. 2008a;158:217–25.
22. Torres AR, Prince MJ, Bebbington PE, et al. Obsessive-compulsive disorder: prevalence, comorbidity, impact, and help-seeking in the British National Psychiatric Morbidity Survey of 2000. Am J Psychiatry. 2006;163:1978–85.
23. Angelakis I, Gooding P, Tarrier N, et al. Suicidality in obsessive compulsive disorder (OCD): a systematic review and meta-analysis. Clin Psychol Rev. 2015;39:1–15.
24. Albert U, De Ronchi D, Maina G, et al. Suicide risk in obsessive-compulsive disorder and exploration of risk factors: a systematic review. Curr Neuropharmacol. 2019a;17:681–96.

25. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry. 2020;19(3):313–27.
26. McGuinness M, Blissett J, Jones C. OCD in the perinatal period: is postpartum OCD (ppOCD) a distinct subtype? A review of the literature. Behav Cogn Psychother. 2011;39:285–310.
27. McKee K, Admon LK, Winkelman TNA, et al. Perinatal mood and anxiety disorders, serious mental illness, and delivery-related health outcomes, United States, 2006–2015. BMC Womens Health. 2020;20(1):150.
28. Fawcett EJ, Fairbrother N, Cox ML, et al. The prevalence of anxiety disorders during pregnancy and the postpartum period: a multivariate bayesian meta-analysis. J Clin Psychiatry. 2019;80(4):18.
29. Uguz F, Gezginc K, Zeytinci IE, et al. Obsessive-compulsive disorder in pregnant women during the third trimester of pregnancy. Compr Psychiatry. 2007;48(5):441–5.
30. Sharma V, Sommerdyk C. Obsessive–compulsive disorder in the postpartum period: diagnosis, differential diagnosis and management. Womens Health. 2015;11(4):543–52.
31. House SJ, Tripathi SP, Knight BT, et al. Obsessive-compulsive disorder in pregnancy and the postpartum period: course of illness and obstetrical outcome. Arch Womens Ment Health. 2016;19(1):3–10.
32. Steiner M, Dunn E, Born L. Hormones and mood: from menarche to menopause and beyond. J Affect Disord. 2003;74(1):67–8.
33. Chaudron LH, Nirodi N. The obsessive–compulsive spectrum in the perinatal period: a prospective pilot study. Arch Womens Ment Health. 2010;13(5):403–10.
34. Leckman JF, Goodman WK, North WG, et al. The role of central oxytocin in obsessive compulsive disorder and related normal behaviour. Psychoneuroendocrinology. 1994;19(8):723–49.
35. Forray A, Focseneanu M, Pittman B, et al. Onset and exacerbation of obsessive-compulsive disorder in pregnancy and the postpartum period. J Clin Psychiatry. 2010;71(8):1061–8.
36. Zambaldi CF, Cantilino A, Montenegro AC, et al. Postpartum obsessive-compulsive disorder: prevalence and clinical characteristics. Compr Psychiatry. 2009;50(6):503–9.
37. Obeysekare JL, Cohen ZL, Coles ME, et al. Delayed sleep timing and circadian rhythms in pregnancy and transdiagnostic symptoms associated with postpartum depression. Transl Psychiatry. 2020;10(1):14.
38. Sharma V. Role of sleep deprivation in the causation of postpartum obsessive-compulsive disorder. Med Hypotheses. 2019;122:58–61.
39. Chang JJ, Pien GW, Duntley SP, et al. Sleep deprivation during pregnancy and maternal and fetal outcomes: is there a relationship? Sleep Med Rev. 2010;14(2):107–14.
40. Manchanda S, Singh H, Kaur T, et al. Low-grade neuroinflammation due to chronic sleep deprivation results in anxiety and learning and memory impairments. Mol Cell Biochem. 2018;449(1–2):63–72.
41. Uguz F, Ayhan MG. Epidemiology and clinical features of obsessive- compulsive disorder during pregnancy and postpartum period: a review. J Mood Disord. 2011;1(4):178–86.
42. Rosso G, Bechon E, Bogetto F, et al. OCD during pregnancy and post-partum. Riv Psichiatr. 2012b;47(3):200–4.
43. Starcevic V, Eslick GD, Viswasam K, et al. Symptoms of obsessive-compulsive disorder during pregnancy and the postpartum period: a systematic review and meta-analysis. Psychiatr Q. 2020;91:965–81.
44. Fairbrother N, Abramowitz JS. New parenthood as a risk factor for the development of obsessional problems. Behav Res Ther. 2007;45:2155–63.
45. Miller ES, Chu C, Gollan J, et al. Obsessive-compulsive symptoms during the postpartum period. J Reprod Med. 2013;58(3–4):115–22.
46. Yakut E, Uguz F, Aydogan S, et al. The course and clinical correlates of obsessive-compulsive disorder during the postpartum period: a naturalistic observational study. J Affect Disord. 2019;254:69–73.
47. Kaya V, Uguz F, Sahingoz M, et al. Pregnancy-onset obsessive-compulsive disorder: clinical features, comorbidity, and associated factors. Bull Clin Psychopharmacol. 2016;25(3):248–58.

48. Kaminsky ZA, Osborne LM, Guglielmi V, et al. Postpartum depression biomarkers predict exacerbation of OCD symptoms during pregnancy. Psychiatry Res. 2020;293:113332.
49. Miller ES, Hoxha D, Wisner KL, et al. The impact of perinatal depression on the evolution of anxiety and obsessive-compulsive symptoms. Arch Womens Ment Health. 2015;18(3):457–61.
50. Overbeek T, Schruers K, Vermetten E, et al. Comorbidity of obsessive-compulsive disorder and depression: prevalence, symptom severity, and treatment effect. J Clin Psychiatry. 2002;63(12):1106–111210.
51. Arnold LM. A case series of women with postpartum-onset obsessive-compulsive disorder. Prim Care Companion J Clin Psychiatry. 1999;1(4):103–8.
52. Abramowitz JS, Franklin ME, Schwartz SA, et al. Symptom presentation and outcome of cognitive-behavioral therapy for obsessive-compulsive disorder. J Consult Clin Psychol. 2003;71(6):1049–57.
53. Williams KE, Koleva H. Identification and treatment of peripartum anxiety disorders. Obstet Gynecol Clin North Am. 2018;45(3):469–81.
54. Rodriguez-Cabezas L, Clark C. Psychiatric emergencies in pregnancy and postpartum. Clin Obstet Gynecol. 2018;61(3):615–27.
55. Sinesi A, Maxwell M, O'Carroll R, et al. Anxiety scales used in pregnancy: systematic review. BJPsych Open. 2019;5(1):e5.
56. Goodman WK, Price LH, Rasmussen SA, et al. The yale-brown obsessive compulsive scale. I. Development, use, and reliability. Arch Gen Psychiatry. 1989;46(11):1006–11.
57. Speisman BB, Storch EA, Abramowitz JS. Postpartum obsessive-compulsive disorder. J Obstetr Gynecol Neonatal Nurs. 2011;40(6):680–90.
58. Lord C, Rieder A, Hall GBC, et al. Piloting the perinatal obsessive-compulsive scale (POCS): development and validation. J Anxiety Disord. 2011;25(8):1079–84.
59. Cox J, Holden J, Sagovsky R, et al. Detection of postnatal depression: development of the 10-item Edinburgh Postanatal depression scale. Br J Psychiatry. 1987;150(6):782–6.
60. Spielberg CD, Gorsuch RL, Luschene R, et al. State-trait anxiety inventory for adults; 1983.
61. Nillni YI, Mehralizade A, Mayer L, et al. Treatment of depression, anxiety, and trauma-related disorders during the perinatal period: a systematic review. Clin Psychol Rev. 2018;66:136–48.
62. Albert U, Di Salvo G, Solia F, et al. Combining drug and psychological treatments for obsessive-compulsive disorder: what is the evidence, when and for whom. Curr Med Chem. 2018b;25(41):5632–46.
63. Del Casale A, Sorice S, Padovano A, et al. Psychopharmacological treatment of obsessive-compulsive disorder (OCD). Curr Neuropharmacol. 2019;17:710–36.
64. Katzman MA, Bleau P, Blier P, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry. 2014;14(1):S1.
65. Maina G, Rosso G, Rigardetto S, et al. No effect of adding brief dynamic therapy to pharmacotherapy in the treatment of obsessive-compulsive disorder with concurrent major depression. Psychother Psychosom. 2010a;79(5):295–302.
66. Sharma V. Pharmacotherapy of postpartum obsessive-compulsive disorder: a systematic review. Expert Rev Neurother. 2018;18(12):925–31.
67. Koran LM, Hanna GL, Hollander E, et al. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Am J Psychiatry. 2007;164(7):5–53.
68. Maina G, Saracco P, Giolito MR, et al. Impact of maternal psychological distress on fetal weight, prematurity and intrauterine growth retardation. J Affect Disord. 2008b;111(2–3):214–22.
69. Fumeaux CJF, Harari MM, Weisskopf E, et al. Risk-benefit balance assessment of SSRI antidepressant use during pregnancy and lactation based on best available evidence - an update. Expert Opin Drug Saf. 2019;18(10):949–63.
70. Albert U, Marazziti D, Di Salvo G, et al. A systematic review of evidence-based treatment strategies for obsessive- compulsive disorder resistant to first-line pharmacotherapy. Curr Med Chem. 2018a;25(41):5647–61.

71. Albert U, Barbaro F, Bramante S, et al. Duration of untreated illness and response to SRI treatment in obsessive-compulsive disorder. Eur Psychiatry. 2019b;58:19–26.
72. Damkier P, Videbech P. The safety of second-generation antipsychotics during pregnancy: a clinically focused review. CNS Drugs. 2018;32(4):351–66.
73. Belzeaux R, Sanguinetti C, Murru A, et al. Pharmacotherapy for the peripartum management of bipolar disorder. Expert Opin Pharmacother. 2019;20(14):1731–41.
74. Panchaud A, Weisskopf E, Winterfeld U, et al. Pharmacokinetic alterations in pregnancy and use of therapeutic drug monitoring. Therapie. 2014;69(3):223–34.
75. Chad L, Pupco A, Bozzo P, et al. Update on antidepressant use during breastfeeding. Can Fam Physician. 2013;59(6):633–4.
76. Cuomo A, Maina G, Neal SM, et al. Using sertraline in postpartum and breastfeeding: balancing risks and benefits. Expert Opin Drug Saf. 2018;17(7):719–25.
77. Creeley CE, Denton LK. Use of prescribed psychotropics during pregnancy: a systematic review of pregnancy, neonatal, and childhood outcomes. Brain Sci. 2019;9(9):235.
78. Fineberg NA, Hollanderd E, Pallanti S, et al. Clinical advances in obsessive-compulsive disorder: a position statement by the International College of Obsessive- Compulsive Spectrum Disorders. Int Clin Psychopharmacol. 2020;35(4):173–93.

Unwanted, Intrusive Thoughts of Infant-Related Harm

6

Nichole Fairbrother, Rachel Martin, and Fiona Challacombe

6.1 Overview

The arrival of a newborn infant is an exciting and joyous experience for most parents. Despite being a positive experience, it is also a stressful time involving significant changes. This is particularly true for birthing people for whom pregnancy, birth, and postpartum are also accompanied by a host of physiological and neurobiological changes [1–3]. A relatively unknown aspect of early parenting is the experience of unwanted, intrusive thoughts (UITs; thoughts, images, and impulses) related to the newborn, in particular UITs of infant-related harm. Unwanted, intrusive, postpartum thoughts of infant-related harm are a ubiquitous experience for almost all new parents and may involve thoughts of accidental harm (e.g., What if my baby falls off the bed?) and thoughts of intentional harm (e.g., What if I scream at my baby?). Although thoughts of harming one's infant can occur in other contexts, *unwanted intrusive* thoughts of infant-related harm are those that do not fit with the desires, values and motivation of the person, and it is these far more common experiences that we focus on here.

In this chapter, we begin by describing what is known about UITs in general, outside of pregnancy and the postpartum. Following this, we provide detailed

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information about the prevalence, content, and course of perinatal UITs, as well as their relationship with mental health problems (e.g., depression and obsessive–compulsive disorder) and parenting. We also describe how parents respond to UITs of infant-related harm, in particular how they feel and behave. Postpartum UITs of infant-related harm are ubiquitous for both mothers and fathers, but there are some gender differences that we briefly outline. We conclude by offering recommendations for healthcare professionals about how to normalize UITs if parents disclose them, and importantly how professionals can respond in more positive ways that are less stigmatizing and ultimately support new parents adjusting to their caregiving role.

6.2 Nonperinatal UITs

In any given day, thousands of positive, neutral, and negative thoughts will occur to us. They may be in the form of words, images, doubts, or urges. For brevity, we will use the term "thoughts" to refer to all of these. In many instances, they are related to our current situation, past experiences, or future ones, but they can also occur seemingly without any obvious reason. The capacity to experience thoughts in this way without planning allows for lateral thinking and creativity and is an important part of human experience [4].

When our spontaneous thoughts relate to things we are worried about, that is, things we do not want to happen, or content that we deem unacceptable, they may be experienced as unwanted, difficult to control, and intruding into consciousness [5]. When this happens, they are referred to as unwanted, intrusive thoughts (UITs), which Rachman (1981) defined as thoughts that interfere with an ongoing or current activity, are attributed to an internal origin, and are difficult to control [6]. Consider the common examples of an image of pushing a fellow traveler in front of the train at a busy platform or a fleeting urge to jump when at the top of a high monument. UITs may therefore serve a function of alerting us to all sources of personally relevant and sometimes threat-related information in order that we can make micro-adjustments to avoid these outcomes if needed or ignore them if not. Put another way, Salkovskis (1988) argued that UITs ensure that our thoughts are noticed and evaluated for their relevance to our goals and priorities in order to facilitate problem-solving [7]. For example, a UIT about falling from a high ledge may lead us to take a step or two back.

UITs are reported by 74% to 99% of individuals in the general population [8–10] and are generally experienced as fleeting and easily dismissed. The content of UITs typically relates to our current preoccupations and concerns (i.e., the things we are focused on and the things we are worried about) [11]. UITs are also more likely to occur when we are stressed and anxious [12]. Rachman (1978) suggested that individuals who are more sensitive to threats or danger in their surrounding environment may be more likely to experience UITs. Due to their sensitivity to threat, these individuals are both more prone to experience UITs and to notice and attend to them [13].

6.3 Perinatal UITs of Infant-Related Harm

6.3.1 Overview

UITs of infant-related harm are a common and normative part of the transition to parenthood and tend to be more frequent among first-time parents [14]. Several studies have estimated that between 70 and 100% of mothers of infants experience UITs of infant-related harm [14–16]. The frequency of UITs of infant-related harm tends to peak within the first few weeks following childbirth [17]. This is not surprising, given the often preoccupying and stressful nature of the early postpartum and the relationship between preoccupation, stress, and the content and occurrence of UITs in general [18]. The steep learning curve entailed in caring for a precious, fragile newborn can be challenging, with parents needing to understand and navigate all sources of threat including potentially themselves. Therefore, given that new parents are often hypervigilant to potential sources of danger in the caregiving environment, this may increase the frequency and likelihood of experiencing UITs of infant-related harm [19]. The content of postpartum UITs tends to be experienced as thoughts of accidentally harming one's infant (e.g., what if my baby falls off the bed?) or thoughts of intentionally harming one's infant (e.g., what if I throw my baby out of the window?). The level of distress associated with the experience of UITs of infant-related harm varies across individuals; however, intentional thoughts of harming one's own infant are particularly distressing [14, 20].

6.4 Prevalence of UITs of Infant-Related Harm among New Parents

A recent review by Brok and colleagues [17] identified four studies examining the prevalence of UITs of infant-related harm among parents [14, 19, 21, 22]. To our knowledge, the first study on this topic was conducted by Leckman and colleagues (1999) [21]. They measured the prevalence of infant-related preoccupations (intrusive thoughts and concerns), in particular preoccupations related to infant harm, among 41 pairs of mothers and fathers. The authors reported that 95% of mothers and 80% of fathers worried about something bad happening to their infant, and this included having concerns about their infant's health, development, or appearance. In particular, 37% of parents (n = 14 mothers, n = 16 fathers) reported preoccupations of infant-related harm [21]. Unlike the other three studies discussed below, this initial study did not focus exclusively on UITs (i.e., unwanted and intrusive ideation) but may also have included worry thoughts, for example, "I hope he sleeps tonight."

Abramowitz and colleagues (2003) have assessed the prevalence of UITs of infant-related harm among parents of infants in two separate studies [19, 22]. In the first [19], UITs of infant-related harm were assessed among both mothers and fathers, with 65% of the 76 parents in the sample reporting them [19]. The prevalence of perinatal UITs of infant-related harm was again later assessed in a cross-sectional study by Abramowitz and colleagues (2010) [22]. This study utilized the Postpartum Thoughts and Behaviors Checklist (PTBC), a modified version of the

YBOCS, to assess the prevalence of UITs. The PTBC is similar to the PPII [14] and includes a checklist of 10 different types of UITs of infant-related harm (e.g., thoughts that the infant could stop breathing while asleep; thoughts that the infant could die of SIDS; fears about dropping the infant). Among the sample of postpartum women, 87% of mothers ($n = 52$) reported experiencing at least one of the 10 UITs of infant-related harm.

In their study, Fairbrother and Woody (2008) [14] found that UITs of accidental infant-related harm were a universal experience, reported by all mothers ($n = 91$) at 4 weeks postpartum. This remained stable at 12 weeks postpartum, with slightly over 95% of the mothers continuing to report UITs of accidental infant-related harm. Regarding UITs of intentional harm, almost 50% of mothers in the study reported UITs of intentional harm toward their infant at 4 weeks postpartum. This rate decreased to just under 27% of all mothers who reported UITs of intentional harm at 12 weeks postpartum. In this study, maternal UITs of infant-related harm were assessed using the Postpartum Intrusions Interview (PPII), a semi-structured interview developed by the study authors. The PPII examines the content and behavioral and emotional responses to UITs, as well as the interference of UITs with parenting and functioning more generally [14].

Finally, a randomized controlled trial examining the efficacy of a cognitive-behavioral prevention program for postpartum OCD in 71 expectant mothers also reported data on the prevalence of UITs of infant-related harm [23]. This study utilized the PTBC to assess intrusive thoughts of infant-related harm at three points in postpartum. Only the control group prevalence estimates are reported here as the intervention likely impacted UIT prevalence (it was designed with this goal in mind). Specifically, among control participants, a minimum of 84% reported thoughts of infant-related harm at one or more of the postpartum assessments [23].

Taken together, these studies provide support that UITs of infant-related harm are a common and universal experience among new parents, with prevalence estimates ranging from 65% to 100%. However, there was significant variability in the assessment method used across studies, which may explain the differences observed in prevalence rates among each of the samples.

6.5 The Content of Perinatal UITs of Infant-Related Harm

In general, the content of perinatal UITs relates to concerns about accidental harm befalling the infant or harming the infant on purpose. To date, perinatal UITs of infant-related harm are generally poorly understood. As such, healthcare providers tend to respond to disclosures of these kinds of thoughts, especially thoughts of intentional harm, as evidence of increased risk for child abuse. In light of this, research investigators have, in some studies, made a distinction between perinatal UITs of accidental and intentional harm in order to test the hypothesis that UITs of intentional harm may be a risk factor for child abuse, with the hypothesis, derived from all other studies of normal intrusive thoughts, that this is not the case.

UITs of accidental and intentional harm differ slightly in terms of their prevalence and content. UITs of accidental harm appear to be universal, and to date,

studies have shown that all new mothers report experiencing UITs of accidental infant-related harm [14]. Some examples of the content of UITs of accidental infant-related harm include thoughts of accidentally drowning the baby, the baby falling, or being accidentally dropped from a height.

Examples of Unwanted, Intrusive Thoughts of Accidental Infant-Related Harm

- Suffocation.
- The baby falling or accidentally being dropped from a height.
- Contamination and illness.
- Accidents.
- Neglect.
- Sexual abuse by another person.
- Drowning.
- Burns.
- Abduction or harm by another person.
- Animal attacks.
- Accidentally being responsible for causing harm to one's infant (e.g., stepping on the baby by accident).

In contrast, almost half of new mothers report UITs of harming their infant intentionally [14]. The content of these thoughts may include ideas related to infant suffocation, sudden infant death syndrome, accidents, contamination, or intentional harm [15, 16]. Not surprisingly, intentional UITs of harming one's infant are more distressing than accidental harm thoughts [18]. However, neither accidental nor intentional UITs of infant-related harm have been associated with actual child harming behaviors [14].

Examples of Unwanted, Intrusive Thoughts of Intentional Infant-Related Harm

- Screaming at your baby.
- Shaking your baby.
- Giving your baby away.
- Intentionally hitting your baby too hard when burping him/her.
- Dropping or throwing your baby out the window or off the balcony.
- Touching your baby's genitals in an inappropriate way.
- Intentionally puncturing the soft spot on your baby's head.
- Throwing or dropping your baby on purpose.
- Stabbing your baby.
- Slapping or hitting your baby.
- Intentionally allowing your baby to fall under water in the bath.
- Intentionally smothering your baby.
- Burning your baby with hot water on purpose.
- Leaving baby somewhere where he/she may not be found right away.
- Strangling your baby.
- Stepping on your baby on purpose.

6.6 Onset and Course of Perinatal UITs of Infant-Related Harm: From Pregnancy to Postpartum

Only one study has evaluated the onset of UITs of infant-related harm. Remarkably, in this study, the majority of new mothers (63.2%) reported rapid onset of UITs, and over half (58.3%) of the new mothers in the sample reported that they experienced UITs of infant-related harm for the first time on the day their baby was born [14]. Slightly less than 10% (7.7%) reported onset in pregnancy.

To our knowledge, there are only two studies to date that have evaluated the course and onset of perinatal UITs of infant-related harm at specific times during the prenatal and postpartum periods [14, 23]. In the first of these studies by Fairbrother and Woody (2008), the course of UITs of infant-related harm was assessed across several time points during the postpartum period and distinguished between UITs of accidental and intentional infant-related harm. The authors found that all new mothers (n = 91) reported UITs of accidental infant-related harm at around 1 month postpartum [14]. Almost 50% (n = 45) of those mothers reported UITs of intentional infant-related harm, which tended to relate to intentional physical harm of the infant. Similar rates were observed at 3 months postpartum, in which close to 95% of new mothers reported UITs of accidental infant-related harm, with 19.1% of new mothers continuing to endorse UITs of intentional infant-related harm.

In terms of changes in the frequency of UITs of infant-related harm, from birth to 1 month postpartum, half of the sample (54.4%) reported that they either decreased in frequency, or stopped altogether, with 40% reporting no change and 5.6% reporting an increase in frequency. From 1–3 months postpartum, again over half of the sample (55%) reported continued declines in UIT frequency, with 29% reporting no change and 16% reporting an increase in UIT frequency [14].

The second study by Timpano and colleagues (2011) measured UITs of infant-related harm at 1, 3, and 6 months postpartum [23]. The proportion of participants reporting one or more UITs of infant-related harm was highest at 3 months postpartum (≥ 84%), followed by 1 month postpartum (≥80%) and 6 months postpartum (≥75%) [23].

Overall, findings suggest that UITs of infant-related harm begin most often in the very early postpartum and that their onset is abrupt. The frequency of UITs of infant-related harm, and the proportion of new mothers to report them, appears to decrease over the course of the postpartum period, with evidence from one study that the peak may be closest to 3 months postpartum. Furthermore, for most new mothers, the frequency of UITs of infant-related harm decreases across the postpartum period, but either remains stable or increases for a small proportion of women. It may be that increases in harm UITs across the first 3 months postpartum indicate an onset or exacerbation of mental health difficulties such as obsessive–compulsive disorder (OCD). Further research is needed to better understand predictors of UIT courses over time and the relationship of UIT frequency with mental health. Future research should seek to chart the course of these thoughts further out in the postpartum period.

6.7 Characteristics and Emotional and Behavioral Responses to UITs of Infant-Related Harm

Several studies have specifically explored new parents' emotional and behavioral responses to UITs of infant-related harm, as well as how time-consuming and interfering these thoughts tend to be [14, 15, 19, 22, 24]. We will briefly outline these findings beginning with what the research has shown about how parents feel when they experience UITs of infant-related harm and some of the commonly reported behaviors that parents engage in to both manage and cope with these types of thoughts.

6.7.1 Emotional Responses

A study by Abramowitz and colleagues (2003) found that parents reported mild distress when UITs of infant-related harm occurred [19]. They also reported that they were present for, on average, less than an hour a day, were minimally interfering, and were easy to push out of their mind. Mothers reported spending more time (approx. 1 h per day) thinking about UITs of infant-related harm compared to fathers [19]. In a subsequent study, Fairbrother and Woody (2008) also demonstrated that UITs of accidental infant-related harm tend to result in mild distress, little or no guilt and interference, are fairly easy to get rid of, and occupy less than 10 min a day at 1 month postpartum, and less than 10 min a week at 3 months postpartum [14]. In contrast, UITs of intentional harm were more distressing, resulted in more guilt, and were less time-consuming [14]. More recently, a study conducted by Boyd and Gannon (2019), which involved semi-structured interviews with eight new mothers who experienced UITs of infant-related harm, sought to understand how these thoughts made these new mothers feel and behave [24]. Most mothers described strong emotional responses when UITs occurred. In particular, mothers reported having a lack of control over their UITs and feeling exhausted from not being able to "switch off" from these thoughts. In response to their UITs, most mothers engaged in behaviors to help them have a sense of control over these thoughts, like distracting themselves and/or washing the infant's belongings to stop them from being contaminated in some way. A subset of mothers reported the use of cognitive reappraisal (e.g., self-dialogue) as a means to rationalize their UITs [24].

6.7.2 Behavioral Responses

In a study by Abramowitz and colleagues (2006), over half of all parents utilized "neutralizing" (i.e., behaviors or mental thoughts and images the person engages in to undo the content or the consequences of the UIT) [4, 15]) to cope with their UITs of infant-related harm [15]. The most common strategies reported by parents were self-reassurance (71.8%) and checking on the infant (61.2%) as

strategies to cope with UITs. A few parents (9.4%) reported avoiding the infant as a response to these thoughts [15]. In the study by Fairbrother and Woody (2008), over 90% of the new mothers who participated in the study reported one or more behavioral responses to UITs of both accidental and intentional infant-related harm [14]. Behavioral responses included checking on the baby's well-being, reassurance seeking, avoidance of situations in which the thoughts occur and avoiding specific activities with their infant, washing behaviors, distraction, and "mental undoing" (imagining the thought content not occurring) [14]. Similar behavioral responses were reported by a group of 60 postpartum women in a more recent study [22]. Taken together, findings from these studies indicate that it is common for parents to engage in behaviors in response to UITs of infant-related harm.

6.8 Gender Differences in the Experience of UITs of Infant-Related Harm

It is not only new mothers that experience UITs of infant-related harm following childbirth or when caring for a newborn infant in the early postpartum period. During the transition to parenthood, fathers also experience increased stress associated with the demands of caregiving and adapting to their new parenting role [25, 26].

Prevalence.

Among the available research studies, findings have consistently demonstrated that mothers and fathers experience UITs at similar rates; in other words, almost all new mothers and fathers report UITs of infant-related harm during the postpartum period [15, 18, 19]. In an early study by Abramowitz and colleagues (2003), 75% of new parents reported UITs of infant-related harm [19]. There were no noticeable differences among mothers and fathers in terms of whether or not they reported experiencing UITs of infant-related harm. However, mothers reported spending more time with UITs (M = 1.08 h), compared to fathers (M = 0.91 h) [19]. These findings were supported by a later study by Abramowitz and colleagues (2006), which also found no difference in the likelihood of reporting UITs of infant-related harm among mothers (90.7%) and fathers (88.1%) [15]. In a more recent study, Fairbrother and colleagues (2019) examined UITs of infant-related harm in prepartum and postpartum couples in response to recorded sounds of infant crying and again found no differences in the likelihood of reporting UITs of infant-related harm [18]. In a subsequent study by Fairbrother and colleagues (2019), there were no differences found in the number of UITs of infant-related harm that prepartum and postpartum mothers and fathers reported [18]. Although equal proportions of mothers and fathers report UITs of infant-related harm, mothers appear to experience these thoughts for longer than fathers. In other words, mothers tend to experience UITs of infant-related harm as more time-consuming than do fathers.

6.8.1 Emotional Responses to Harm Thoughts

To our knowledge, two studies have compared the differences between mothers' and fathers' emotional responses to UITs of infant-related harm, with minor gender differences being reported [18, 19]. In the most recent study by Fairbrother and colleagues (2019), prepartum and postpartum mothers' and fathers' emotional responses to infant cries were compared with respect to those parents who reported UITs of infant-related harm. Among prepartum couples, mothers tended to report experiencing more internalizing emotions in response to infant cries, compared with fathers [18]. Among both prepartum and postpartum parents who reported UITs of infant-related harm, mothers and fathers reported more hostile emotions. Compared to postpartum mothers, fathers who reported UITs of infant-related harm in response to infant cries also scored higher on measures of state anger [18].

A second study by Abramowitz and colleagues (2003) also compared gender differences between mothers' and fathers' emotional responses to UITs of infant-related harm [19]. Mothers reported slightly more distress than fathers when experiencing UITs of infant-related harm [19]. Specifically, fathers reported no distress ($M = 0.87$), compared to mothers who reported mild distress ($M = 1.28$), as indicated by parental ratings of distress ranging from one to four, with one being no distress and four being severe distress. The higher levels of distress reported in mothers are likely explained by the differences in time spent with the infant and the differing nature of caregiving tasks in the early postpartum; on average, mothers reported just over 15 h per day with the infant, compared to fathers who reported an average of over 5 h per day with the infant. Both mothers and fathers reported being able to control their UITs and did not feel comfortable disclosing their UITs. Those fathers who had greater difficulty controlling their UITs were less able to disclose such thoughts [19].

Findings are consistent in showing that UITs of infant-related harm are common among both new mothers and new fathers. Nonetheless, there has been less attention given to assessing UITs of infant-related harm among fathers, compared with mothers. Although it is clear that fathers experience UITs of infant-related harm at similar rates to mothers, additional information regarding fathers' experience of these kinds of thoughts is needed.

6.9 Why Do Parents Experience UITs of Infant-Related Harm?

As discussed in an earlier section, UITs among individuals in the general population typically arise in response to stimuli in our environment that is salient (e.g., something we attach meaning to), or goals that motivate us [11, 27] and cause us to behave in a certain way. UITs tend to occur during times of increased stress or following exposure to a stressful event [12, 28]. It is not surprising then that new

parents experience UITs of infant-related harm, which are likely a reaction to caring for a vulnerable infant who is dependent upon the parent to attend to their physical and emotional needs.

Becoming a parent for the first time is a rewarding, albeit stressful experience for almost all parents. First-time parents in particular are adjusting to their new role as caregivers, in which they are solely responsible for providing care to their newborn. UITs of infant-related harm likely arise as a direct result of these particular demands and additional responsibilities that accompany the caregiving role [14]. Specifically, new parents think about their infant all the time. One's newborn is likely most parents' primary preoccupation [21, 29]. Further, new parents are bombarded with information about potential hazards to the health and safety of their infant (e.g., sudden infant death syndrome, car seat safety, electric outlets, the soft spot on the top of the infant's head). This preoccupation with one's infant and all of the information about potential risk heightens a parent's perception of threat and feelings of anxiety, which trigger the occurrence of UITs of infant-related harm [18]. Prior theories (e.g., Rachman (1978)) have proposed that UITs are more prevalent among individuals who are more sensitive to threats in their environment [13]. Therefore, among parents who are especially threat sensitive (i.e., concerned about danger and safety), UITs of infant-related harm may be particularly frequent.

UITs of infant-related harm in the early postpartum period may also be an adaptive evolutionary response, which cues new parents to behave in ways to protect their infant from danger, with the ultimate goal of ensuring infant survival. When they are infants, our children depend almost exclusively on us as parents to ensure their health and safety. UITs of infant-related harm (even UITs of intentional harm) likely trigger protective, safety-seeking behavioral responses and consequently increase infant safety. From an evolutionary perspective, it may not matter if the UITs of infant-related harm are accidental or intentional if both provoke a protective parental response. From what we know about new mothers' behavioral responses to UITs of both accidental and intentional harm, it seems clear that this is the case; both types of UITs of harm are associated with behaviors intended to increase infant safety [14].

Additional predictors of the occurrence of postpartum UITs of infant-related harm include parenting stress, infant crying, and low social support [14, 18, 30]. When these very normal and ubiquitous harm thoughts occur in the context of negative emotions, low social support, and high stress, it is likely that parents will experience them as particularly distressing. Additional research is needed to investigate this relationship.

6.10 Relationship of UITs of Infant-Related Harm to Mental Health

By far, the most common mental health difficulty associated with postpartum UITs of infant-related harm is obsessive–compulsive disorder (OCD) [31]. OCD is an anxiety-related disorder characterized by two primary symptoms: obsessions

(recurrent, persistent, and frequently distressing UITs) and/or compulsions (behaviors, often repetitive, that the person engages in an effort to reduce the distress associated with an obsession or to prevent some dreaded outcome associated with a particular obsession) [32]. Obsessions are unwanted, intrusive thoughts, images, or impulses (i.e., UITs) that are recurrent and that the person attempts to push out of their mind [31]. The content of obsessions often involves contamination, sexual or violent aggression, religious beliefs, or other people being harmed. While UITs are a normal human experience, they can develop into true obsessions (i.e., persistent and recurrent UITs) if the person experiencing them interprets them to imply something terrible (e.g., I am crazy, dangerous, or evil) and consequently tries hard to push the UITs out of their mind [31]. This can result in the paradoxical effect of increasing the frequency of the UITs, and further alarming the person experiencing them [32]. It is this interpretation of negative personal significance rather than the content that differentiates "normal" and "obsessional" intrusive thoughts.

The current DSM-5 diagnostic criteria for OCD [33] requires one of the following: (a) the OC symptoms cause interference to the individual's life, (b) the obsessions and/or compulsions occupy 1 h or more a day, or (c) the person who experiences the obsessions and compulsions experiences them as clinically distressing. The most recent meta-analysis of the prevalence of OCD globally has estimated a lifetime prevalence of 1.3% in the adult population [34]. Compared to men, women are 1.6 times more likely to experience OCD, with a lifetime prevalence of 1.5%, a slightly higher risk compared to men, who have a 1.0% lifetime prevalence rate [34].

OCD has also been associated with an increase in engagement of healthcare services, lower quality of life, and problems with finances [35]. As a result of the stigmatization associated with the content of some obsessions (e.g., those that may be deemed morally repugnant), individuals tend to conceal the true essence and severity of their issues [31]. This has led to delays among individuals seeking treatment for their OCD from the first time they experience symptoms and/or notice significant functional impairments, in some cases for years [36, 37].

6.11 Perinatal OCD

Among the anxiety and anxiety-related disorders, OCD alone has been associated with an increased risk of onset and exacerbation during the perinatal period [31]. It has been hypothesized that the dramatic increase in responsibility for a fragile and precious newborn contributes to this risk [31, 38]. If a new parent interprets their normally occurring thoughts of infant-related harm as implying personal responsibility or fault, this can increase the likelihood that OCD may develop.

In the most recent and methodologically sound meta-analysis of perinatal OCD conducted to date, Fawcett and colleagues (2019) found that 1 in 5 perinatal women met diagnostic criteria for at least one type of anxiety disorder [39]. Pregnant women in particular were 3.1% more vulnerable to having an anxiety disorder, compared to postpartum women who had given birth [39]. Additional evidence has estimated that among recent mothers, approximately 2–9% meet the criteria for a

diagnosis of OCD at 6–26 weeks postpartum [40–42]. Retrospective studies of individuals with OCD have consistently reported that compared to other life events, pregnancy and childbirth trigger the onset and exacerbation of OCD [41, 43–45]. The postpartum period may be a significant period of risk for OCD onset, compared to the prenatal period, with noticeable increases in OCD symptomatology being reported [46].

OCD can arise in the perinatal period as a disorder for the first time, a preexisting condition, or a prior diagnosis of OCD that is exacerbated or recurs during the perinatal period. Perinatal OCD generally has a quick onset and is characterized by obsessions of infant-related harm [47–49]. Among new mothers who suffer from postpartum OCD, compulsions may involve repeated checking on the infant (e.g., check to see that one's infant is breathing), reassurance seeking (e.g., looking things up on the internet), or cleaning rituals (e.g., excessive cleaning of baby-related supplies), as well as while avoiding the infant and/or avoiding engaging in certain activities with the infant (e.g., bathing) [50]. The content of obsessions frequently involves harm related to the infant, which may be accidental or intentional [14, 51], for example, thoughts or images of infant smothering or inappropriate sexual contact toward the infant during diaper changes [14].

PpOCD has been associated with less optimal parenting outcomes, with some mothers displaying less sensitive caregiving interactions with their infant, as well as having lower rates of breastfeeding practices, particularly if mothers were prescribed certain medications that prevented this [50]. However, attachment may be unaffected by OCD itself. Moreover, in a recent study looking at mother–infant bonding, the authors reported that antenatal anxiety disorders were not associated with perceived or observed bonding [52].

6.12 Postpartum Depression

Several studies have explored the relationship between UITs of infant-related harm and postpartum depression [19, 53–55]. These studies assessed UITs of infant-related harm as opposed to the kinds of infant-related harming thoughts that may occur in the context of major depression with either suicidal or psychotic features. UITs are, by definition, unwanted and inconsistent with the person's beliefs and values, whereas the kinds of harming thoughts experienced in the context of a suicidal or psychotic depression may not be.

Two studies have assessed the prevalence of UITs of infant-related harm among women experiencing postpartum depression [53, 54]. In the first such study by Jennings and colleagues (1999), 41% of depressed mothers reported some thoughts of infant-related harm, 20% reported passing thoughts, and 21% reported repeated thoughts, taking precautions, or acting in a way that may be harmful. In contrast, among those mothers who did not experience depression, only 6.5% reported experiencing UITs [53]. However, it is important to mention here that the prevalence of UITs of infant-related harm reported by Jennings and colleagues (1999) is much lower than what has been found in other research studies [14–16]. This may be a

result of the methodology employed by Jennings et al. (1999), in which only one question was used to assess UITs of infant-related harm. In a second study, Wisner and colleagues (1999) found no statistically significant difference ($p = 0.13$) in the likelihood of reporting obsessional thoughts among women suffering from postpartum onset major depression (57%) with non-postpartum onset major depression (36%). However, when limited to those who reported obsessional thoughts, thought frequency was higher for those with postpartum onset major depression compared to those with non-postpartum onset major depression.

Two subsequent studies assessed the relationship between depression and the severity of intrusive thoughts of infant-related harm [19, 55]. In a study of intrusive thoughts of infant-related harm among parents, Abramowitz and colleagues (2003) reported a small to moderate association between depression and UIT severity (i.e., how time-consuming, impairing, distressing, and difficult to control) [19]. Critically, this association was reported in mothers only, and there was no significant association between depressive symptoms and UITs of infant-related harm among fathers. The authors suggest that this may be explained by fathers reporting more difficultly controlling UITs of infant-related harm, who tend to respond by suppressing or concealing such thoughts. A pilot study by Humenik and Fingerhut (2007) used the Child Thoughts Inventory (CTI) (a self-report measure developed by the authors) to examine the relationship between postpartum depression and UITs of infant-related harm in a sample of 50 new mothers (30 of whom were first-time mothers). A positive association between postpartum depression and UITs of infant-related harm was reported [55]. Specifically, mothers who scored higher on the Edinburgh Postnatal Depression Scale (EPDS) [56] also reported more frequent and severe UITs of infant-related harm on the CTI. In addition, mothers who had a more negative self-view of themselves also had more frequent UITs of infant-related harm. It may be that mothers who hold a more negative view of themselves are consequently more likely to negatively appraise and resist their UITs of infant-related harm, thereby increasing their frequency.

Collectively, these studies provide strong support for a relationship between depressed mood and the frequency and severity of UITs of infant-related harm and suggest that mothers with postpartum depression are more likely to report these kinds of thoughts compared to nondepressed new mothers.

6.13 Why Might Parents Who Experience UITs of Infant-Related Harm be Concerned about Disclosing these Thoughts?

Concealment of obsessions is common among OCD sufferers whose obsessions involve content that they consider morally repugnant or potentially indicative that they are a danger to others [37, 57]. The concealment of obsessions has been positively associated with OCD severity and, more specifically, symptoms related to unacceptable thoughts, fears of causing harm, and ordering [37]. Among those individuals with OCD who conceal their obsessions, they are more likely to have

negative attitudes about seeking professional help and lower expectations about the benefits of therapy to treat their OCD [37, 58]. Critically, therefore, the concealment of obsessions may act as a barrier preventing the individual from accessing appropriate treatment.

Mothers with postpartum OCD who experience harming obsessions often conceal their obsessions from others, especially healthcare providers, in fear that if they voice their UITs, their infant will be removed from their care [59]. This is likely also true for parents who experience UITs of infant-related harm, even if they do not suffer from OCD. They may be fearful of disclosing these thoughts to healthcare professionals out of concern that they may be reported to child protection services and/or that their infant may be removed from their care [43, 51]. As such, new parents may conceal these thoughts, preventing them from accessing the necessary education and support that would help them normalize and manage their UITs of infant-related harm [43]. Through our own clinical work and research investigations, mothers have shared stories in which they have had their infant removed from their care or experienced unnecessary risk management because they have disclosed UITs of infant-related harm to a healthcare professional. This is concerning and unnecessary; UITs of infant-related harm do not indicate risk of harm. In addition, we have also heard stories from mothers who disclose UITs of infant-related harm and who are then monitored by healthcare providers and/or child protection services for child abuse [59]. These reactions are not evidence-based and may cause unnecessary distress for mothers and their infants [51]. In particular, these types of reactions would increase the anxiety associated with experiencing UITs of infant-related harm, which may subsequently lead to the development of OCD.

We recommend that healthcare professionals provide evidence-based information about UITs of infant-related harm to their clients and provide meaningful reassurance that these kinds of disclosures will not result in monitoring or child removal. This would help new parents interpret their UITs as normal and would subsequently reduce the high levels of shame, guilt, and distress that tend to be associated with the experience of UITs of infant-related harm [14, 17, 60]. In addition, this would help encourage new parents to disclose harmful thoughts and would increase accessibility to treatment when appropriate.

6.14 Perinatal UITs and Risk of Infant Harm

There is no evidence from empirical research studies [14, 18, 19] nor from our own clinical reports working with new parents to indicate that UITs of infant-related harm lead the parent who experiences UITs to act aggressively or engage in intentional harming behaviors toward their infant. Furthermore, it is widely accepted that OCD sufferers are not at risk of acting on the content of their obsessions, irrespective of how horrific their obsessions may be. A recent meta-analysis by Brok and colleagues (2017), which included a review of several case studies examining UITs and infant harming behaviors, found no evidence of an increased risk of parental

aggression or violence toward the infant among parents who experienced UITs of infant-related harm. This is because these thoughts are ego-dystonic and do not represent a parent's true intentions [17].

Two studies have directly assessed this question. In one study by Fairbrother and Woody (2008), no difference in harsh parenting at 1 month postpartum between those mothers who endorsed UITs of infant-related harm and mothers who did not endorse UITs was found. Consistent with these findings, Murray and Finn (2012) conducted semi-structured interviews with six recent mothers who endorsed UITs of intentional infant-related harm and found no evidence of actual harming behaviors among mothers.

6.15 Non-UIT Harming Ideation and Risk of Infant Harm

Thoughts of infant-related harm that are not UITs can occur for a variety of reasons and, in some cases, may represent a risk to infant safety, for example, the non-UIT harmful thoughts that occur in the context of postpartum psychosis or a major depression with suicidal ideation or intent. Although extremely rare, harmful thoughts in the context of postpartum psychosis or depression may represent a risk of harm to the infant [61, 62]. Although postpartum OCD and postpartum psychosis both involve similar UITs of infant-related harm, these two are distinctly different clinical disorders [31]. A key difference between UITs of infant-related harm and the kinds of harming thoughts that may occur in the context of postpartum psychosis or depression is that UITs of infant-related harm are ego-dystonic (e.g., these thoughts are repugnant, distressing, and unacceptable to a parent's own values and beliefs) [24, 43, 63], while the delusions in postpartum psychosis and the thoughts of harming one's infant in depression with suicidal ideation/intent are ego-syntonic (e.g., they are acceptable to a parent and compatible with their values and beliefs) [17, 43, 64].

6.16 Information and Guidance for Healthcare Providers

To our knowledge, expectant and new parents are rarely educated by healthcare providers about perinatal UITs of infant-related harm. Importantly, psychoeducational programs for new parents would benefit from including normalizing information about UITs of infant-related harm in view of reducing the risk of negative appraisals of these thoughts. New parents who experience UITs of infant-related harm are often distressed and reluctant to disclose harmful thoughts to healthcare providers. This is because they may feel ashamed about having these types of thoughts or fear that if they disclose their UITs, they will be monitored, or worse, that their infant will be removed from their care by social services [65].

Healthcare professionals are often disinclined to enquire about UITs of infant-related harm among new parents because they are concerned that in doing so, parents may act on these thoughts [65]. This is not true and is, in fact, the exact opposite.

Rather, parents will likely feel relieved at having the opportunity to discuss these thoughts and learn that UITs are a normal part of parenthood and do not mean they will actually cause harm to their own infant. By healthcare providers acknowledging such thoughts and having open discussions with parents, this has shown to decrease the significance parents place on UITs of infant-related harm and how frequently they occur [65].

In light of this, we strongly recommend that during prenatal appointments, healthcare providers educate new parents that UITs of infant-related harm following childbirth is a ubiquitous postpartum experience, which likely reflects an adaptive response to protect the infant from danger and ensure the infant's survival [21]. Healthcare providers should differentiate between UITs of accidental and intentional infant-related harm [66] and reassure parents that both are a common and normative postpartum experience, and there is no research or clinical evidence linking UITs of infant-related harm to infant harming behaviors or child abuse. Healthcare providers should not assess for risk of infant-related harm on the basis of UITs of infant-related harm alone. Only when true indicators of child abuse (e.g., prior history of child abuse, harming behaviors, disclosure and/or plans to harm the infant) are present should any assessment or monitoring of the parent be undertaking. Engaging in this type of assessment or monitoring in the absence of any real risk factors for child harm, based exclusively on the presence of UITs of infant-related harm, will significantly increase the likelihood of the development of OCD. As has been discussed in previous sections, prior research [14, 18, 19] provides no evidence that UITs of infant-related harm represent a risk to infant safety.

Educating expectant mothers before childbirth normalizes harmful thoughts as a universal postpartum experience, and critically, would reduce the risk of ppOCD onset. This converges with evidence from a randomized-controlled trial (RCT) examining the efficacy of a prevention program for ppOCD symptoms in 71 pregnant women identified as being psychologically vulnerable to developing OCD [23]. The majority of new mothers in the sample reported UITs of infant-related harm at several timepoints across the 6-month postpartum period. Expectant mothers who received a cognitive-behavioral prevention program beginning in the second or third trimester until childbirth exhibited lower levels of obsessions and compulsions, as indicated by lower scores on the YBOCS at 6 months postpartum [23]. Therefore, demonstrating that addressing UITs of infant-related harm through early educational programs prenatally minimizes the risk of ppOCD onset.

In our lab (the Perinatal Anxiety Research Lab, led by Dr. Nichole Fairbrother at the University of British Columbia), we are currently designing an educational video with the aim of providing specific information to new parents about perinatal UITs of infant-related harm. We hope that this will help destigmatize and normalize these thoughts for new parents. We are also conducting further research in this area, which we anticipate will provide additional evidence to support UITs of infant-related harm as a ubiquitous postpartum experience.

Resources

- British Journal of General Practice: https://bjgp.org/content/bjgp/67/661/376.full.pdf.
- The Postpartum Stress Center. *What if I'm having scary thoughts?* https://postpartumstress.com/get-help-2/are-you-having-scary-thoughts/.
- International OCD Foundation. Beyond the Blues: Postpartum OCD: https://iocdf.org/expert-opinions/postpartum-ocd/.
- UK Royal College of General Practitioners Perinatal mental health toolkit: https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/perinatal-mental-health-toolkit.aspx.
- Anxiety and Depression Association of America: https://iocdf.org/. Provides a wealth of materials and resources for clinicians on perinatal OCD and other conditions.
- Anxiety Canada: https://www.anxietycanada.com/.
- International OCD Foundation: https://iocdf.org/.
- UKRCP free leaflet for women with OCD co-authored with service users https://www.rcpsych.ac.uk/mental-health/problems-disorders/perinatal-ocd and partners/carers https://www.rcpsych.ac.uk/mental-health/problems-disorders/perinatal-ocd-for-carers.
- Charity Maternal OCD: www.maternalocd.org. Founded by two women who have recovered from perinatal OCD in order to raise awareness of the condition and provide support for sufferers and resources for all.
- National Institute of Clinical Excellence Guidance on treatments in Antenatal and Postnatal Mental Health: https://www.nice.org.uk/guidance/cg192.

References

1. Fan F, Zou Y, Ma A, Yue Y, Mao W, Ma X. Hormonal changes and somatopsychologic manifestations in the first trimester of pregnancy and post partum. Int J Gynecol Obstet. 2009;105(1):46–9.
2. Leifer M. Psychological changes accompanying pregnancy and motherhood. Genet Psychol Monogr. 1977;95(1):55–96.
3. Hoekzema E, Barba-Muller E, Pozzobon C, Picado M, Lucco F, Garcia-Garcia D, et al. Pregnancy leads to long-lasting changes in human brain structure. Nat Neurosci. 2017;20(2):287–96.
4. Salkovskis PM. Cognitive-behavioural factors and the persistence of intrusive thoughts in obsessional problems. Behav Res Ther. 1989;27(6):677–82.
5. Clark DA, Rhyno S. Unwanted intrusive thoughts in nonclinical individuals. Intrusive thoughts in clinical disorders: Theory, research, and treatment; 2005:1–29.
6. Rachman S, Part I. Unwanted intrusive cognitions. Adv Behav Res Ther. 1981;3(3):89–99.
7. Salkovskis P. Intrusive thoughts and obsessional disorders. Curr Issues Clin Psychol. 1988;4:96–110.
8. Langlois F, Freeston MH, Ladouceur R. Differences and similarities between obsessive intrusive thoughts and worry in a non-clinical population: study 1. Behav Res Ther. 2000;38(2):157–73.

9. Belloch A, Morillo C, Lucero M, Cabedo E, Carrió C. Intrusive thoughts in non-clinical subjects: the role of frequency and unpleasantness on appraisal ratings and control strategies. Clin Psychol Psychother. 2004;11(2):100–10.
10. Radomsky AS, Alcolado GM, Abramowitz JS, Alonso P, Belloch A, Bouvard M, et al. Part 1—you can run but you can't hide: intrusive thoughts on six continents. J Obsessive Compul Relat Disord. 2014;3(3):269–79.
11. Klinger E. The contents of thoughts: interference as the downside of adaptive normal mechanisms in thought flow. In: Sarason IG, Pierce GR, Sarason BR, editors. Cognitive interference: theories, methods, and findings. Mahwah, NJ: Erlbaum; 1996. p. 3–23.
12. Nassif Y, Wells A. Attention training reduces intrusive thoughts cued by a narrative of stressful life events: a controlled study. J Clin Psychol. 2014;70(6):510–7.
13. Rachman S. An anatomy of obsessions. Behav Analy Modif. 1978;2(4):253–78.
14. Fairbrother N, Woody SR. New mothers' thoughts of harm related to the newborn. Arch Womens Ment Health. 2008;11(3):221–9.
15. Abramowitz JS, Khandker M, Nelson CA, Deacon BJ, Rygwall R. The role of cognitive factors in the pathogenesis of obsessive–compulsive symptoms: a prospective study. Behav Res Ther. 2006;44(9):1361–74.
16. Abramowitz JS, Nelson CA, Rygwall R, Khandker M. The cognitive mediation of obsessive-compulsive symptoms: a longitudinal study. J Anxiety Disord. 2007;21(1):91–104.
17. Brok EC, Lok P, Oosterbaan DB, Schene AH, Tendolkar I, van Eijndhoven PF. Infant-related intrusive thoughts of harm in the postpartum period: a critical review. J Clin Psychiatry. 2017;78(8):913–23.
18. Fairbrother N, Barr RG, Chen M, Riar S, Miller E, Brant R, et al. Prepartum and postpartum mothers' and fathers' unwanted, intrusive thoughts in response to infant crying. Behav Cogn Psychother. 2019;47(2):129–47.
19. Abramowitz JS, Schwartz SA, Moore KM. Obsessional thoughts in postpartum females and their partners: content, severity, and relationship with depression. J Clin Psychol Med Settings. 2003;10(3):157–64.
20. Fairbrother N, Thordarson DS, Challacombe FL, Sakaluk JK. Correlates and predictors of new mothers' responses to postpartum thoughts of accidental and intentional harm and obsessive compulsive symptoms. Behav Cogn Psychother. 2018;46(4):437–53.
21. Leckman JF, Mayes LC, Feldman R, Evans DW, King RA, Cohen DJ. Early parental preoccupations and behaviors and their possible relationship to the symptoms of obsessive-compulsive disorder. Acta Psychiatr Scand. 1999;100:1–26.
22. Abramowitz JS, Meltzer-Brody S, Leserman J, Killenberg S, Rinaldi K, Mahaffey BL, et al. Obsessional thoughts and compulsive behaviors in a sample of women with postpartum mood symptoms. Arch Womens Ment Health. 2010;13(6):523–30.
23. Timpano KR, Abramowitz JS, Mahaffey BL, Mitchell MA, Schmidt NB. Efficacy of a prevention program for postpartum obsessive–compulsive symptoms. J Psychiat Res. 2011;45(11):1511–7.
24. Boyd CF, Gannon K. How do new/recent mothers experience unwanted harm thoughts related to their newborn? A thematic analysis. J Reprod Infant Psychol. 2019:1–13.
25. Baldwin S, Bick D. Mental health of first time fathers–it's time to put evidence into practice. LWW. 2018;16(11):2064–5.
26. Baldwin S, Malone M, Sandall J, Bick D. Mental health and wellbeing during the transition to fatherhood: a systematic review of first time fathers' experiences. JBI Database System Rev Implement Rep. 2018;16(11):2118.
27. Klinger E. Modes of normal conscious flow. In: Pope KS, Singer JL, editors. The stream of consciousness. New York: Plenum Press; 1978. p. 225–58.
28. Horowitz MJ. Intrusive and repetitive thoughts after experimental stress: a summary. Arch Gen Psychiatry. 1975;32(11):1457–63.
29. Kim P, Mayes L, Feldman R, Leckman JF, Swain JE. Early postpartum parental preoccupation and positive parenting thoughts: relationship with parent–infant interaction. Infant Ment Health J. 2013;34(2):104–16.

30. Fairbrother N, Barr RG, Pauwels J, Brant R, Green J. Maternal thoughts of harm in response to infant crying: an experimental analysis. Arch Womens Ment Health. 2015;18(3):447–55.
31. Fairbrother N, Abramowitz JS. Postpartum obsessive-compulsive disorder. Oxford Handbook of Perinatal Psychology. Wenzel, A. Ed, Oxford University Press; 2016.
32. Abramowitz JS, Blakey SM, Reuman L, Buchholz JL. New directions in the cognitive-behavioral treatment of OCD: theory, research, and practice. Behav Ther. 2018;49(3):311–22.
33. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). Arlington, VA: American Psychiatric Publishing; 2013.
34. Fawcett EJ, Power H, Fawcett JM. Women are at greater risk of OCD than men: a meta-analytic review of OCD prevalence worldwide. J Clin Psychiatry. 2020;81(4)
35. Bobes J, González M, Bascaran M, Arango C, Saiz P, Bousono M. Quality of life and disability in patients with obsessive-compulsive disorder. Eur Psychiatry. 2001;16(4):239–45.
36. Belloch A, Del Valle G, Morillo C, Carrió C, Cabedo E. To seek advice or not to seek advice about the problem: the help-seeking dilemma for obsessive-compulsive disorder. Soc Psychiatry Psychiatr Epidemiol. 2009;44(4):257.
37. Wheaton MG, Sternberg L, McFarlane K, Sarda A. Self-concealment in obsessive-compulsive disorder: associations with symptom dimensions, help seeking attitudes, and treatment expectancy. J Obsessive Compul Relat Disord. 2016;11:43–8.
38. Blakey S, Abramowitz J. Postpartum obsessive-compulsive disorder. The Wiley handbook of obsessive compulsive disorders; 2017:511–526.
39. Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The prevalence of anxiety disorders during pregnancy and the postpartum period: a multivariate Bayesian meta-analysis. J Clin Psychiatry. 2019;80(4)
40. Wenzel A, Haugen E, Jackson L, Robinson K. Prevalence of generalized anxiety at eight weeks postpartum. Arch Womens Ment Health. 2003;6(1):43–9.
41. Zambaldi CF, Cantilino A, Montenegro AC, Paes JA, de Albuquerque TLC, Sougey EB. Postpartum obsessive-compulsive disorder: prevalence and clinical characteristics. Compr Psychiatry. 2009;50(6):503–9.
42. Akman C, Uguz F, Kaya N. Postpartum-onset major depression is associated with personality disorders. Compr Psychiatry. 2007;48(4):343–7.
43. Abramowitz JS, Schwartz SA, Moore KM, Luenzmann KR. Obsessive-compulsive symptoms in pregnancy and the puerperium: a review of the literature. J Anxiety Disord. 2003;17(4):461–78.
44. Wenzel A, Haugen EN, Jackson LC, Brendle JR. Anxiety symptoms and disorders at eight weeks postpartum. J Anxiety Disord. 2005;19(3):295–311.
45. Uguz F, Akman C, Kaya N, Cilli AS. Postpartum-onset obsessive-compulsive disorder: incidence, clinical features, and related factors. J Clin Psychiatry. 2007;68(1):132–8.
46. Osnes RS, Eberhard-Gran M, Follestad T, Kallestad H, Morken G, Roaldset JO. Mid-pregnancy insomnia is associated with concurrent and postpartum maternal anxiety and obsessive-compulsive symptoms: a prospective cohort study. J Affect Disord. 2020;266:319–26.
47. Russell EJ, Fawcett JM, Mazmanian D. Focus on Women's mental health meta-analysis. J Clin Psychiatry. 2013;74(4):377–85.
48. Speisman BB, Storch EA, Abramowitz JS. Postpartum obsessive-compulsive disorder. J Obstet Gynecol Neonatal Nurs. 2011;40(6):680–90.
49. Fairbrother N, Abramowitz JS. New parenthood as a risk factor for the development of obsessional problems. Behav Res Ther. 2007;45(9):2155–63.
50. Challacombe FL, Salkovskis PM, Woolgar M, Wilkinson EL, Read J, Acheson R. Parenting and mother-infant interactions in the context of maternal postpartum obsessive-compulsive disorder: effects of obsessional symptoms and mood. Infant Behav Dev. 2016;44:11–20.
51. Collardeau F, Corbyn B, Abramowitz J, Janssen PA, Woody S, Fairbrother N. Maternal unwanted and intrusive thoughts of infant-related harm, obsessive-compulsive disorder and depression in the perinatal period: study protocol. BMC Psychiatry. 2019;19(1):94.

52. Challacombe FL, Nath S, Trevillion K, Pawlby S, Howard LM. Fear of childbirth during pregnancy: associations with observed mother-infant interactions and perceived bonding. Arch Womens Ment Health. 2020;1-10
53. Jennings KD, Ross S, Popper S, Elmore M. Thoughts of harming infants in depressed and nondepressed mothers. J Affect Disord. 1999;54(1–2):21–8.
54. Wisner KL, Peindl KS, Hanusa BH. Obsessions and compulsions in women with postpartum depression. J Clin Psychiatry. 1999;60(3):176–80.
55. Humenik ALF, Fingerhut R. A pilot study assessing the relationship between child harming thoughts and postpartum depression. J Clin Psychol Med Settings. 2007;14(4):360–6.
56. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150(6):782–6.
57. Newth S, Rachman S. The concealment of obsessions. Behav Res Ther. 2001;39(4):457–64.
58. Nam SK, Choi SI, Lee JH, Lee MK, Kim AR, Lee SM. Psychological factors in college students' attitudes toward seeking professional psychological help: a meta-analysis. Prof Psychol Res Pract. 2013;44(1):37.
59. Challacombe FL, Wroe AL. A hidden problem: consequences of the misdiagnosis of perinatal obsessive–compulsive disorder. Br J Gen Pract. 2013;63(610):275–6.
60. Murray L, Finn M. Good mothers, bad thoughts: new mothers' thoughts of intentionally harming their newborns. Fem Psychol. 2012;22(1):41–59.
61. Lopez-Garcia P, Ashby S, Patel P, Pierce KM, Meyer M, Rosenthal A, et al. Clinical and neurodevelopmental correlates of aggression in early psychosis. Schizophr Res. 2019;212:171–6.
62. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. J Women's Health. 2006;15(4):352–68.
63. Challacombe FL, Bavetta M, DeGiorgio S. Intrusive thoughts in perinatal obsessive-compulsive disorder. BMJ. 2019;367
64. Tinkelman A, Hill EA, Deligiannidis KM. Management of new onset psychosis in the postpartum period. J Clin Psychiatry. 2017;78(9):1423–4.
65. Lawrence PJ, Craske MG, Kempton C, Stewart A, Stein A. Intrusive thoughts and images of intentional harm to infants in the context of maternal postnatal depression, anxiety, and OCD. Br J Gen Pract. 2017;67(661):376–7.
66. Hudak R, Wisner KL. Diagnosis and treatment of postpartum obsessions and compulsions that involve infant harm. Am J Psychiatr. 2012;169(4):360–3.

Sleep Disorders and Peripartum

7

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7.1 Introduction

Sleep is an important regulatory psychophysiological behavior in life, influencing mood, emotion regulation, and impulse behavior, which are key mediators of stress adjustments commonly needed in the perinatal period [1]. Consistently, sleep problems are recognized as a major risk factor for mental health and health problems in general [2, 3], while sleep is commonly impaired during peripartum [1, 4–7]. Women's sleep during pregnancy and postpartum is altered by anatomical, endocrinological, physiological, psychological, behavioral, socioeconomic, and cultural factors [6].

These changes have the potential to affect sleep duration, sleep quality, sleep pattern, and breathing during sleep, hence predisposing pregnant women to sleep disturbances during peripartum [1, 4–7]. In fact, evidence clearly shows that peripartum sleep disruption is reported by most women. Most common problems during all three trimesters include short sleep duration, poor sleep quality, and

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insomnia [1, 4–7], which tend to persist and worsen during postpartum [8], but also nightmares, sleep-disordered breathing, and restless legs syndrome [6, 7]. Cumulative evidence suggests that disrupted sleep in pregnancy has been linked to negative gestational and birth outcomes [9], emergency cesarean section [10], and gestational diabetes [11]. Most importantly, insomnia and poor sleep quality during peripartum have been found to be prospective risk factors for peripartum psychopathology, including mood disorders, postpartum blues, and psychosis. In particular, disturbed sleep has been considered a risk factor for unipolar and bipolar depression during the prenatal and postpartum periods [1, 4, 12, 13]. Disturbed sleep has been associated with the emergence of new depressive symptoms in pregnancy, such that sleep disturbances in early pregnancy predict depressive symptoms in late pregnancy. Similarly, sleep disturbances in late pregnancy assessed both objectively and subjectively have been shown to independently predict symptoms of postpartum depression [1, 4, 12, 13]. In addition, potentially, sleep disruption during pregnancy may mediate the relation between postpartum blues and increased risk of postpartum depression [14]. Sharma et al. (2003) [15] have discussed that sleep loss/disruption may be the final common pathway in the development of postpartum psychotic episodes. Most importantly, sleep disturbances during peripartum have been linked to an increased suicidal risk [16, 17].

Maternal sleep patterns in pregnancy may also entrain infant sleep patterns, such that disrupted maternal sleep in pregnancy is associated with worse infant sleep, which can in turn lead to disrupted maternal postpartum sleep [8, 18]. Sleep in the perinatal period has been considered a family issue with potential short-term consequences on child and whole family mental health and, in the long-term, modifying child's vulnerability to mental health during adult life [1, 18].

In this framework, assessing and treating sleep disturbances during peripartum should be a priority in clinical practice. It might reduce the risk for postpartum psychopathology and prevent short-term/long-term consequences on the whole family's mental health. Alternatively, modulation of sleep–wake patterns could offer relief to women in whom symptoms of these disorders have already developed. In this chapter, pregnancy-related changes in sleep physiology and the most frequent sleep disturbances in peripartum are discussed.

7.2 Pregnancy-Related Changes in Sleep Physiology

Pregnancy is a physiological condition characterized by profound biological changes, which have a significant influence on sleep [6, 7]. The typically increased secretion of several hormones across pregnancy considerably affects both the circadian and homeostatic components of sleep regulation, leading to modifications of sleep architecture [6, 14]. Pregnancy causes changes in melatonin and cortisol as well as gonadal steroids such as estrogen and progesterone and pituitary hormones such as gonadotropins, prolactin, and growth hormone, and these changes may affect sleep [6]. In human studies, nonrapid eye movement sleep (NREM) has been shown to be enhanced by progesterone and prolactin, while rapid eye movement sleep (REM) is decreased by progesterone and increased by estrogens. In particular, progesterone

has sleep-inducing action on brain gamma-aminobutyric acid (GABA) receptors, producing a soporific effect and a significant increase in nonrapid eye movement (NREM) sleep. This effect may partly explain daytime sleepiness and fatigue in the first trimester when progesterone is steadily rising. The increased respiratory rate caused by progesterone may protect the airway from occlusion, protecting from SDB. Indeed, the thermogenic effect of progesterone elevates core body temperature, and its inhibitory effect on smooth muscle (including gastrointestinal tract, ureters, and bladder) indirectly influences sleep and favors more awakenings during the night with low sleep quality disturbances [6, 19, 20]. Estrogen secreted by the placenta increases significantly during pregnancy, reaching peak levels before birth and declining thereafter. Estrogen has excitatory effects on the nervous system and selectively decreases REM sleep, its concentration during pregnancy causes vasodilation, and women typically experience nasal congestion that might contribute to SDB. Estrogen also stimulates prolactin production and suppresses dopamine release, contributing to RLS disturbances [6, 19, 20]. Oxytocin peaks during the night, promoting uterine contractions, might lead to sleep fragmentation. Cortisol and growth hormone levels are also elevated, affecting sleep quality and inducing daytime sleepiness [6, 7]. Melatonin, which is the major regulator of circadian rhythms, is secreted by the pineal gland and is activated by darkness and suppressed by light; melatonin levels increase in the third trimester. Melatonin synergizes with oxytocin to promote the birth process. Altered rhythm or low levels of melatonin secretion, which is related to sleep disturbances, might potentially result in some pregnancy complications and in pregnancy psychopathology (for an overview, see Izci-Balserak et al. 2017, Kay-Stacey et al. 2017) [19, 20]. Besides hormones, other factors that are essential to maintain a healthy pregnancy may contribute to sleep disruption during pregnancy, such as gastroesophageal reflux, affecting up to 75% of pregnant women, nocturnal micturition, due to an increase in overnight sodium excretion, anatomical changes related to the growing uterus, and increased body weight [6, 19, 20]. Moreover, iron and folate deficiency may play a role in the occurrence of sleep-related movement disorders in pregnant women [6, 19, 20].

With the physical and hormonal adaptations in pregnancy, changes in sleep are common, from 66% to 97% of women [19, 20]. During the first trimester, women experience daytime sleepiness and fatigue and report more frequent naps, an increase in total sleep time (TST), longer sleep onset latency, and more wake time after sleep onset (WASO). Overall sleep quality, sleep duration, and deep sleep decrease in this period. Hormones are responsible for fatigue and daytime sleepiness, morning sickness, waking with nausea, increased urinary frequency, physical discomforts such as back pain, and mood changes, which may all contribute to sleep disturbances in this period [19, 20]. Psychosocial stressors, if in the case of first-time or unplanned pregnancies, might also contribute to sleep disturbances in this first trimester [4, 19, 20]. In the second trimester, most women report less fatigue and less wake time after sleep onset (WASO) compared to the first one, with an average of more than 7 h per night in the second trimester likely due to the stabilization of hormone levels. By the end of the second trimester, however, the number of awakenings increases. Accordingly, women may experience disturbed sleep because of the onset of snoring, heartburn, irregular uterine contractions, fetal movements,

or leg cramps [4, 19, 20]. Vivid dreams and pain in the back, neck, and joints were additional reasons for sleep disruption during the second trimester. The majority, from 75% to 98%, of women report sleep disturbances during the third trimester of pregnancy with high WASO and increased light sleep and reduction in deep sleep [1, 4, 19, 20]. Nocturnal sleep time is lower than the first two trimesters, with more frequent and longer daytime naps. Physical changes associated with a rapidly growing uterus, urinary frequency, general physical discomfort (backache), heartburn, and leg cramps, in addition to hormonal fluctuations, are the main causes of sleep disturbances in the third trimester. Fetal movements, shortness of breath, vivid dreams/nightmares associated with labor/delivery, the health of the fetus, and pregnancy complications also contribute to disturbing sleep during the night during the third trimester. During childbirth, pain, anxiety, uterine contractions, long labor, and administration of medications all affect sleep and result in sleep loss and low sleep quality during labor and immediately after delivery. In summary, each trimester may lead to disrupting sleep. Pregnant women have more light sleep and less deep sleep (i.e., slow-wave sleep), owing to nocturnal awakenings [1, 4, 19, 20].

Pathogenetic mechanisms behind these associations have been postulated but remain to be proven [1, 4, 6, 19, 20]. The placenta has been proposed as a potential target organ in mediating adverse pregnancy outcomes in relation to sleep disturbances. For example, evidence of placental hypoxia and alterations in placenta-secreted markers have been shown in sleep disordered breathing (SDB) during pregnancy. It is biologically plausible that other sleep disturbances may affect placental function as well, given associations of sleep deprivation with similar placenta-mediated outcomes. The hypothalamic–pituitary–adrenal axis has been postulated to play a potential role in the association between SDB and gestational diabetes. Other potential mechanisms include an enhanced inflammatory profile, endothelial dysfunction, and oxidative stress but remain to be proven. The allostatic load hypothesis has also been proposed, suggesting that chronic sleep loss is both a precipitant of stress and a consequence of it and may lead to the "overload" of the stress system, which may account for adverse pregnancy outcomes. In summary, sleep is significantly disturbed in pregnancy, and sleep disruptions might have significant implications on perinatal health outcomes. Future research needs to focus on understanding the pathogenesis of these associations and examining the impact of sleep-targeted interventions on perinatal outcomes [1, 4, 6, 19, 20].

7.3 Pregnancy-Related Most Frequent Sleep Disturbances

7.3.1 Insomnia: Epidemiological and Clinical Characteristic During Peripartum

Chronic insomnia, also currently referred to as "insomnia disorder," now has similar diagnostic criteria in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) [21] and in other sleep manuals. Insomnia disorder is now considered a 24-h *sleep*–wake *disorder*

[21] characterized by nocturnal and diurnal symptoms. Insomnia can be episodic, lasting for a period within 1 month or between 1 month–3 months, or persistent, lasting longer than 3 months; transient-episodic forms tend, in the majority of the cases, to chronicity.

Insomnia is defined as difficulty initiating or maintaining sleep, early-morning awakening, or nonrestorative sleep associated with daytime consequences such as fatigue, irritability, and lack of concentration [21]. It is the most frequent sleep disturbance, affecting almost one-third of the general population [22, 23]. Frequency, severity, and pattern of insomnia can vary during pregnancy, with insomnia affecting >50% of pregnant women and reaching 80% during the third trimester. Insomnia symptoms increase in the first 6 months after childbirth with a total nocturnal sleep time of less than 6 h, and almost 10% of women develop an insomnia disorder in the long term [1, 4, 6, 19, 20].

The evolving models of chronic insomnia according to neurobiological, neurophysiological, cognitive, behavioral, or other perspectives [24] made the evaluation of insomnia progressively more complex. Although details of current models are beyond the scope of this chapter, concepts are critical for insomnia evaluation. The most heuristic model of insomnia is the diathesis-stress model, commonly known as the "3-P" model, describing predisposing, precipitating, and perpetuating factors relevant to the development and maintenance of insomnia (for an overview, see Palagini et al. 2020) [23]. *Predisposing factors* include genetic, physiological, or psychological diatheses that confer differential susceptibility to individuals in response to stress. *Precipitating factors* include physiological, environmental, or psychological stressors interacting with predisposing factors to produce acute symptoms. *Perpetuating factors*, especially behavioral, cognitive, and environmental factors, intervene in the perpetuation of insomnia. Hormonal and physical factors during pregnancy act as predisposing factors while maladaptive sleep behaviors and coping strategies such as napping, spending more time in bed, or increasing caffeine intake can perpetuate insomnia. Other risk factors for insomnia in pregnancy include age older than 30 years, nulliparity, single motherhood, preeclampsia or pregnancy-induced hypertension, prepregnancy affective disorders, perinatal depression, and environmental factors such as noise from other children or bed partners. Emotional distress related to pregnancy might be considered a precipitating factor per se, especially in the first trimester [1, 4, 6, 19, 20]. Weight gain and obesity contribute to sleep-onset or maintenance insomnia and SDB, favoring multiple awakenings during the night.

Decades of research into the cause of chronic insomnia have identified hyperarousal as a key factor [25] with increased levels of physiological, cognitive, and emotional levels of arousal in insomnia. The hyperarousal has been hypothesized to interact with unhelpful cognitive beliefs and negative behaviors contributing to the perpetuation of insomnia [26]. It is commonly seen in pregnancy as a higher body temperature and metabolic rate, with increased secretion of cortisol. The allostatic load hypothesis has been proposed and suggested that sleep loss is both a precipitant of stress as well as a consequence of it and by leading to a stress "overload" may account for adverse pregnancy outcomes, including peripartum psychopathology [4].

7.4 Evaluation of Insomnia During Peripartum

Insomnia evaluation needs a careful patient history and examination addressing sleep and waking functions as well as common medical, psychiatric, and medication/substance-related comorbidities. International guidelines suggest evaluating insomnia symptoms firstly using the Consensus Sleep Diary for at least 1/2 weeks to assess the insomnia day-to-day variability [23, 27]. In addition, the administration of questionnaires and survey instruments has been suggested to assess outcomes and guide treatment: the Insomnia Severity Index (ISI) [24] and the Epworth Sleepiness Scale (ESS) [28] are the questionnaires that have been suggested for the evaluation of insomnia and of its daytime consequences [23, 27]. The Insomnia Symptom Questionnaire was validated among pregnant women; therefore, it can be used as a reasonable screening tool for insomnia during pregnancy [29].

7.5 Management of Insomnia During Peripartum

Timely assessment and appropriate management are essential to prevent potential adverse pregnancy outcomes and the reoccurrence of chronic insomnia. It is of importance to know that many pregnant women do not seek treatment for insomnia because they either think it will naturally resolve after birth or wish to avoid medication owing to concerns about adverse effects on the fetus [20]. Therefore, it seems of utmost importance to clinically assess and manage sleep disruption from the beginning of pregnancy.

For chronic insomnia, cognitive behavioral therapy for insomnia (CBT-I) is the internationally considered first-line treatment [23, 30, 31]. Cognitive behavioral therapy for insomnia usually consists of behavioral strategies including psychoeducation/sleep hygiene, relaxation training, stimulus control therapy, sleep restriction therapy, and cognitive strategies such as sleep/related cognitive restructuring. In the context of CBT-I, psychoeducation typically includes the so-called "sleep hygiene rules" about health practices and environmental factors (e.g., light, noise, temperature) that may promote or disrupt sleep. Relaxation therapy is aimed at reducing somatic tension or intrusive thoughts at bedtime. Behavioral strategies include sleep restriction and stimulus control therapies; sleep restriction is a method designed to curtail the time in bed to the actual amount of sleep being achieved, and stimulus control therapy is a set of behavioral instructions designed to re-associate the bed/bedroom with sleep and to re-establish a consistent sleep–wake schedule. A recent systematic review pointed out a severe lack of knowledge on effective clinical interventions for insomnia during pregnancy [32]. The review selected 16 studies including in total 1252 expecting mothers. Four studies evaluated cognitive behavioral interventions for insomnia, one study pharmacotherapy, one study acupuncture, three studies mindfulness or yoga, five studies relaxation techniques, and two studies herbal medication. Of those, only six were randomized controlled trials. Although some preliminary support for clinically assessing insomnia during pregnancy is reported, the lack of evidence is severe. Specifically, preliminary support was evidenced for cognitive behavioral interventions for insomnia, which was also

found to be the preferred therapy for pregnant women [33]. Furthermore, so far, no specific adaptation of the standard cognitive-behavioral therapy for insomnia protocol for pregnant women has been developed, but improving sleep hygiene, using relaxation, mindfulness techniques and yoga, and implementation of lifestyle modifications such as regular exercise have been used and suggested in pregnancy [32].

If nonpharmacologic therapies have failed for moderate insomnia during pregnancy, antihistamines like doxylamine or diphenhydramine (histamine H1 receptor antagonists) are categorized as possible but unlikely to harm the fetus. Based on animal and human studies, these drugs are not expected to be teratogenic. There are, however, some concerns with first-trimester use and minor birth defects. Breastfeeding is not recommended, but no reports of adverse effects exist in the medical literature [19, 20]. If a patient's insomnia is more severe, then treatment with a sedating antidepressant or sedative-hypnotic may be considered. However, there are limited safety data on the sedative hypnotics during pregnancy. Zolpidem, with no known teratogenicity but with potentials of low birth weight and preterm delivery, need futher studies to be suggested. This drug is indeed considered safe in breastfeeding by the American Academy of Pediatrics [34]. Most other sedative hypnotics should be avoided or used with extreme caution in pregnancy. The available human data suggest no teratogenicity with zopiclone or eszopiclone, but there have been reports of withdrawal in infants after birth with chronic maternal use. Safety in breastfeeding has not been established. Sedating antidepressants such as tricyclic antidepressants (TCAs) might be better alternatives when patients have comorbid depression with insomnia. Based on case reports and on animal and human studies, the two antidepressants amitriptyline and trazodone are not expected to be teratogenic. Low-dose benzodiazepines (i.e., lorazepam) might also be considered if a patient also has issues with anxiety; however, caution must be used due to the potential risk for withdrawal and toxicity for the infant postpartum as well as an increased risk of cleft palate. For pregnant women with extreme sleep, mood, or anxiety symptoms, the benefits of using low-dose benzodiazepines may outweigh these reported concerns; however, the lowest effective dose should be prescribed to lower the risk of withdrawal and toxicity in infants postpartum [20]. Occasional use seems to be compatible with breastfeeding [34]. Finally, ramelteon, a melatonin receptor agonist, is associated with teratogenicity, but no human data on either pregnancy or breastfeeding are available [34]. Alternative therapies, herbal or dietary supplements, such as chamomile tea, lavender pillows, or acupuncture, are also used as sleep aids, but controlled studies are needed to assess the benefits and risks to fetal and maternal health [32].

7.6 Sleep Disordered Breathing (SDB): Epidemiological and Clinical Characteristic During Peripartum

Sleep disordered breathing (SDB) includes the spectrum of snoring, upper airway resistance syndrome and obstructive sleep apnea (OSA), and hypopnea syndrome. It is a breathing-related sleep disorder characterized by repeated episodes of apnea (cessation of breathing) or hypopnea (decrease in the flow of breathing

accompanied by oxygen desaturation) secondary to obstruction of airflow in the upper airway [20]. The estimated prevalence in pregnant women has been reported to be higher than the general population, and it is reported to be between 10% and 25%. Normal physiological and hormonal changes in pregnancy, including weight gain, edema, and diaphragmatic displacement secondary to enlarging uterus, can contribute to breathing-related sleep difficulties. In addition, higher circulating levels of estrogen cause edema of mucous membranes, which can lead to nasal congestion and pharyngeal constriction, another cause of breathing-related sleep disorders. On the other hand, progesterone stimulates the ventilatory drive and increases the electromyographic activity of the upper airway dilator muscle. Progesterone's stimulating properties enhance the responsiveness of the upper airway dilator muscles to chemical stimuli during sleep. This effect of progesterone theoretically protects against the development of SDB. Sleeping in the lateral position and the reduction in the time spent in REM sleep in late pregnancy are both protective against apneic and hypopneic events [19, 20].

7.7 Evaluation of SDB During Peripartum

Clinical manifestations of SDB during pregnancy include snoring and symptoms of daytime hypersomnolence, which can be evaluated with the Epworth Sleepiness Scale (ESS). A score of >10 is indicative of pathological hypersomnolence. SDB during pregnancy represents a risk factor for adverse pregnancy outcomes [6]. Therefore, it is of particular importance to evaluate and treat SDB during pregnancy.

7.8 Management of SDB in Pregnancy

Although no recommendations exist for the pregnant population specifically, it has been considered reasonable to follow those same guidelines in pregnancy [19, 20].

The decision to treat pregnant women with SDB should probably be made the same way as in the nonpregnant population [19, 20]. A particular concern regards fetal well-being in women with recurrent episodes of intermittent apnea and potential intermittent desaturations and hypoventilation. Continuous positive airway pressure (CPAP) is the preferred method of treatment of SDB in the general population and helps treat over 90% of patients with OSA. Although there is a theoretical concern regarding an increased risk of aspiration in pregnancy with the use of CPAP, it has been shown to be well tolerated in pregnancy and does not seem to be associated with a higher risk of complications in this population [19, 20]. CPAP pressures may have to be titrated during the course of pregnancy because of weight gain, but the required increase in pressures may only be 1–2 cm. CPAP therapy has been shown to improve hemodynamic parameters nocturnal cardiac output on the treatment night in patients with preeclampsia. Although the studies mentioned above involve only a small number of subjects, they are supportive of a potential hemodynamic benefit to the use of CPAP therapy in patients with preeclampsia. Other

therapies for OSAs include oral appliances that have a well-documented benefit in eliminating apneas in patients with mild to moderate disease. The effect of this therapy on patients with severe disease is less well documented. Although not all sleep apnea cases will resolve postpartum, those that do persist in the postpartum period may need a different CPAP prescription following weight loss. Given that a supine position could worsen OSA in about half of the general population, lateral-recumbent or head-elevated positions are recommended. It is possible that pregnant patients may also have position-dependent OSA, so positional therapy could be an alternative that is less invasive than CPAP. Positional therapy includes wearing something around one's waist or back (i.e., tennis balls or foam in a backpack or fanny pack) as well as newer devices, such as sleep-position trainers, that incorporate vibrations while a patient is in a supine position that continues until the patient changes position [19, 20].

7.9 Restless Legs Syndrome (RLS): Epidemiological and Clinical Characteristics During Peripartum

Restless legs syndrome (RLS) is characterized by an unpleasant leg sensation that causes an almost irresistible urge to move the legs [21]. A diagnosis of RLS is established when four clinical features are present: (1) the urge to move the legs; (2) the urge is worse when the patient is sedentary; (3) the abnormal sensation in the legs or the urge to move improves or resolves when the movement of the legs occurs; and (4) the symptoms have a circadian pattern and get worse during the evening or night [19, 20].

RLS occurs more frequently in pregnancy than in the general population and is reported in as many as 27% of pregnant women. RLS is considered a dysfunction of dopamine within the nigrostriatal circuit, but when RLS is associated with pregnancy, this syndrome is related to iron deficiency anemia, folate deficiency, advanced renal disease, and peripheral neuropathy. Other theories in pregnancy include iron deficiency and dopamine insufficiency as well as hormonal causes related to progesterone and prolactin. RLS is often under-diagnosed during pregnancy also because symptoms can be similar to leg cramps that are quite common in pregnancy. Untreated RLS increases the risk of depressed mood, and RLS-related sleep deprivation is linked to adverse effects like prolonged labor, heightened pain perception and discomfort during labor, higher rates of C-section, preterm labor, and elevated inflammatory cytokine. Therefore, it is of importance to evaluate RLS during pregnancy [19, 20].

7.10 Evaluation of RLS During Peripartum

A sleep history that includes the diagnostic criteria of RLS can help with an accurate diagnosis. History of RLS in a previous pregnancy and in the nonpregnant state, family history, multiparity, anemia, low folate level, low iron level, and high

estrogen level are associated with an increased risk of RLS during pregnancy [20]. Specific questionnaires may help in the diagnosis such as the Restless Legs Syndrome Rating Scale that was developed by the International Restless Legs Syndrome Study Group (IRLSSG) to assess the severity of a patient's RLS symptoms [35]. It consists of 10 questions and has been commonly used to assess RLS in pregnant women.

7.11 Management of RLS During Peripartum

First, managing the symptoms of RLS should begin with a nonpharmacological approach, including mental alerting activities, abstinence from caffeine, and removal of drugs known to aggravate RLS such as antidepressants, neuroleptics, antiemetics, and sedating antihistamines. If the above approach does not reduce the symptoms of RLS, then a pharmacological approach should be considered for further management. When treating RLS during pregnancy, the physician must consider the effect of medication on the fetus, especially the possibility of congenital malformations. Controlled studies of RLS during pregnancy have been limited. As a result, most evidence of therapeutic results come from reported cases or small case series. The medications that were studied include iron supplementation, dopaminergic agents, benzodiazepines, opioids, and anti-epileptic agents [19, 20].

Treatment of RLS in pregnancy aims at identifying iron or folate deficiency and replenishing the stores. Although the mainstay of therapy for this syndrome is monotherapy with levodopa and dopaminergic agents, levodopa has been associated with adverse pregnancy outcomes in experimental animals after high-dose treatment. Safety in human pregnancies has not been established, despite case reports in humans describing no evidence of abnormal embryological or fetal development [19, 20].

There are no data to support the safety of pramipexole or ropinirole use in pregnancy. Benzodiazepine, in particular clonazepam, may potentially be used to treat RLS during pregnancy as adjunct treatment, and there is no evidence that it causes an increased rate of major malformations; however, the incidence of minor congenital malformations including cleft lip and palate is more frequent with benzodiazepine use. Due to the risks of congenital malformations and neonatal abstinence syndrome, opioids should be avoided for treating the symptoms of RLS during pregnancy if possible. Anti-epileptic agents should be considered the last choice for treating RLS during pregnancy. Gabapentin, carbamazepine, and oxcarbazepine may be reasonable choices due to their lower rates of teratogenicity [19, 20].

7.12 Nightmare and Bad Dreams During Peripartum

Women during their first pregnancy experience frequently pregnancy-related dreams [36]. An higher frequency of disturbing dreams has been described in pregnant women compared to nonpregnant women. Research indicated that

pregnancy-related worries like loss, danger to the fetus/baby, or giving birth to a deformed baby also occurred in dreams during pregnancy. The number of these negatively toned dreams correlated with daytime depressive mood and trait anxiety; i.e., the dreams including pregnancy-related worries also reflect the daytime worries of pregnant women. Nightmares are defined as well-remembered dreams that usually involve a threat to survival, security, or physical integrity and, thus, represent an extreme form of negatively toned dreams. About 40–50% of pregnant women experience nightmares, at least about 6–10% of pregnant women reported severe nightmares related to fear of childbirth with dream recall higher than once per week. The findings clearly indicated a heightened nightmare frequency in pregnant women in their last trimester. If a substantial number of pregnant women suffer from nightmare disorders, it would be very interesting to learn whether short-term interventions like imagery rehearsal therapy, which have been shown to be very effective in different samples, are also beneficial for pregnant women with nightmares. Imagery rehearsal therapy is based on principles of cognitive therapy and encompasses three steps: confrontation (recording the dream), coping (imagining a new, more satisfying dream ending), and rehearsal (imagining the new coping strategy once a day for 5–10 min over 2 weeks) [36].

References

1. Baglioni C, Tang NK, Johann AF, Altena E, Bramante A, Riemann D, et al. Insomnia and poor sleep quality during peripartum: a family issue with potential long term consequences on mental health. J Matern Fetal Neonatal Med. 2020;2:1–9. https://doi.org/10.1080/14767058.2020.1854718.
2. Palagini L, Bruno RM, Gemignani A, Baglioni C, Ghiadoni L, Riemann D. Sleep loss and hypertension: a systematic review. Curr Pharm Des. 2013;19(13):2409–19. https://doi.org/10.2174/1381612811319130009.
3. Hertenstein E, Feige B, Gmeiner T, Kienzler C, Spiegelhalder K, Johann A. Insomnia as a predictor of mental disorders: a systematic review and meta-analysis. Sleep Med Rev. 2019;43:96–105. https://doi.org/10.1016/j.smrv.2018.10.006.
4. Palagini L, Gemignani A, Banti S, Manconi M, Mauri M, Riemann D. Chronic sleep loss during pregnancy as a determinant of stress: impact on pregnancy outcome. Sleep Med. 2014;15(8):853–9. https://doi.org/10.1016/j.sleep.2014.02.013.
5. Mindell JA, Cook RA, Nikolovski J. Sleep patterns and sleep disturbances across pregnancy. Sleep Med. 2015;16(4):483–8. https://doi.org/10.1016/j.sleep.2014.12.006.
6. Pengo MF, Won CH, Bourjeily G. Sleep in women across the life span. Chest. 2018;154(1):196–206. https://doi.org/10.1016/j.chest.2018.04.005.
7. Garbazza C, Hackethal S, Riccardi S, Cajochen C, Cicolin A, D'Agostino A, et al. Polysomnographic features of pregnancy: a systematic review. Sleep Med Rev. 2020;50:101249. https://doi.org/10.1016/j.smrv.2019.101249.
8. Meltzer LJ, Montgomery-Downs HE. Sleep in the family. Pediatr Clin N Am. 2011;58(3):765–74. https://doi.org/10.1016/j.pcl.2011.03.010.
9. Okun ML, Schetter CD, Glynn LM. Glynn LM. Poor sleep quality is associated with preterm birth. Sleep 2011;34(11):1493–1498. doi: https://doi.org/10.5665/sleep.1384.
10. Paine SJ, Signal TL, Sweeney B, Priston M, Muller D, Smith A, et al. Maternal sleep disturbances in late pregnancy and the association with emergency caesarean section: a prospective cohort study. Sleep Health. 2020;6(1):65–70. https://doi.org/10.1016/j.sleh.2019.11.004.

11. Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A. Sleep disturbances compared to traditional risk factors for diabetes development: systematic review and meta-analysis. Sleep Med Rev. 2016;30:11–24. https://doi.org/10.1016/j.smrv.2015.10.002.
12. Tomfohr LM, Buliga E, Letourneau NL, Campbell TS, Giesbrecht GF. Trajectories of sleep quality and associations with mood during the perinatal period. Sleep. 2015;38(8):1237–45. https://doi.org/10.5665/sleep.4900.
13. Emamian F, Khazaie H, Okun ML, Tahmasian M, Sepehry AA. Link between insomnia and perinatal depressive symptoms: a metaanalysis. J Sleep Res. 2019;28(6):e12858. https://doi.org/10.1111/jsr.12858.
14. Ross LE, Murray BJ, Steiner M. Sleep and perinatal mood disorders: a critical review. J Psychiatry Neurosci. 2005;30(4):247–56.
15. Sharma V, Mazmanian D. Sleep loss and postpartum psychosis. Bipolar Disord. 2003;5:98–105. https://doi.org/10.1034/j.1399-5618.2003.00015.x.
16. Palagini L, Cipollone G, Masci I, Novi M, Caruso D, Kalmbach DA, et al. Stress-related sleep reactivity is associated with insomnia, psychopathology and suicidality in pregnant women: preliminary results. Sleep Med. 2019;56:145–50. https://doi.org/10.1016/j.sleep.2019.01.009.
17. Kalmbach DA, Cheng P, Ong JC, Ciesla JA, Kingsberg SA, Sangha R, et al. Depression and suicidal ideation in pregnancy: exploring relationships with insomnia, short sleep, and nocturnal rumination. Sleep Med. 2020;65:62–73. https://doi.org/10.1016/j.sleep.2019.07.010.
18. Mindell JA, Leichman ES, DuMond C, Sadeh A. Sleep and social-emotional development in infants and toddlers. J Clin Child Adolesc Psychol. 2017;46(2):236–46. https://doi.org/10.1080/15374416.2016.1188701.
19. Izci-Balserak B, Lee KA. Sleep and sleep disorders associated with pregnancy. In: Kryger M, Roth T, Dement W, editors. Principles and practice of sleep medicine. 6th ed. Philadelphia, PA: Saunders; 2017. p. 1525–39.
20. Kay-Stacey M, Attarian HP. Managing sleep disorders during pregnancy. Gender Genome. 2017;1:34–45. https://doi.org/10.1089/gg.2016.0006.
21. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5). Arlington, VA: American Psychiatric Publishing; 2013.
22. Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis JG, et al. European guideline for the diagnosis and treatment of insomnia. J Sleep Res. 2017;26:675–700. https://doi.org/10.1111/jsr.12594.
23. Palagini L, Manni R, Aguglia E, Amore M, Brugnoli R, Girardi P, et al. Expert opinions and consensus recommendations for the evaluation and management of insomnia in clinical practice: joint statements of five Italian scientific societies. Front Psychiatry. 2020;11:558. https://doi.org/10.3389/fpsyt.2020.00558.
24. Morin CM. Insomnia: psychological assessment and management. New York: Guilford Press; 1993.
25. Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M, et al. The hyperarousal model of insomnia: a review of the concept and its evidence. Sleep Med Rev. 2010;14:19–31. https://doi.org/10.1016/j.smrv.2009.04.002.
26. Riemann D, Nissen C, Palagini L, Otte A, Perlis ML, Spiegelhalder K. The neurobiology, investigation, and treatment of chronic insomnia. Lancet Neurol. 2015;14(5):547–58. https://doi.org/10.1016/S1474-4422(15)00021-6.
27. Carney CE, Buysse DJ, Ancoli-Israel S, Edinger J, Krystal AD, Lichstein KL, et al. The consensus sleep diary: standardizing prospective sleep self-monitoring. Sleep. 2012;35:287–302. https://doi.org/10.5665/sleep.1642.
28. Johns MW. A new method of measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14:540. https://doi.org/10.1093/sleep/14.6.540.
29. Okun ML, Kravitz HM, Sowers MF, Moul DE, Buysse DJ, Hall M. Psychometric evaluation of the insomnia symptom questionnaire: a self-report measure to identify chronic insomnia. J Clin Sleep Med. 2009;5:41–51.
30. Baglioni C, Altena E, Bjorvatn B, Blom K, Bothelius K, Devoto A, et al. The European academy for cognitive behavioural therapy for insomnia: an initiative of the European insomnia network

to promote implementation and dissemination of treatment. J Sleep Res. 2020;29(2):e12967. https://doi.org/10.1111/jsr.12967.
31. Baglioni C, Bostanova Z, Bacaro V, Benz F, Hertenstein E, Spiegelhalder K, et al. A systematic review and network meta-analysis of randomized controlled trials evaluating the evidence base of melatonin, light exposure, exercise, and complementary and alternative medicine for patients with insomnia disorder. J Clin Med. 2020;9(6):1949. https://doi.org/10.3390/jcm9061949.
32. Bacaro V, Benz F, Pappaccogli A, De Bartolo P, Johann AF, Palagini L, et al. Interventions for sleep problems during pregnancy: a systematic review. Sleep Med Rev. 2020;50:101234. https://doi.org/10.1016/j.smrv.2019.101234.
33. Sedov ID, Goodman SH, Tomfohr-Madsen LM. Insomnia treatment preferences during pregnancy. J Obstet Gynecol Neonat Nurs. 2017;46(3):e95–e104. https://doi.org/10.1016/j.jogn.2017.01.005.
34. Oyiengo D, Louis M, Hott B, Bourjeily G. Sleep disorders in pregnancy. Clin Chest Med. 2014;35:571–87. https://doi.org/10.1016/j.ccm.2014.06.012.
35. The International Restless Legs Syndrome Study Group. Validation of the international restless legs syndrome study group rating scale for restless legs syndrome. Sleep Med. 2003;4(2):121–32. https://doi.org/10.1016/s1389-9457(02)00258-7.
36. Schredl M, Gilles M, Wolf I, Peus V, Scharnholz B, Sütterlin M, et al. Nightmare frequency in last trimester of pregnancy. BMC Pregnancy Childbirth. 2016;16(1):346. https://doi.org/10.1186/s12884-016-1147-x.

Eating Disorders in Pregnancy and Postpartum Period

8

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8.1 Eating Disorders (ED) in Pregnancy: Introduction

EDs are serious mental disorders characterized by severe disturbances in eating behaviours and distorted body image that considerably impair physical health and psychosocial functioning. The primary diagnosis classification of ED includes anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED) [1], and they typically develop in women during reproductive age [2].

A large body of evidence suggests that maternal ED is associated with adverse outcomes for the mother and the baby. Maternal AN, characterized by extremely low body weight and restriction of food intake, has been associated with intrauterine growth restriction, small for gestational age and low birth weight [3, 4], BN with induced labour and BED with larger birth weight and large for gestational age [4]. Drawing from the existing literature, Bulik et al. suggested a cycle of risk that may be playing in AN, whereby the maternal effect of AN on offspring via perinatal

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complications is hypothesized as being influenced by environmental, genetic and environmental factors that are highly influenced by maternal genotypes (i.e. pregnancy nutrition, weight gain in utero, appearance focus and restrictive eating during childhood/adolescence) [5]. In 2009, Micali and Treasure proposed a risk model for the impact of maternal ED on child development that embraces all ED focusing on in utero mechanisms. Specifically, the model described the effect of a maternal ED in pregnancy on the foetus via nutritional factors (i.e. protein deficiency, low folate and low iron intake) and comorbid psychopathology (i.e. comorbid anxiety and depression and in turn via increased glucocorticoids and corticotrophin-releasing hormone) leading to obstetric complications, which in turn predispose offspring to a later ED [6].

8.1.1 Current Prevalence

The estimated prevalence of ED during pregnancy varies considerably across studies, ranging from 0.6% to 27.8%. These rates differ depending on the characteristics of the sample (i.e. pregnancy stage), the component of ED being investigated (e.g. cognitive vs. affective vs. behavioural), the psychometric instrument employed (e.g. screening tool vs. self-report inventory vs. clinical interview) and the various instrument thresholds used to determine clinically significant scores [7]. Prevalence estimates for ED in pregnancy have ranged from 5.5 to 23.4% for shape and weight concerns, 0.3 to 2.5% for dietary restraint, and 8.4 to 36.1% for binge eating in the general population [8]. For women with a past diagnosis of ED, it has been estimated that, on average, 54% of women report improvement and even remission of ED symptoms during pregnancy. However, research has also identified a worsening of symptoms or emergence of new ED symptoms during pregnancy, particularly in association with binge eating behaviour [9, 10].

8.1.2 Behavioural Aspects

In terms of behavioural aspects of eating, pregnancy is associated with an overall improvement in the severity of ED behaviours for most women [11]. Reasons for the improvement in ED may include the relief of a sense of responsibility for body weight and shape and the woman's worries about its harmful effects on her unborn child. However, pregnancy might also be a trigger for the deterioration of binge eating and overeating. Ten percent of pregnant women with a recent ED report restrictive intake [12]. Reasons for the intensification of ED behaviours may include increased anxiety over weight gain. Furthermore, physiological changes in the course of pregnancy, such as changes in satiety associated with altered leptin levels, may have important influences on eating behaviour [13].

A qualitative study investigating possible factors responsible for the remission of ED symptoms seen during pregnancy in women with anorexia nervosa concluded

that there are likely three main categories of influence: biological (biological neuroendocrine changes during pregnancy are hypothesized to play a role in increasing the likelihood of high remission rates during pregnancy), psychological (women with anorexia nervosa reported a sense of maternal responsibility for recovery or a changed perception of their body during pregnancy) and social (pregnant women with anorexia nervosa reported greater support during pregnancy from the father of their child, family, friends and health care providers) [13].

Pregnant women with ED need enhanced perinatal and postnatal support. From a nutritional point of view, the latter is of great importance regarding (breast)feeding practices in women with ED [14].

8.1.3 Psychological Aspects

A recent review on women's experiences of pregnancy and ED found that women experienced turmoil related to fear and guilt about their changing body and the sense of self, wanting to be 'good mothers' and concern about how others would perceive their behaviour during pregnancy [15].

Common psychological presentations of ED in pregnant women are concern, distress or preoccupation with weight gain even when weight is within the expected range; dissatisfaction with body shape, even despite reassurance about expecting normal body shape changes with stages of pregnancy; negative or unusual attitudes towards food and/or eating; negative attitudes towards the unborn baby; depression; anxiety about pregnancy; and anxiety about caring for their baby.

It is important to remember that a woman with an ED may worry about how the ED might affect her unborn baby [11].

8.1.4 Comorbidity with Other Perinatal Psychopathology

A few studies have investigated levels of comorbid psychopathology during the perinatal period among women with ED. These studies show that pregnant women with ED may have an increased risk of comorbid psychiatric illnesses, particularly anxiety (in particular pregnancy-related anxieties, specifically for the well-being of their unborn child and weight gain during pregnancy), depression and obsessive–compulsive disorder [9, 16, 17]. Moreover, hormonal changes, body transformation and psychological adjustments during pregnancy have been linked to mood difficulties and ED [9].

Although it has been shown that anxiety generally precedes anorexia nervosa or bulimia nervosa onset, anxiety, depression and ED likely have common risk factors and similar underlying psychopathologic traits [17].

Carter et al. in 2003 found that 40% of women with ED also had a major depressive episode during the year of childbirth [12]. One large epidemiological study reported that women with a history of ED had increased levels of anxiety and depression during the antenatal and postnatal periods [17].

8.1.5 Risk Factors, Birth and Obstetric Outcomes

A large body of evidence has reported an increased risk of adverse pregnancy and neonatal outcomes for women with ED [18].

It is important for providers who care for women to understand the unique reproductive needs of women with ED and the gynaecological and obstetrical complications that may arise [13]. Endocrine abnormalities and intimate relationship problems associated with ED meant that a long-time pregnancy was believed to be a rare occurrence in this population. However, amenorrhea does not necessarily imply a lack of ovulation, and gestation can begin even at very low weight [11]. Due to having irregular menses, women with ED might have a strong belief that pregnancy is unlikely or impossible, and as a result, may be less vigilant about contraception. Failure to use contraception may lead to sexually transmitted infections in addition to an unplanned pregnancy. Moreover, if a patient does become pregnant when struggling with an active ED, she may be at higher risk for complications during pregnancy with a consequent negative impact on her child's development both in utero and in the postpartum period [14].

Large cohort studies and register data show that maternal ED behaviour and dysregulated body weight have detrimental effects on the course of pregnancy and birth outcomes. Pregnant women with an active ED are at increased risk of experiencing the following: antepartum haemorrhage, hyperemesis gravidarum, higher rates of miscarriage, caesarean sections and postpartum depression. The literature on foetal outcomes of women with ED displays lower and higher birth weights, intrauterine growth restriction, small head circumferences, neurobehavioral dysregulation early after birth, as well as premature deliveries, and perinatal mortality. Disturbances and dysfunctions related to nutrition and eating behaviours, which are core symptoms of ED, might contribute to these adverse pregnancy outcomes seen in women with ED [14].

Similarly, in a very large longitudinal cohort study, women with lifetime AN or AN + BN were more likely to have babies with restricted foetal growth, and acute maternal AN was associated with lower birth weight, length, head and abdominal circumference, ponderal index, and higher rates of preterm birth in offspring compared with unexposed women [19].

In an intergenerational study adjusting for grandmaternal pregnancy outcomes, Watson and colleagues found that irrespective of covariates, maternal AN was associated with smaller birth length, maternal BN with induced labour, and maternal BED with larger birth weight and being large for gestational age [4].

In summary, increased risk for pregnancy and obstetric complications can occur in women with ED, and the growth of their offspring (in utero) can be affected.

8.2 ED in Postpartum Period

8.2.1 Effect of ED on Postpartum Mothers

During the postpartum period, dissatisfaction with body weight and shape is common, even in women without a history of ED. In the first month after delivery, 75% of mothers report being concerned about their weight; by 4 months, 70% of women attempt to lose weight [20]. A study in a non-clinical population indicated that the percentage of women with ED nearly triplicates from pregnancy to the postpartum period [21]. Previous literature is consistent, indicating that the postpartum period is a high-risk time for relapse and exacerbation of ED symptomatology. Although during pregnancy women with ED seem to be more accepting of their body changes due to understanding that their body is serving the function of growing their child [22], during the postpartum women do not appear to be as accepting of body changes. Research has shown that relapse of symptoms and a return to baseline ED psychopathology levels is a common course in the first year postpartum [23], but the desire to lose weight can itself be a trigger for the development of an ED [24, 25].

Some studies have also explored comorbid psychopathology in women with ED. In a case–control study, Easter and colleagues found that ED symptoms during pregnancy predicted anxiety and depressive symptoms at 8 weeks and 6 months postpartum [16].

High levels of anxiety and depression were also identified at 8 months postpartum in a large prospective study of women with lifetime ED symptoms and active ED symptoms conducted by our group [17]. The prevalence of depressive symptoms in the above studies was consistent with earlier studies that have reported a prevalence of 30% in women with ED [12, 26, 27].

In summary, the above evidence suggests that the postpartum period is an extremely vulnerable window for women with past or current ED. Women are in fact prone to an exacerbation of ED symptomatology, with a particular increase in shape and weight concerns but are also more likely to develop comorbid anxious and depressive symptomatology.

8.2.2 Breastfeeding, Infant Feeding and Growth Trajectories

Given its relevance, the effect of maternal ED on a child's feeding and growth has received considerable attention in the literature. Infant feeding is one of the most important parental responsibilities and also one of the most important means of communication between the mother and the child. Research has shown that feeding difficulties starting early on in life can often persevere over the years and impact child and adolescent development and emotional well-being [28, 29]. Furthermore, children with feeding difficulties could be a major source of stress for families, which can worsen premorbid conditions such as depression and anxiety.

Numerous studies have examined breastfeeding patterns in mothers with ED, though findings are not consistent, possibly due to different study designs and populations [30, 31]. A large population-based study found a longer breastfeeding duration in mothers with ED, especially in mothers with BN [31]. Prolonged breastfeeding practice might in fact prevent from dysfunctional eating behaviours [32].

A similar study found a similar rate of initial breastfeeding practice in both the ED group and controls; however, mothers with ED were more likely to stop early [33]. On the contrary, Nguyen and colleagues stated that mothers with a history of ED were slightly less likely to initiate breastfeeding, although no longer significant after adjustment (socio-demographics, body mass index (BMI), maternal psychiatric symptoms) [34]. Despite feeding difficulties being common in infants, mothers with AN reported increased feeding difficulties, including exhaustion during feeding, slow feeding and no established routine [30, 31]. Infants of women with BN displayed higher levels of refusal to take solids compared to controls [31].

Body image distortion, a core symptom of both AN and BN, can also have an impact on feeding practices. In a study carried out by our group, mothers with both past and current ED expressed higher concerns about their infant being/becoming overweight compared with HC, respectively, at 8 weeks and 6 months postpartum only [35], which might have a direct effect on their child's dietary intake and in the severe case has been associated with reduction of their child's food intake and endorsement of dieting behaviours [36, 37].

Given the evidence of feeding difficulties amongst mothers with ED highlighted above, growth in children of mothers with ED remains an under-researched area. Although offspring weight and height are highly heritable, they can also be modified by environmental factors [4]. Preliminary evidence suggests that growth in children in mothers with ED may be affected. Maternal AN is associated with smaller weight at birth [22] and smaller birth length [4]. Some studies focused on the role of gender in the growth of children of mothers with ED. An early study conducted by Hodes and colleagues proposed that there was a gender influence with girls being more at risk of being underweight compared to boys [38]. However, the sample size in this study was small, and further investigation of the influence of gender on childhood growth is required.

In conclusion, research has demonstrated that children of mothers with ED tend to experience more difficulties in feeding their infants. Despite the literature on breastfeeding yielding mixed results, women with ED often experience difficulties with this. During toddler years, difficulties such as slow feeding, small quantity feeding and lack of established feeding routines appeared as common among ED mothers. Children of mothers with ED are at higher risk of displaying feeding difficulties compared to controls, dietary patterns deviating from norm and ED later in life. Most recent studies are consistent with earlier ones [26, 37, 39]. Future research should aim at exploring genotype-environmental interplay to provide new insights.

8.2.3 General Parenting

There is evidence that ED, like other psychiatric disorders, can impact general parenting abilities [28]. Women might struggle to integrate the demands of an ED and the challenges of motherhood. The ED itself can be time consuming; excessive preoccupation with food and weight and consequent compensatory behaviours can take up a substantial part of the day and impact sensitive responses to their child's needs [24]. In an early study, Stein and colleagues found that mothers with ED were more controlling and intrusive and engaged in more expressed emotions compared to controls during mealtimes and play [40]. In the same study, infants of mothers with ED displayed less positive effects with their mothers during feeding and play [40]. Likewise, mothers with lifetime ED in the Danish National Birth Cohort study reported greater difficulties in parenting their 18-month-old daughters and mothers with lifetime BN in looking after their children compared to controls [41]. Furthermore, a few studies have also shown that children of women with ED take the "carer role" including comforting their parents, monitoring their diet and cooking [28]. Ultimately, social factors such as unstable relationships and marital discord may also interfere with parenting function [42] and have implications for development in their offspring.

8.2.4 Parent–Child Bonding

Although limited literature explored mother–child interaction in ED mothers and their infants, preliminary results showed that maternal ED might affect mother–child interaction.

Research has shown that non-adequate parent–child relationships are potential risk factors for other psychopathological disorders later in life [43].

Mothers with ED report more problems in adapting to the new maternal role 3 months after delivery [44] and, as detailed above, are more prone to experience higher levels of anxiety and depression postnatally compared to controls [16]. ED mothers with comorbid depression and anxiety may have lower psychological resources to focus on their child, thus potentially decreasing the mother's ability to read the child's behavioural signals and to select and provide appropriate responses.

In a videotaped study of mother–child play interactions, children of mothers with ED were reported to be less involved and less responsive. Mothers were rated as less sensitive, more controlling and more hostile towards their children in comparison to the control group [45]. In the same study, they also found a correlation between maternal perceptions of a child's psychological problems and a decreased emotional availability in mother–child interactions [45].

In a review of literature on ED in the postpartum period, Astrachan-Fletcher and colleagues concluded that increased vulnerability to postnatal depression in

addition to body image concerns intensified by body changes that occurred during pregnancy might have a negative impact on mother–child relationship and consequently attachment in the postpartum period [24].

8.2.5 Barriers to Identifying ED during Pregnancy and the Postpartum Period

There are numerous potential barriers to the identification of eating disorders in pregnancy and the postnatal period. Evidence suggests that women with ED are frequently reluctant to disclose their illnesses to professionals [15]. Research showed that fear of being stigmatized, along with health care professionals' poor confidence to enquire and identify ED, has a major impact on women's disclosure of ED [46]. In a recent qualitative study aimed at exploring experiences of maternity care in women with ED, women expressed feeling shameful, embarrassed and feeling judged by health professionals based on their physical appearance. Women also reported a lack of opportunity and time to disclose an ED in a comfortable way and insufficient enquiry by health professionals. Other themes that emerged in the study were preference for self-management, current ED symptomatology and illness awareness [46].

Research demonstrated that the overarching factors that impact disclosure and barriers to accessing health care treatment for eating disorders are comparable amongst pregnant and non-pregnant women. These embrace the severity of the ED psychopathology, stigma of maternal ED, poor personal awareness of ED, and lack of knowledge amongst clinicians to identify an eating disorder. It is also important to note that while women with ED who are not pregnant may decide not to disclose and seek any medical treatment, pregnant women with ED are often already seeking care through a maternity care provider and may have frequent visits with a maternity care provider, thus providing multiple potential opportunities for disclosure [47].

8.3 Practical Issues: How to Best Support Women with ED During Pregnancy and Postpartum Period

ED in pregnancy and postpartum can negatively impact maternal and infant outcomes, as highlighted in the above sections. It is therefore of paramount importance that health professionals have the appropriate skills to assess and identify an ED in the early stages.

Below we summarize recommendations from NICE guidelines (NICE 2008, 2014, 2017) integrated with the most recent research:

1. Antenatal care should entail questions related to whether a person has ever suffered from an ED in the past (NICE 2014) and to identify those who might be at risk of relapse.

2. If a woman discloses a past or current ED, a referral for a full assessment and treatment within an ED service should be considered. It is also important to note that thresholds for referral to specialist services should be low in pregnancy and the postpartum period. Potential reasons for concerns are women being underweight (i.e. BMI below 19), failure to gain physiological weight during pregnancy, engaging in purging behaviours (i.e. vomiting, abuse of laxatives or diuretics), high preoccupation about her weight and shape and limited motivation to change.
3. A multidisciplinary approach to monitoring the mental and physical condition and antenatal care with clear and open communication between health professionals and women should be pursued (NICE 2008).
4. Pregnancy is a good window to offer treatment as motivation to change is likely to be high during this period.
5. Pregnant women with ED might need sensitive advice and increased support on how they plan to feed their babies, which may entail discussing the benefits of breastfeeding and practical advice on how to breastfeed (NICE 2008) whilst involving partners of the women since the beginning [48].
6. Having a discussion with a woman about her diet and her eating behaviours could be very beneficial. This could give the opportunity to address any concerns she may have, offer information on the benefits of a healthy balanced diet and deliver tailored advice on how to eat healthily during pregnancy and postnatally (see nutrition leaflets for women with eating disorders at http://www.eatingdisordersandpregnancy.co.uk/nutrition-leaflets-women/) [49].
7. Women with ED require higher levels of postnatal support in view of the higher vulnerability to develop postnatal depression and relapse of ED symptomatology.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: fifth edition, DSM5. Washington DC/London: American Psychiatric Publishing; 2013.
2. Treasure J, Duarte T, Schmidt U. Seminar eating disorders. Lancet. 2020;395:583–93.
3. Solmi F, Sallis H, Stahl D, Treasure J, Micali N. Low birth weight in the offspring of women with anorexia nervosa. Epidemiol Rev. 2014;36:49–56.
4. Watson HJ, Zerwas S, Torgersen L, Diemer EW, Knudsen GP, Reichborn-Kjennerud T, et al. Maternal eating disorders and perinatal outcomes: a three-generation study in the Norwegian mother and child cohort study. J Abnorm Psychol. 2017;126(5):552–64.
5. Bulik CM, Reba L, Siega-Riz AM, Reichborn-Kjennerud T. Anorexia nervosa: definition, epidemiology, and cycle of risk. Int J Eat Disord. 2005;37(SUPPL)
6. Micali N, Treasure J. Biological effects of a maternal ED on pregnancy and foetal development : a review. Eur Eat Disord Rev. 2009;17:448–54.
7. Bannatyne AJ, Mcneil E, Stapleton P, Mackenzie-Shalder K, Watt B. Disordered eating measures validated in pregnancy samples: a systematic review. J Treat Prev. 2021;29(4):421–46.
8. Baskin R, Meyer D. Psychosocial factors , mental health symptoms, and disordered eating during pregnancy. Int J Eat Disord. 2020;53(6):873–82.
9. Baskin R, Galligan R. Disordered eating and the perinatal period : a systematic review and best evidence synthesis of mental health and psychosocial correlates. Eur Eat Disord Rev. 2019;27(5):462–80.

10. Bulik CM, Von Holle A, Hamer R, Berg CK, Torgersen L, Magnus P, et al. Pattern of remission, continuation, and incidence of broadly defined eating disorders during early pregnancy in the Norwegian Mother and Child Cohort Study (MoBa). Psychol Med. 2007;37(8):1109–18.
11. Micali N. Eating disorders and pregnancy; 2008: 191–3. http://discovery.ucl.ac.uk/1338822/.
12. Carter F, a., McIntosh VVW, Joyce PR, Frampton CM, Bulik CM. Bulimia nervosa, childbirth, and psychopathology. J Psychosom Res. 2003;55(4):357–61.
13. Kimmel MC, Ferguson EH, Zerwas S, Bulik CM, Meltzer-Brody S. Obstetric and gynecologic problems associated with eating disorders. Int J Eat Disord. 2016;49(3):260–75.
14. Dorsam A, Preibi H, Micali N, Lorcher S, Zipfel S, Giel K. The impact of maternal eating disorders on dietary intake and eating patterns during pregnancy: a systematic review. Nutrients. 2019;11(840):1–17.
15. Fogarty S, Elmir R, Hay P, Schmied V. The experience of women with an eating disorder in the perinatal period : a meta- ethnographic study. BMC Pregnancy Childbirth. 2018;18(121):1–18.
16. Easter A, Solmi F, Bye A, Taborelli E, Corfield F, Schmidt U, et al. Antenatal and postnatal psychopathology among women with current and past eating disorders: longitudinal patterns. Eur Eat Disord Rev. 2015;23(1):19–27. https://doi.org/10.1002/erv.2328.
17. Micali N, Simonoff E, Treasure J. Pregnancy and post-partum depression and anxiety in a longitudinal general population cohort: the effect of eating disorders and past depression. J Affect Disord. 2011;131(1–3):150–7. https://doi.org/10.1016/j.jad.2010.09.034.
18. Mantel A, Hirschberg AL, Stephansson O. Association of maternal eating disorders with pregnancy and neonatal outcomes. JAMA Psychiatry. 2020;77(3):285–93.
19. Micali N, Stemann Larsen P, Strandberg-Larsen K, Nybo Andersen AM. Size at birth and preterm birth in women with lifetime eating disorders: a prospective population-based study. BJOG An Int J Obstet Gynaecol. 2016;123(8):1301–10.
20. Martinez-Olcina M, Rubio-Arias J, Reche-García C, Leyva-Vela B, Hernández-García M, Hernández-Morante JJ, et al. Eating disorders in pregnant and breastfeeding women : a systematic review. Medicina (B Aires). 2020;56(352):1–18.
21. Pettersson CB, Zandian M, Clinton D. Eating disorder symptoms pre- and postpartum. Arch Womens Ment Health. 2016;19:675–80. https://doi.org/10.1007/s00737-016-0619-3.
22. Micali N, Simonoff E, Treasure J. Risk of major adverse perinatal outcomes in women with eating disorders; 2007. http://discovery.ucl.ac.uk/1304482/
23. Micali N, Treasure J, Simonoff E. Eating disorders symptoms in pregnancy: a longitudinal study of women with recent and past eating disorders and obesity. J Psychosom Res. 2007;63(3):297–303. http://www.sciencedirect.com/science/article/pii/S0022399907002073
24. Astrachan-Fletcher E, Veldhuis C, Lively N, Fowler C, Marcks B. The reciprocal effects of eating disorders and the postpartum period: a review of the literature and recommendations for clinical care. J Women's Heal. 2008;17(2):227–39.
25. Mazzeo SE, Zucker NL, Gerke CK, Mitchell KS, Bulik CM. Parenting concerns of women with histories of eating disorders. Int J Eat Disord. 2005;37(Suppl):77–9.
26. Morgan JF, Lacey JH, Sedgwick PM. Impact of pregnancy on bulimia nervosa. Br J Psychiatry. 1999;174:135–40.
27. Franko DL, Blais MA, Becker AE, Delinsky SS, Greenwood DN, Flores AT, et al. Pregnancy complications and neonatal outcomes in women with eating disorders. Am J Psychiatry. 2001;158(9):1461–6.
28. Patel P, Wheatcroft R, Park R, Stein A. The children of mothers with eating disorders. Clin Child Fam Psychol Rev. 2002;5(1):1–19.
29. Motion S, Northstone K, Emond A. And the AlSPAC study team. Persistent early feeding difficulties and subsequent growth and developmental outcomes. Ambul Child Heal. 2001;7:231–7.
30. Micali N, Simonoff E, Stahl D, Treasure J. Maternal eating disorders and infant feeding difficulties : maternal and child mediators in a longitudinal general population study. J Child Psychol Psychiatry. 2011;52(7):800–7.
31. Micali N, Simonoff E, Treasure J. Infant feeding and weight in the first year of life in babies of women with eating disorders. J Pediatr. 2009;154:55–60.

32. Stapleton H, Fielder A, Kirkham M. Breast or bottle ? Eating disordered childbearing women and infant-feeding decisions. Matern Child Nutr. 2008;2008(4):106–20.
33. Torgersen L, Ystrom E, Haugen M, Meltzer HM, Von Holle A, Berg CK, et al. Breastfeeding practice in mothers with eating disorders. Matern Child Nutr. 2010;6(3):243–52.
34. Nguyen AN, de Barse LM, Tiemeier H, Jaddoe VWV, Franco OH, Jansen PW, et al. Maternal history of eating disorders: diet quality during pregnancy and infant feeding. Appetite. 2017;109:108–14. https://doi.org/10.1016/j.appet.2016.11.030.
35. Martini MG, Taborelli E, Schmidt U, Treasure J, Micali N. Infant feeding behaviours and attitudes to feeding amongst mothers with eating disorders: a longitudinal study. Eur Eat Disord Rev. 2018:1–10.
36. Waugh E, Bulik CM. Offspring of women with eating disorders. Int J Eat Disord. 1999;25(2):123–33.
37. Lacey JH, Smith G. Bulimia nervosa: the impact of pregnancy on mother and baby. Br J Psychiatry. 1987;150(6):777–81.
38. Hodes M, Timimi S, Robinson P. Children of mothers with eating disorders: a preliminary study. Eur Eat Disord Rev. 1997;5(1):11–24. https://doi.org/10.1002/(SICI)1099-0968(199703)5:1%3C11::AID-ERV179%3E3.0.CO;2-7.
39. Martini MG, Barona-Martinez M, Micali N. Eating disorders mothers and their children: a systematic review of the literature. Arch Womens Ment Health. 2020;23(4):449–67.
40. Stein A, Woolley H, Cooper S, Fairburn C. An observational study of mothers with eating disorders and their infants. J Child Psychol Psychiatry. 1994;35(4):733–48.
41. Barona M, Nybo Andersen AM, Micali N. Childhood psychopathology in children of women with eating disorders. Acta Psychiatr Scand. 2016;134(4):295–304.
42. Arcelus J, Yates A, Whiteley R. Sexual and relationship therapy romantic relationships, clinical and sub-clinical eating disorders : a review of the literature. Sex Relatsh Ther. 2012;27(2):147–61.
43. Lobera J, Rios bolanos. Parenting styles and eating disorders. J Psychiatr Ment Health Nurs. 2011;18:728–35.
44. Koubaa S, Hallstrom T, Hirschberg AL. Early maternal adjustment in women with eating disorders. Int J Eat Disord. 2008;41:405–10.
45. Sadeh-Sharvit S, Levy-Shiff R, Arnow KD, Lock JD. The interactions of mothers with eating disorders with their toddlers: identifying broader risk factors. Attach Hum Dev. 2016;18(4):418–28. https://doi.org/10.1080/14616734.2016.1164201.
46. Bye A, Shawe J, Bick D, Easter A, Kash-macdonald M, Micali N. Barriers to identifying eating disorders in pregnancy and in the postnatal period : a qualitative approach. BMC Pregnancy Childbirth. 2018;18(114):1–10.
47. Thompson C, Park S. Barriers to access and utilization of eating disorder treatment among women. Arch Womens Ment Health. 2016;19:753–60. https://doi.org/10.1007/s00737-016-0618-4.
48. Watson HJ, O'Brien A, Sadeh-Sharvit S. Children of parents with eating disorders. Curr Psychiatry Rep. 2018;20(11)
49. Bye A, Walker M, Mackintosh N, Sandall J, Easter A. Supporting women with eating disorders during pregnancy and the postnatal period. J Heal Visit. 2018;6(5):224–8.

Puerperal Psychosis

9

Jessica Mei Kay Yang, Ian Jones, and Arianna Di Florio

9.1 Introduction

The perinatal period is a time when women are at the highest risk of mental health difficulties [1], with suicide remaining a leading cause of maternal death within a year of childbirth [2, 3]. The most severe perinatal mental health disorder is postpartum psychosis. Postpartum psychosis is rare, affecting around 1–2 in 1000 deliveries; however, despite this very low incidence, the postpartum represents a period of incredibly high risk of developing such severe psychopathology—23 times higher than any other period in women's lives [4].

Characterised by a rich variation in symptomology, this rare disorder is not currently included in current diagnostic systems such as the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) or International Classification of Diseases (ICD) [2, 4, 5]. It exists only as an umbrella term, encompassing a number of severe psychiatric presentations affecting women after childbirth [2, 4].

Women with postpartum psychosis will frequently present with severe affective episodes; for some this may be mania or psychotic depression, whilst others develop mixed episodes of high and low mood [2]. Psychotic features—such as paranoia,

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hallucinations and delusions—are common, estimated to be present in over 70% of cases [6, 7]. Some also report neurological symptoms, including decreased consciousness and motor difficulties [4, 5]. Often, symptom onset will occur abruptly and dramatically, typically within 4–6 weeks after childbirth [2, 8].

For the majority of these women, this severe postpartum episode will be their first experience of any acute psychiatric history, hereafter described as first-onset postpartum psychosis [5]. Nevertheless, one of the strongest predictors of postpartum psychosis onset is a previous diagnosis of bipolar disorder [9, 10]. Postpartum mood episodes across the mood disorder spectrum are highly prevalent, but the relationship between postpartum psychosis and bipolar disorder has been evidenced most consistently [11–13]. Indeed, early research considered postpartum psychosis to be a specific presentation of bipolar disorder, triggered by parturition [3, 14, 15]. It is likely that women with bipolar disorder are particularly susceptible to relapse during this period compared to other psychiatric disorders such as schizophrenia [16].

This chapter will introduce the specific course and risk factors involved in postpartum psychosis. Based on clinical and academic research across the world, it will establish this severe disorder as a psychiatric emergency. Finally, it will highlight the necessary factors that should be considered when dealing with the treatment and management of these cases in order to minimise harm to the mother, child and their outer network.

9.2 Epidemiology

9.2.1 Burden of Disease

Estimating the global prevalence of a rare disorder such as postpartum psychosis poses several challenges. Incidence rates—which vary between 1 and 2 per 1000 childbirths—are typically based on inpatient admissions in Western societies [1, 2, 4]. This results in an under-representation which limits understanding of global and, in particular, non-Western outpatient cases. A recent meta-analysis conducted by the World Health Organization found incidence rates in lower-income countries to be relatively comparable to Western estimates, despite Nigeria reporting the highest incidence at 2.6 in 1000 childbirths [1]. These findings must be considered alongside the caveat that postpartum psychosis is a highly heterogenous term, due to inadequate diagnostic systems and poorly understood cultural differences. Contact with services may present another opportunity to estimate prevalence, being that hospital admissions are frequently necessary following a postpartum episode [2]. One population-based study estimated the risk of being admitted during the first 30 days postpartum with a first-onset postpartum bipolar disorder diagnosis to be 23.33% [17]. Although a valuable starting point, this estimate does not take into consideration the considerable likelihood of being misdiagnosed [18].

Despite the low prevalence, women are far more likely to develop a first-onset affective psychosis during the postpartum period than any other time point in their

lives [4]. For women with bipolar type I disorder, incidence sharply increases to 1 in 5 [19]. Subsequent pregnancies for women with a history of postpartum psychosis confer greater risk still, at one in two childbirths [2, 20]. The true incidence is likely to be much higher given the need for additional data.

It is unsurprising that the financial burden of such a severe mental illness is steep. In a 2014 report by the Centre for Mental Health in the UK, postpartum psychosis was estimated to cost the economy £53,000—roughly $68,800 in US dollar—*per case* [21]. These costs—based on prolonged service use and losses to productivity and quality-adjusted life years—are likely to be much higher due to insufficient data on adverse effects on the child. The economic costs relating to the mother alone are double that of perinatal depression or anxiety, with costs to the public sector being at least 20 times higher for postpartum psychosis. These findings demonstrate the need to address what can only be described as a psychiatric emergency.

9.3 Aetiology

The relationship between postpartum psychosis and the childbirth trigger is indisputable when considering the highly specific risk profile. A meta-analysis found that over 40% of women with first-onset postpartum psychosis experienced affective psychosis isolated to the postpartum period [22], with others reporting that this figure could be up to 50% [4]. Based on population studies, where increased risk for postpartum depression persisted up to 5 months postpartum, the risk for bipolar-type disorders remained increased for only 2 months [17]. Postpartum disorders classified as schizophrenia-type were even more specific still, with increased risk persisting for just 30 days following childbirth. Pregnancy seemed to be protective against accessing services, and overall, the window of highest risk fell between 10 and 19 days postpartum for first-onset and readmission risk [17, 23]. Childbirth may be the key instigator in the onset of postpartum psychosis, yet it is likely that a complex interaction between a range of biological and psychological risk factors is also at play.

9.3.1 Bipolar Disorder

In the DSM, most postpartum psychosis cases fall under the mood disorder nosology, making it almost impossible to distinguish from bipolar disorder with a postpartum recurrence. This is understandable in view of the significant overlap between symptoms, risk factors and prognosis. For women with a first-time onset of psychiatric disorder within 2 weeks of delivery, the likelihood of converting to a bipolar disorder diagnosis has been reported to be over three times higher than for women who present outside of the perinatal period [18]. Similarly, women with bipolar disorder are at significant risk of a postpartum psychosis diagnosis [23], with a history of bipolar disorder—familial or individual—remaining one of the strongest risk factors for postpartum psychosis [9, 14, 15].

9.3.2 Risk Factors

9.3.2.1 Obstetrics

Based on the specificity of the puerperal trigger, it is reasonable to presume that obstetric factors play a role, the most cited of which is primiparity. In one study, 35% of women with bipolar type I disorder reported psychosis or mania following their first child. This dropped to 20.5% for a second pregnancy and reached just over 14% for subsequent pregnancies [19]. This was the case despite excluding women with only one pregnancy from the analyses as a way of controlling for the possibility that women chose not to have further pregnancies following their first. These findings therefore suggest possible differences between the first and subsequent pregnancies that impress greater risk for affective psychosis.

Postpartum psychosis is not the only condition that is more common following a first pregnancy. Pre-eclampsia—which has been associated with primiparity—has been shown to increase risk of psychiatric postpartum episodes [2, 24]. Given the similar risk profiles of postpartum psychosis and pre-eclampsia, it seems possible that they share common disease mechanisms. Notably, pre-eclampsia begins during pregnancy, signalling a marked difference to postpartum psychosis. It is suspected that pre-eclampsia induces a hyperinflammatory state which could promote changes in brain function due to disruptions to the blood-brain barrier [24]. Similar comorbidities may also aid understanding of the disease mechanisms underpinning postpartum psychosis.

Research has also shown that affective psychosis is more likely following a full-term live or stillbirth delivery compared to termination or miscarriage [25]. This provides further evidence for the significance of the childbirth trigger. Other obstetric factors, including delivery complications, Caesarean section and having a female baby, have been previously cited as increasing risk of postpartum psychosis; however, a retrospective study found no robust evidence for these [26].

9.3.2.2 Reproductive Hormones

Hormones offer an obvious candidate for the aetiology of postpartum psychosis due to the array of hormonal changes that occur during the postpartum period. Research in the past has implicated the typical drop in gonadal steroids, such as oestrogen, following childbirth with psychosis onset [27]. Others cite improvements in psychotic symptoms following oestradiol treatment [28]. Yet many of these studies remain largely outdated and irreplicable [4]. This lack of reliable evidence for the role of hormones in postpartum psychosis is also true for progesterone and oxytocin.

Nonetheless, it is important to remember that these hormones do not occur in isolation but interact in a complex system of neurotransmitters and other hormones. Consequently, the differential sensitivity to hormone shifts during the postpartum period—which is exhibited by women with a history of postpartum episodes—is likely mediated by other factors linked to this system. Evidence for this can be inferred from a study of women with postpartum depression, where perinatal hormone conditions were pharmacologically mimicked [29]. The abrupt withdrawal of increased oestradiol and progesterone (a hallmark of parturition) marked a peak in

depressive symptoms in women with a history of postpartum depression. These findings illustrate the possibility that gonadal steroids may play a role in the aetiology of postpartum psychiatric episodes, despite the overall levels of these hormones remaining largely the same as for women without a similar history [7, 29].

One potential mechanism through which these hormones may contribute to postpartum psychosis is the dopaminergic system. Dopamine, along with other neurotransmitters such as noradrenaline and serotonin, is often implicated in the aetiology of nonpuerperal affective or psychotic disorders [7], suggesting they may have a potential role in postpartum psychosis. Further evidence for the role of dopamine can be found in case studies of women outside of the postpartum period where administration of dopamine agonists induced mania or psychosis; however, this phenomenon seems to be rare [30, 31].

9.3.2.3 Immunological Disease

Psychosis has long been linked to immune system function—from infectious agents leading to psychosis to several autoimmune disorders such as multiple sclerosis including psychosis as a symptom [32]. A comprehensive review of this relationship is beyond the scope of this chapter; nevertheless, several eminent findings are worth mentioning.

Microglia—the brain-based counterpart of macrophages—are heavily involved in immune response as well as neurodevelopment and synaptic functioning. Due to the difficulty in studying microglia in vivo, most research has opted to indirectly measure their functioning through their production of inflammatory cytokines which promote immune response. In a meta-analysis of 30 studies, inflammatory cytokines were aberrant in individuals with bipolar disorder compared to healthy controls [33]. Further evidence demonstrates that levels of inflammatory cytokines are positively associated with the acute phases of bipolar disorder—in particular mania—yet testimony of their relationship with depressive episodes remains inconsistent [34, 35]. Notably, these same markers were not associated with any states or symptoms of non-affective psychosis (schizophrenia), suggestive of an immune mechanism aetiology specific to affective psychosis [34].

Natural killer cells may also be implicated due to their role in cytokine production and cytotoxic functions. A recent study found that natural killer cell activation was much higher in individuals with first-onset psychosis who were subsequently diagnosed with bipolar disorder [36]. The authors cited inappropriate NKG2C expression (a cell-surface receptor) as the possible mechanism, as this has been linked to abnormal cytokine production, toxicity and severity of psychotic or manic symptoms. Circulating monocytes (part of the same developmental lineage as microglia) and T cells (which interact with monocytes and microglia) are white blood cells that also exhibit abnormal levels in individuals with bipolar disorder [32, 37]. Finally, not only do bipolar disorder patients show high prevalence for autoantibodies—a marker of an autoimmune response—but so do their first-degree relatives, implying a potential familial immune abnormality [32].

Given the close relationship between bipolar disorder and postpartum psychosis, concurrent findings are to be expected for the latter group. Research into immune

dysfunction and postpartum psychosis is much more sparse, with most evidence originating from centres in the Netherlands [24, 37, 38] and India [39]. There is some variation in these studies, with one reporting robust increases in cytokines and monocytes in women with postpartum psychosis [37] and another a decrease [39]. Similarly, one reports an overall decrease in T cell activation in women with postpartum psychosis compared to controls [37], whilst another reports a specific decrease in CD4 helper and CD8 cytotoxic T cells alongside an increase in natural killer cells and regulatory T cells [39]. Still, the consistent finding of immune system abnormality across two very different cultural contexts advocates a strong link between postpartum psychosis and immune response.

The increase in prevalence of both affective psychosis and autoimmune disease during the postpartum period further supports a common underlying immunological mechanism. Postpartum psychosis has been reported to co-occur with or exacerbate symptoms of autoimmune thyroiditis, multiple sclerosis and rheumatoid arthritis [4, 32, 40], indicative of an immune dysfunction mechanism underpinning these conditions. This is further supported by research that has shown central nervous system antibodies in a subset of women with postpartum psychosis, suggesting comorbid autoimmune encephalitis [38]. These immune dysregulations—and the vast number of symptoms related to them—likely reflect an interaction between a number of genetic, epigenetic and environmental traits.

9.3.2.4 Genetic Factors

There exists a strong body of evidence for a genetic component in postpartum psychosis. Mood disorders including bipolar disorder have consistently been found to aggregate in families [14, 15]. A family history of postpartum psychosis has been reported to increase risk of relapse by over twofold in women with bipolar disorder [15]. Further exploration of this familial component in a seminal linkage analysis led to the discovery of one genome-wide significant loci on chromosome 16p13 and, to a lesser extent, 8q24 [41]. Specific genes associated with increased postpartum psychosis risk, however, remain elusive.

Previous research has focused on candidate genes relating to serotoninergic, hormonal and inflammatory pathways. Serotonin-related genes offer interesting candidates as they are modulated by oestrogen. Whilst no evidence has been found linking postpartum psychosis with the 5HT2A serotonin receptor [42, 43], there has been some evidence for an association with two loci within the serotonin reuptake transporter (SERT/5-HTT) gene [42]. Exploration into hormonal pathways has found no relationship between postpartum psychosis and the oestrogen receptor alpha (ESR1) gene [44, 45]. Nonetheless, one study reported an association with the methyltransferase-like 13 (METTL13) gene—which regulates oestrogen receptor-related gene transcription [45]. Genes encoding inflammatory cytokines such as tumour necrosis factor alpha (TNFα) are also found to be regulated by oestrogen yet do not seem to be associated with postpartum psychosis risk [46]. In spite of this, it is likely that immunological genes may contribute a peripheral role. Supportive of this is the upregulation of immune-related gene expression in the monocytes of women with postpartum psychosis [37] which coincides with the downregulation of microRNA that moderates these immune-related genes [47].

More recently, researchers in the UK have used a case-control approach to compare genetic risk for different mental health conditions in women with first-onset postpartum psychosis, women with bipolar disorder (with and without history of postpartum relapse) and control women [48]. When looking at schizophrenia and bipolar disorder genetic risk, women with first-onset postpartum psychosis and women with bipolar disorder had very similar levels of risk - higher than that of control women. Looking at genetic risk for major depression however, woment with first-onset postpartum psychosis and women with bipolar disorder differed. Women with first-onset postpartum psychosis had risk levels similar to that of controls whilst women with bipolar disorder had higher levels of genetic risk for major depression. This research is the first to suggest that postpartum psychosis may be partially genetically distinct from bipolar disorder, supporting its recognition as its own disease entity within the bipolar disorder spectrum.

These collective findings, though promising, do not conclusively elucidate the genetic risk associated with postpartum psychosis. Replication is required, along with unbiased, genome-wide association approaches with large sample sizes to reach sufficient statistical power. Given the rarity of the disorder and the robust sample sizes required for such complex disorders—tens of thousands at least—these studies will likely require large-scale, international consortia similar to those established for bipolar disorder and schizophrenia [49, 50].

9.3.2.5 Medication Changes

Women with an established bipolar disorder are faced with the difficult decision of whether to continue their medication during pregnancy. Previous research has shown that discontinuing lithium treatment during pregnancy did not increase risk of recurrence compared to women who were not pregnant [51]. Following childbirth however, risk of relapse rose drastically for women having discontinued treatment. More recent research also reported a twofold increase in risk of recurrence during pregnancy after mood stabiliser discontinuation [52]. These findings demonstrate the need for improved treatment planning that considers risk to both mother and baby.

9.3.2.6 Sleep Deprivation

For some individuals with bipolar disorder, sleep deprivation has been linked to increased risk of manic episodes, particularly for women [53, 54]. This relationship has been shown to exacerbate risk during the postpartum period, a time of significant sleep loss. Women with bipolar disorder who described sleep loss as a trigger for manic episodes were twice as likely to experience postpartum psychosis than those whose episodes were not triggered by sleep loss [53].

The evidence relating sleep loss and postpartum psychosis remains sparse but compelling. Firstly, disruptions to the circadian rhythm are commonly reported in postpartum psychosis, often preceding the postpartum episode [4]. Second, indirect evidence on the importance of sleep comes from the observation that targeting sleep loss alone can lead to remission in about 6% of cases [55]. Finally, neurotransmitters—already discussed as a mechanism in the aetiology of postpartum psychosis—are also likely to play a role in sleep [7]. Sleep disturbance therefore offers an

important and easily monitored risk factor when considering disorder prevention for women at high risk.

9.3.2.7 No Association with Personality or Adverse Childhood Events

Bipolar disorder has been associated with a number of personality traits, including impulsivity, neuroticism and low extraversion [56, 57]. In light of this, it is easy to assume that postpartum psychosis would follow a similar pattern. This is not the case. Neither personality traits, cognitive styles nor affective temperaments were found to differentiate women with postpartum psychosis and women with bipolar disorder [56]. Similarly, rates of adverse childhood events, including abuse, deaths, parental separation and serious illness, seem to be no different [58], demonstrating that there is little evidence of a link between psychosocial factors and postpartum psychosis.

First-onset postpartum psychosis

The number of women who develop postpartum psychosis yet have no family or individual history that would predispose them to it is estimated to be 50% or higher [2]. A subset of these women go on to be diagnosed with bipolar disorder and will continue to experience episodes outside of the postpartum period [13]. For these women, it is possible that childbirth triggers a bipolar diathesis that was undetectable up to that point [13].

Generally those with affective psychosis confined to the postpartum period will have a more favourable disease course than women with postpartum psychosis within the context of an existing bipolar disorder [22, 59]. One study found that women with first-onset postpartum psychosis remained stable during pregnancy and were less likely to relapse during the postpartum period—provided they began treatment with lithium prophylaxis following childbirth [59]. Furthermore, researchers have shown that women with first-onset postpartum psychosis do not show significant enrichment of obstetric risk factors [60]. These women also exhibited delayed symptom onset and mood incongruent psychotic symptoms, which stands in contrast to bipolar disorder. These differences have led researchers to consider first-onset postpartum psychosis to be its own distinct category, making management yet more complex [22, 55]

9.4 Management

9.4.1 Diagnosis

Despite difficulties with diagnosis due to poor stratification in diagnostic manuals, the temporal link to childbirth and severity of symptoms facilitates identification. Clinical presentation is rapid, with over half of symptom onsets taking place by postpartum day three [2]. Researchers have identified three overarching symptom profiles—manic, depressive and atypical—the latter of which is characterised by disorientation and delirium-like symptoms [61]. The majority of women in this sample presented with the depressive profile, and the most prevalent symptoms were irritability, abnormal thoughts and anxiety. It is important to note that women who presented with a depressive profile also demonstrated psychotic or manic symptoms; however, depressive symptoms were most prevalent. Data from South

India has shown that over half of women reported infant-related delusions which could affect mother-child interactions [62].

One major setback for diagnosis of postpartum psychosis is the lack of recognition in the DSM and ICD. As a result, diagnosis relies on women meeting the criteria for a severe mood episode as well as the post-natal onset specifier [2]. Women are therefore often misdiagnosed, which can contribute to inappropriate management plans and unwarranted stigma. Symptoms can fluctuate over time, and intrusive thoughts of harming their children are common for new mothers even within the general population, creating additional complications with diagnosis [63]. This may be further exacerbated by comorbidities such as autoimmune encephalitis which may be the root of psychotic symptoms. As such, extensive examinations and laboratory tests are necessary to determine whether an organic cause of symptoms is present [2, 55].

9.4.2 Primary Prevention

Women at high risk first need to be identified based on the described risk factors. They will require a prebirth plan, involving close family, friends and health care professionals [63]. This is necessary to reduce stress, increase support and coordinate all those involved [4]. Women should be advised to prioritise sufficient rest during the postpartum period, and many recommend beginning lithium prophylaxis immediately following childbirth [4, 55, 63]. Rates of recurrence are much higher for women with a history of postpartum psychosis should they decline prophylaxis [9, 16, 55]. Some research reports that response to lithium prophylaxis tends to cluster in families [64]; therefore, if the woman in question has a lithium-responsive family member, prescribing lithium is likely to be an appropriate option.

Other preventative measures that have been explored include antipsychotics and hormone therapy [9]; however there exists very little reliable evidence for the efficacy of these. Furthermore, for women with first-onset postpartum psychosis, preventative measures are unlikely to have been taken, meaning that treatment is the only option.

9.4.3 Treatment

To date, there have been no randomised controlled trials for the treatment of postpartum psychosis. This has contributed to a lack of internationally recognised, specific guidelines for treatment [9, 55]. Despite this, antipsychotics are typically used globally as the first-line treatment [55].

Most research has focused on lithium treatment, perhaps due to its success for patients with bipolar disorder. One specific treatment plan of note was developed at the Erasmus Medical Centre in the Netherlands. This consisted of a four-step additive method, utilising first benzodiazepines, antipsychotics, mood stabilisers and finally electroconvulsive therapy (ECT) [55]. Whether women required the next

level of treatment was dependent on whether their symptoms persisted. Using this method, the majority of women remitted within 2 months, which is consistent with other evidence for the efficacy of pharmacotherapy [63]. In fact, all women included in the study ($N = 64$), except for one, achieved full remission by step three of the method, suggesting that ECT is not necessary in the majority of cases. The most effective treatment was lithium and antipsychotic adjunctive therapy; however, the performance of these treatments alone was not tested and therefore cannot be supported based on this research [55].

ECT has been predominantly recommended for treatment of postpartum psychosis with depressive or catatonic features due to its longer disease duration than postpartum mania [4, 55]. The little evidence published suggests that ECT is highly effective, particularly for those with treatment refractory postpartum psychosis; however, this is based on dated research [3, 4]. More recently, some have advocated ECT as a first-line treatment option [65, 66]. ECT has also been credited with improving mortality rates associated with postpartum psychosis, after being more widely prescribed in the 1940s and inducing rapid symptom resolution [3]. Nonetheless, due to the efficacy of pharmacotherapy in many cases, ECT is often deemed unnecessary [55]. Women who are concerned about drug treatment and breastfeeding may choose ECT as this is reported to have minimal impact on the baby through breastfeeding [66]. The decision on whether individuals should use ECT or pharmacotherapy should ultimately be discussed with the patient and their family, with consideration of their specific symptoms and needs.

Women who require drug treatment are not expected to continue pharmacological maintenance therapy indefinitely. Particularly for those with episodes isolated to the postpartum period, gradual tapering off of lithium maintenance therapy is advised [4, 55]. This is providing that women remain in full remission for a significant period postpartum.

9.4.4 Prognosis

Following appropriate treatment, symptom remission can occur within several weeks [6, 55, 63]. Some reports show that women who exhibit manic features have less than half the duration of illness compared to women who exhibit mixed or depressed symptoms [4, 60]. The short-term prognosis for postpartum psychosis is therefore relatively positive; however, this is based on treatment compliance. Women who do not receive appropriate treatment suffer a much longer course of illness, around 8 months on average [55]. In addition, it has been reported that more than half of women require a year or more to achieve complete symptom resolution [13].

The prognosis tends to remain overall positive in the months following remission. One prospective follow-up study found that the majority of women reported good functioning, in terms of work and interpersonal relationships, 9 months postpartum [67]. Yet these women also reported higher rates of depression and anxiety, and the small subset of women who relapsed reported substantially worse functioning.

In the long term, the recurrence rate of postpartum psychosis has been reported to be high, although estimates are variable depending on a woman's personal and familial psychiatric history. Considering overall relapse rates for women with any psychiatric history of postpartum psychosis, bipolar disorder or both, one retrospective cohort study reported 52.2% in any subsequent delivery [13], whilst a meta-analysis which included this study reported an overall recurrence rate of 35% [16]. Similarly, a recent report suggests that women with a history of both bipolar disorder and postpartum psychosis have a 43% risk of severe relapse related to a subsequent pregnancy [7]. Whilst women with bipolar disorder have a postpartum relapse risk of around 35% following their first child, this risk decreases with subsequent pregnancies [16, 19]. For women with first-onset postpartum psychosis, the relapse risk for subsequent pregnancies is 31% [4, 16]. One review suggested that postpartum relapse is more severe for women with a history of postpartum psychosis compared to bipolar disorder [16]. Despite this, women with bipolar disorder are more likely to relapse during the postpartum period even with the use of lithium prophylaxis [59]. For women with first-onset postpartum psychosis, the risk of experiencing non-puerperal episodes after the incipient episode is high [4, 13, 16]. A recent meta-analysis using longitudinal data that spanned up to 26 years showed that women with first-onset postpartum psychosis (i.e. without co-existing bipolar disorder) have a 43.5% risk of recurrence outside of the postpartum period [22]. These episodes will typically fall within the bipolar disorder spectrum [4]. Indeed, the presence of any type of psychiatric episode during the postpartum period is expected to substantially increase a women's risk of developing bipolar disorder in the years following childbirth [18]. In spite of this, there are a number of women who only experience symptoms during the postpartum period [22].

9.4.4.1 Complications

An ongoing drawback in treatment and management is the lack of appropriate services. Within the UK, around half of women cannot access specialist services for perinatal mental health [21]. This figure is estimated by the World Health Organization to be much higher for women living in low- and lower middle-income countries [68]. The rarity of the disorder feeds into a lack of understanding within society, leading to women often being isolated socially as well. It has been estimated that one out of five marriages ends due to postpartum psychosis [69].

This absence of support can have severe consequences. Women are at 70% increased risk for suicide during the postpartum period compared to any other period in their lives; and for every 1000 women who experience postpartum psychosis, 2 complete suicide [3]. There have also been reports of a slight increase in risk of women with postpartum psychosis committing infanticide [28]; however, the data on this is minimal. These reports are already devastating, yet these cases are often exaggerated in mainstream media, contributing to the overall stigma endured by these women [63].

The relationship between mother and child can be adversely affected by a mother's mental state. Women with postpartum psychosis are less likely to have impaired mother-to-infant bonding compared to women with postpartum depression [70].

Although bonding can improve following treatment, some women will continue to experience impaired bonding which could impact the long-term development of their child. Women who have delusions about someone wanting to harm their child can remain affectionate and bond well with them, whilst women who believe their baby is evil may be more likely to be unable to care for its needs or harm them [62].

It is also important to consider the fact that cultural differences in the presentation and understanding of this disorder may be at play. The global prevalence of postpartum psychosis is relatively consistent [1]; however, it is possible that the concept of postpartum psychosis is incongruent between cultures. The types of symptoms that are expressed by women with postpartum depression have been found to differ even between Western countries that are considered comparable such as the USA and the UK [71]. Research from India has demonstrated that only 1/3 of women and their carers believed their symptoms had biomedical origins, with others citing psychosocial stressors or supernatural causes [72]. Psychoeducation may be beneficial to improve understanding and social support for women and the people around them.

9.5 Conclusion

Whilst childbirth can be a powerful trigger for many psychiatric disorders, few are as severe as postpartum psychosis. For some women, this may be the incipient episode of a bipolar-type disorder. For others, their symptoms will be limited to the postpartum period. The unique specificity of this disorder—isolated to an especially small window of time—allows for an unprecedented opportunity to study its aetiology. Research in this area has identified obstetric, hormonal, immunological and genetic risk factors. An understanding of these risk factors will effectively improve management. Fortunately, with appropriate care and planning, overall prognosis can be good, with women typically responding well to treatment. Several limitations of prevailing research within this area remain, illustrating the need for larger and more diverse samples. The potential benefits of this approach are immeasurable. Utilising international datasets will improve understanding of this disorder, which will lead to more informed nosology and homogeneity in diagnosis. This will, in turn, provide further insight into clinical management and treatment.

References

1. VanderKruik R, Barreix M, Chou D, Allen T, Say L, Cohen LS, et al. The global prevalence of postpartum psychosis: a systematic review. BMC Psychiatry. 2017;17(1):272.
2. Di Florio A, Smith S, Jones I. Postpartum psychosis. Obstetr Gynaecol. 2013;15(3):145–50.
3. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. J Womens Health (Larchmt). 2006;15(4):352–68.
4. Bergink V, Rasgon N, Wisner KL. Postpartum psychosis: madness, mania, and melancholia in motherhood. Am J Psychiatr. 2016;173(12):1179–88.

5. Di Florio A, Munk-Olsen T, Bergink V. The birth of a psychiatric orphan disorder: postpartum psychosis. Lancet Psychiatry. 2016;3(6):502.
6. Forde R, Peters S, Wittkowski A. Recovery from postpartum psychosis: a systematic review and metasynthesis of women's and families' experiences. Arch Womens Ment Health. 2020;23(5):597–612.
7. Perry A, Gordon-Smith K, Jones L, Jones I. Phenomenology, epidemiology and aetiology of postpartum psychosis: a review. Brain Sci. 2021;11(1):47.
8. Bergink V, Boyce P, Munk-Olsen T. Postpartum psychosis: a valuable misnomer. Aust N Z J Psychiatry. 2015;49(2):102–3.
9. Doucet S, Jones I, Letourneau N, Dennis C-L, Blackmore ER. Interventions for the prevention and treatment of postpartum psychosis: a systematic review. Arch Womens Ment Health. 2011;14(2):89–98.
10. Chaudron LH, Pies RW. The relationship between postpartum psychosis and bipolar disorder: a review. J Clin Psychiatry. 2003;64(11):1284–92.
11. Di Florio A, Forty L, Gordon-Smith K, Heron J, Jones L, Craddock N, et al. Perinatal episodes across the mood disorder spectrum. JAMA Psychiatry. 2013;70(2):168–75.
12. Jones I, Cantwell R, on behalf of the Nosology Working Group RCoPPS. The classification of perinatal mood disorders—suggestions for DSMV and ICD11. Arch Womens Ment Health. 2010;13(1):33–6.
13. Blackmore E, Rubinow D, O'Connor T, Liu X, Tang W, Craddock NJ, et al. Reproductive outcomes and risk of subsequent illness in women diagnosed with postpartum psychosis; 2013.
14. Jones I, Craddock N. Do puerperal psychotic episodes identify a more familial subtype of bipolar disorder? Results of a family history study. Psychiatr Genet. 2002;12(3):177–80.
15. Jones I, Craddock N. Familiality of the puerperal trigger in bipolar disorder: results of a family study. Am J Psychiatr. 2001;158(6):913–7.
16. Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJM, Kushner SA, Bergink V. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatr. 2016;173(2):117–27.
17. Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB. New parents and mental disorders: a population-based register study. JAMA. 2006;296(21):2582–9.
18. Munk-Olsen T, Laursen TM, Meltzer-Brody S, Mortensen PB, Jones I. Psychiatric disorders with postpartum onset: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry. 2012;69(4):428–34.
19. Di Florio A, Jones L, Forty L, Gordon-Smith K, Blackmore ER, Heron J, et al. Mood disorders and parity - a clue to the aetiology of the postpartum trigger. J Affect Disord. 2014;152–154:334–9.
20. Di Florio A, Gordon-Smith K, Forty L, Kosorok MR, Fraser C, Perry A, et al. Stratification of the risk of bipolar disorder recurrences in pregnancy and postpartum. Br J Psychiatry. 2018;213(3):542–7.
21. Bauer A, Parsonage M, Knapp M, Iemmi V, Adelaja B. The costs of perinatal mental health problems; 2014.
22. Gilden J, Kamperman AM, Munk-Olsen T, Hoogendijk WJG, Kushner SA, Bergink V. Long-term outcomes of postpartum psychosis: a systematic review and meta-analysis. J Clin Psychiatry. 2020;81(2)
23. Munk-Olsen T, Laursen TM, Mendelson T, Pedersen CB, Mors O, Mortensen PB. Risks and predictors of readmission for a mental disorder during the postpartum period. Arch Gen Psychiatry. 2009;66(2):189–95.
24. Bergink V, Laursen TM, Johannsen BM, Kushner SA, Meltzer-Brody S, Munk-Olsen T. Pre-eclampsia and first-onset postpartum psychiatric episodes: a Danish population-based cohort study. Psychol Med. 2015;45(16):3481–9.
25. Di Florio A, Jones L, Forty L, Gordon-Smith K, Craddock N, Jones I. Bipolar disorder, miscarriage, and termination. Bipolar Disord. 2015;17(1):102–5.

26. Blackmore ER, Jones I, Doshi M, Haque S, Holder R, Brockington I, et al. Obstetric variables associated with bipolar affective puerperal psychosis. Br J Psychiatry. 2006;188(1):32–6.
27. Wieck A, Kumar R, Hirst A, Marks M, Campbell I, Checkley S. Increased sensitivity of dopamine receptors and recurrence of affective psychosis after childbirth. Br Med J. 1991;303(6803):613–6.
28. Maguire J. Hormonal and immunological factors in postpartum psychosis. Biomarkers of Postpartum Psychiatric Disorders. Elsevier in Amsterdam, Netherlands; 2020. p. 159–79.
29. Bloch M, Schmidt PJ, Danaceau M, Murphy J, Nieman L, Rubinow DR. Effects of gonadal steroids in women with a history of postpartum depression. Am J Psychiatr. 2000;157(6):924–30.
30. Chang S-C, Chen C-H, Lu M-L. Cabergoline-induced psychotic exacerbation in schizophrenic patients. Gen Hosp Psychiatry. 2008;30(4):378–80.
31. Harris YT, Harris AZ, Deasis JM, Ferrando SJ, Reddy N, Young RC. Cabergoline associated with first episode mania. Psychosomatics. 2012;53(6):595.
32. Bergink V, Gibney SM, Drexhage HA. Autoimmunity, inflammation, and psychosis: a search for peripheral markers. Biol Psychiatry. 2014;75(4):324–31.
33. Modabbernia A, Taslimi S, Brietzke E, Ashrafi M. Cytokine alterations in bipolar disorder: a meta-analysis of 30 studies. Biol Psychiatry. 2013;74(1):15–25.
34. Hope S, Dieset I, Agartz I, Steen NE, Ueland T, Melle I, et al. Affective symptoms are associated with markers of inflammation and immune activation in bipolar disorders but not in schizophrenia. J Psychiatr Res. 2011;45(12):1608–16.
35. Sayana P, Colpo GD, Simoes LR, Giridharan VV, Teixeira AL, Quevedo J, et al. A systematic review of evidence for the role of inflammatory biomarkers in bipolar patients. J Psychiatr Res. 2017;92:160–82.
36. Tarantino N, Leboyer M, Bouleau A, Hamdani N, Richard JR, Boukouaci W, et al. Natural killer cells in first-episode psychosis: an innate immune signature? Mol Psychiatry. 2021:1–10.
37. Bergink V, Burgerhout KM, Weigelt K, Pop VJ, de Wit H, Drexhage RC, et al. Immune system dysregulation in first-onset postpartum psychosis. Biol Psychiatry. 2013;73(10):1000–7.
38. Bergink V, Armangue T, Titulaer MJ, Markx S, Dalmau J, Kushner SA. Autoimmune encephalitis in postpartum psychosis. Am J Psychiatr. 2015;172(9):901–8.
39. Kumar MM, Venkataswamy MM, Sathyanarayanan G, Thippeswamy H, Chandra PS, Mani RS. Immune system aberrations in postpartum psychosis: an immunophenotyping study from a tertiary care neuropsychiatric hospital in India. J Neuroimmunol. 2017;310:8–13.
40. Bergink V, Kushner SA, Pop V, Kuijpens H, Lambregtse-van den Berg MP, Drexhage RC, et al. Prevalence of autoimmune thyroid dysfunction in postpartum psychosis. Br J Psychiatry. 2011;198(4):264–8.
41. Jones I, Hamshere M, Nangle J-M, Bennett P, Green E, Heron J, et al. Bipolar affective puerperal psychosis: genome-wide significant evidence for linkage to chromosome 16. Am J Psychiatr. 2007;164(7):1099–104.
42. Kumar HK, Purushottam M, Kubendran S, Gayathri P, Mukherjee O, Murthy AR, et al. Serotonergic candidate genes and puerperal psychosis: an association study. Psychiatr Genet. 2007;17(5):253–60.
43. Robertson E, Jones I, Middle F, Moray J, Craddock N. No association between two polymorphisms at the 5HT2A gene and bipolar affective puerperal psychosis. Acta Psychiatr Scand. 2003;108(5):387–91.
44. Middle F, Jones I, Robertson E, Morey J, Lendon C, Craddock N. Variation in the coding sequence and flanking splice junctions of the estrogen receptor alpha (ERα) gene does not play an important role in genetic susceptibility to bipolar disorder or bipolar affective puerperal psychosis. Am J Med Genet B Neuropsychiatr Genet. 2003;118(1):72–5.
45. Thippeswamy H, Paul P, Purushottam M, Philip M, Jain S, Chandra PS. Estrogen pathway related genes and their association with risk of postpartum psychosis: a case control study. Asian J Psychiatr. 2017;26:82–5.
46. Middle F, Jones I, Robertson E, Lendon C, Craddock N. Tumour necrosis factor alpha and bipolar affective puerperal psychosis. Psychiatr Genet. 2000;10(4):195–8.

47. Weigelt K, Bergink V, Burgerhout KM, Pescatori M, Wijkhuijs A, Drexhage HA. Down-regulation of inflammation-protective microRNAs 146a and 212 in monocytes of patients with postpartum psychosis. Brain Behav Immun. 2013;29:147–55.
48. Di Florio A, Yang J, Crawford K, Bergink V, Leonenko G, Pardiñas A, Escott-Price V, Gordon-Smith K, Owen M, Craddock N, and Jones L. Postpartum psychosis and its relationship with bipolar disorder: a polygenic risk score analysis in the UK. The Lancet Psychiatry. 2021.
49. Pardiñas AF, Holmans P, Pocklington AJ, Escott-Price V, Ripke S, Carrera N, et al. Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. Nat Genet. 2018;50(3):381–9.
50. Stahl EA, Breen G, Forstner AJ, McQuillin A, Ripke S, Trubetskoy V, et al. Genome-wide association study identifies 30 loci associated with bipolar disorder. Nat Genet. 2019;51(5):793–803.
51. Viguera AC, Nonacs R, Cohen LS, Tondo L, Murray A, Baldessarini RJ. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. Am J Psychiatr. 2000;157(2):179–84.
52. Viguera AC, Whitfield T, Baldessarini RJ, Newport DJ, Stowe Z, Reminick A, et al. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. Am J Psychiatr. 2007;164(12):1817–24.
53. Lewis KJ, Di Florio A, Forty L, Gordon-Smith K, Perry A, Craddock N, et al. Mania triggered by sleep loss and risk of postpartum psychosis in women with bipolar disorder. J Affect Disord. 2018;225:624–9.
54. Lewis KS, Gordon-Smith K, Forty L, Di Florio A, Craddock N, Jones L, et al. Sleep loss as a trigger of mood episodes in bipolar disorder: individual differences based on diagnostic subtype and gender. Br J Psychiatry. 2017;211(3):169–74.
55. Bergink V, Burgerhout KM, Koorengevel KM, Kamperman AM, Hoogendijk WJ, Lambregtse-van den Berg MP, et al. Treatment of psychosis and mania in the postpartum period. Am J Psychiatr. 2015;172(2):115–23.
56. Perry A, Gordon-Smith K, Webb I, Fone E, Di Florio A, Craddock N, et al. Postpartum psychosis in bipolar disorder: no evidence of association with personality traits, cognitive style or affective temperaments. BMC Psychiatry. 2019;19(1):395.
57. Barnett J, Huang J, Perlis R, Young M, Rosenbaum J, Nierenberg A, et al. Personality and bipolar disorder: dissecting state and trait associations between mood and personality. Psychol Med. 2011;41(8):1593.
58. Perry A, Gordon-Smith K, Di Florio A, Forty L, Craddock N, Jones L, et al. Adverse childhood life events and postpartum psychosis in bipolar disorder. J Affect Disord. 2016;205:69–72.
59. Bergink V, Bouvy PF, Vervoort JSP, Koorengevel KM, Steegers EAP, Kushner SA. Prevention of postpartum psychosis and mania in women at high risk. Am J Psychiatr. 2012;169(6):609–15.
60. Bergink V, Lambregtse-van den Berg MP, Koorengevel KM, Kupka R, Kushner SA. First-onset psychosis occurring in the postpartum period: a prospective cohort study. J Clin Psychiatry. 2011;72(11):1531–7.
61. Kamperman AM, Veldman-Hoek MJ, Wesseloo R, Robertson Blackmore E, Bergink V. Phenotypical characteristics of postpartum psychosis: a clinical cohort study. Bipolar Disord. 2017;19(6):450–7.
62. Chandra PS, Bhargavaraman R, Raghunandan V, Shaligram D. Delusions related to infant and their association with mother–infant interactions in postpartum psychotic disorders. Arch Womens Ment Health. 2006;9(5):285–8.
63. Luykx JJ, Di Florio A, Bergink V. Prevention of infanticide and suicide in the postpartum period—the importance of emergency care. JAMA Psychiatry. 2019;76(12):1221–2.
64. Grof P, Duffy A, Cavazzoni P, Grof E, Garnham J, MacDougall M, et al. Is response to prophylactic lithium a familial trait? J Clin Psychiatry. 2002;63(10):942–7.
65. Babu GN, Thippeswamy H, Chandra PS. Use of electroconvulsive therapy (ECT) in postpartum psychosis—a naturalistic prospective study. Arch Womens Ment Health. 2013;16(3):247–51.

66. Focht A, Kellner CH. Electroconvulsive therapy (ECT) in the treatment of postpartum psychosis. J ECT. 2012;28(1):31–3.
67. Burgerhout KM, Kamperman AM, Roza SJ, Lambregtse-Van den Berg MP, Koorengevel KM, Hoogendijk WJ, et al. Functional recovery after postpartum psychosis: a prospective longitudinal study. J Clin Psychiatry. 2017;78(1):122–8.
68. Fisher J, Mello MC, Patel V, Rahman A, Tran T, Holton S, et al. Prevalence and determinants of common perinatal mental disorders in women in low-and lower-middle-income countries: a systematic review. Bull World Health Organ. 2012;90:139–49.
69. Blackmore ER, Rubinow DR, O'Connor TG, Liu X, Tang W, Craddock N, et al. Reproductive outcomes and risk of subsequent illness in women diagnosed with postpartum psychosis. Bipolar Disord. 2013;15(4):394–404.
70. Gilden J, Molenaar NM, Smit AK, Hoogendijk WJ, Rommel A-S, Kamperman AM, et al. Mother-to-infant bonding in women with postpartum psychosis and severe postpartum depression: a clinical cohort study. J Clin Med. 2020;9(7):2291.
71. Di Florio A, Putnam K, Altemus M, Apter G, Bergink V, Bilszta J, et al. The impact of education, country, race and ethnicity on the self-report of postpartum depression using the Edinburgh postnatal depression scale. Psychol Med. 2017;47(5):787–99.
72. Thippeswamy H, Dahale A, Desai G, Chandra PS. What is in a name? Causative explanatory models of postpartum psychosis among patients and caregivers in India. Int J Soc Psychiatry. 2015;61(8):818–23.

Trauma, Stress, and Post-Traumatic Stress Disorder (PTSD) in Perinatal Period

10

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Stress is a universal experience and an adaptive reaction to *stressors* (i.e., the causes or sources of stress), wherein the environmental, physical, or emotional demands exceed an individual's resources, yielding a reactive and involuntary cascade of physiological and bodily responses. Although the term "stress" encompasses a range of positive and negative experiences, an individual's acute stress response (e.g., secretion of adrenal hormones, increased heart rate and respiration) is typically transient, and the body returns to baseline homeostasis after a stressor is removed. Nevertheless, certain stressors may disrupt or recalibrate the body's stress response, resulting in persistent or maladaptive stress reactivity that continues even after the original threat is no longer present. Such dysregulation of the body's stress response is likely to occur when stressors are prolonged and uncontrollable in nature, commonly referred to as *chronic stress* [1] or *toxic stress* [2]. As a related construct, *trauma* is a specific and extreme stressor, defined as disturbing events or experiences involving actual or perceived threat of death, injury, or bodily harm [3, 4]. Traumatic stress inherently overwhelms an individual's coping mechanisms [5] and may yield lasting effects on psychological, relational, and physical health. When the traumatic experiences are interpersonal in nature (e.g., inflicted by a

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caregiver or romantic partner) and occur early in development (i.e., during the first decade of life; [6]), trauma can have especially deleterious consequences.

In the context of current or lifetime trauma, the perinatal period may be a time of increased risk for the initial onset, recurrence, and exacerbation of post-traumatic stress symptoms and other psychopathology [7–9]. For example, risks for perinatal mental health concerns are particularly high for women with a history of reproductive trauma and childhood sexual abuse, given the psychosexual changes associated with pregnancy and prenatal care procedures that may be perceived as invasive and triggering [10–12]. Furthermore, although childbirth in and of itself is not traumatic, birth trauma and childbirth-related post-traumatic stress disorder can occur following subjective appraisals of actual or threatened death, injury, or bodily harm to the mother or child [13–15]. Overall, the physical and psychological effects of trauma may detrimentally impact a birthing person's health and behavior during pregnancy; delivery and birth outcomes; postpartum mental health and maternal functioning; and the developing parent-child relationship.

Identifying risks for perinatal traumatic stress and minimizing its detrimental effects is especially important, given that pregnancy and postpartum inherently overlap with sensitive periods of child brain development. The intergenerational transmission of trauma and stress can occur through unique and combined genetic, epigenetic, parenting, and environmental mechanisms, which can translate into neuroendocrine and neuroanatomical changes in offspring, thereby altering behavior and development across the life span [1, 16, 17]. As such, a mother's well-being during the perinatal period has significant implications for her own physical and mental health *as well as* the health and well-being of her offspring.

In the current chapter, we focus on trauma, stress, and post-traumatic stress symptoms during pregnancy and postpartum. We begin the chapter with a general overview of trauma effects on the individual, briefly highlighting common physiological and psychological outcomes. Next, we provide an overview of three specific types of traumatic stress and their effects on pregnant and postpartum women: birth trauma, childhood maltreatment, and the COVID-19 pandemic. Finally, we end with a discussion of assessment and treatment options for birthing people with a history of trauma and stress, focusing on the importance of timely screening and effective treatments for both individuals and caregiver-infant dyads, which may help mitigate the intergenerational transmission of trauma and toxic stress.

10.1 Physical and Psychological Trauma Effects

Individual reactions to traumatic events fall on a continuum, from resilient and adaptive responses to significant psychiatric distress and poor functioning. Although the vast majority of people who experience trauma do not develop significant or ongoing psychological sequelae, trauma can detrimentally alter an individual's beliefs, functioning, and interpersonal behavior [1, 18, 19]. Even when individuals do not experience trauma-related mental health symptoms or consciously recall what happened to them, trauma may leave a physiological imprint on the brain and

the body. For example, childhood abuse and maltreatment can alter brain pathways involved in stress regulation (e.g., the hypothalamic pituitary adrenal axis), as well as connectivity between regions crucial to emotional health (e.g., the limbic system and medial prefrontal cortex; for review, see [20]). Furthermore, cumulative adverse childhood experiences or "ACEs" substantially increase risk for adult-onset disease, including cancer, cardiovascular, metabolic, gastrointestinal, and other inflammatory diseases [21–24]. This link between traumatic stress and health outcomes is critically important in the perinatal period, as both proximal and distal stressors can impact pregnancy and birth outcomes, including hypertension, impaired uterine blood flow, preterm birth, and low birth weight [25–32].

Based on a combination of retrospective and prospective research, trauma exposure is consistently associated with increased risk for negative mental health outcomes, including post-traumatic stress disorder (PTSD), depression, anxiety disorders, substance use disorders, and more generalized emotion dysregulation. And yet, many of the symptoms associated with such psychological "dysfunction" may have been protective in the context of ongoing trauma, wherein the individual developed responses or behaviors to actively cope with the stress or prevent further harm [19]. From a strengths-based and trauma-informed perspective, we therefore acknowledge that current diagnostic systems may pathologize behavior and functioning that once served an adaptive role in the face of trauma [33, 34].

Despite the variety of psychological responses that may emerge secondary to traumatic stress, in this chapter we primarily highlight and focus on perinatal PTSD. In order to meet criteria for PTSD, individuals must identify a criterion traumatic event and endorse a combination of symptoms that include re-experiencing (e.g., flashbacks or intrusive memories), avoidance of trauma reminders, negative changes in mood/cognition, and increased arousal or activation in response to trauma-related stimuli [35]. In the perinatal period, estimated prevalence rates for PTSD vary widely depending on the period of assessment, measurement methods, and sample type. Within an urban and racially diverse pregnant sample, Seng et al. [11] found the risk of developing PTSD during pregnancy was six times higher among individuals with demographic risk factors (e.g., younger age, poverty, less than high school education) and those with a history of prior miscarriage or terminated pregnancy. Consistent with the broader obstetric literature on racial differences in perinatal outcomes (see, e.g., American College of Obstetricians and Gynecologists [36] and Hardeman et al. [37]), one study among pregnant women in the United States found Black women were slightly more likely to have higher rates of lifetime PTSD, but had four times the rate of concurrent PTSD during pregnancy [38, 39]. Unfortunately, other studies have reported perinatal women with combined demographic risk and PTSD symptoms are also more likely to have comorbid psychopathology, including a fivefold increase in risk for major depressive disorder and threefold risk for generalized anxiety disorder [40].

In two separate meta-analytic investigations, substantial differences in PTSD prevalence emerged when comparing high-risk perinatal women to community samples [41, 42]. Of note, high-risk groups in both studies included individuals with psychological risk factors (e.g., history of sexual violence, childhood abuse, high

fear of giving birth, prior birth trauma), as well as individuals with notable medical risks for the mother or fetus (e.g., preeclampsia, prior preterm birth or emergency caesarean, identified fetal anomalies). Grekin and O'Hara [41] found a PTSD prevalence of 3.1% in community samples but 15.7% in high-risk samples. More recently, Yildiz et al. [42] showed a similar postpartum PTSD prevalence of 4.0% in community samples but 18.5% in high-risk samples. One novel aspect of Yildiz et al.'s [42] meta-analysis was the focus on PTSD prevalence during pregnancy *and* postpartum. Once again, a stark differential risk pattern emerged in pregnancy: the prevalence of prenatal PTSD was 3.3% in community samples and 18.95% in high-risk samples. Across both pregnancy and postpartum, Yildiz et al. [42] found the course of perinatal PTSD was generally characterized by increases in PTSD prevalence during the first 6 months after birth. Although prospective longitudinal studies of perinatal PTSD are somewhat limited (see, e.g., [43]), it is possible that the higher point prevalence in the immediate postpartum period may relate to acute birth trauma or childbirth experiences that are re-traumatizing for women with prior trauma or a history of PTSD [42].

Looking more closely at risk for postpartum PTSD, symptoms typically occur via two etiological patterns: (1) a continuation, exacerbation, or recurrence of PTSD symptoms in the context of more general trauma history and (2) new-onset PTSD symptoms triggered specifically by childbirth experiences [41, 44–46]. In the former group, postpartum PTSD symptoms emerge or *re*-emerge secondary to lifetime events that occurred prior to birth, pregnancy, or even conception, including criterion stressors such as childhood sexual abuse, rape, or intimate partner violence [41, 45]. Within the latter group, wherein childbirth itself is the traumatic event, PTSD symptoms emerge secondary to distressing labor and delivery experiences [41, 42, 44, 46–48]. In the next sections, we further elaborate on birth trauma and two other types of traumatic stress (i.e., childhood maltreatment and the COVID-19 pandemic), exploring ways in which these traumatic and stressful experiences may detrimentally impact perinatal women's mental and physical health, birth outcomes, and the developing parent-child relationship.

10.2 Birth Trauma and Childbirth-Related PTSD

Historically, studies of postpartum PTSD have not consistently distinguished childbirth-related PTSD (i.e., CB-PTSD) from more general postpartum PTSD precipitated by lifetime traumatic events; however, the study of birth trauma and risk for CB-PTSD is a growing field [42, 44, 47, 49]. Objectively, labor and delivery involve acute physiological changes, from drastic hormonal shifts to extreme bodily pain, changes in cardiac and respiratory output, and blood loss. Although the majority of birthing people do not develop PTSD following childbirth, given the complexity of labor and delivery, it is perhaps unsurprising that even full-term, healthy births may be experienced as stressful or traumatic [44, 50]. Using established PTSD criteria (APA 2013), childbirth can be characterized as a criterion traumatic event when there is actual *or* threatened death or bodily harm to the mother or neonate.

Based on data from phenomenological interviews among women with a history of birth trauma [51], further expanded this definition of birth trauma to include traumatic experiences in which women feel dehumanized or stripped of their dignity during labor and delivery.

Consistent with PTSD in the general population [52, 53], *subjective* appraisals of traumatic birth experiences are a strong predictor of CB-PTSD [54–56]. Notably, women's birth appraisals may substantially differ from the perceptions of obstetricians and other clinical staff, who may otherwise deem certain birth-related medical events and procedures as "routine" [49]. The prevalence of CB-PTSD among birthing people who describe their labor and delivery as traumatic varies widely across prior studies, ranging from 9% to 44% [57]. In the United States, Black, Indigenous, People of Color (BIPOC) are more likely to report mistreatment during labor and delivery [58], including behaviors frequently associated with traumatic birth appraisals, such as loss of autonomy and being ignored by providers. As noted, however, only a minority of women who identify their birth experiences as traumatic go on to develop clinically significant CB-PTSD. In a study of CB-PTSD, Alcorn et al. [59] found 43% of the sample subjectively described childbirth as a trauma event; however, only 3.6% developed clinically significant postpartum PTSD. In a prospective, longitudinal, observational study, Kountanis et al. [60] recently reported rates of new-onset CB-PTSD at 6 weeks and 3 months postpartum of 6.2% and 5.1%, respectively. In comparison, when considering subclinical symptoms (e.g., hyperarousal, re-experiencing, avoidance), another study found up to one third of first-time mothers experience some form of post-traumatic stress symptoms secondary to childbirth [61].

When identifying and differentiating individuals who go on to develop CB-PTSD from those who do not experience post-traumatic stress symptoms, attention must be paid to interactive and multifaceted risk factors. The emergence of CB-PTSD is often conceptualized within a diathesis-stress model, wherein a combination of pre-birth vulnerability factors and birth-specific risk factors predicts negative outcomes [44, 62]. In a meta-analysis exploring the etiology of CB-PTSD, Ayers et al. [47] reported the *vulnerability factors* most strongly associated with CB-PTSD were a prior history of trauma and PTSD; depression during pregnancy; fear of childbirth; and health complications during pregnancy. The birth-related *risk factors* most strongly associated with CB-PTSD included negative subjective appraisals of birth; dissociation during labor and delivery; having an operative delivery (i.e., assisted vaginal or caesarean); and poor support during birth [47]. Overall, these results are highly consistent with more general (i.e., not childbirth-specific) risks for postpartum PTSD [41]. Qualitative and interview-based data further highlight higher risk for birth trauma associated with perceptions of low control and poor communication during labor and delivery; across multiple studies, traumatic birth experiences are often characterized by limited information from medical staff about what is occurring, lack of consent, and not involving women in medical decision-making [49, 57, 63]. In particular, Beck [64] identified risk for traumatic birth when women have low feelings of self-agency combined with the perception that medical procedures were "acted on" them. Additional experiences common to traumatic birth may

include feeling abandoned or alone during labor and delivery; limited or poor-quality birthing support (e.g., from partners, doulas); and discrepancies between birth expectations and reality [49, 57, 63].

Similar to the broader PTSD literature, there is also a strong association between CB-PTSD and perinatal depression [41, 47], with moderate to high rates of comorbidity [65]. For example, as many as 72% of women with postpartum PTSD may endorse clinically significant depressive symptoms [42]. Given the degree of comorbidity, Dekel et al. [65] recently explored whether CB-PTSD and postpartum depression may actually represent a "single posttraumatic stress-depressive response" (p. 562). Within their sample, the authors found 90% of women classified with CB-PTSD had elevated levels of depression, whereas 31% of those with postpartum depression had comorbid symptoms of CB-PTSD. Factor-analytic results further supported a one-factor model, even after controlling for overlapping symptoms within CB-PTSD and depression diagnostic criteria [65]. Given these results, Dekel et al. [65] concluded that a distinct subset of women may develop a unique depression-stress phenotype secondary to traumatic childbirth, and when this is the case, it is critical for effective treatments to address the depressive symptoms in the context of comorbid post-traumatic stress and the underlying traumatic event.

Birth trauma and CB-PTSD may also pose unique intergenerational challenges to offspring development and the early parent-child relationship. Although up to one quarter of women may develop CB-PTSD in the context of a healthy full-term birth [44], Grekin and O'Hara found a strong relationship between infant complications (e.g., low birth weight, preterm birth, NICU stay) and PTSD among high-risk postpartum samples. Thus, some mothers may be faced with the dual challenges of attending to their child's medical and developmental complications while also managing their own postpartum PTSD symptoms. Within the growing literature on motherhood and parenting outcomes among women with postpartum PTSD, only a select number of studies have focused on mothers with CB-PTSD. Ostensibly, given that the criterion trauma in CB-PTSD involves the birth of the child, one might expect difficulties with maternal bonding or connecting with the infant. Prior findings indicate that mothers with CB-PTSD describe their 6-week-old newborns as less emotionally warm and more demanding [66]; rate their 18-month-old children higher in internalizing and externalizing disorders [67]; and self-report interactions with their 24-month-old toddlers as difficult [68]. Among a relatively large sample of 685 postpartum women, Dekel et al. [69] compared subgroups of mothers with probable CB-PTSD, those with postpartum PTSD unrelated to birth trauma, and those with no PTSD symptoms. The authors found that the CB-PTSD group had the poorest self-reported ratings of mother-to-infant attachment, even after controlling for other demographic, psychiatric, and childbirth-related confounds (e.g., parity, type of delivery, NICU admission; [69]). In one of the few qualitative studies examining the parenting experiences of women with CB-PTSD, Beck and Watson [70] identified phenomenological parenting themes of numbness/detachment, high reactivity (i.e., anger, crying), distressing cognitive changes (e.g., catastrophic thinking), and limited social interactions outside the home. Overall, these findings underscore the potential intergenerational impact of birth trauma and CB-PTSD,

with parent-child interactions representing an important behavioral target for intervention among high-risk dyads. In the next section, we will expand our focus on the risk factors and consequences of perinatal traumatic stress by examining how a mother's history of maltreatment in her own childhood may impact birth outcomes, perinatal mental health, and parenting practices.

10.3 Childhood Maltreatment

Although the perinatal period is generally a time of heightened vulnerability for physical and mental health challenges, such risks are significantly heightened for individuals with childhood maltreatment histories [71–73]. Childhood maltreatment (CM) is defined as "…all types of physical and/or emotional ill-treatment, sexual abuse, neglect, negligence, and commercial or other exploitation, which results in actual or potential harm to the child's health, survival, development or dignity in the context of a relationship of responsibility, trust or power" [74]. Though prevalence rates vary by definition and population, 61% of adults report at least one adverse childhood experience prior to the age of 18 (e.g., abuse, neglect, household dysfunction; [75]); and globally, approximately 20% of women report experiences of childhood sexual abuse [76]. Among women in the perinatal period, prevalence rates of CM range from 11% to 35% in community samples [77] and 47% to 80% among higher-risk mothers (e.g., teen mothers, low-income mothers [78, 79]).

It is well established that a history of CM puts women at greater risk for physiological and psychological disruptions during pregnancy [16, 38, 39, 71]. Broadly speaking, women with CM histories have heightened risk for antenatal complications such as premature contractions, cervical insufficiency, gestational diabetes, previa, abruption, preeclampsia, intrauterine growth restriction, being of overweight status, and/or being hospitalized during pregnancy [38, 39, 80, 81]. Some of the physiological disruptions associated with CM histories may help explain the greater risk for health complications during pregnancy. For example, women with CM histories have greater risk for thyroid dysfunction and subclinical hypothyroidism during pregnancy [82], as well as higher levels of placental corticotropin-releasing hormone (pCRH) and a steeper increase in release of pCRH [83]. The association between CM history and mental health symptoms is also well-replicated in the perinatal period. A systemic review that included research with over 26,000 participants found that CM is strongly associated with a greater risk for depression and PTSD during pregnancy and postpartum, even when controlling for history of mental illness, sociodemographic variables, and psychosocial factors [71].

The combination of CM history and perinatal psychopathology may be particularly detrimental to birth outcomes and child development. For example, in the context of CM and maternal PTSD symptoms, risks for low birth weight and shorter gestation are heightened [38, 39], as are risks for breastfeeding challenges and bonding impairment [8, 9]. Consistent with the idea of intergenerational transmission of risk, offspring of women with CM histories may be at greater risk for subsequent mental and physical health challenges [16, 43, 83]. More specifically,

endocrine and immune processes play an essential role in fetal development, and disruptions to these neurobiological processes may partially explain the transmission of risk from maternal CM history to negative neurodevelopmental outcomes among children [16, 82–85]. For example, Moog et al. [85] found newborns of mothers with CM histories had smaller brain size and gray matter volume at birth compared to newborns of mothers who did not have a history of CM. Further, research suggests there is a dose-dependent effect of CM, such that worse severity (i.e., frequency/intensity) is associated with worse offspring outcomes [16]. In sum, CM has the potential to impact maternal physical and psychological well-being during the perinatal period, and in turn, these maternal changes can influence intrauterine development in profound ways.

Nevertheless, the impact of CM on perinatal risk is probabilistic rather than deterministic, and processes of risk and resilience are complex and multifaceted. Although it is well known that postpartum depression increases risk for parenting difficulties—and subsequent child biopsychosocial outcomes [86–89]—research on the unique impact of CM and/or postpartum PTSD symptoms on parenting outcomes has a less consistent and clear picture [90, 91]. For example, although mothers with CM histories may perceive themselves as being less confident or competent in parenting, these perceptions are not always associated with observed challenges in parenting behaviors [92]. Further, prior observational research documented that CM history *in the absence of psychopathology* did not confer risk for negative parenting behaviors [91], nor was CM history associated with maternal parenting behaviors or reflective functioning [93]. In another study, mothers with CM histories reported higher bonding impairment with their infants than mothers without CM histories, but the persistence of bonding problems across the postpartum period was predicted by psychological symptoms rather than CM status [72].

One way to help make sense of the contradictory results around CM and parenting is to think about the numerous risk and protective factors across the mother's own developmental trajectory [71], as well as the complexity of the post-traumatic changes that may emerge as a mother transitions into parenthood [94]. In a study of CM survivors during the postpartum period, Fava et al. [94] found higher CM severity combined with higher demographic risk was associated with greater *positive* post-traumatic change (e.g., being intentional about protecting their child from abuse and staying calm in the face of challenging child behaviors because they want to give their child a better childhood than they experienced [94]). Thus, although CM history may increase risk for perinatal mental health difficulties, and these symptoms can in turn increase risk for parenting challenges, the pathway from CM to parenting is one marked by both risk and resilience. Ultimately, it is important to recognize that women with CM histories are very much capable of nurturing, safe, and effective parenting, despite what happened to them.

In the subsequent section, we will end our review of specific traumatic stressors and their effects on perinatal mental health by highlighting a far-reaching, once-in-a-century stressor that has detrimentally affected individuals and communities across the globe: the COVID-19 pandemic. We will specifically highlight unique

challenges facing perinatal women and explore the impact of the pandemic on increased risk for perinatal mental health concerns, including high levels of stress, depression, anxiety, and perinatal PTSD.

10.4 COVID-19 Pandemic

In 2020, the global coronavirus pandemic brought an accumulation of physical, psychological, and social stressors for much of the world population. Given the widespread and multifaceted consequences—including the threat of severe illness, death, or loss of a loved one—attention to the mental health impact of COVID-19 (i.e., the disease caused by SARS-CoV-2) among perinatal women is warranted. At the time of this chapter's publication, rapidly emerging data on pregnancy and birth outcomes associated with COVID-19 created a moving target of literature to review. Understanding the risks and consequences associated with prenatal COVID-19 infection was further complicated by difficulties separating the direct effects of the disease from indirect changes to maternity care and other social determinants of health [95], as well as challenges in identifying infected individuals given limited universal testing and indications that up to 90% of pregnant women infected with SARS-CoV-2 are asymptomatic [95, 96]. Nevertheless, several recent systematic reviews and meta-analyses indicate that prenatal COVID-19 infection is associated with heightened risk for preterm birth prior to 37 weeks [95, 97, 98], caesarean delivery [95, 98], and maternal intensive care unit admission [97]. These risks are particularly high for infected women of increased maternal age and those with pre-existing medical comorbidities [95, 97]. Thus far, risk of vertical transmission to the neonate appears rare [95, 98], although one review found higher risk of NICU admission among babies born to mothers with COVID-19 [97]. Taken together, the emerging data on COVID-19 appear somewhat contradictory insofar as positive pregnant women may present as asymptomatic *or* severely ill (e.g., requiring admission to intensive care unit), which ultimately heightens confusion among this population and adds to the rising mental health toll in perinatal women.

Emerging research indicates that perinatal women may be particularly vulnerable to intense worries or distress about the novel coronavirus [99, 100], including concerns about the health and safety of themselves, their unborn child, and other family members [101, 102]. Among pregnant women in the United States, Preis and colleagues identified two categories of pandemic-related stress: (1) feeling unprepared for birth due to the pandemic (i.e., "preparedness stress") and (2) fear of perinatal COVID-19 infection [103], with 30% of 4451 pregnant women reporting high levels of stress in each of these domains. In a similarly large sample pregnant women in the United States, fear of infection was endorsed by 93% of participants [104]. Liu et al. [105] also assessed levels of COVID-19-specific health worries and grief and loss associated with the pandemic (e.g., feelings of sadness related to not

being able to celebrate the birth of one's child with loved ones; bitterness at changes in daily routine or limited social support); within this perinatal sample, 18% reported high levels of COVID-19 health worries, and 9% reported high levels of grief [105].

Beyond the direct distress associated with fear of contracting COVID-19, indirect pandemic-related stressors may particularly affect perinatal women, resulting in chronic stress and high cumulative stress load. Notably, COVID-19 abruptly and dramatically changed the face of prenatal care, birth experiences, parenting support, and other psychosocial resources. In order to minimize COVID-19 disease risks for the mother and fetus, health systems and providers understandably adopted new approaches to perinatal care, including remote or telehealth consultations with providers, fewer consultation and postpartum services, or limiting the presence of partners or labor support staff during birth [106, 107]. Given the important and protective role a supportive partner, family member, or doula may have on labor and birth experiences—especially for women with prior trauma histories and BIPOC women—it is reasonable to expect associated increases in traumatic birth experiences [106]. Moyer et al. [104] reported that 25.8% of pregnant women stopped prenatal care during the COVID-19 pandemic, whereas 15.2% used video visits, and 31.8% used phone visits for prenatal care; in turn, these reductions in prenatal care and use of phone-based visits were associated with increases in pregnancy-related anxiety [104].

Other psychosocial stressors exacerbated by COVID-19 include financial stress, unemployment, eviction, and food insecurity [100, 107, 108]. Within their sample of 2740 pregnant women in the United States, Moyer et al. [104] found high levels of stress related to concerns about food availability (59%), loss of work or household income (63.7%), loss of childcare (56.3%), and conflict between household members (37.5%). As families spend more time together at home under these stressful circumstances, pandemic-related increases in domestic and intimate partner violence also pose significant safety risks for perinatal women and their children [100, 107, 108]. Finally, broader public health initiatives and social distancing guidelines (e.g., limiting contact with others outside one's immediate household) inherently reduce or eliminate access to social connections and concrete parenting support for postpartum women [100, 106, 108]. For multiparous women, the negative psychosocial impact of social distancing may include simultaneous demands of childcare, homeschooling, and remote work [108, 109]. The necessary and lifesaving importance of COVID-19 social distancing practices notwithstanding, such measures conflict with the instinctive human drive for social connection [100] and may limit empirically supported intervention approaches that aim to increase positive social support or feelings of belonging, known to reduce stress and promote resilience among perinatal women.

Relying on outcomes from prior epidemics and public health emergencies (e.g., severe acute respiratory syndrome [SARS], Middle East respiratory syndrome coronavirus [MERS-CoV] [110, 111]), stress induced by such extreme events can increase risks for negative perinatal outcomes, including perinatal mental health disorders [107]. For pregnant and postpartum women already at elevated risk for perinatal mood and anxiety disorders, the mental health implications of COVID-19

may therefore be profound [106], especially among women from marginalized populations or otherwise under-resourced communities [108]. Based on preliminary cross-cultural findings, prevalence rates of perinatal depression and anxiety increased during the COVID-19 pandemic. Across pregnancy and postpartum, rates of clinically significant perinatal mental health concerns have ranged from 23.6% to 37% among five studies assessing depression [105, 112–114]; 13.6% to 57% among six studies assessing general anxiety [102, 105, 112–115]; and 10.2% to 10.3% among two studies assessing PTSD [102, 105]. Two studies also looked at rates of pregnancy-specific anxiety (i.e., worries about the pregnancy and birth itself) in the context of COVID-19, with one reporting pregnancy-specific anxiety scores almost three times higher than similar samples assessed prior to the pandemic [115] and the other study identifying within-individual increases in pregnancy-specific anxiety from pre- to post-pandemic onset [104].

Data on risks for perinatal mental health concerns in the context of the COVID-19 pandemic are somewhat comparable to the general literature on high-risk perinatal groups, wherein depression and anxiety is higher among individuals with greater sociodemographic risk (e.g., low education, income, financial strain, food insecurity, being a woman of color [103, 104, 112]; comorbid medical complexity (e.g., pre-existing condition, high-risk pregnancy [103]); current relationship strain or tension in the home [104, 112, 115]; social isolation [112, 115]; or a history of abuse [103]. Unique to the pandemic, fear of infection, health concerns, COVID-19-related grief, and altered prenatal care were also predictive of higher depression, anxiety, and pregnancy-specific anxiety [104, 105, 115]. In particular, women with prior histories of anxiety and depression appear more likely to report increased levels of mental health concerns during the pandemic [104, 105, 112]. Although only two studies have examined perinatal PTSD in the context of COVID-19, perinatal women with a prior diagnosis of PTSD were 3.73 times more likely to develop perinatal PTSD during the pandemic [105]. Furthermore, among a sample of pregnant women in Italy recruited during a period of lockdown in March 2020, those with a history of depression or anxiety had 2.3 times the risk of developing PTSD, and this risk increased to a magnitude of 5.66 for those with a history of comorbid depression and anxiety [102].

Ultimately, conclusions across studies are limited by different measurement tools, reproductive timing, and variable community-level risks for COVID-19; however, the reviewed findings underscore the far-reaching impact and critical importance of attending to perinatal mental health concerns in the ongoing wake of the coronavirus pandemic, especially among certain high-risk groups. Such results contribute to the broader literature on the acute and long-term effects of disasters and traumatic life stress on perinatal mental health [8, 9, 116–119]. In time, a more thorough and nuanced understanding of long-term implications and potential cohort effects among offspring will emerge with ongoing longitudinal follow-up. Nevertheless, given the importance of mitigating risks for mothers, children, and families, targeted interventions may be paramount to preventing greater downstream effects. We will therefore end our chapter with a brief overview of assessment and treatment options that may help minimize the effects of trauma and stress

on perinatal women and their young children, including recommendations for minimizing risks associated with current COVID-19 stressors.

10.5 Assessment and Treatment

Although an extensive review of assessment and treatment recommendations specific to perinatal stress, trauma, and PTSD is beyond the scope of this chapter, we want to highlight several clinical recommendations that may be beneficial for individual maternal mental health and well-being, as well as evidence-based treatments that can help mitigate the transmission of intergenerational risks for trauma and toxic stress. First and foremost, preventative interventions in the context of obstetric care may help minimize stress and trauma for high-risk perinatal women. Maternity care providers, such as obstetricians, midwives, and nurses, may help reduce risks for re-traumatization or new-onset birth trauma through the promotion of effective communication, informed consent for medical procedures, and respect for birthing people's agency in making healthcare decisions [63]. The presence of a supportive person (e.g., partner, doula) during birth has also emerged as one of the most important protective factors that can mediate the relationship between prior trauma history and postpartum PTSD, as well as birth trauma and new-onset CB-PTSD [47]. As mentioned, however, many hospitals and medical systems limited the number of supportive people who can be present with a birthing person in the wake of the COVID-19 pandemic. Given these necessary limitations, other trauma-informed approaches to perinatal care may be especially crucial. In this regard, Choi et al. [108] highlighted numerous ways in which medical staff may continue to promote women's voice and choice during pregnancy, birth, and early postpartum—despite workplace restrictions related to COVID-19. Specific trauma-informed strategies medical systems may consider implementing include naming and acknowledging COVID-19 effects on birth and parenting experiences; implementing telehealth check-ins to ensure connection with hospital specialists (e.g., social workers, lactation consultants); introducing consultation-liaison services to help meet the increased mental health needs of birthing patients; and connecting medical staff with additional coping, stress relief, and psychological support as they continue to care for pregnant and postpartum patients [106–108].

In addition to sensitive and trauma-informed medical practices, adequate and systematic assessment for perinatal PTSD is an essential step toward identifying women and dyads at highest risk for negative trauma and stress-induced outcomes. Given the high psychiatric comorbidity of perinatal PTSD and depression [41, 47, 65], we join others in recommending that women with elevated depression symptoms be screened for PTSD. Furthermore, the development of postpartum PTSD may be partially mitigated by identifying women who describe their experiences during childbirth as traumatic. Once again, it is important to note that *subjective* childbirth experiences are a critical risk factor; thus, even women with uncomplicated, full-term births should be asked about their thoughts concerning labor and delivery [57]. Perinatal women with significant trauma histories and

PTSD—regardless of the criterion event—may benefit from a number of individual psychotherapies. Although there is very limited clinical literature on the efficacy and effectiveness of trauma-focused interventions among pregnant and postpartum women, combining current knowledge of perinatal PTSD with the broader PTSD treatment literature (e.g., "gold standard" exposure-based treatment [120]) is current best practice [121]. Unfortunately, however, the highest-risk mothers with significant trauma histories are often the least likely to have access to therapeutic care. As a result, assessment and treatment referrals are not sufficient, and additional emphasis must be placed on increasing access to and engagement with high-quality, trauma-focused interventions in integrated settings (e.g., integrating mental health into OB-GYN practices). Time-limited, soft-safe entry programs for high-risk mothers of young children, such as Mom Power [122], can also help perinatal women with a history of trauma and PTSD connect to additional therapeutic resources and treatment options.

Given the intergenerational impact of trauma, stress, and perinatal PTSD, mothers and their young children may particularly benefit from dyadic or two-generation treatments. The early parent-child relationship plays a critical role in the intergenerational transmission of risks *or* resilience. If a young child experiences traumatic stress, his caregiver can help him build resiliency by soothing him and helping him regulate his distress; however, when a mother herself is overwhelmed by her own trauma symptoms, she may be less able to attend to her child's needs. Specifically, children who experience prolonged and intense physiological stress, *without a sensitive and responsive caregiver*, are at greater risk for maladaptive physiological stress responses and later problems with behavioral and emotional development [123]. Dyadic approaches to mental health care thereby view the parent-child relationship as the vehicle for positive, intergenerational, healing change; and a mother's mental well-being, parenting behaviors, representations of her child, and reflective capacity are targets for intervention. A number of evidenced-based interventions were developed for high-risk parent-child dyads, including perinatal women and infants exposed to toxic stress and trauma (for reviews, see [7, 124, 125]). A summary of several dyadic treatments previously published by the authors [7] is provided in Table 10.1. The interventions in Table 10.1 share a common foundation in attachment theory but vary in their specific modality, length, and treatment components. Notably, several of interventions, such as Child-Parent Psychotherapy (CPP; [142, 160]) and Attachment and Biobehavioral Catch-up (ABC; [127]), were designed for young children and their parents exposed to early adversity or trauma. Among the clinical targets, these programs help young children develop a play-based narrative of traumatic experiences (CPP) or help mothers support their child's emerging regulatory skills in the face of ongoing stressors (ABC). As an illustrative example, CPP places explicit emphasis on the caregiver's own trauma history and how this may affect her thoughts about and behaviors toward her child [142, 160]. As we understand more about the intergenerational importance of intervening as early as possible, an extension of CPP was recently created for the period of pregnancy through the first 6 months postpartum [161]. Ultimately, the Perinatal Child-Parent Psychotherapy (P-CPP) approach supports birthing people and their partners

Table 10.1 Description of existing two-generation interventions targeting parenting and attachment relationships within high-risk dyads[a]

Intervention	Population/participants/duration/ setting	Treatment description and modality	Evidence base
Attachment and biobehavioral catch-up (ABC) *For infants (ABC-I)* [126–136] *For toddlers (ABC-T)* [137]	Children with experiences of early adversity ABC-I: 6 months–2 years old ABC-T: 2–4 years old Parent-child dyad 10 weeks of 1-h sessions Home	• Help caregivers provide nurturing care, even if the child pushes the caregiver away • Help caregivers provide a responsive, predictable environment that helps the child develop regulatory abilities • Coach caregivers to follow the child's lead and show delight in the child • Help caregivers decrease behaviors that may be frightening or overwhelming to the child • ABC-T (specifically): Teach caregivers ways to co-regulate their children when they are distressed • Video feedback, homework, and in-the-moment feedback are used to reach these goals	ABC-I: RCTs with at-risk children (N = 24 to 120) and children in foster care (N = 46 to 173). ABC-I is associated with: • Lower rates of child disorganized attachment, higher rates of secure attachment, less avoidant behavior • Lower child negative affect during a challenging task • Lower child internalizing and externalizing behavior • Higher child cognitive flexibility, theory of mind skills, and receptive vocabulary • More normative child diurnal pattern of cortisol production, with effects persisting into preschool age • Improvements in sensitive caregiving, decreases in intrusive caregiving • Lower scores on measures of child abuse potential and parenting stress • Enhanced maternal ERP responses for emotional faces relative to neutral faces ABC-T: RCT with children in foster care (N = 173). ABC-T is associated with: • Lower rates of attention problems, higher cognitive flexibility

Child and family interagency resource, support, and training (Child FIRST) [138]	Children at high risk of emotional, behavioral, or developmental problems, or child maltreatment 0–5 years old Parent-child dyad 6–12 months; 2x/week for first month, then weekly sessions for 1–1.5 h Home or early care and education setting	• Treatment team consists of mental health/developmental clinician and a care coordinator • Provide trauma-informed child-parent psychotherapy and parent guidance • Offer care coordination and connection to community services • Observe and collaborate with teachers in early care and education settings	RCT with multi-risk urban mothers and children ($N = 157$). Child FIRST is associated with: • Improved child language • Improved child externalizing symptoms • Less parenting stress • Lower maternal psychopathology symptoms • Less protective service involvement • Greater access to wanted services
Child-parent psychotherapy (CPP) [139–144]	Children exposed to trauma 0–5 years old Parent-child dyad, with some parent-only sessions ~1 year ($M = 32$ sessions) of 1–1.5 h weekly sessions Home or clinic	• Focus on safety, affect regulation, reciprocity in relationships, continuity of daily living, with emphasis on the traumatic event • Create shared positive memories • Help dyad develop a play-based narrative of traumatic experience • Foundational phase: Develop trauma-informed formulation of dyad's functioning • Core intervention phase: Provide play-based developmental-relational therapy • Sustainability and termination phase: Help the family process upcoming goodbye and reviews family story • Utilizes reflective supervision for the providing clinician	RCTs with anxiously attached dyads ($N = 93$), children with depressed mothers ($N = 108, 198$), low-income families with a history of maltreatment ($N = 122, 137$), witnesses of domestic violence ($N = 75, 50$). CPP is associated with: • More positive mother-child relationship expectations • Higher parental empathic responsiveness and goal-corrected partnership, lower angry behavior • Lower likelihood of child anxious attachment • Increases in levels of child secure attachment • Decreases in child traumatic stress disorder symptoms and behavior problems • Reductions in problematic maternal representations • Decline in maternal avoidant symptoms, general distress, and PTSD symptoms

(continued)

Table 10.1 (continued)

Intervention	Population/participants/duration/ setting	Treatment description and modality	Evidence base
Circle of security (COS) *Home Visiting-4 (COS-HV4)* [145] *COS group* [146, 147] *COS-parenting (COS-P)* [148] *COS-perinatal protocol (COS-PP)* [149]	High-risk populations (e.g., enrolled in early head start, teen moms, irritable babies, incarcerated perinatal women) Prenatal—5 years old Parent-only (COS-HV4) Parent group (COS group, COS-P, COS-PP) COS-HV4, 1 3-h assessment session and 4 1.5-h sessions over 3 months; COS group, 20 weekly 1.25-h sessions; COS-P, 10 weekly 1.5-h sessions; COS-PP, twice-weekly 90-min group sessions from third trimester through 12 months postpartum Home (COS-HV4); clinic, facility, or community (COS group, COS-P, COS-PP)	• Teach caregivers about attachment theory using the "circle" graphic • Help parents provide a "safe haven" in times of distress or threat and a "secure base" in times of exploration • Teach parents about ways children might "miscue" what they need • Help caregivers see how their own strong feelings influence their responses to their children • COS-HV4, COS group, COS-PP: Review of video of caregiver interacting with his or her own child (or stock footage of mother-infant interactions for pregnant participants in COS-PP) • COS-P DVD-based delivery of key COS concepts in order to make program more accessible	COS-HV4 RCT with low-income mothers with irritable infants ($N = 220$). COS-HV4 is associated with: • Reduced risk of child insecure attachment, for dismissing mothers with highly irritable infants COS group pre-post design with low-income children and their caregivers ($N = 65$) and clinically referred children and their caregivers ($N = 83$). COS group is associated with: • Shift from child disorganized to organized (mostly secure) attachment classifications • Improved caregiver reflective functioning and caregiving representations COS-P RCT with low-income children and their caregivers ($N = 141$). COS-P is associated with: • Improved child inhibitory control • Fewer unsupportive maternal responses to child distress COS-PP pre-post design with high-risk perinatal women in a jail diversion program for nonviolent offenders with a history of substance abuse ($N = 20$). COS-PP is associated with: • Improvements in maternal depressive symptomatology • Rates of infant attachment security and disorganization comparable to existing rates in low-risk samples • Comparable levels of maternal sensitivity to existing community comparisons

Minding the baby [150]	First-time parents at high risk for problems (e.g., young maternal age, poverty, history of trauma) Prenatal—2 years old Parent-child dyad Weekly 1-h sessions prenatally through the first year, then biweekly sessions until age 2 Home	• Help parents become more reflective and responsive during interactions with their infant • Team consists of pediatric nurse practitioner and clinical social worker; providers alternate who attends home visit • When applicable, social worker conducts mental health assessment and provides treatment to parent • Home visitors maintain close contact with mother's and child's physicians and coach families with regard to healthcare information and accessing social services	RCT with primiparous women receiving care at a community health center ($N = 105$). Minding the baby is associated with: • Higher likelihood of being on-track with child immunization schedule • Lower rates of rapid subsequent childbearing • Lower likelihood of referral to child protective services • Higher likelihood of child secure attachment relationship; lower likelihood of child disorganized attachment relationship • Improved maternal capacity to reflect on their own and their child's experience for mothers who were high-risk • Less likely to have disrupted mother-infant interactions when mothers were teenagers

(continued)

Table 10.1 (continued)

Intervention	Population/participants/duration/ setting	Treatment description and modality	Evidence base
Mom power (MP) [8, 9, 122, 151–156]	High-risk populations, often with maternal trauma and psychopathology Prenatal—6 years old Group-based: Separate mother and child groups run simultaneously, in conjunction with guided parent-child interactions 10 weeks of 3-h group sessions, plus 1–3 individual sessions Clinic or community setting (e.g., church, community center)	• Teach mothers an attachment-based parenting education curriculum using the "tree" metaphor of "building roots" (connecting) and "branching out" (exploring) • Focus on maternal self-care skills such as diaphragmatic breathing and progressive muscle relaxation • Enhance peer/social support with other group members and with external parenting support in mothers' lives • Engage and connect mothers to ongoing care, when indicated • Corresponding child curriculum focuses on child-led play • Includes in vivo guided parent-child interactions (separations and reunions)	Pre-post design with low income mothers and their children ($N = 99$). MP is associated with: • Decreased maternal depression, PTSD, and caregiving helplessness • Improved maternal reflective capacity • Improved parenting confidence, social support, and connection to care RCT with high-risk mothers and their children ($N = 122$). MP is associated with: • Improvements in mental health symptoms and parenting stress • Improved maternal reflective capacity • Increase in "balanced" maternal representations • Better outcomes for mothers with a history of interpersonal trauma • Improvement in mothers' brain-based indices of social cognition and empathy

Mother-infant therapy group (M-ITG) [157, 158]	High-risk mothers with postpartum depression and their infants 1 month–2 years old Group-based: Separate mother, child, and dyadic group components; 2 sessions with mother's romantic partner 12 weeks of 1.5-h group sessions, plus initial intake Clinic or community setting	• Address postpartum depression symptoms, including the impact on infant development, relationships with others, and the parent-child relationship, specifically • Teach more adaptive relational and coping skills • Reduce social isolation and facilitate peer support and learning through the experiences of others • Corresponding infant group provides an emotionally responsive environment to support child development • Includes dyadic component to foster positive interactions between mothers and infants	Pre-post designs with depressed mothers and their children (N = 13, 18). M-ITG is associated with: • Decreases in maternal depressive symptoms • Increases in maternal reports of their infants as reinforcing and adaptable • Improvements in mother's positive affect, verbalization, and communication during interactions with their infants

[a] Note: Table is reprinted with permission from [7]; adapted from [125, 159]

as they make sense of how their adverse and traumatic life experiences have affected them; how these experiences may be evoked within the parent-child relationship; and how they can create a loving, caring, and safe environment for themselves and their babies, despite what happened.

10.6 Conclusion

A trauma-informed approach to supporting women and families in the perinatal period must recognize the proximal and distal risk factors that may put perinatal women at risk for developing PTSD. In the current chapter, we summarized the literature on perinatal PTSD, focusing on birth trauma, childhood maltreatment, and the COVID-19 pandemic as three critical traumatic stressors that may confer risk. Trauma-informed perinatal mental health care must consider the multifaceted strengths and vulnerabilities of each birthing person and create space to consider how what happened to an individual before, during, and after birth may impact her own mental health and the well-being of her family. Given the potential intergenerational impact of untreated and unresolved trauma, we briefly identified assessment and treatment options for perinatal women and mothers of young children exposed to trauma or significant adversity, and we highlighted several evidence-based dyadic interventions. Our hope is that the field of perinatal mental health can continue to integrate, acknowledge, and attend to the role of traumatic stress using a multigenerational lens that considers a mother's own childhood experiences (e.g., childhood maltreatment), her subjective appraisals of labor and delivery, and other contextual stressors and risk factors that may contribute to the development or exacerbation of PTSD. Ultimately, such an approach to perinatal mental health has the potential to build resiliency and effect change across generations.

References

1. Bowers ME, Yehuda R. Intergenerational transmission of stress in humans. Neuropsychopharmacol Rev. 2016;41:232–44. https://doi.org/10.1038/npp.2015.247.
2. Brisson D, McCune S, Wilson JH, Speer SR, McCrae JS, Hoops Calhoun K. A systematic review of the association between poverty and biomarkers of toxic stress. J Evid Based Soc Work. 2020;17(6):696–713.
3. American Psychological Association. APA dictionary of psychology; 2020. Retrieved August 26 from 2020 from https://dictionary.apa.org/trauma
4. International Society for Traumatic Stress Studies. What is traumatic stress?; 2016. Retrieved on August 26, 2020 from https://istss.org/public-resources/what-is-traumatic-stress
5. Herman JL. Trauma and recovery: from domestic abuse to political terror. London: Pandora; 1992.
6. Van Der Kolk BA, Roth S, Pelcovitz D, Sunday S, Spinazzola J. Disorders of extreme stress: the empirical foundation of a complex adaptation to trauma. J Trauma Stress. 2005;18(5):389–99. https://doi.org/10.1002/jts.20047.
7. Erickson NL, Julian M, Muzik M. Perinatal depression, PTSD, and trauma: impact on mother-infant attachment and interventions to mitigate the transmission of risk. Int Rev Psychiatry. 2019;31(3):245–63. https://doi.org/10.1080/09540261.2018.1563529. Epub 2019 Feb 27

8. Muzik M, Mcginnis EW, Bocknek E, Morelen D, Rosenblum K, Liberzon I, et al. PTSD symptoms across pregnancy and early postpartum among women with lifetime PTSD diagnosis. Depress Anxiety. 2016a;33:584–91. https://doi.org/10.1002/da.22465.
9. Muzik M, Rosenblum KL, Schuster MM, Kohler ES, Alfafara EA, Miller NM. A mental health and parenting intervention for adolescent and young adult mothers and their infants. J Depress Anxiety. 2016b;5(3):2167–1044. https://doi.org/10.4200/2167-1044.1000233.
10. Banyard VL, Williams LM, Siegel JA. The long-term mental health consequences of child sexual abuse: an exploratory study of the impact of multiple traumas in a sample of women. J Trauma Stress. 2001;14:697–715. https://doi.org/10.1023/A:1013085904337.
11. Seng JS, Low LK, Sperlich M, Ronis DL, Liberzon I. Prevalence, trauma history, and risk for posttraumatic stress disorder among nulliparous women in maternity care. Obstet Gynecol. 2009;114(4):839–47. https://doi.org/10.1097/AOG.0b013e3181b8f8a2.
12. Sperlich M, Seng JS. Survivor moms: women's narratives of birthing, mothering, and healing after sexual abuse. Eugene, OR: Motherbaby Press; 2008.
13. Bastos MH, Furuta M, Small R, McKenzie-McHarg K, Bick D. Debriefing interventions for the prevention of psychological trauma in women following childbirth. Cochrane Database Syst Rev. 2015;4:Art. No. CD007194. https://doi.org/10.1002/14651858.CD007194.pub2.
14. Beck CT. Birth trauma: in the eye of the beholder. Nurs Res. 2004;53:28–35. https://doi.org/10.1097/00006199-200401000-00005.
15. Boorman RJ, Devilly GJ, Gamble J, Creedy DK, Fenwick J. Childbirth and criteria for traumatic events. Midwifery. 2014;30:255–61. https://doi.org/10.1016/j.midw.2013.03.001. Epub 2013 Apr 26
16. Buss C, Entringer S, Moog NK, Toepfer P, Fair DA, Simhan HN, Heim CM, Wadhwa PD. Intergenerational transmission of maternal childhood maltreatment exposure: implications for fetal brain development. J Am Acad Child Adolesc Psychiatry. 2017;56(5):373–82. https://doi.org/10.1016/j.jaac.2017.03.001.
17. Schwerdtfeger KL, Nelson Goff BS. Intergenerational transmission of trauma: exploring mother-infant prenatal attachment. J Trauma Stress. 2007;20:39–51. https://doi.org/10.1002/jts.
18. Agorastos A, Pervanidou P, Chrousos GP, Baker DG. Developmental trajectories of early life stress and trauma: a narrative review on neurobiological aspects beyond stress system dysregulation. Front Psychiatry. 2019;10:118. https://doi.org/10.3389/fpsyt.2019.00118.
19. Sexton MB, Bennet DC, Muzik M, Rosenblum KL. Resilience, recovery, and therapeutic interventions for peripartum women with histories of trauma. In: Muzik M, Rosenblum KL, editors. Motherhood in the face of trauma. London: Springer; 2018. p. 115–30.
20. Thomason ME, Marusak HA. Review toward understanding the impact of trauma on the early developing human brain. Neuroscience. 2017;342:55–67. https://doi.org/10.1016/j.neuroscience.2016.02.022.
21. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards E, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the adverse childhood experiences (ACE) study. Am J Prevent Med. 1998;14:245–58.
22. Huang H, Yan P, Shan Z, Chen S, Li M, Luo C, Gao H, Hao L, Liu L. Adverse childhood experiences and risk of type 2 diabetes: a systematic review and meta-analysis. Metab Clin Exp. 2015;64(11):1408–18. https://doi.org/10.1016/j.metabol.2015.08.019.
23. Ports KA, Holman DM, Guinn AS, Pampati S, Dyer KE, Merrick MT, Lunsford NB, Metzler M. Adverse childhood experiences and the presence of cancer risk factors in adulthood: a scoping review of the literature from 2005 to 2015. J Pediatr Nurs. 2019;44:81–96. https://doi.org/10.1016/j.pedn.2018.10.009.
24. Su S, Jimenez MP, Roberts CT, Loucks EB. The role of adverse childhood experiences in cardiovascular disease risk: a review with emphasis on plausible mechanisms. Curr Cardiol Rep. 2015;17(10):88. https://doi.org/10.1007/s11886-015-0645-1.
25. Berkowitz G, Wolff M, Janevic T, Holzman I, Yehuda R, Landrigan P. The world trade center disaster and intrauterine growth restriction. J Am Med Assoc. 2003;290:595–6.
26. Cederbaum JA, Putnam-Hornstein E, King B, Gilbert K, Needell B. Infant birth weight and maltreatment of adolescent mothers. Am J Prevent Med. 2013;45:197–201.

27. Christiaens I, Hegadoren K, Olson DM. Adverse childhood experiences are associated with spontaneous preterm birth: a case-control study. BMC Med. 2015;13:124. https://doi.org/10.1186/s12916-015-0353-0.
28. Coussons-Read ME, Okun ML, Schmitt MP, Giese S. Prenatal stress alters cytokine levels in a manner that may endanger human pregnancy. Psychosom Med. 2005;67:625–31.
29. Glover V. Maternal stress or anxiety in pregnancy and emotional development of the child. Br J Psychiatry. 1997;171:105–6.
30. Lederman SA, Rauh V, Weiss L, Stein JL, Hoepner LA, Becker M, Perera FP. The effects of the world trade center event on birth outcomes among term deliveries at three lower Manhattan hospitals. Environ Health Perspect. 2004;112:1772–8. https://doi.org/10.1289/ehp.7348.
31. Wadhwa PD, Sandman CA, Porto M, Dunkel Schetter C, Garite TJ. The association between prenatal stress and infant birth weight and gestational age at birth: a prospective investigation. Am J Obstetr Gynecol. 1993;164:858–65.
32. Yonkers KA, Smith MV, Forray A, Epperson CN, Costello D, Lin H, Belanger K. Pregnant women with posttraumatic stress disorder and risk of preterm birth. JAMA Psychiatry. 2014;71(8):897–904.
33. Kezelman CA, Stavropoulos PA Practice guidelines for clinical treatment of complex trauma. Blue knot foundation; 2019. Retrieved February 20, 2021 from https://www.blueknot.org.au/Portals/2/Practice%20Guidelines/BlueKnot_Practice_Guidelines_2019.pdf
34. Ross CA, Halpern N. Trauma model therapy: a treatment approach for trauma, Dissociation and Complex Comorbidity Richardson, TXL Manitou Communications; 2009
35. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author. 2013.
36. American College of Obstetricians and Gynecologists. Racial and ethnic disparities in obstetrics and gynecology. Committee opinion no. 649. Obstet Gynecol. 2015;126:e130–4.
37. Hardeman RR, Karbeah J, Kozhimannil KB. Applying a critical race lens to relationship-centered care in pregnancy and childbirth: an antidote to structural racism. Birth. 2019;47:3–7. https://doi.org/10.1111/birt.12462.
38. Seng JS, Kohn-Wood LP, Mcpherson MD, Sperlich M, Seng JS, Kohn-Wood LP, et al. Disparity in posttraumatic stress disorder diagnosis among African American pregnant women. Arch Womens Ment Health. 2011a;14:295–306. https://doi.org/10.1007/s00737-011-0218-2.
39. Seng JS, Low LK, Sperlich M, Ronis DL, Liberzon I. Post-traumatic stress disorder, child abuse history, birthweight and gestational age: A prospective cohort study. BJOG Int J Obstet Gynaecol. 2011b;118(11):1329–39. https://doi.org/10.1111/j.1471-0528.2011.03071.x.
40. Loveland Cook CA, Flick LH, Homan SM, Campbell C, McSweeney M, Gallagher ME. Posttraumatic stress disorder in pregnancy: prevalence, risk factors, and treatment. Obstet Gynecol. 2004;103(4):710–7. https://doi.org/10.1097/01.AOG.0000119222.40241.fb.
41. Grekin R, O'Hara MW. Prevalence and risk factors of postpartum posttraumatic stress disorder: a meta-analysis. Clin Psychol Rev. 2014;34(5):389–401. https://doi.org/10.1016/j.cpr.2014.05.003.
42. Yildiz PD, Ayers S, Phillips L. The prevalence of posttraumatic stress disorder in pregnancy and after birth: a systematic review and meta-analysis. J Affect Disord. 2017;208:634–45. https://doi.org/10.1016/j.jad.2016.10.009.
43. Oh W, Muzik M, McGinnis EW, Hamilton L, Menke RA, Rosenblum KL. Comorbid trajectories of postpartum depression and PTSD among mothers with childhood trauma history: course, predictors, processes and child adjustment. J Affect Disord. 2016;200:133–41. https://doi.org/10.1016/j.jad.2016.04.037.
44. Dekel S, Stuebe C, Dishy G. Childbirth induced posttraumatic stress syndrome: a systematic review of prevalence and risk factors. Front Psychol. 2017;8:560. https://doi.org/10.3389/fpsyg.2017.00560.
45. Fisher J, Acton C, Rowe H. Mental health problems among childbearing women: historical perspectives and social determinants. In: Muzik M, Rosenblum KL, editors. Motherhood in the face of trauma. Cham: Springer; 2018. p. 3–22.

46. Thiel F, Dekel S. Peritraumatic dissociation in childbirth-evoked posttraumatic stress and postpartum mental health. Arch Womens Ment Health. 2020;23(2):189–97. https://doi.org/10.1007/s00737-019-00978-0.
47. Ayers S, Bond R, Bertullies S, Wijma K. The aetiology of post-traumatic stress following childbirth: a meta-analysis and theoretical framework. Psychol Med. 2016;46(6):1121–34. https://doi.org/10.1017/S0033291715002706.
48. Thiel F, Ein-Dor T, Dishy G, King A, Dekel S. Examining symptom clusters of childbirth-related posttraumatic stress disorder. Prim Care Companion CNS Disord. 2018;20(5):18m02322. https://doi.org/10.4088/PCC.18m02322.
49. Beck CT. The slippery slope of birth trauma. In: Muzik M, Rosenblum KL, editors. Motherhood in the face of trauma. Springer; 2018. p. 55–68.
50. Andersen LB, Melvaer LB, Videbech P, Lamont RF, Joergensen JS. Risk factors for developing post-traumatic stress disorder following childbirth: a systematic review. Acta Obstet Gynecol Scand. 2012;91:1261–72. https://doi.org/10.1111/j.1600-0412.2012.01476.x.
51. Beck, CT, & Watson S. Subsequent childbirth after a previous traumatic birth. Nursing research. 2010;59(4):241–249. https://doi.org/10.1097/NNR.0b013e3181e501fd
52. Bowman ML. Individual differences in posttraumatic distress: problems with the DSM-IV model. Can J Psychiatr. 1999;44:21–33. https://doi.org/10.1177/070674379904400103.
53. Dekel S, Hankin IT, Pratt JA, Hackler DR, Lanman ON. Posttraumatic growth in trauma recollections of 9/11 survivors: a narrative approach. J Loss Trauma. 2016;21:315–24. https://doi.org/10.1080/15325024.2015.1108791.
54. Czarnocka J, Slade P. Prevalence and predictors of post-traumatic stress symptoms following childbirth. Br J Clin Psychol. 2000;39:35–51. https://doi.org/10.1348/014466500163095.
55. Olde E, van der Hart O, Kleber RJ, van Son MJM, Wijnen HAA, Pop VJM. Peritraumatic dissociation and emotions as predictors of PTSD symptoms following childbirth. J Trauma Dissociation. 2005;6:125–42.
56. Verreault N, Da Costa D, Marchand A, Ireland K, Banack H, Dritsa M, et al. PTSD following childbirth: a prospective study of incidence and risk factors in Canadian women. J Psychosom Res. 2012;73:257–63. https://doi.org/10.1016/j.jpsychores.2012.07.010.
57. de Graaff LF, Honig A, van Pampus MG, Stramrood CAI. Preventing post-traumatic stress disorder following childbirth and traumatic birth experiences: a systematic review. Acta Obstet Gynecol Scand. 2018;97(6):648–56. https://doi.org/10.1111/aogs.13291.
58. Vedam S, Stoll K, Taiwo TK, et al. The giving voice to mothers study: inequity and mistreatment during pregnancy and childbirth in the United States. Reprod Health. 2019;16:77. https://doi.org/10.1186/s12978-019-0729-2.
59. Alcorn KL, O'Donovan A, Patrick JC, Creedy D, Devilly GJ. A prospective longitudinal study of the prevalence of post-traumatic stress disorder resulting from childbirth events. Psychol Med. 2010;40:1849–59.
60. Kountanis JA, Muzik M, Chang T, Langen E, Cassidy R, Mashour GA, Bauer ME. Relationship between postpartum mood disorder and birth experience: a prospective observational study. Int J Obstet Anesth. 2020;44:90–9. https://doi.org/10.1016/j.ijoa.2020.07.008.
61. Olde E, van der Hart O, Kleber R, van Son M. Posttraumatic stress following childbirth: A review. Clin Psychol Rev. 2006;26:1–16. https://doi.org/10.1016/j.cpr.2005.07.002.
62. Ayers S. Delivery as a traumatic event: prevalence, risk factors, and treatment for postnatal posttraumatic stress disorder. Clin Obstet Gynecol. 2004;47:552–67.
63. Koster D, Romijn C, Sakko E, Stam C, Steenhuis N, de Vries D, et al. Traumatic childbirth experiences: practice-based implications for maternity care professionals from the woman's perspective. Scand J Caring Sci. 2020;34(3):792–9. https://doi.org/10.1111/scs.12786.
64. Beck CT. Pentadic cartography: mapping birth trauma narratives. Qual Health Res. 2006;16:453–66.
65. Dekel S, Ein-Dor T, Dishy GA, Mayopoulos PA. Beyond postpartum depression: posttraumatic stress-depressive response following childbirth. Arch Womens Ment Health. 2020;23:557–64. https://doi.org/10.1007/s00737-019-01006-x/Published.

66. Davies J, Slade P, Wright I, Stewart P. Posttraumatic stress symptoms following childbirth and mothers' perceptions of their infants. Infant Ment Health J. 2008;29(6):537–54. https://doi.org/10.1002/imhj.20197.
67. DiBlasio P, Camisasca E, Miragoli S, Ionio C, Milani L. Does maternal parenting stress mediate the association between postpartum PTSD symptoms and children's internalizing and externalizing problems? A longitudinal perspective. Child Youth Care Forum. 2017;46(5):685–701. https://doi.org/10.1007/s10566-017-9400-7.
68. McDonald S, Slade P, Spiby H, Iles J. Posttraumatic stress symptoms, parenting stress, and mother-child relationships following childbirth and at 2 years postpartum. J Psychosom Obstet Gynecol. 2011;32(2):141–6. https://doi.org/10.3109/0167482X.2011.596962.
69. Dekel S, Ein-Dor T, Berman Z, Barsoumian IS, Agarwal S, Pitman RK. Delivery mode is associated with maternal mental health following childbirth. Arch Womens Ment Health. 2019;22(6):817–24. https://doi.org/10.1007/s00737-019-00968-2.
70. Beck CT, Watson S. Mothers' experiences interacting with infants after traumatic childbirth. MCN Ame J Matern Child Nurs. 2019;44(6):338–44. https://doi.org/10.1097/NMC.0000000000000565.
71. Choi KW, Sikkema KJ. Childhood maltreatment and perinatal mood and anxiety disorders: a systematic review. Trauma Violence Abuse. 2016;17(5):427–53. https://doi.org/10.1177/1524838015584369.
72. Muzik M, Bocknek EL, Broderick A, Richardson P, Rosenblum KL, Thelen K, Seng JS. Mother–infant bonding impairment across the first 6 months postpartum: the primacy of psychopathology in women with childhood abuse and neglect histories. Arch Womens Ment Health. 2013;16(1):29–38. https://doi.org/10.1007/s00737-012-0312-0.
73. Onoye JM, Shafer LA, Goebert DA, Morland LA, Matsu CR, Hamagami F. Changes in PTSD symptomatology and mental health during pregnancy and postpartum. Arch Womens Ment Health. 2013;16(6):453–63. https://doi.org/10.1007/s00737-013-0365-8.
74. World Health Organization. (2020, June 8). Child Maltreatment. https://www.who.int/news-room/fact-sheets/detail/child-maltreatment.
75. Centers for Disease Control and Prevention. Preventing Adverse Childhood Experiences; 2020. https://www.cdc.gov/violenceprevention/aces/fastfact.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fviolenceprevention%2Facestudy%2Ffastfact.html.
76. Singh MM, Parsekar SS, Nair SN. An epidemiological overview of child sexual abuse. J Fam Med Prim Care. 2014;3(4):430–5. https://doi.org/10.4103/2249-4863.148139.
77. Gilbert LK, Breiding MJ, Merrick MT, Thompson WW, Ford DC, Dhingra SS, Parks SE. Childhood adversity and adult chronic disease: an update from ten states and the District of Columbia, 2010. Am J Prev Med. 2015;48(3):345–9. https://doi.org/10.1016/j.amepre.2014.09.006.
78. Bert SC, Guner BM, Lanzi RG. The influence of maternal history of abuse on parenting knowledge and behavior. Fam Relat. 2009;58(2):176–87. https://doi.org/10.1111/j.1741-3729.2008.00545.x.
79. Smith AL, Cross D, Winkler J, Jovanovic T, Bradley B. Emotional dysregulation and negative affect mediate the relationship between maternal history of child maltreatment and maternal child abuse potential. J Fam Violence. 2014;29(5):483–94. https://doi.org/10.1007/s10896-014-9606-5.
80. Leeners B, Stiller R, Block E, Görres G, Rath W. Pregnancy complications in women with childhood sexual abuse experiences. J Psychosom Res. 2010;69(5):503–10. https://doi.org/10.1016/j.jpsychores.2010.04.017.
81. Nagl M, Steinig J, Klinitzke G, Stepan H, Kersting A. Childhood maltreatment and prepregnancy obesity: a comparison of obese, overweight, and normal weight pregnant women. Arch Womens Ment Health. 2016;19(2):355–65. https://doi.org/10.1007/s00737-015-0573-5.
82. Moog NK, Heim CM, Entringer S, Kathmann N, Wadhwa PD, Buss C. Childhood maltreatment is associated with increased risk of subclinical hypothyroidism in pregnancy. Psychoneuroendocrinology. 2017;84:190–6. https://doi.org/10.1016/j.psyneuen.2017.07.482.

83. Moog NK, Buss C, Entringer S, Shahbaba B, Gillen DL, Hobel CJ, Wadhwa PD. Maternal exposure to childhood trauma is associated during pregnancy with placental-fetal stress physiology. Biol Psychiatry. 2016;79(10):831–9. https://doi.org/10.1016/j.biopsych.2015.08.032.
84. Heim C, Shugart M, Craighead WE, Nemeroff CB. Neurobiological and psychiatric consequences of child abuse and neglect. Dev Psychobiol. 2010;52(7):671–90. https://doi.org/10.1002/dev.20494.
85. Moog NK, Entringer S, Rasmussen JM, Styner M, Gilmore JH, Kathmann N, Heim CM, Wadhwa PD, Buss C. Intergenerational effect of maternal exposure to childhood maltreatment on newborn brain anatomy. Biol Psychiatry. 2018;83(2):120–7. https://doi.org/10.1016/j.biopsych.2017.07.009.
86. Davalos DB, Yadon CA, Tregellas HC. Untreated prenatal maternal depression and the potential risks to offspring: a review. Arch Womens Ment Health. 2012;15(1):1–14. https://doi.org/10.1007/s00737-011-0251-1.
87. Deave T, Heron J, Evans J, Emond A. The impact of maternal depression in pregnancy on early child development. BJOG Int J Obstet Gynaecol. 2008;115(8):1043–51. https://doi.org/10.1111/j.1471-0528.2008.01752.x.
88. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: A meta-analytic review. Clin Psychol Rev. 2000;20(5):561–92. https://doi.org/10.1016/S0272-7358(98)00100-7.
89. O'Hara MW, McCabe JE. Postpartum depression: current status and future directions. Annu Rev Clin Psychol. 2013;9(1):379–407. https://doi.org/10.1146/annurev-clinpsy-050212-185612.
90. Morelen D, Rosenblum KL, Muzik M. Childhood maltreatment and motherhood: implications for maternal well-being and mothering. Motherhood in the Face of Trauma. Springer; 2018. p. 23–37.
91. Muzik M, Morelen D, Hruschak J, Rosenblum KL, Bocknek E, Beeghly M. Psychopathology and parenting: an examination of perceived and observed parenting in mothers with depression and PTSD. J Affect Disord. 2017;207:242–50. https://doi.org/10.1016/j.jad.2016.08.035.
92. Bailey HN, DeOliveira C, Wolfe V V, Evans EM, & Hartwick C. The impact of childhood maltreatment history on parenting: a comparison of maltreatment types and assessment methods. Child abuse & neglect. 2012;36(3):236–246. https://doi.org/10.1016/j.chiabu.2011.11.005.
93. Stacks, A. M., Muzik, M., Wong, K., Beeghly, M., Huth-Bocks, A., Irwin, J. L., & Rosenblum, K. L. (2014). Maternal reflective functioning among mothers with childhood maltreatment histories: links to sensitive parenting and infant attachment security. Attachment & human development. 16(5):515–533. https://doi.org/10.1080/14616734.2014.935452.
94. Fava NM, Simon VA, Smith E, Khan M, Kovacevic M, Rosenblum KL, Menke R, Muzik M. Perceptions of general and parenting-specific posttraumatic change among postpartum mothers with histories of childhood maltreatment. Child Abuse Negl. 2016;56:20–9. https://doi.org/10.1016/j.chiabu.2016.04.007.
95. Khalil A, Kalafat E, Benlioglu C, O'Brien P, Morris E, Draycott T, et al. SARS-CoV-2 infection in pregnancy: a systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 2020;25:100446. https://doi.org/10.1016/j.eclinm.2020.100446.
96. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. N Engl J Med. 2020;382(22):2163–4. https://doi.org/10.1056/NEJMc2009316.
97. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370 https://doi.org/10.1136/bmj.m3320.
98. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2020;2(2):100107. https://doi.org/10.1016/j.ajogmf.2020.100107.

99. Brooks SK, Weston D, Greenberg N. Psychological impact of infectious disease outbreaks on pregnant women: rapid evidence review. Public Health. 2020;189:26–36. https://doi.org/10.1016/j.puhe.2020.09.006.
100. Caparros-Gonzalez RA, Alderdice F. The COVID-19 pandemic and perinatal mental health. J Reprod Infant Psychol. 2020;38(3):223–5. https://doi.org/10.1080/02646838.2020.1786910.
101. Corbett GA, Milne SJ, Hehir MP, Lindow SW, O'Connell MP. Health anxiety and behavioural changes of pregnant women during the COVID-19 pandemic. Eur J Obstet Gynecol Reprod Biol. 2020;249:96–7. https://doi.org/10.1016/j.ejogrb.2020.04.022.
102. Ravaldi C, Ricca V, Wilson A, Homer C, Vannacci A. Previous psychopathology predicted severe COVID-19 concern, anxiety and PTSD symptoms in pregnant women during lockdown in Italy. Arch Women's Mental Health. 2020;23(6):783–6. https://doi.org/10.1101/2020.08.26.20182436.
103. Preis H, Mahaffey B, Heiselman C, Lobel M. Vulnerability and resilience to pandemic-related stress among U.S. women pregnant at the start of the COVID-19 pandemic. Soc Sci Med. 2020;266:113348. https://doi.org/10.1016/j.socscimed.2020.113348.
104. Moyer CA, Compton SD, Kaselitz E, Muzik M. Pregnancy-related anxiety during COVID-19: a nationwide survey of 2740 pregnant women. Arch Womens Ment Health. 2020;23(6):757–65. https://doi.org/10.1007/s00737-020-01073-5.
105. Liu CH, Erdei C, Mittal L. Risk factors for depression, anxiety, and PTSD symptoms in perinatal women during the COVID-19 pandemic. Psychiatry Res. 2021;295:113552. https://doi.org/10.1016/j.psychres.2020.113552.
106. Hermann A, Fitelson EM, Bergink V. Meeting maternal mental health needs during the COVID-19 pandemic. JAMA Psychiatry. 2021;78(2):123–4. https://doi.org/10.1001/jamapsychiatry.2020.1947.
107. Thapa SB, Mainali A, Schwank SE, Acharya G. Maternal mental health in the time of the COVID-19 pandemic. Acta Obstet Gynecol Scand. 2020, July 1;99(7):817–8. https://doi.org/10.1111/aogs.13894.
108. Choi KR, Records K, Low LK, Alhusen JL, Kenner C, Bloch JR, et al. Promotion of maternal–infant mental health and trauma-informed care during the COVID-19 pandemic. J Obstet Gynecol Neonatal Nurs. 2020;49(5):409–15. https://doi.org/10.1016/j.jogn.2020.07.004.
109. Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. Lancet Psychiatry. 2020;S2215-0366(20):30168–71.
110. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiatry. 2020;7(7):611–27. https://doi.org/10.1016/S2215-0366(20)30203-0.
111. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. Brain Behav Immun. 2020;89:531–42. https://doi.org/10.1016/j.bbi.2020.05.048.
112. Cameron EE, Joyce KM, Delaquis CP, Reynolds K, Protudjer JLP, Roos LE. Maternal psychological distress & mental health service use during the COVID-19 pandemic. J Affect Disord. 2020;276:765–74. https://doi.org/10.1016/j.jad.2020.07.081.
113. Ceulemans M, Hompes T, Foulon V. Mental health status of pregnant and breastfeeding women during the COVID-19 pandemic: A call for action. Int J Gynecol Obstet. 2020;151(1):146–7. https://doi.org/10.1002/ijgo.13295.
114. Farrell T, Reagu S, Mohan S, Elmidany R, Qaddoura F, Ahmed EE, et al. The impact of the COVID-19 pandemic on the perinatal mental health of women. J Perinat Med. 2020;48(9):971–6. https://doi.org/10.1515/jpm-2020-0415.
115. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. J Affect Disord. 2020;277:5–13. https://doi.org/10.1016/j.jad.2020.07.126.
116. Huizink AC, Bartels M, Rose RJ, Pulkkinen L, Eriksson CJ, Kaprio J. Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring. J Epidemiol Community Health. 2008;62(4):e5.

117. Laplante DP, Brunet A, Schmitz N, Ciampi A, King S. Project ice storm: prenatal maternal stress affects cognitive and linguistic functioning in 5 1/2-year-old children. J Am Acad Child Adolesc Psychiatry. 2008;47(9):1063–72.
118. Seng JS, Rauch SA, Resnick H, Reed CD, King A, Low LK, McPherson M, Muzik M, Abelson J, Liberzon I. Exploring posttraumatic stress disorder symptom profile among pregnant women. J Psychosom Obstet Gynaecol. 2010;31(3):176–87.
119. Yehuda R, Engel SM, Brand SR, Seckl J, Marcus SM, Berkowitz GS. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the world trade center attacks during pregnancy. J Clin Endocrinol Metab. 2005;90:4115–8.
120. Foa EB, Meadows EA. Psychosocial treatments for posttraumatic stress disorder: a critical review. In: Spence J, Darley JM, Foss DJ, editors. Annual review of psychology, vol. 49. Palo Alto, CA: Annual Reviews; 1997. p. 449–80.
121. Cirino NH, Knapp JM. Perinatal posttraumatic stress disorder: a review of risk factors, diagnosis, and treatment. Obstet Gynecol Surv. 2019;74(6):369–76. https://doi.org/10.1097/OGX.0000000000000680.
122. Muzik M, Rosenblum KL, Alfafara EA, Schuster MM, Miller NM, Waddell RM, et al. Mom power: preliminary outcomes of a group intervention to improve mental health and parenting among high-risk mothers. Arch Womens Ment Health. 2015;18(3):507–21. https://doi.org/10.1007/s00737-014-0490-z.
123. Gunnar MR, Quevedo K. The neurobiology of stress and development. Annu Rev Psychol. 2007;58:145–73. https://doi.org/10.1146/annurev.psych.58.110405.085605.
124. Julian MM, Muzik M. Interventions to enhance mother-infant attachment in the context of trauma, depression, and substance abuse. In: Chandra P, Herrman H, Fisher J, Riecher-Rössler A, editors. Mental health and illness of women. Mental health and illness worldwide. Singapore: Springer; 2019. https://doi.org/10.1007/978-981-10-0371-4_29-1.
125. Julian MM, Muzik M, Rosenblum KL. Parenting in the context of trauma: dyadic interventions for trauma-exposed parents and their young children. In: Muzik M, Rosenblum KL, editors. Motherhood in the face of trauma. Springer; 2018. p. 131–50.
126. Bernard K, Dozier M, Bick J, Gordon MK. Intervening to enhance cortisol regulation among children at risk for neglect: results of a randomized clinical trial. Dev Psychopathol. 2015a;27(03):829–41. https://doi.org/10.1017/S095457941400073X.
127. Bernard K, Dozier M, Bick J, Lewis-Morrarty E, Lindhiem O, Carlson EA. Enhancing attachment organization among maltreated children: results of a randomized clinical trial. Child Dev. 2012;83(2):623–36. https://doi.org/10.1111/j.1467-8624.2011.01712.x.
128. Bernard K, Hostinar CE, Dozier M. Intervention effects on diurnal cortisol rhythms of child protective services–referred infants in early childhood. JAMA Pediatr. 2015b;169(2):112–9. https://doi.org/10.1001/jamapediatrics.2014.2369.
129. Bernard K, Lee AH, Dozier M. Effects of the ABC intervention on foster children's receptive vocabulary. Child Maltreat. 2017;22(2):174–9. https://doi.org/10.1177/1077559517691126.
130. Bernard K, Simons R, Dozier M. Effects of an attachment-based intervention on child protective services-referred mothers' event-related potentials to children's emotions. Child Dev. 2015c;86(6):1673–84. https://doi.org/10.1111/cdev.12418.
131. Bick J, Dozier M. The effectiveness of an attachment-based intervention in promoting foster mothers' sensitivity toward foster infants. Infant Ment Health J. 2013;34(2):95–103. https://doi.org/10.1002/imhj.21373.
132. Dozier M, Lindhiem O, Lewis E, Bick J, Bernard K, Peloso E. Effects of a foster parent training program on young children's attachment behaviors: preliminary evidence from a randomized clinical trial. Child Adolesc Soc Work J. 2009;26(4):321–32. https://doi.org/10.1007/s10560-009-0165-1.
133. Lewis-Morrarty E, Dozier M, Bernard K, Terracciano SM, Moore SV. Cognitive flexibility and theory of mind outcomes among foster children: preschool follow-up results of a randomized clinical trial. J Adolesc Health. 2012;51(2) https://doi.org/10.1016/j.jadohealth.2012.05.005.

134. Lind T, Bernard K, Ross E, Dozier M. Intervention effects on negative affect of CPS-referred children: results of a randomized clinical trial. Child Abuse Negl. 2014;38(9) https://doi.org/10.1016/j.chiabu.2014.04.004.
135. Sprang G. The efficacy of a relational treatment for maltreated children and their families. Child Adolesc Mental Health. 2009;14(2):81–8. https://doi.org/10.1111/j.1475-3588.2008.00499.x.
136. Yarger HA, Hoye JR, Dozier M. Trajectories of change in attachment and biobehavioral catch-up among high-risk mothers: A randomized clinical trial. Infant Ment Health J. 2016;37(5):525–36. https://doi.org/10.1002/imhj.21585.
137. Lind T, Raby KL, Caron EB, Roben CKP, Dozier M. Enhancing executive functioning among toddlers in foster care with an attachment-based intervention. Dev Psychopathol. 2017;29(02):575–86. https://doi.org/10.1017/S0954579417000190.
138. Lowell DI, Carter AS, Godoy L, Paulicin B, Briggs-Gowan MJ. A randomized controlled trial of child FIRST: a comprehensive home-based intervention translating research into early childhood practice. Child Dev. 2011;82(1):193–208. https://doi.org/10.1111/j.1467-8624.2010.01550.x.
139. Cicchetti D, Rogosch FA, Toth SL. Fostering secure attachment in infants in maltreating families through preventive interventions. Dev Psychopathol. 2006;18(3):623–49.
140. Cicchetti D, Toth SL, Rogosch FA. The efficacy of toddler-parent psychotherapy to increase attachment security in offspring of depressed mothers. Attach Hum Dev. 1999;1(1):34–66. https://doi.org/10.1080/14616739900134021.
141. Lieberman AF, Ghosh Ippen C, Van Horn P. Child-parent psychotherapy: 6-month follow-up of a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2006;45(8):913–8. https://doi.org/10.1097/01.chi.0000222784.03735.92.
142. Lieberman AF, Van Horn P, Ghosh Ippen C. Toward evidence-based treatment: child-parent psychotherapy with preschoolers exposed to marital violence. J Am Acad Child Adolesc Psychiatry. 2005;44(12):1241–8. https://doi.org/10.1097/01.chi.0000181047.59702.58.
143. Lieberman AF, Weston DR, Pawl JH. Preventive intervention and outcome with anxiously attached dyads. Child Dev. 1991;62(1):199. https://doi.org/10.2307/1130715.
144. Toth SL, Maughan A, Manly JT, Spagnola M, Cicchetti D. The relative efficacy of two interventions in altering maltreated preschool children's representational models: implications for attachment theory. Dev Psychopathol. 2002;14(04):877–908. https://doi.org/10.1017/S095457940200411X.
145. Cassidy J, Woodhouse SS, Sherman LJ, Stupica B, Lejuez CW. Enhancing infant attachment security: an examination of treatment efficacy and differential susceptibility. Dev Psychopathol. 2011;23(1):131–48. https://doi.org/10.1017/S0954579410000696.
146. Hoffman KT, Marvin RS, Cooper G, Powell B. Changing toddlers' and preschoolers' attachment classifications: the circle of security intervention. J Consult Clin Psychol. 2006;74(6):1017–26. https://doi.org/10.1037/0022-006X.74.6.1017.
147. Huber A, McMahon CA, Sweller N. Efficacy of the 20-week circle of security intervention: changes in caregiver reflective functioning, representations, and child attachment in an Australian clinical sample. Infant Ment Health J. 2015;36(6):556–74. https://doi.org/10.1002/imhj.21540.
148. Cassidy J, Brett BE, Gross JT, Stern JA, Martin DR, Mohr JJ, Woodhouse SS. Circle of security–parenting: a randomized controlled trial in head start. Dev Psychopathol. 2017;29(02):651–73. https://doi.org/10.1017/S0954579417000244.
149. Cassidy J, Ziv Y, Stupica B, Sherman LJ, Butler H, Karfgin A, et al. Enhancing attachment security in the infants of women in a jail-diversion program. Attach Hum Dev. 2010;12(4):333–53. https://doi.org/10.1080/14616730903416955.
150. Sadler LS, Slade A, Close N, Webb DL, Simpson T, Fennie K, Mayes LC. Minding the baby: enhancing reflectiveness to improve early health and relationship outcomes in an interdisciplinary home-visiting program. Infant Ment Health J. 2013;34(5):391–405. https://doi.org/10.1002/imhj.21406.

151. LePlatte D, Rosenblum KL, Stanton E, Miller NM, Muzik M. Mental health in primary care for adolescent parents. Ment Health Fam Med. 2012;9(1):39–45.
152. Muzik M, Cameron HG, Fezzey A, Rosenblum KL. Motherhood in the face of trauma: PTSD in the childbearing year. Zero Three. 2009;29(5):28–33.
153. Muzik M, Schmicker M, Alfafara EA, Dayton CJ, Schuster MM, Rosenblum KL. Predictors of treatment engagement to the parenting intervention mom power among Caucasian and African American mothers. J Soc Serv Res. 2014;40(5):662–80. https://doi.org/10.1080/01488376.2014.917451.
154. Rosenblum KL, Lawler JM, Alfafara E, Miller N, Schuster M, Muzik M. Improving maternal representations in high-risk mothers: a randomized, controlled trial of the mom power parenting intervention. Child Psychiatry Hum Dev. 2017;(49, 3):372–84. https://doi.org/10.1007/s10578-017-0757-5.
155. Swain JE, Ho SS, Rosenblum KL, Morelen D, Dayton CJ, Muzik M. Parent–child intervention decreases stress and increases maternal brain activity and connectivity during own baby-cry: an exploratory study. Dev Psychopathol. 2017;29(02):535–53. https://doi.org/10.1017/S0954579417000165.
156. Swain JE, Ho SS, Rosenblum KL, Morelen D, Muzik M. Emotion processing and psychopathological risk in the parental brain: psychosocial intervention increases activity and decreases stress. J Am Acad Child Adolesc Psychiatry. 2016;55(10):S320–1. https://doi.org/10.1016/j.jaac.2016.07.350.
157. Clark R, Tluczek A, Brown R. A mother-infant therapy group model for postpartum depression. Infant Ment Health J. 2008;29:514–36. https://doi.org/10.1002/imhj.
158. Clark R, Tluczek A, Wenzel A. Psychotherapy for postpartum depression: a preliminary report. Am J Orthopsychiatry. 2003;73(4):441–54. https://doi.org/10.1037/0002-9432.73.4.441.
159. Julian M, Lawler J, Rosenblum K. Caregiver-child relationships in early childhood: interventions to promote well-being and reduce risk for psychopathology. Curr Behav Neurosci Rep. 2017;4:87–98. https://doi.org/10.1007/s40473-017-0110-0.
160. Lieberman AF, Ghosh Ippen C, Van Horn P. "Don't hit my mommy!": a manual for child-parent psychotherapy with young children exposed to violence and other trauma. Zero to Three; 2015.
161. Lieberman AF, Diaz MA, Castro G, Bucio GO. Make room for baby: perinatal child-parent psychotherapy to repair trauma and promote attachment. Guilford Publications; 2020.

Maternal Suicide and Filicide

11

Margaret Spinelli and Alessandra Bramante

11.1 Suicide in the Perinatal Period: Introduction

Suicide is a global public health concern. The World Health Organization reports approximately 800.000 global suicide death annually, which is 1 person every 40 s [1]. Suicide is the second leading cause of death among women 25–34 years of age and has steadily increased in prevalence since 2001. Death from suicide occurs in a lower percentage in pregnant or postpartum women than in women in the general population; however the rates of suicide following childbirth are higher than previously thought. Some studies indicate that suicide is the number one cause of death for women in the first year postpartum [2]. The Confidential Enquiry into Maternal Deaths identifies suicide as the leading cause of maternal death. Maternal death is the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes. In addition, a late maternal death is one which occurs more than 6 weeks but less than 1 year after the end of pregnancy [3].

11.2 Maternal Death Classification

Maternal deaths can be further divided by cause into the following: *direct deaths*, resulting from obstetric complications of the pregnant state (e.g. amniotic fluid embolism, pre-eclampsia); *indirect deaths*, resulting from medical health

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conditions exacerbated by pregnancy (e.g. cardiac disease); and *coincidental deaths*, where the cause is unrelated to pregnancy (e.g. traffic collision, homicide). The CEMD reports on all maternal deaths in the United Kingdom and Ireland, including those that are late and/or coincidental. Maternal death can be divided by time into *early death*, when **it occurs** in pregnancy, or within 42 days of delivery, and *late death* when **it occurs** after 42 days to 1 year postpartum [3]. Maternal suicide is included **with** maternal death due to psychiatric cause. A death is described as being due to a psychiatric cause if it would not have occurred in the absence of psychiatric disorder.

The majority are due to suicide, with a minority due to substance misuse (mainly accidental overdoses of heroin) and a few other causes (e.g. adverse drug reactions). All psychiatric deaths are classified as indirect. According to the CEMD, the profile of women who died from suicide seems different **from those** of men and non-childbearing women. The woman most likely to kill herself is one who has had a previous experience of hospitalized mental illness without her baby and who suffers from a severe mental illness with an early onset following childbirth, who is older and free from social adversity and whose act of deliberate self-harm is violent [3].

11.3 Maternal Death Rates

Maternal death rates (per 100,000 women) reported in different countries are as follows: 2.0 in the United States, 2.6 in Canada, 8.7 in Japan, 2.5 in the United Kingdom, 5.9 in Finland, 3.7 in Sweden and 1.3 in Italy [4]. Analysing data from ICD-9 and ICD-10 codes derived from the medical records of 595.237 childbearing women 15–44 years of age, researchers observed that, during the time period extending from 1 year before to 1 year after childbirth, the prevalence of suicidality (defined as suicidal ideation or intentional self-harm) has increased from 0.2% in 2006 to 0.6% in 2017 [5].

11.4 Maternal Suicide in the Literature

Contrary to the belief that pregnancy may be a protective factor against suicide, there is concern relating to the increased incidence of suicidal ideation (thoughts about committing suicide) in pregnant women [6]. Suicidal ideation is currently reported as a common complication of pregnancy and has been recognized as a predictor for suicidal attempts and completed suicide, informing the need for better understanding of this issue during pregnancy and the postpartum period [7]. Rates of suicidal ideation during pregnancy range from 13.1% to 46%. However, these estimates have been based on small psychiatric or drug-dependent treatment high-risk samples [8]. Kubota et al. reported that unintentionally pregnant women who had neither been in a union nor had a child were at a significantly higher risk for suicidal ideation compared with non-pregnant and non-postpartum women [4]. Fewer studies have examined the occurrence of suicide attempts (following through

with the act of trying to commit suicide) during pregnancy and postpartum compared with non-pregnancy; however, some research has investigated related outcomes, such as suicidal ideation and completed suicide. In general, while suicidal ideation may be higher during this time, the perinatal period is likely one of lower suicide risk [9]. From a global perspective, rates of postpartum suicide are difficult to glean from the research literature, due to differences in time periods included, the nature of study cohorts, reporting methods and years under consideration.

Thus, rates of postpartum suicide per 100,000 live births have varied. For example, in Washington State it was reported at 1.4, in Finland at 5.9, while in Taiwan 6.9. Many studies related to the entire perinatal period [from pregnancy to 1 year postpartum], including reports of perinatal suicide rates per 100,000 live births of 2.6 in Canada, 2.0 in the United Kingdom and 3.7 in Sweden [10].

Because suicide in this population is rare, we have limited information regarding risk factors for suicide during the perinatal period. A study published in *The Lancet Psychiatry* attempts to identify risk factors in this population. This study analysed data collected from 1997 to 2012 as part of the UK National Confidential Inquiry into Suicide and Homicide by People with Mental Illness. This database included only suicides by people who had contact with psychiatric services within the previous year. The researchers focused on women between the ages of 16 and 50 years who died by suicide during pregnancy or the first postpartum year (perinatal suicides) and compared this group to a similarly aged women who died by suicide outside of this timeframe (non-perinatal suicides). A total of 4.785 women died by suicide. A minority of those suicides occurred during the perinatal period (98 or 2%). Compared with non-perinatal women, women who died by suicide in the perinatal period were more likely to have a diagnosis of depression, were less likely to be receiving any active treatment at the time of death and were also more likely to be younger and married, with shorter illness duration [11]. Women with a history of depression or a major mental illness, passive smoking or cigarette smoking and women experiencing intimate partner violence or from low socio-economic backgrounds are all at higher risk of suicidal ideation in the perinatal period [6]. A systematic review of 57 articles carried out by Gelaye et al. identified intimate partner violence, less than 12 years of education and MDD as risk factors for antenatal suicidal ideation [7]. The diagnosis of a comorbid psychiatric condition was identified as a risk factor for suicidal ideation, specifically a diagnosis of depression in the antenatal and postnatal period. Women with a history of abuse and intimate partner violence are at risk of suicidal ideation during pregnancy [6]. In pregnant women, suicidal ideations appear more likely among those with a lifetime history of mood disorder, anxiety disorder or substance use disorder, but not of psychotic disorder. In another study, in postpartum women consecutively admitted to a psychiatric unit, suicidal ideation was associated with depression but not with psychotic disorder [12].

Various psychosocial factors, involved in maternal suicide, have been reported: younger age, unmarried, a history of family suicide, poverty, domestic violence, a history of abuse, racial issues, regional isolation, anxiety, suicidal ideation, a history of suicidal attempts, unexpected pregnancy, foetal and infant death and mental

disorders such as major depressive disorder (MDD), bipolar disorder and substance-related disorders [4]. Suicide risk is also higher in women with a history of suicide attempts, sleep disturbances during the postpartum period, stillbirth and abrupt discontinuation of psychotropic medications during pregnancy [13]. Moreover, the women in pharmacotherapy for severe mental illness often discontinue their antidepressant medication in the perinatal period, mostly because of fears of potential harm to the unborn baby or breastfeeding infant, leaving them vulnerable to relapse in pregnancy and beyond [11]. The most important risk factor for perinatal suicidality seems to be a history of psychiatric illness. Women diagnosed with severe mental disorders (such as schizophrenia or bipolar disorder) are more likely to complete suicide during pregnancy [11]. Women with a diagnosis of bipolar disorder have a higher risk for suicide and are more likely to die by suicide during pregnancy than women with unipolar depression [11]. Regarding mental health, a personal history of psychiatric disorder increases the risk of attempted suicide (women with a history of psychiatric hospitalization have a risk of postpartum suicide attempts that is 27 times higher), and over two thirds of perinatal suicides concerned women with a current psychiatric disorder (women hospitalized in psychiatric unit in the first year postpartum have a risk of suicide that is 70 times greater than women in the general population) [12].

The majority of women who died by suicide in the perinatal period used a violent method, mainly by hanging or jumping. Roughly a quarter died by self-poisoning, with only 4% dying by overdose of psychotropics [11]. This is sign of severe psychopathology and strong suicidal intention.

Suicidal ideation and intent may be extremely distressing for the mother, and suicidal behaviour and complete suicide may have devastating and intergenerational consequences for the family [11]. Indeed, they can have long lasting adverse health outcomes that extend beyond the peripartum period, effecting both maternal and neonatal wellbeing. Serious injury during the antepartum period from failed suicide attempts can also have devastating implications for the woman and foetus [7].

11.5 Implications for Practice

Many authors pointed out the urgent need for innovative approaches to improve the screening and detection of antepartum suicidal ideation, given that a substantial proportion of women with suicidal ideation do not meet the clinical thresholds for depression and that the stress–diathesis model shows susceptibility to suicidal behaviour independent of depressive disorders. Identifying the factors that cause suicidal ideation independent of depressive disorders is very important [4].

All healthcare providers who work with childbearing women should be prepared to discuss and screen for mental health issues [14]. They need to be reminded that a minority of women will suffer from a severe illness of sudden onset in the early puerperium that requires specialist management, and they also need to be reminded of the high rate of recurrence after subsequent pregnancies and that the timing and

severity of these illnesses are likely to be as before. Women who have suffered from severe non-postpartum illness also face a high risk of recurrence. At the booking clinic, asking specifically about the history of serious mental illness is as essential as asking questions about diabetes and epilepsy [3]. Medical professionals working in the emergency room should also be trained on these matters as the majority of new mothers who die by suicide visit an ER within 1 month prior to taking their lives [14]. Nevertheless, policymakers, health plan and clinicians should ensure access to universal suicidality screening and appropriate treatment for pregnant and postpartum individuals and seek health system and policy avenues to mitigate this public health crisis, particularly for high-risk groups [5].

While psychiatrists regularly screen for suicide, the findings from many studies highlight how important it is to screen perinatal women for suicide in primary care or obstetric offices, as many of the women who go on to complete suicide may never see a psychiatrist. Moreover, paediatricians may play a particularly helpful role in helping identify women at risk for suicide as at-risk women may be less likely to engage in paediatric care for their children [15].

11.6 Recommendation

11.6.1 Primary Prevention

Increase culturally and linguistically relevant public awareness about maternal mental health risk factors, signs, symptoms, treatment and recovery [16]. Reduce social isolation during and after pregnancy by increasing availability to evidence-based, culturally and linguistically relevant group prenatal care, peer-led support or home visiting programme [16]. Support incentives to routine screening of pregnant and postpartum women for mental health conditions by both obstetric providers and paediatricians during well-child visits [16].

11.6.2 Secondary Prevention

Protocols for the management of women at risk of a serious mental illness following delivery should be in place in every maternity service [17]. Enquiries about previous psychiatric history should be made routinely at the antenatal booking clinic [17]. The term “postnatal depression” should not be used as a term for all types of psychiatric disorder [17]. Women who have a past history of serious psychiatric disorder (postpartum or non-postpartum) should be assessed by a psychiatrist in the antenatal period with regard to the high risk of recurrence following delivery [17]. For women with mental health conditions, incorporate routine suicide risk assessment using a validated scale [16]. Mental health professional should provide support and education for family members of women with mental health conditions [16].

11.6.3 Tertiary Prevention

Improve education for obstetric and psychiatric providers regarding perinatal mental health diagnoses and treatment, particularly around management of medications in pregnancy and medical management of psychosis in postpartum patients [16]. Educate psychiatrist on the value of keeping mother and baby together during day treatments or hospitalizations [16].

11.7 Infanticide

Maternal infanticide or the murder of an infant in the first year of life by its mother is a subject both compelling and repulsive. The killing of an innocent elicits horror, sorrow and anger. Yet the perpetrator of this act is often a victim too, and that recognition makes for a more paradoxical response. On one hand, there is the image of a defenceless infant killed by the very person on whom he or she depended for survival. On the other hand, there is the image of a mother insane, isolated and incarcerated for a crime unthinkable to many [18]. In this chapter we discuss two categories of maternal infanticide associated with mental illness, infanticide and neonaticide. *Infanticide* is the murder of an infant in the first year of life, usually by a mother with psychosis, while *neonaticide* is infant murder within 24 h of birth [19].

11.8 History

This very same pull between the demand for condemnation and the impulse towards mercy describes the evolution and implications of infanticide laws from ancient times in both Western society and non-Western cultures [18, 20, 21]. In Babylonian and Chaldean civilizations, abnormal infants were left on the roadside to die. In the Greek and Roman era, fathers who had absolute rule over the family decided the fate of the infant. When the church elevated infant murder to a mortal sin, societies adopted laws in hopes for prevention [18], and secular penalties became increasingly severe.

In 1647, Russia became the first country to adopt a more humane attitude, and by 1888, all European states except England established a legal distinction between infanticide and murder by assigning more lenient penalties to infanticide [20, 22]. In 1922 and 1938, England passed the Infanticide Act in recognition of the time surrounding childbirth as biologically vulnerable and made infanticide a less severe crime proscribing sentences of probation and mandatory psychiatric treatment for women found guilty [22]. Today, almost all Western societies except the United States have adjusted the penalty for infanticide [18]. The United States has no particular laws governing infanticide. In the United States, it is a crime. It demands retribution. That is the law. A woman who kills an infant is charged with the crime

of homicide. If convicted in the American judicial system, she may face a long prison sentence or even the death penalty [18].

Seven incidence studies between 1994 and 2006 suggest that the rate of infanticide/neonaticide in industrialized countries (England, Scotland, Wales, United States, Canada, New Zealand) ranges from 2.4 per 100,000 to 7.0 per 100,000. The infanticide rate in the United States is 7.2 per 100,000 births [23]. Despite severe punishments the infanticide rate in the United States is higher than all Western countries. In Canada, however, the incidence is estimated at less than 3.0 per 100,000, while New Zealand is 4.5 in 100,000 [24, 25]. Wales found that infants less than 1 year old are at four times greater risk of being murdered than any other age group, with the first day of life being the highest risk.

11.9 Categories of Infanticide

Resnick has placed infanticide into categories [19]. The first category is *neonaticide* in which an infant is killed within 24 h of birth. This is usually after a denied or hidden pregnancy. *Assisted/coerced* infanticide occurs when a woman, often caught in an abusive relationship, kills an infant in conjunction with a partner. The third category involves mothers who kill because of *neglect. Abuse-related infanticide* involves a death that occurs when a mother is abusing her infant. The final category is acute psychosis in a woman with *mental illness.* For the purpose of this chapter, we will discuss mental illness-related infanticide in the setting of a postpartum psychotic episode and/or neonaticide.

11.10 Postpartum Psychosis

Postpartum psychosis is a rare and severe disorder that occurs in 1–2/1000 childbearing women. It occurs at a rate 23 times higher in the first weeks after childbirth than any other time in a woman's life [26–28]. Core features include rapid onset, profound confusion, inability to function, alternating affective states and delusional beliefs, a state that represents a profound change from baseline. Postpartum psychosis is a psychiatric emergency with a rapid progression from wellness to severe disorder. It is the only psychiatric illness that is notably associated with homicide (infanticide). The study of postpartum psychosis is rapidly evolving and requires an understanding of the complex interaction of neurochemistry, genetics and endocrine events [29–31]. More recent research reveals that the majority of postpartum psychotic episodes occur in women with underlying bipolar illness. Alternatively, women with no pre-existing mental illness may experience a first onset of psychosis after childbirth. Finally, some women with postpartum depression may experience mood symptoms that progress to psychotic symptoms and loss of contact with reality [30].

11.11 Presentation

Postpartum psychosis presents as an isolated event or an expression of bipolar disorder with a range of mood, behavioural and cognitive dysfunction, a state that frequently has a disorganized or delirious quality [18].

In 1984 James Hamilton [32] described postpartum psychosis as a picture puzzle to include mood symptoms, psychotic symptoms and cognitive disorganization, a delirium-like state of confusion and disorientation. A fluctuating state of "waxing and waning" psychotic symptoms describes a mother who looks well at one moment and then floridly psychotic in the next. In short, she may commit violent acts, despite being lucid in other contexts.

Mothers suffering from this mental illness can experience hallucinations that may take the form of threatening images or commanding voices, bizarre delusions racing thoughts, insomnia, mood lability, delirium and confusion. Most significantly postpartum psychosis is frequently accompanied by cognitive impairment, which distorts the mother's judgment, awareness of her surroundings, memory and ability to make decisions. While in the grips of psychosis, some mothers have become so dominated by uncontrollable thoughts that they have killed their children. A mother must be separated from her infant until she is well [33]. Upon presentation the clinician must inquire about suicidal or infanticidal ideation. The patient should be admitted to the hospital and separated from the infant. A metabolic workup should include relevant laboratory tests such as blood count, chemistry, thyroid function tests, antithyroid antibodies, B12 and urine cultures. Brain scans are usually unnecessary unless neurological symptoms are present. Treatment includes antipsychotic medication and mood stabilizer [33].

11.12 A Case of Postpartum Psychosis

A well-known case illustrates the complexity of this illness [34]. In 2001, during an episode of postpartum psychosis, Andrea Yates felt the presence of Satan directing her to drown her children in the bathtub of her Houston, Texas, home. Satan dictated that drowning them was the only way to save them from the fires of hell. If she ended their lives, they would go to heaven. It makes sense that any good mother would want to save her children from endless pain and suffering. The psychotic individual like Andrea inhabits an alternate reality, a mental state in which she interprets events differently from those around her. Her reality is her space in time, crowded and confused with delusions, visions and voices meant only for her. And so, when Satan directed Andrea to drown her five children to save them from burning in hell, she did. With this fundamental understanding, she prepared them for their journey to heaven by placing them in bed according to age—each one's arm around the younger for protection. Andrea Yates was misdiagnosed and incorrectly medicated by a psychiatrist. With appropriate treatment and provisions for safety, the Yates tragedy could have been avoided.

11.13 Postpartum Psychosis and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM)

Due to the absence of formal DSM-5 diagnosis [35], American psychiatrists often fail to identify and properly treat postpartum psychosis keeping our infanticide rates soaring above those in other countries. The absence of formal diagnostic criteria for postpartum psychosis in the DSM flies in the face of biology. It disregards the neurohormonal triggering factors of childbirth and the impact of hormone changes on the brain.

Still today, recent editions of the DSM (DSM-IV and DSM-5) continue to deny a formal diagnostic classification for postpartum illness suggesting that psychiatric symptoms do not differ from non-puerperal disorders [35, 36]. If the atypical symptoms of postpartum psychosis are not properly identified and treated, the associated morbidity and mortality have grave consequences for mothers, children and their families. Postpartum psychosis is associated with homicide and suicide, and yet we deny this the formal diagnosis that it deserves and the further possibility of saving mothers and infants. Recently the DSM-5 committee has agreed to place postpartum psychosis in Section III of the DSM-5, which includes diagnosis that requires further research for inclusion in the DSM [33].

11.14 Neonaticide

Neonaticide is often associated with denial of pregnancy and may be viewed in the category of infanticide with mental illness. Although neonaticide is associated with denial of pregnancy, the spectrum of denial is broad. Unlike infanticide, neonaticide is not associated with an obvious diagnosis, identifiable symptoms, biological determinants or obvious mental incapacity [18]. In 2002 US neonaticides on the first day of life were 222.2 per 100,000 person-years with a significant decrease since the onset of Safe Haven Laws [25]. In Europe, incidence varied from 0.07 (Finland, 1980–2000 period) to 8.5 neonaticides per 100,000 births (Austria, 1975–2001 period) [25]. Infant death statistics are often glaringly underestimated [37]. There is a scarcity of data on infant fatalities from abuse or neglect particularly as related to the perpetrators. This underreporting is accounted for by poor documentation, infanticides reported as SIDS deaths, lack of death certificates and undocumented births due to pregnancy denial and unfound corpses.

11.15 Categories of Denial

Miller [38] described three qualitatively different forms of pregnancy denial. Affective denial is associated with feelings of detachment. The woman acknowledges intellectually that she is pregnant but experiences few or none of the accompanying emotional or behavioural changes. A more extreme form of denial is

pervasive denial when not only the significance of pregnancy but the very existence is kept from awareness. The shock of pregnancy may cause the pregnancy to remain out of conscious awareness because it is so traumatic that pregnancy is suppressed. Finally, women with psychotic disorders may deny pregnancy in the context of a delusion.

11.16 Psychopathology

The preponderance of the literature on neonaticide is derived from judicial statistics or retrospective chart reviews. Research shows a fairly common pattern of unmarried women with unwanted pregnancies. In the general population studies, maternal perpetrators of neonaticide are usually young (mean age in late teens to 20s), single with unwanted pregnancies, lacking prenatal care and fearful of the repercussions of their pregnancy [19].

The clinical profiles of the women in my own case series [39] match those described in Janet's writings on hysteria and dissociative hallucinosis [40]. Brezinka [41] published well-documented clinical case reports of neonaticide observed in 27 women with pregnancy denial without neonaticide. Bonnet [42] described a presentation of pregnancy denial, dissociative symptoms or psychosis in 22 women. Bonnet described a failed dissociative response followed by ego disintegration or hysterical psychosis when the sight of the new-born erupts into consciousness. Family dynamics were consistent with those of the women in the following study. The prevalence of sexual abuse was 20% of Bonnet's subjects, compared to 56% of the women in the following study [39].

The case series presented here are from Spinelli's evaluation of women charged with murder for neonaticide [39]. All of the women gave informed consent and were cognizant of the purpose of the interviews. Several women who missed menstruation believed that intermitted staining was menses. Bloating was interpreted as weight gain. Even labour was thought to be the need for a bowel movement. While the concept of denial is difficult to comprehend, these women have often had family members and other third parties who had no idea that the woman was pregnant even at 36 weeks. Many women delivered by surprise alone in their home or in a bathroom. Although many mothers may kill the infant, many of these infants succumb due to lack of respiratory support [39].

We were also struck by the similarities of personal and family histories. Each woman presented with a childlike demeanour and *la belle indifference* [40]. The women, family and significant others denied awareness of the physical changes of pregnancy. A spectrum of disavowal was described, and several themes were outlined. Five denied knowledge of their gravid state until the childbirth. Twelve described intermittent awareness of an intolerable reality, which was subsequently decompartmentalized. Gravid symptoms were either absent or misinterpreted. Labour was associated with minimal or "no pain". Many experienced dissociative symptoms and some had dissociative hallucinations at the time of delivery. Family histories were strikingly similar to those families with abuse histories. Parental

relationships were strained and often bizarre; social isolation and suspicion were prominent; boundary violations and emotional neglect were pronounced. The women themselves were mostly "good girls" with no history of legal problems. Sixty-five per cent experienced physical or sexual trauma.

All of the women described "watching" themselves during the birth. Eleven denied pain, and five described the pain as "not bad". Twelve women experienced dissociative hallucinations as an internal commentary of critical and argumentative voices. Nine of those women described associated psychotic symptoms at the sight of the infant. Upon reintegration, the women could not account for the dead infant. Nine women reported a history of childhood sexual trauma and six women reported a history of physical abuse. Spinelli's review has been criticized because malingering by subjects must be considered in women who may deliberately conceal their pregnancy to escape charges of murder. Therefore, the possibility of malingering by subjects must be considered. Bizarre behaviour with the infant corpses included travelling to the airport with the dead infant in a knapsack to bring it home to Europe. One woman left the dead infant in a shared office file cabinet while she went on vacation. The putrefied corpse was found 2 weeks after delivery. Another girl placed the deceased new-born under a bed and told her friend "it is a dolly".

11.17 Prevention

In order to prevent infant death, anonymous delivery was implemented in France during the French Revolution in 1793 and enacted again in 1940. Luxemburg followed in 1993, Italy in 1997 and Austria in 2001 [43]. Some form of "baby hatches" or anonymous birth can be found in many nations. Baby hatches are incubators in the walls of hospitals and religious buildings. The incubator signals staff when a baby is placed inside. Almost 200 have been installed across the continent in the past decade in nations as diverse as Germany, Switzerland, Poland, Czech Republic and Latvia. By 2008 all 50 states and Puerto Rico had enacted Safe Haven Laws. Most Safe Haven Laws allow anonymous legal abandonment of unharmed newborns at designated sites [43]. Most state laws designate "safe havens" as hospitals, police stations and fire stations where mother can leave the baby and remain anonymous.

The CDC analysed infant homicides in the United States during 2008–2017 to determine whether rates changed after nationwide implementation of Safe Haven Laws [44] and to examine the association between infant homicide rates and state-specific Safe Haven age limits. In 2002 the rate of neonaticides was 222.2 per 100,000 in the United States. The CDC analysed rates during 2008–2017 to determine whether rates changed after nationwide implementation of Safe Haven Laws and to examine the association between infant homicide rates and state-specific Safe Haven Laws. During 2008–2017, the overall infant homicide rate on the first day of life was 74.0 per 100,000 person-years, representing a 66.7% decrease from 1989 to 1998.

As part of a comprehensive initiative in Germany, there is also a 24-h helpline and anonymous birth option. If these mothers seek custody of the infant within the first 8 weeks of life, they can obtain it. Austria passed an "anonymous birth" law in 2001 [43]. The law allows women to give birth in a hospital without giving their name and without charge. Main outcome measures included neonaticide rates before (1991–2001) and after (2002–2009) the introduction of anonymous delivery legislation per 100,000 births. Before the law the neonaticide rate was 7.2 per 100,000 births and 3.1 per 100,000 births after the law was passed. A significant decrease in neonaticide was observed in Austria after the implementation of anonymous delivery. Whereas the Finnish and Swedish rates were lower than the Austrian rates before and after the implementation of the Austrian law, they remained unchanged over the study period [43]. The question remains whether women with denial of pregnancy possess the mental acuity to reach out for this assistance. Despite social and institutional changes, neonaticide persists even in the most socially advanced, liberal and prosperous societies in the world. Nevertheless, these mechanisms of prevention have saved the lives of many neonates [44].

References

1. Naghavi M. Global, regional, and national burden of suicide mortality 1990 to 2016: systematic analysis for the global burden of disease study 2016. BMJ. 2019;364:l94.
2. Davis N, Goodman D, Smoots A. Pregnancy-related deaths: data from 14 U.S. maternal mortality review committees, 2008-2017. Centre for Disease Control and Prevention; 2019
3. Confidential Enquiry into Maternal and Child Health. Why mothers die 2000–2002. The sixth report of the confidential enquiries into maternal death in the United Kingdom. London: RCOG Press; 2004.
4. Kubota C, Inada I, Shiino T, Ando M, Sato M, Nakamura Y, Yamauchi A, et al. The risk factors predicting suicidal ideation among perinatal women in Japan. Front Psychiatry. 2020;11
5. Admon LK, Dalton VK, Kolenic GE, Ettner SL, Tilea A, Haffajee RL, Brownlee RM, Zochowski MK, Tabb KM, Muzik M, Zivin K. Trends in suicidality 1 year before and after birth among commercially insured childbearing individuals in the United States, 2006-2017. JAMA Psychiatry. 2021;78(2):171–6.
6. O'Connor A, Geraghty S, Doleman G, De Leo A. Suicidal ideation in the perinatal period: a systematic review. Mental Health Prevent. 2018;12:67–75.
7. Gelaye B, Kajeepeta S, Williams MA. Suicidal ideation in pregnancy: an epidemiologic review. Arch Women's Mental Health. 2016;19(5):741–51.
8. Tabb K, Gavin AR, Guo Y, Huang H, Debiek K, Katon W. Views and experiences of suicidal ideation during pregnancy and the postpartum: findings from interviews with maternal care clinic patients. Women Health. 2013;53:519–35.
9. Mota NP, Chartier M, Ekuma O, Nie Y, Hensel JM, MacWilliam L, McDougall C, Vigod S, Bolton JM. Mental disorders and suicide attempts in the pregnancy and postpartum periods compared with non-pregnancy: a population-based study. Can J Psychiatry. 2019;64(7):482–91.
10. Glasser S, Levinson D, Gordon ES, Braun T, Haklai Z, Goldberger N. The tip of the iceberg: postpartum suicidality in Israel. Isr J Health Policy Res. 2018;7:34.
11. Khalifeh H, Hunt IM, Appleby L, Howard LM. Suicide in perinatal and non-perinatal women in contact with psychiatric services: 15-year findings from a UK national inquiry. Lancet Psychiatry. 2016;3:233–42.

12. Gressier F, Guillard V, Cazas O, Falissard B, Glangeaud-Freudenthal NMC, Sutter-Dallay AL. Risk factors for suicide attempt in pregnancy and the post-partum period in women with serious mental illnesses. J Psychiatr Res. 2016;84:284–91.
13. Sit D, Luther J, Buysse D, Dills JL, Eng H, Okun M, Wisner KL. Suicidal ideation in depressed postpartum women: associations with childhood trauma, sleep disturbance and anxiety. J Psychiatr Res. 2015;66–67:95–104.
14. Goldman-Mellor S, Margerison C. Maternal drug-related death and suicide are leading causes of postpartum death in California. Am J Obstetr Gynecol. 2019;221(5):489–505.
15. Grigoriadis S, Wilton AS, Kurdyak PA, et al. Perinatal suicide in Ontario, Canada: a 15-year population-based study. Can Med Assoc J. 2017;189:E1085–92.
16. CA-PAMR Report: Pregnancy-Associated Suicide, 2002–2012; 2019.
17. Oates M. Suicide: the leading cause of maternal death. Br J Psychiatry. 2003;183:279–81.
18. Spinelli M. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: American Psychiatric Press; 2002.
19. Resnick PJ. Murder of the newborn: a psychiatric review of neonaticide. Am J Psychiatry. 1970;126(10):1414–20.
20. Oberman M. A brief history of infanticide and the law. In: Spinelli M, editor. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: American Psychiatric Press; 2002. p. 3–18.
21. Mosely KL. History of infanticide in the western society. Issues Law Med. 1986;I:346–57.
22. http://www.childtrends.org/wp-content/uploads/2014/07/72_Infant_Homicide.pdf
23. https://www150.statcan.gc.ca/n1/pub/85-224-x/2008000/fv3-eng.htm
24. Porter T, Gavin H. Infanticide and neonaticide: a review of 40 years of research literature on incidence and causes. Trauma Violence Abuse. 2010;11(3):99–112.
25. Tanaka CT, Berger W, Valencia AM, Evandro SF, Coutinho ESF, Jean-Louis G, Fontenelle LF, Mendlowicz MV. The worldwide incidence of infanticide. Arch Womens Ment Health. 2017;20(2):249–56.
26. Kendell RE, Chalmers JC, Platz C. Epidemiology of puerperal psychoses. Brit J Psychiatry. 1987;150:662–773.
27. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson G. Postpartum depression: a systematic review of prevalence and incidence. Obstet Gynecol. 106:1071–83.
28. Chaudron LH, Pies RW. The relationship between postpartum psychosis and bipolar disorder: a review. J Clin Psychiatry. 2003;64(11):1284–92.
29. Sichel D. Neurohormonal aspects of postpartum depression and psychosis. In: Spinelli MG, editor. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: American Psychiatric Publishing; 2002. p. 61–80.
30. Bergink V, Burgerhout KM, Weigelt K. Immune system dysregulation in first-onset postpartum psychosis. Biol Psychiatry. 2013;73(10):1000–7.
31. Jones I, Craddock N. Searching for the puerperal trigger: molecular genetic studies of bipolar affective puerperal psychosis. Psychopharmacol Bull. 2007;40(2):115–28.
32. Hamilton J. Postpartum psychiatric illness: a picture puzzle. Philadelphia, PA: University of Pennsylvania Press; 1992.
33. Spinelli M. Proposal to DSM committee for inclusion of postpartum psychosis in the DSM. Arch Womens Ment Health. 2021;24(5):817–82.
34. Denno D. Who is Andrea yates? A short story about insanity. Duke J Gender Law Policy. 2003;10:61–75.
35. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM4). 4th ed. Arlington, VA: American Psychiatric Association; 1994.
36. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM5). 5th ed. Washington, DC: American Psychiatric Association; 2013.
37. Overpeck M. Epidemiology of infanticide. In: Spinelli M, editor. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: American Psychiatric Press; 2002. p. 19–32.

38. Miller LJ. Denial of pregnancy. In: Spinelli MG, editor. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: APPI Press; 2003. p. 81–104.
39. Spinelli M. Neonaticide: a systematic investigation of 17 cases. In: Spinelli M, editor. Infanticide: psychosocial and legal perspectives on mothers who kill. Washington, DC: American Psychiatric Press; 2002. p. 105–18.
40. Janet P. The major symptoms of hysteria: fifteen lectures given to the medical School at Harvard University. London: MacMillan; 1907.
41. Brezinka C, Huter O, Biebl W, Kinzl J. Denial of pregnancy: obstetrical aspects. Psychosom Obstet Gynaecol. 1994;15(1):1–8.
42. Bonnet C. Adoption at birth: prevention against abandonment or neonaticide. Child Abuse Negl. 1993;17(4):501–13.
43. Klier C, Chryssa G, Amon S, Fiala C, Weizmann-Henelius G, Pruitt S, Putkonen H. Is the introduction of anonymous delivery associated with a reduction of high neonaticide rates in Austria. A retrospective study? BJOG. 2012;120(4):428–34.
44. Wilson RF, Klevens J, Williams D, Xu L. Infant homicides within the context of safe haven laws — United States, 2008–2017. MMWR Morb Mortal Wkly Rep. 2020;69:1385–90. https://doi.org/10.15585/mmwr.mm6939a1externalicon.

Perinatal Affective Disorders in Fathers: Anthropological, Neuroendocrine, and Clinical Observations

12

Franco Baldoni and Michele Giannotti

12.1 Some Anthropological Observations on the Role of the Father

In the human species, the discovery of a link between the sexual act and procreation, the awareness of the male's procreative capacities (the fact that the father's semen contributes to the birth of children), and consequently the social enhancement of the father's role are relatively recent acquisitions, dating back to about 4000–5000 years before Christ [1]. Until then, for thousands of years, mothers were considered the only sources of life and creativity. At least this was the opinion of Johann Jakob Bachofen (1815–1878), a highly respected nineteenth-century scholar who influenced Freud himself. A testimony of this is given by the numerous statues of mother goddesses found in the excavations, some of which date back to 23,000–25,000 years ago, such as the Venus of Willendorf, found in Austria. These images represent life, creativity, and nature's ability to reproduce. The female alone was responsible for the birth and growth of the children and therefore represented the family. Only following the awareness of the link between sexual intercourse and procreation in ancient iconography (sculptures, graffiti, paintings) do men begin to be represented alongside mothers as paternal figures. In Egypt, for example, in the Middle Kingdom (2055–1790 BC), a smaller male figure appears next to the mother goddess (*Mut*), representing the father (son-lover, servant, or husband *Amon*, deity of Thebes).

Previously, motherhood is believed to have been linked to natural elements (moon, flower, fruit, stars, rain, and wind), and this seems to have led to a long

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matriarchal or gynecocratic phase in the Paleolithic period (2000,000–8000 BC) [2] in which the feminine principle would dominate.

In primitive cultures, the importance of the mother and the reduced role of the father have remained unequal for thousands of years and are found in the indigenous peoples of the *Trobriand* Islands studied at the beginning of the last century by the famous anthropologist Bronislaw Malinowski (1884–1942). Malinowski, a Pole who was in Australia for a congress in 1914, was considered an enemy of Australia (as a citizen of the Austro-Hungarian Empire) and interned at the beginning of the First World War. However, he was allowed to continue his studies in the Trobriand Islands (Melanesia), an Australian protectorate near present-day New Guinea, where, using his innovative technique of participant observation, Malinowski lived for three years (1915–1918) studying indigenous society life. The Trobriand tribes still had a matrilineal society in which only women, who had economic ceremonial and even magical responsibilities, determined social relations through kinship. The natives still ignored the link between fertilization and birth (the male semen was not thought to determine birth), even if the mating between a man and a woman was considered necessary to prepare the female sexual organ for the entrance of the spirits. Each newborn, in fact, was considered to be the reincarnation of the spirit of a maternal relative who had returned from death by penetrating the maternal body. In these societies, the only males who played an important role in the family were the mother's brothers, who protected the family but who also prevented the sons from sexually uniting with their sisters. Based on these observations, Malinowski took a critical position toward Freudian psychoanalysis, arguing that the Oedipus complex was not universal and found itself absent or modified in some primitive societies. In the Trobriand Islands, in fact, the Oedipus complex seemed to manifest itself with the young male's desire to join with his sister and with an aversion toward the maternal uncle (who prevented the realization of this desire).

Until the last century, therefore, there were still matriarchal organized societies. Obviously, the male was also important in primitive societies; due to his strength and physical constitution, he could establish himself as a more powerful figure than the female and participate in battles and war events, but child-rearing was considered a maternal practice. The etymology of the same word father, from the Sanskrit root *pā*, similar to *Patis* (lord), refers to protecting (Sanskrit *Pâti*) and nurturing, but not to a procreative function or to a biological role [1]. In primitive societies, the only male figure who assumed a role in the management of the children was the mother's brother, the only one who was surely linked to the offspring by a blood bond. This great importance given to the mother is also found in ancient Rome, where, following the tradition of the Lici (an ancient population of Anatolia), children were often given the name of the mother while the older brothers of the mothers acted as protectors of the family and the offspring (avunculate, from the Latin *avunculus*, mother's brother).

While in ancient Greece the (very important) link between fathers and sons was connected above all to the need of fathers' need, to be protected and cared for in old age by the value and power of their children (see in the Iliad and in the Homer's Odyssey) [1], the Romans were decisive in the legal and social recognition of the role of the *paterfamilias* (laws of the XII tables, 451–450 BC). The whole *familia* (a family society made up of wives, children, relatives, and slaves) was subjected to

this, and, overall, the *patria potestas* (which tradition is considered one of the first legislative acts of Romulus) was exercised. The paterfamilias had many rights, among which are the *ius exponendi* (the right to abandon the newborn in a public place), the *ius vendendi* (the right to sell children as slaves), the *ius noxae dandi* (the power to give a child or a slave to others to get rid of the judicial consequences of an offense), and the *ius vitae et necis* (the right of life and death over the child). These rights were maintained for many years. It seems that the emperor Hadrian (76-138 AD), who was cultured, sensitive, and enlightened, was the first to put a limit to this power by deporting a father who had killed his son after the latter had committed adultery with his stepmother.

Over time, therefore, the importance of mother and father in different societies has changed, as we have seen, above all as a result of men becoming aware of their contribution (their seed) to the birth of children and the existence of a blood bond.

12.2 From the Patriarchal Family to the Modern Nuclear Family

During the twentieth century in most societies, especially in Western countries, there has been a gradual transition from families organized in a "patriarchal" way to a form of contemporary family organization that is usually called "nuclear" and is currently the most common.

In the patriarchal family, several related families tended to live close together (sometimes in the same house). The women experienced motherhood and the birth of their children supported by a network of other women (their mother, aunts, cousins, and nurses) who assisted them during pregnancy and in the birth and rearing of the offspring. Each family tended to have many children (up to ten or more), who, as adults, would contribute their work to the family. The children were looked after by the women of the house and played with cousins and friends. The fathers (but also the other men in the family, such as uncles and grandparents) dedicated themselves to work and the family economy and were scarcely involved in the care of their offspring, except to impart rules and educational aspects. Normative power, in fact, was managed by men and was of an authoritarian type: whoever violated it was punished.

With the advent of the industrial revolution, the situation began to change [3]. Many people have moved from rural areas to cities, where there was work, and lived in homes suitable for small families. The drastic reduction in infant mortality, as a consequence of better scientific knowledge and the spread of hygiene practices and greater birth control, led families and the whole of society to invest more attention in childcare while recognizing the emotional and psychological needs of children. At the same time, families began to undergo a transformation, and the number of children decreased, as the possibility of survival increased.

The functions and role of the father in the contemporary nuclear family are the consequence of this transformation. Today the birth rate is constantly decreasing (especially in Western countries), alongside an increase in the average life span and in the number of elderly people. Families that have children (rarely more than one) are almost always made up of only parents and children. The elderly are rarely

housed in the family home, and help from grandparents and other relatives (such as uncles) is increasingly rare. Infants are raised by both parents, with the help of grandparents, if available, and babysitters. Children spend most of their time indoors and are rarely able to play with other children because they are isolated in the house. They already learn at a few months of age to distract themselves with technology (smartphones and tablets) which is also used outside the home (e.g., in a restaurant). Both parents usually work, and it is necessary to take the children to daycare or kindergarten as soon as possible. In this context, life as a couple and the role of parents has changed profoundly.

The contemporary father (or the male partner, in the case of a non-biological father) is increasingly the point of reference of the mother during the pregnancy (sometimes the only one) [4–7]. He must not only deal with practical problems such as guaranteeing a comfortable and safe home and financial support, procuring food and other necessary goods relating to the extra-family environment, protecting the family, and resolving any problems and conflicts; another paternal function of great importance that has long been underestimated but is highlighted by attachment studies is to protect the female partner (we have seen that the etymology of the word father refers to protection) in the periods in which she is most exposed to potentially dangerous conditions and physical and emotional problems. This protective role becomes especially important during the perinatal period and is realized by providing mother with security and emotional support, encouraging her to carry out her maternal function and protecting her from an excess of psychological suffering [8], particularly of an emotional nature. From the perspective of attachment theory, this protective function can be interpreted as a "secure base" effect [4, 9–11], that is, as the result of the atmosphere of security and trust that characterizes an attachment relationship (as is usually the case of a romantic couple). Young fathers today, moreover, are much more involved in the care of their offspring and have to support the mother (without replacing her or competing with her) in functions such as cradling, putting to sleep, dressing, feeding, washing, and changing the newborn. These are the same handling functions that Donald Winnicott [12] described as characteristics of a "good enough mother." In today's family, therefore, the father has acquired greater importance as an attachment figure for the mother and in the care of offspring. It follows that in the perinatal period, both during pregnancy and after the birth of a child, a father (or a male partner) who is too worried, anxious, or depressed, or with problems adjusting to fatherhood, represents a disadvantage for his partner's mental health and a threat to the positive progress of the relationship between mother and child. These issues regarding fatherhood, however, must be addressed while taking into account the attachment functions of the father within a family system and with an ecological perspective that considers the mother-father and child as a triad [4–7].

12.3 Hormonal and Neurobiological Aspects

The significative changes in the functions of the contemporary father are also evidenced by hormonal and neurobiological changes that occur both during pregnancy and when the father cares for a newborn [13–18] highlighting a natural biological predisposition, on an evolutionary basis to childcare, also in the male.

These modifications concern:

1. The decrease of *testosterone* and *estradiol* (which makes fathers more sensitive, less aggressive, and better disposed toward the newborn and the mother) [19–21], particularly if the father is involved in the care of the newborn. Research and meta-analytic studies have confirmed that fathers tend to have lower testosterone levels than other males and that fathers with lower testosterone levels tend to look after their children better [22].
2. Increased level of *oxytocin* (which promotes empathic abilities, social activities, and willingness to play) [23–25]. Giving intranasal oxytocin to the father appears to increase his willingness to play [26].
3. Higher *prolactin* levels (which increases when the infant cries or is more vulnerable and in need of care) [27, 28].
4. Increase of *vasopressin* (which in animals favors the territoriality and protection of the partner). Levels can be related to the interaction between father and child [25]. Experimentally administering vasopressin to the father promotes attention to virtual baby-related avatars and influences the neural and behavioral response to the baby's crying [29].
5. Increase in the level of *cortisol*, a classic stress hormone (which increases in response to the baby's cry by intensifying attention to the newborn but which decreases in skin-to-skin contact) [23, 27, 30]. A higher prenatal level of cortisol, however, is predictive of a lower quality of postnatal parenting of the father [31].

These hormonal changes are accompanied by significant neural changes and responses. The areas and brain circuits activated when caring for a newborn are in fact similar in men and women and concern emotional-empathic and socio-cognitive brain functions [13, 16, 17]. In particular, using modern neuroimaging techniques, the following were described in the father:

1. *Gray matter changes* in the postnatal period (2–16 weeks after birth) [32], particularly in areas sensitive to oxytocin and vasopressin (such as the superior temporal sulcus). These alterations appear to be favored by caring for the baby and have been described both in natural fathers, when caring for the newborn, and in homosexual males who serve as primary caregiver after the birth of their first child [13]. In both cases, an activation of the *superior temporal sulcus* (important for social understanding) has been recorded when the father interacts directly with the newborn, which differentiates them from the mothers, while the response of the *amygdala* (important for the processing of emotions) is similar to that of mothers. The connectivity between the superior temporal sulcus and

the amygdala appears to increase linearly with the time spent caring directly for the newborn.
2. In a meta-analysis of brain responses to newborn crying (350 subjects including 95 fathers) [33], it emerged that fathers showed greater activation of the *right inferior frontal gyrus* (involved in mentalization processes) which stretched to the left *angular gyrus* of the temporal lobe (important for semantic processing). On the contrary, the mothers showed greater activation of the *insula* (at the base of the emotional response) [17].

These important hormonal and neural changes inevitably influence the father's behavior as well as his psychological health.

12.4 Paternal Affective Perinatal Disorders

For decades, research on perinatal affective disorders (particularly postpartum/postnatal depression) has been focused almost exclusively on mothers. The paucity of data on paternal perinatal disorder could be related to different reasons [4, 34, 35]:

(a) The role of the father is often underestimated by health professionals (pediatricians, gynecologists, obstetricians, nurses), who are inclined to consider pregnancy and childbirth as predominantly female issues. This attitude, called *maternal gatekeeping* by the Anglo-Saxons [36, 37], tends to exclude fathers or to legitimize their disengagement and is often favored and shared by mothers.
(b) Fathers show little willingness to be studied and are often reluctant to ask for help and to communicate their problems, especially psychological ones.
(c) Men tend to manifest their difficulties, especially those of an emotional type, in a different way than women, minimizing the depressive aspects [4]. As a result, paternal affective disorders tend to be considered less clinically severe.
(d) Self-report tools designed to assess female depressive symptoms, and which do not take into account gender differences are usually used for screening and diagnosis [34, 35].

Despite these difficulties, recent meta-analysis and systematic reviews have shown that in the perinatal period, fathers frequently manifest affective disorders almost as frequently as mothers. In fact, compared to about 13% of women suffering from perinatal affective disorders, from 8.4% to over 10% of men have the same problem [38–40]. Furthermore, about 50% of males with a partner suffering from postpartum depression are also depressed; in the same way, 50% of mothers with a partner who manifests a perinatal affective disorder suffer from the same malaise. In fact, throughout the perinatal period, the mental states of the father and mother influence each other, and the risk of developing a psychological disorder when the partner is also affected increases [4, 35, 38, 40–43].

Paternal perinatal disorders, such as *paternal perinatal depression* (PPND), are therefore very common, but their diagnosis is difficult. In fact, in men, depressive symptoms tend to manifest themselves in a different way from those of mothers and are frequently accompanied by other disorders (in particular anxiety) which as a whole express the affective suffering of the male [4, 11, 39, 44, 45]; for this reason the definition of *paternal perinatal affective disorders* (PPAD) was proposed for them [4, 35]. The most frequent alterations manifested by men are:

1. *Anxiety disorders* (generalized anxiety disorder, panic attacks, phobias, post-traumatic stress disorder), which affect up to 18% of fathers [39, 46, 47].
2. *Abnormal illness behavior* (somatization disorders, functional medical syndromes, hypochondriacal concerns).
3. *Behavioral problems* (anger attacks, aggression and violence, compulsive physical or sexual activity, extramarital affairs, escaping from home or from work).
4. *Addictions* (smoking, alcohol, drugs) and other addictive disorders (such as those involving gambling or the internet).

These disorders, which can overlap or mask depressive symptoms, generating complex and difficult-to-define clinical pictures, tend to occur more frequently in the third trimester of pregnancy and three to four months after birth, almost three times more often than in the general population [48]. Early screening and prevention of these affective disorders is clearly very important as they have negative consequences not only for the father but for the well-being of the mother and the development of the child, and the risks increase in the case of a preterm birth.

12.5 Diagnosis and Screening of Paternal Perinatal Affective Disorders

Although the relevance of paternal perinatal affective disorder has been widely acknowledged, it is still not clear whether this label could be considered as a clinical diagnosis itself. In general, the diagnosis *of paternal perinatal depression* (PPND) is preferred to paternal *postpartum depression* or *paternal postnatal depression*, since affective alterations in men tend to be observed during the prenatal period. In this regard, the assessment and diagnosis of paternal perinatal affective disorder should take its complex clinical expression into consideration. To date, none of the available screening tools is appropriate to sufficiently capture the multifaceted expression of men's psychological distress during the perinatal period [34, 35]. Both in a clinical setting and in research, these questionnaires were originally developed to detect traditional symptoms of maternal depression and are rarely complemented by clinical interviews. For instance, the *Edinburgh Postnatal Depression Scale* [49] was developed for mothers but has also been validated on the male population [50]. Nevertheless, the authors highlighted different cutoff scores for fathers and mothers [51]. The EPDS is considered suitable for screening paternal affective disorders in the transition to parenthood, but only a minimal part of epidemiological

studies takes the cutoff values indicated for fathers into account, thus providing conflicting data on the distribution of these disorders. Only a few studies available have compared the most widely used questionnaires (e.g., EPDS, CES-D) with those specifically developed for the assessment of depression in men, such as the *Gotland Male Depression Scale* (GMDS) [52]. One of these studies [53] revealed that the EPDS might not be appropriate to evaluate paternal symptoms since 20% of fathers exceed the cutoff only on the GMDS. In fact, it seems that EPDS and GMDS are associated with different risk factors and produce different rates of PPND [54]. In general, fathers may tend to minimize their difficulties, especially those that are an expression of a depressive disorder. For most of them, it could be easier to recognize that they are feeling anxious, stressed, or physically distressed. According to a sociocultural perspective, these manifestations may be more adherent to traditional masculine gender norms [55]. For these reasons, the assessment of perinatal affective disorders should include specific gender-sensitive instruments, which carefully consider the male-type behaviors and signs of discomfort that can mask conventional symptoms of depression [35].

To this purpose, a new screening questionnaire, the *Perinatal Assessment of Paternal Affectivity* (PAPA) [56], has recently been developed. It is a self-report questionnaire that investigates eight dimensions using a 5-points Likert-type scale: anxiety, depression, perceived stress, irritability/anger, relationship problems (couple, family, friends, etc.), abnormal illness behavior (somatizations, functional medical syndromes, hypochondriacal complaints), physiological disturbances (sleep, appetite, or sexual desire disorders), addictive disorders, and behavioral acting out. Specific questions related to the paternal experience and the possible influence of sociocultural factors are also included. It is a user-friendly scale, which is suitable for a number of different contexts and can be used by professionals with different backgrounds, both in public and private care settings.

In general, to accurately investigate the course and severity of paternal perinatal affective symptoms and their impact on the couple's relationship and child development, it is essential to integrate data obtained from validated questionnaires with those from individual and couple's clinical interviews as well as standardized observational procedures.

12.6 Prevention and Treatment of Paternal Perinatal Affective Disorder

Paternal affective disorders require specific prevention programs [48]. Although more attention has been paid to the paternal figure in the last decades, fathers are still only partially involved in birth preparation courses and gynecological visits. Similarly, prospective studies focusing on the role of the father and his contribution to child development starting from the prenatal period are lacking [5]. For an appropriate prevention activity, some specific indications should be taken into account [34] (see Table 12.1):

Table 12.1 Recommendations for prevention of paternal perinatal affective disorders

Recognition of the importance of the father, involving him from the first medical visit to (at least) one year after the birth of the child
Implementation of parenting education and support programs involving both parents
Addressing paternal perinatal affective disorders within a family perspective, given the interrelationship between paternal and maternal symptoms
Informing both mothers and fathers about the difficulties they may experience in the transition to parenthood
Consideration of the possible clinical manifestation of affective disorder in both mothers and fathers
Consideration of the quality of marital adjustment, which can be negatively affected by perinatal affective disorder
Assessment of the different clinical manifestations in fathers that can mask depressive symptoms
Raising awareness among professionals regarding gender differences in the clinical expression of perinatal psychological distress

1. Recognition of the importance of the father, involving him from the first medical checkup to (at least) one year after the birth of the child. It is essential to promote and facilitate the fathers' access to pre- and postnatal healthcare services, in particular to gynecological visits.
2. Implementation of parenting education and support programs involving both mothers and fathers.
3. Addressing paternal perinatal affective disorders within a family perspective. This is of particular importance given the impact of paternal affective disorder on children's development and the interrelationship between paternal and maternal symptoms.
4. Informing both mothers and fathers about the difficulties they may experience in the transition to parenthood. It is essential to offer information on maternal and paternal affective disorders, providing specific indications concerning the services and specialists they can contact for advice or psychological help. The contribution of the partner is crucial to limit the manifestations of perinatal depression [57].
5. Consideration of the possible clinical expression of affective disorder in both mothers and fathers. When one parent is depressed, the partner is at a greater risk of showing a similar symptomatology [38, 41].
6. Consideration of the quality of marital adjustment which can be negatively affected by perinatal affective disorder [43]. Prevention programs should consider this aspect by promoting communication in the couple and helping them to deal with any problems and conflicts [57].
7. Assessment of the different clinical manifestations in fathers that can mask depressive symptoms (anxiety disorders, abnormal illness behavior, acting out, addictive disorders, and other behavioral problems) [35, 53].
8. Raising awareness among professionals regarding gender differences in the clinical expression of perinatal psychological distress. In addition, including fathers

from the first appointments, and promoting their involvement throughout the perinatal period, should constitute a priority for parenting practitioners.

Focusing on the treatment, public and private health services offer individual, family, or group help programs to support fathers during the transition to parenthood [34]. A study carried out in Canada [58], focused on which paternal needs and thoughts were related to perinatal depression, found that fathers prefer individual support and home intervention rather than group therapy. Specifically, home support interventions seem to have a positive influence on their parenting abilities and consequently on the whole family. This could be particularly useful when a child manifests behavioral difficulty that can generate negative effects in their parents such as frustration, anger, and guilt. Parents should be supported in attributing an appropriate meaning to children's emotional reactions and behaviors. For this purpose, parent training techniques that integrate psychodynamic and/or cognitive-behavioral interventions with a psychoeducational approach have proved to be particularly effective [4, 59]. In this scenario, attachment studies have shown that contradicting and inconsistent parenting behaviors increase the possibility of children engaging in maladaptive behaviors in order to cope with an unpredictable parental environment. By contrast, when parents show optimal responsiveness and sensitivity, children tend to manifest security and confidence in facing developmental challenges, perceiving the attachment figure as a source of protection (secure base effect). Thus, promoting parental sensitivity (i.e., the ability to perceive children's needs and respond adequately to them) and mentalization (i.e., the ability to think about states of mind in the self and the child) constitutes two crucial aspects of parenting support programs. Although more studies are needed, video-feedback techniques can be considered an appropriate method to promote the development of more secure attachment bonds [4, 34, 60]. These methods, which are grounded in attachment theory and social learning theory as well as in infant research and developmental psychology, are intended to promote parental sensitivity and mentalization skills, adopting a triadic perspective. Audiovisual recording is particularly useful in order to examine the interactive processes which occur within the family context.

Moreover, some studies suggest the utility of mindfulness interventions for couples, such as the *Mindfulness-Based Relationship Enhancement* (MBRE) in reducing parental worries, anxious feelings, and negative emotions associated with child-rearing [61].

In conclusion, the treatment of paternal perinatal affective disorders should take into account not only individual factors but also relational and sociocultural problems that can increase personal vulnerability. It is important to implement specific preventive programs that consider fathers throughout the perinatal period, involving them from the first gynecological visit. At-risk fathers require a more in-depth diagnostic assessment and a personalized treatment. Psychological interventions should be tailored on specific paternal needs, considering the possible expression of male-type depressive equivalents [62]. Evidence as to the effectiveness of different psychotherapeutic approaches (CBT, psychodynamic, systemic family treatment, psychoeducational) and treatment programs for perinatal affective disorders are still scarce; however, the first wave of studies has produced promising results.

References

1. Quilici M. Storia della paternità. Dal pater familias al mammo. Roma: Fazi editore; 2010.
2. Bachofen JJ. (1881) Das Mutterrecht. Trad It. Il matriarcato. Ricerca sulla ginecocrazia nel mondo antico nei suoi aspetti religiosi e giuridici. Torino: Giulio Einaudi editore, Nuova PBE, 2016.
3. Aries P. L'enfant et la vie familiale sous l'ancien régime. Trad. It. Padri e figli nell'Europa medievale e moderna, Bari: Laterza, 1994. 1960.
4. Baldoni F. I disturbi affettivi nei padri. In: Grussu P, Bramante A, editors. Manuale di Psicopatologia Perinatale. Erickson: Trento; 2016. p. 443–86.
5. Cabrera NJ, Volling BL, Barr R. Fathers are parents, too! Widening the lens on the parenting for children's development. Child Dev Perspect. 2018;12(3):152–7.
6. Cabrera NJ, Volling BL. Moving research on fathering and children's development forward: priorities and recommendations for the future. In B. L. Volling & N. J. Cabrera (Eds.), advancing research and measurement on fathering and children's development. Monogr Soc Res Child Dev. 2019;84(1):107–17.
7. Ahnert L, Schoppe-Sullivan SJ. Fathers from an attachment perspective. Attach Hum Dev. 2020;22(1):1–3.
8. Kaitz M, Katzir D. Temporal changes in the affective experience of new fathers and their spouses. Infant Ment Health J. 2004;25(6):540–55.
9. Bowlby J. A secure base: parent-child attachment and healthy human development. London: Routledge; 1988.
10. Whiffen V, Johnson S. An attachment theory framework for the treatment of childbearing depression. Clin Psychol Sci Pract. 1998;5(4):478–93.
11. Baldoni F. Attachment, danger and role of the father in family life span. Transylvanian J Psychol (EPSZ). 2010;4:375–402.
12. Winnicott DW. Letter to Roger Money-Kyrle, 27th November in The Spontaneous Gesture: Selected Letters of D.W. Winnicott. London: Karnac Books (1952); 1987. p. 38–43.
13. Abraham E, Hendler T, Shapira-Lichter I, Kanat-Maymone Y, Zagoory-Sharona O, Feldman R. Father's brain is sensitive to childcare experiences. Proc Natl Acad Sci U S A. 2014;111(27):9792–7.
14. Swain JE, Kim P, Spicer J, Ho SS, Dayton CJ, Elmadih A, Abel KM. Approaching the biology of human parental attachment: brain imaging, oxytocin and coordinated assessments of mothers and fathers. Brain Res. 2014;1580:78–101.
15. Fisher D, Khashu M, Adama EA, Feeley N, Garfield CF, Ireland J, Koliuli F, Lindberg B, Nørgaard B, Provenzi L, Thompson-Salo F, van Teijlingen E. Fathers in neonatal units: improving infant health by supporting the baby-father bond and mother-father coparenting. J Neonatal Nurs. 2018;24:306–12.
16. Feldman R, Braun K, Champagne FA. The neural mechanisms and consequences of paternal caregiving. Neuroscience. 2019;20:205–24.
17. Bakermans-Kranenburg MJ, Lotz A, Alyousefi-van Dijk K, van IJzendoorn M. Birth of a father: fathering in the first 1,000 days. Child Dev Perspect. 2019;13(4):247–53.
18. Baldoni F. Essere padre di un bambino nato pretermine. Psichiatria Psicoterapia. 2020;39(1):225–38.
19. Weisman O, Zagoory-Sharon O, Feldman R. Oxytocin administration, salivary testosterone, and father–infant social behaviour. Prog Neuropsychopharmacol Biol Psychiatry. 2014;49(3):47–52.
20. Gettler LT, McDade TW, Agustin SS, Feranil AB, Kuzawa CW. Longitudinal perspectives on fathers' residence status, time allocation, and testosterone in the Philippines. Adapt Hum Behav Physiol. 2015;1(2):124–49.
21. Saxbe DE, Edelstein RS, Lyden HM, Wardecker BM, Chopik WJ, Moors AC. Fathers' decline in testosterone and synchrony with partner testosterone during pregnancy predicts greater postpartum relationship investment. Horm Behav. 2017;90:39–47.

22. Meijer WM, Van IJzendoorn MH, Bakermans-Kranenburg MJ. Challenging the challenge hypothesis on testosterone in fathers: A meta-analysis. Psychoneuroendocrinology. 2019;110:104435.
23. Cong X, Ludington-Hoe SM, Hussain N, Cusson RM, Walsh S, Vazquez V, Briere C, Vittner D. Parental oxytocin responses during skin-to-skin contact in preterm infants. Early Hum Dev. 2015;91(7):401–6.
24. Abraham E, Hendler T, Zagoory-Sharon O, Feldman R. Network integrity of the parental brain in infancy supports the development of children's social competencies. Soc Cogn Affect Neurosci. 2016;11(11):1707–18.
25. Abraham E, Feldman R. The neurobiology of human allomaternal care: implications for fathering, coparenting, and children's social development. Physiol Behav. 2018;193:25–34.
26. Naber FBA, Van IJzendoorn MH, Deschamps P, Van Engeland H, Bakermans-Kranenburg MJ. Intranasal oxytocin increases fathers' observed responsiveness during play with their children: a double-blind within-subject experiment. Psychoneuroendocrinology. 2010;35:1583–6.
27. Fleming AS, Corter C, Stallings J, Steiner M. Testosterone and prolactin are associated with emotional responses to infant cries in new fathers. Horm Behav. 2002;42(4):399–413.
28. Gettler LT. Applying socioendocrinology to evolutionary models: fatherhood and physiology. Evol Anthropol. 2014;23(4):146–60.
29. Cohen-Bendahan CC, Beijers R, Van Doornen LJ, de Weerth C. Explicit and implicit caregiving interests in expectant fathers: do endogenous and exogenous oxytocin and vasopressin matter? Infant Behav Dev. 2015;41:26–37.
30. Kuo PX, Braungart-Rieker JM, Burke Lefever J, Sarma MS, O'Neill M, Gettler LT. Fathers' cortisol and testosterone in the days around infants' births predict later paternal involvement. Horm Behav. 2018;106:28–34.
31. Bos PA, Hechler C, Beijers R, Shinohara K, Esposito G, de Weerth C. Prenatal and postnatal cortisol and testosterone are related to parental caregiving quality in fathers, but not in mothers. Psychoneuroendocrinology. 2018;97:94–103.
32. Kim P, Rigo P, Mayes LC, Feldman R, Leckman JF, Swain JE. Neural plasticity in fathers of human infants. Soc Neurosci. 2014;9:522–35.
33. Witteman J, Van IJzendoorn MH, Rilling JK, Bos PA, Schiller NO, Bakermans-Kranenburg MJ. Towards a neural model of infant cry perception. Neurosci Biobehav Rev. 2019;99:23–32.
34. Baldoni F, Giannotti M. I disturbi affettivi perinatali paterni: valutazione, prevenzione e trattamento. In: Imbasciati A, Cena L, editors. Psicologia Clinica Perinatale. Neuroscienze e psicoanalisi. Milano: Franco Angeli; 2017. p. 218–39.
35. Baldoni F, Giannotti M. Perinatal distress in fathers: toward a gender-based screening of paternal perinatal depressive and affective disorders. Front Psychol. 2020;11:1–5.
36. Allen S, Hawkins A. Maternal gatekeeping: mothers' beliefs and behaviors that inhibit greater father involvement in family work. J Marriage Fam. 1999;61(1):199–212.
37. Gaunt R. Maternal gatekeeping: antecedents and consequences. J Fam Issues. 2008;29:373–95.
38. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression. JAMA. 2010;303(19):1961–9.
39. Leach LS, Poyser C, Cooklin AR, Giallo R. Prevalence and course of anxiety disorders (and symptom levels) in men across the perinatal period: a systematic review. J Affect Disord. 2016;190:675–86.
40. Cameron EE, Sedov ID, Tomfohr-Madsen LM. Prevalence of paternal depression in pregnancy and the postpartum: an updated meta-analysis. J Affect Disord. 2016;206:189–203.
41. Baldoni F, Baldaro B, Benassi M. Affective disorders and illness behaviour in perinatal period: correlations between fathers and mothers. Child Devel Disabil. 2009;36(3):25–44.
42. Baldoni F, Agostini F, editors. Proceedings international congress fathers and perinatality. attachment, adaptation and psychopathology (Bologna, May 10 2013). Bologna: Department of Psychology, University of Bologna (CD-ROM); 2013.
43. Baldoni F, Giannotti M, Casu G, Luperini V, Spelzini F. A dyadic study on perceived stress and couple adjustment during pregnancy: the mediating role of depressive symptoms. J Fam Issues. 2020;41(11):1935–55.

44. Baldoni F, Ceccarelli L. La depressione perinatale paterna. Una rassegna della ricerca clinica ed empirica. Infanzia e Adolescenza. 2010;9(2):79–92.
45. Philpott LF, Savage E, Leahy-Warren P, FitzGerald S. Paternal perinatal depression: a narrative review. Int J Mens Com Soc Health. 2020;3:e1–e15.46.
46. Matthey S, Barnett B, Howie P, Kavanagh DJ. Diagnosing postpartum depression in mothers and fathers: whatever happened to anxiety? J Affect Disord. 2003;74(2):139–47.
47. Bradley R, Slade P. A review of mental health problems in fathers following the birth of a child. J Reprod Infant Psychol. 2011;29(1):19–42.
48. Fletcher RJ, Garfield CF, Matthey S. Fathers' perinatal mental health. In: Milgrom J, e Gemmil A.W., editors. Identifying perinatal depression and anxiety: evidence-based practice in screening, psychosocial assessment, and management. Oxford: Wiley &Sons; 2015. p. 165–76.
49. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150(6):782–6.
50. Matthey S, Barnett B, Kavanagh DJ, Howie P. Validation of the Edinburgh postnatal depression scale for men, and comparison of item endorsement with their partners. J Affect Disord. 2001;64(2–3):175–84.
51. Loscalzo Y, Giannini M, Contena B, Gori A, Benvenuti P. The Edinburgh postnatal depression scale for fathers: a contribution to the validation for an Italian sample. Gen Hosp Psychiatry. 2015;37(3):251–6.
52. Zierau F, Bille A, Rutz W, Bech P. The Gotland male depression scale: a validity study in patients with alcohol use disorder. Nord J Psychiatry. 2002;56(4):265–71.
53. Madsen SA, Juhl T. Paternal depression in the postnatal period assessed with traditional and male depression scales. J Men's Health Gend. 2007;4(1):26–31.
54. Carlberg M, Edhborg M, Lindberg L. Paternal perinatal depression assessed by the Edinburgh postnatal depression scale and the Gotland male depression scale: prevalence and possible risk factors. Am J Mens Health. 2018;12(4):720–9.
55. Schumacher M, Zubaran C, White G. Bringing birth-related paternal depression to the fore. Women Birth. 2008;21(2):65–70.
56. Baldoni F, Matthey S, Agostini F, Schimmenti A, Caretti V. Perinatal assessment of paternal affectivity (PAPA): preliminary report on a new screening tool. Infant Ment Health J. 2016;37(Suppl 1):132–3.
57. Pilkington PD, Milne LC, Cairns KE, Lewis J, Whelan TA. Modifiable partner factors associated with perinatal depression and anxiety: a systematic review and meta-analysis. J Affect Disord. 2015;178:165–80.
58. Letourneau N, Duffett-Leger L, Dennis CL, Stewart M, Tryphonopoulos PD. Identifying the support needs of fathers affected by post-partum depression: a pilot study. J Psychiatr Ment Health Nurs. 2011;18(1):41–7.
59. Fletcher R, Freeman E, Matthey S. The impact of behavioural parent training on father's parenting: a meta-analysis of the triple P-positive parenting program. Fathering. 2011;9(3)
60. Juffer F, Bakermans-Kranenburg MJ, Van IJzendoorn MH. Attachment-based interventions. In Farnfield S, Holmes P. (Eds.), The Routledge Handbook of Attachment: Implications and interventions, London: Routledge. 2014, pp. 83–103.
61. Vieten C, Astin J. Effects of a mindfulness-based intervention during pregnancy on prenatal stress and mood: results of a pilot study. Arch Womens Ment Health. 2008;11(1):67–74.
62. Mangialavori S, Giannotti M, Cacioppo M, Spelzini F, Baldoni F. Screening for early signs of paternal perinatal affective disorder in expectant fathers: a cluster analysis approach. J Personal Med. 2021;11(10):1–15.

Italian Experience of Mother-Infant Bonding Disorders

13

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13.1 Introduction

The maternal emotional response, in human beings as in all mammals, is one of the strongest and most enduring of all emotions and leads to the most powerful bond between two living creatures. It is an almost universal expectation that mothers will love their infants. But the occasional failure of this emotional response became obvious at an early stage in medical literature. First, it became known that many infants were savagely murdered by their mothers, who had been impregnated out of wedlock and concealed their pregnancy and birth; this was a huge public health problem in the eighteenth and nineteenth centuries. Then it was noticed that a few infants, who survived the early days, were deliberately starved to death. Other children were subjected to brutal ill-treatment, day after day. These observations were drawn together in a classic article, written in 1860 by the French pathologist, Ambroise Tardieu [1], which gave details of 18 infants and children who died from beatings or starvation. He also described a new atrocity—the torture of a child by its parents: Adeline Defert was reared, up to the age of 8, by her grandparents but then had to be returned to her mother and father; they whipped her every day, hung up her up by her thumbs and beat her with a nailed plank, burnt her with hot coals and

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bathed her wounds in nitric acid and even raped her with a baton. Surveying this catalogue of maternal persecution, he commented:

> *When we face the fact that the tormenters of these poor defenceless beings are the very mothers that gave them life, we are confronted with one of the most appalling problems that can disturb the soul of a moralist, or the conscience of justice. This ferocious brutality can only be explained by a sort of madness.*

Only a few French colleagues showed any interest in his observations, which failed to cross the language barrier into the English and Italian literature. It was fully 100 years before "the battered baby syndrome" [2] grabbed the attention of paediatricians and became one of the main concerns of the world community.

We can identify some of deviant personality traits that might explain such horrors—traits of cruelty, or irritability aggravated by sleep deprivation and/or depression; but another "form of madness" had already been reported by Tardieu's predecessor, Orfila [3]:

> *Élisabeth Prat, Mrs Sarrat, an irascible and violent woman, was accused of assaulting her 3-year-old, Émilie, who died 2 days later. Mme Sarrat had cursed the birth of her daughter, gave her over to a wet-nurse and rarely visited her. When it was necessary to take on her care, she hard-heartedly made her life miserable. She secluded her in a small room at the top of the house, and ignored her cries when she was hungry, thirsty or ill. The neighbours became accustomed to the toddler's continual distress, but, one morning they heard the dull sound of a body hitting the floor, followed by heart-breaking screams, and then other blows. Mme Sarrat managed to get her buried early, but the neighbours alerted the authorities; the body was exhumed, and necropsy showed multiple bruising and fractures of her skull caused by her mother.*

Nowadays we would recognize that this child had been emotionally rejected by her mother.

13.2 The Syndrome

Emotional rejection is marked by a triad of symptoms:

- Instead of the overwhelming love that most mothers feel, the baby evokes dislike or even hatred (**aversion**). In addition, there is often a curious detachment from the infant, who seems to belong to someone else, not the mother (**estrangement**).
- There is a desire to escape from the incessant toil and burden of childcare. The mother feels better when away from the baby, avoids its company as much as possible or, when holding the infant, avoids looking at it. She may take active steps to escape, by running away, transferring care to a relative or pressing for its fostering or adoption (**avoidance of care**). The desire to escape reaches its acme when the mother considers permanent relinquishment.
- If rejection is severe, a characteristic symptom is the desire for the disappearance of the baby—rarely by theft, more commonly for the extraordinary symptom of the wish for cot death (**wish for the loss of the baby**). This surprisingly common

wish is remarkable because, of all the ways in which an infant can be lost—miscarriage, late termination, foetal death in utero, stillbirth, neonatal death and sudden infant death syndrome—cot death ("crib death" in the USA) is perhaps the most severe. The mother is usually fully bonded with the infant and absorbed in the relationship. There is no warning or preparation, and the death is followed by a forensic investigation. The desire to be rid of the baby altogether testifies to the strength of maternal rejection.

In addition to this triad, there is mounting **anger** if the mother is compelled to attend to the infant's demands. This is dangerous, and can lead to maltreatment, especially by shaking the baby. It can lead to filicide. Explosions of rage are the most frequent cause of maltreatment associated with emotional rejection. Although strongly related to rejection, pathological anger should be regarded as a different morbid, clinical phenomenon and come under separate scrutiny. Parents are frequently angry with their children, when they are disobedient or act in a dangerous or aggressive manner, or when the mother is under excessive stress, but anger with an infant is more unusual. Because of the risk of child maltreatment, rejection with pathological anger is an emergency.

13.3 Two Illustrative Cases

Luisa was first referred to a perinatal outpatient unit in March 2010, 13 days after her first delivery because of a suspected major depressive disorder. Her family of origin consisted of her father (a man with a heart condition and severely hypochondriac), her mother (diagnosed with myopathy, diabetes and chronic anxiety) and an older sister. She married her first husband when she was very young, just to escape from an atmosphere characterized by strong apprehension and little chance of pleasure. When she met her colleague Mario, she gradually fell in love and decided to get divorced. She began this new relationship and was satisfied. Apart from a few episodes of anxiety and traits of emotional dependency, she had never experienced major psychiatric difficulties, only a sense of fatigue due to the highly conflictual relationship with elderly and controlling parents.

She had wanted to be a mother and, after many failed attempts, opted for medically assisted reproduction. It took her 6 years and eight rounds—five of micro-assisted fertilization and three of in vitro fertilization. She finally became pregnant, and, even though she lost her occasional job, her lifestyle was not affected since all her happiness focused on her achievement. She was aware that such massive hormonal stimulation might involve mood swings, but she described the period as peaceful and spent in a positive state of mind. Only the patient's mother-in-law expressed concerns about a sort of immaturity that would impact the mother's capability to look after the newborn.

During the assessment session, she appeared anxious, cried a lot, complained about insomnia and asked for information about the prescription of lorazepam that she had been given for an "incongruous affective reaction." She immediately

declared that she was unable to take care of the baby and that his large size, not predicted, made the delivery traumatic: she had been hospitalized 11 days after the expected date and received a gel induction which failed to initiate labour. Doctors decided to break her waters and to administrate oxytocin, although Luisa insistently asked for a Caesarean birth, strongly opposed by the obstetric team. The expulsive phase was rapid but dominated by impotence, inability and anger; the obstetricians finally chose an assisted birth with vacuum cup. It took several manoeuvres for her son Federico to be born: Luisa suffered a heavy haemorrhage and severe lacerations. She also had a fever and for this reason the baby was shown to her and immediately taken to the nursery.

She saw the baby on the following day, and the midwives urged her to keep him in her room, not complying with her requests to keep him in the nursery. During the first few days, her attention was focused exclusively on her physical condition, and she calmed down only when she felt safe. Once she was back home, she immediately realized that something was wrong.

> *I keep telling myself: What do I do now? He depends on me only. I need somebody to take care of him. I am sure normal mothers don't ask to take care of their baby, what kind of mother am I?*

In April, the psychologist recorded a partial improvement in her self-care, and there was a new desire to spend time with friends, with her husband, but everything took place in the absence of the baby. She timidly told the psychologist that the thought of not wanting the child was the one that scared her most, her husband minimized the problem and the mother-in-law accused her of being a bad parent. From the clinician's point of view, it was very difficult to attribute all her problems to depression because Luisa was lively with friends, responded emotionally and affectively to them and to her husband and felt some kind of relief when she was with them; this was the reason why her mother-in-law called her spoiled. She thought she was overprotected and an immature girl with a baby and that, after 2 months, it was impossible that she wasn't able to love her son, since she had wanted him so much. In May she deteriorated: she explicitly regretted having had her son and confessed in tears that she felt hatred and anger, as if Federico was a stranger with too many needs. Bath time was the worst moment: all that fragility and dependency exhausted her. Thinking about all the people she had met, whose attempts at procreation had failed, she felt a monster.

> *I feel a constant sense of agitation, I do not accept Federico and I blame him for my state of mind and for the fact that everything is going wrong. I delegate everything that concerns him with a thousand of excuses. I constantly have memories of my time before the birth, when I was younger. I keep telling myself that I shouldn't have had a child and it's a deeply rooted thought. I don't want what this new life entails. I am afraid of ruining the relationship with my husband and my family, so I do important stuff for Federico reluctantly: I feel very selfish towards him and don't even want to spend money on him. I don't feel like a good mother and I'm so afraid: when I go out I can't wait to escape. This afternoon I was alone with him and I had to cuddle him, it was a tragedy, luckily he slept all afternoon. Today Federico is three months old, I should be happy and fill him with kisses and instead I cry and he cries too, he is always nervous with me while when my mother-in-law touches him, he calms down: he can feel I don't want him, I'm sure.*

The child contracted a urinary tract infection that required a 1-week hospitalization: she was forced to stay with him 24 h a day, and, when she asked to be replaced by her husband, the nurses told her that it was the first time that a mother had refused to stay by her child. When they were discharged, she phoned her psychologist and asked for an urgent appointment. She arrived with the pram and a bag containing baby gear and, crying desperately, said she wanted to leave him, that the week had been a nightmare and the comparison with other mothers was devastating. She ran away and, at that point, was committed to the psychiatric ward and put on involuntary psychiatric hold: she was given an antidepressant agent (escitalopram oxalate, 10 mg/day). As the days went by, she showed a minimal improvement: family members were summoned and were explained that the reason behind her situation was not a lack of will or traits of selfishness and wickedness but to disorder. The psychologist asked to see her with her baby, in order to monitor their interaction. To overcome his avoidant behaviour, they tried changing his diaper together, with basic interaction and play, trying to attribute a meaning to his expressions and to her feelings. Anxiety and anger decreased and she slowly and steadily improved. When discharged, she tried to reproduce at home what she did in the clinic and felt that the child considered her more. After 3 months of psychotherapy, she first realized she had a bond with her baby when she felt jealous towards her mother-in-law; perhaps, love was starting to bloom. Antidepressant therapy could be discontinued in December 2010 and psychological sessions ended in June 2011.

After a miscarriage and the death of her father, in the summer of 2018, Luisa became pregnant again and decided to meet with her psychologist as suggested by her gynaecologist who also recommended a Caesarean section. This time, when she first saw the baby, she felt quite good. She needed less family support and everything proceeded serenely until the day she returned home: entering the house with Alice in her arms, Luisa was assailed by the well-known feeling of having made a mistake. She became distraught, did not want to spend time with the newborn and had moments in which she thought that the baby had ruined everything, especially her relationship with Federico and other family members; this time, they seemed unwilling to support her.

She saw her psychologist, who told her about bonding disorders and explained that this was the name that could also be given to her experience in 2010. Completing the Postpartum Bonding Questionnaire was a very intense experience: scrolling through the sentences, she recognized the nature of the thoughts and feelings that she was experiencing, and allowing her to name them, she felt not alone. Although less severe with this second child, her symptoms indicated a serious disturbance in the mother-child relationship. A mild pharmacological support was offered and psychotherapy alternated between individual sessions and sessions with the baby with the aim of favouring opportunities of progressive greater connection to Alice and trust in her maternal identity. She received home visits, and, while addressing some issues that weighed her down before conception, they interacted with the baby. The recovery was more rapid and less painful and the accurate diagnosis allowed her to receive appropriate help.

In summary, her illness in 2010 started with anxiety and progressed to rejection, with regrets about the pregnancy, hatred of the baby, anger, running away and other

attempts to escape from infant care. In 2018 she had a milder recurrence, and measurement of severity by the PBQ was 59.

Fabiola is an only child, the "daughter of Mulino Bianco's Family." When she was 20 years old, her father left "overnight" having fallen in love with a much younger woman. Immediately afterwards, her mother stopped eating and was admitted to a psychiatry unit with depression. Fabiola also became very anxious and depressed for a few months. After some difficult years, they recovered, and Fabiola started working in the fashion field where she met Paolo, who became her husband after about 6 years of engagement.

At the age of 35, they decided to try to have a child, more desired by Paolo than by Fabiola who still felt too much the daughter attached to her mother. After 3 years' failure to conceive, they decided to go to a medically assisted procreation centre "because Paolo wanted a family more than anything else in the world." Fabiola felt sad about the failure of her reproductive function, rather than not having a child. Three months later, with second intrauterine insemination, she became pregnant. "They were twins, I lost one in the second month." She immediately became unwell and began to think that the child would upset her life and her marriage. She told the family that she did not want the pregnancy and the baby. "I don't want this baby any more, I want a voluntary termination of pregnancy." The family could not understand and were angry with her. She went to the hospital for the termination of pregnancy, but she was unable to do it because "I was afraid of losing my husband." The pregnancy proceeded well from the physical point of view but emotionally she felt anaesthetized. Elisa was born in August with a planned Caesarean section: "I didn't want to suffer, and I was afraid of pain." After the birth, "I had absolutely rejected her from the first moment I saw her. I didn't touch or pick her up for about a month, and always kept her at a distance." She immediately decided not to breastfeed because she could not tolerate the physical contact. Her mother, husband and a babysitter, at home day and night, did everything with the baby. "I was very sad because I didn't feel love for her." She found it difficult to remain at home with the child and "sometimes I went out and stayed in the car nearby crying." Rather than putting the baby to sleep in the evening, she preferred to clean all the windows. The baby's crying was "a tragedy" for Fabiola, starting from the first night.

When the baby was already 1 year old, she presented for therapy. "I've got a crying anxiety ... my anger comes up and I lose control." When Elisa cries, she did not know what to do and she cried with her or screamed at her to stop. "She doesn't cry, she screams, it seems like she has a megaphone in her throat. It affects me in the head, and I start saying horrible things to her, punch the wall and would like to break something." She sees the fear in the child's eyes, so she locks her alone in another room "to protect her, not to punish her." She feels guilty about the effects on Elisa but said "It is Elisa who is destroying my life and my marriage." Because of Elisa's crying, they never took her anywhere; they never take her to a restaurant or shopping because "I'm afraid that she can cry and I will go crazy." "She is not the child that I wanted: she is a pet that has sneaked into my couple's life. I would have a child more manageable, quiet as a doll. But she always cries, screams and she is not like me, she is ugly ... her hair looks like the toilet brush!." When the baby is about 3 months old,

she started having "bad and scary" thoughts—that if she disappeared, everyone would be happier, including the baby for whom she felt nothing and who, consequently, does not recognize her as a mother. She expressed the wish that "someone will run over me, like the subway because someone pushes me. Don't commit suicide but die from an accident or for a heart attack." These thoughts alternate with thoughts about Elisa "who made me do it! I wanted another family to take her away and raise her." On the one hand, this thought made her feel "free and relieved"; on the other hand, she frightened her because she was afraid of losing her husband. Fabiola says "I don't want to be with the baby, I look her in the face, and I think I won't be able to do anything. I thought it would be natural and easy to love a child, but I don't like anything anymore, neither with her nor without her." She was worried about the conflict in her marital relationship. Her husband was very angry with her for considering termination of the pregnancy. "He would like me to want to be with the baby, instead I would just want to be with him, as we did before."

Fabiola began psychotherapy when Elisa was 1 year old, and she had been under treatment with venlafaxine antidepressant therapy for 4 months, with little improvement. After some clinical sessions and the administration of the Postpartum Bonding Questionnaire (PBQ), where Fabiola obtained a score of 47, a diagnosis of bonding disorder is made, and a clinical work on the dyad is set up. Knowing the correct diagnosis made Fabiola's clinical situation much better.

A pharmacological therapy was offered for the high irritability. She has made individual psychotherapy sessions with some session with the husband and some with the baby for favouring the mother-baby bonding. The diagnosis of bonding disorder allowed her a rapid recovery, and the work on the couple allowed Fabiola and Paolo to elaborate the anger felt in pregnancy and in the first year of their child's life.

In summary, this was an unwanted pregnancy, and emotional rejection began at birth, with a lack of love, almost total avoidance of the baby and its care and wish for its disappearance. She had the unusual symptom of the wish for her own death to escape the baby, which has occasionally been seen in these mothers [4] (Brockington, 2017, pages 38–39). Pathological anger was a prominent symptom, and she admitted to screaming at the baby and punching the wall. This infant was in danger throughout the 12 months before her referral and initiation of effective treatment.

13.4 Discussion

The Role of Depression. In the clinic, it is obvious that rejecting mothers are almost always depressed. The association with depression is beyond doubt, but the direction of causation is uncertain. In some cases, there are indications that it was the primary disorder, complicated by a failure to bond:

- Some mothers develop a normal bond but lose it when they became depressed.
- Some mothers' response to antidepressant treatment, such as electro-convulsive therapy, includes the prompt development of a normal infant relationship.
- In a few mothers, depression has a psychotic or bipolar quality [4]. (Brockington, 2017, pages 97–99).

Failure to develop warm maternal feelings is a potent cause of guilt, shame and severe loss of self-respect, all of which lead to depression. In a few mothers, effective treatment of the bonding problem has dramatically cured treatment-resistant depression, suggesting that it was the primary cause [5]. The close association with depression has been a reason why many "perinatal" psychiatrists have discounted the separate existence of this syndrome and added it to the list of symptoms in "postnatal depression." This is a mistake for a number of reasons:

- Depression is a pathological mood state, with the accompaniment of depressive cognitions, such as guilt, hopelessness and suicidal ideas. Moods are cerebral functions quite different from relationships.
- A few rejecting mothers are not depressed. In those that are, the degree and timing of depression may not match that of infant rejection—Luisa is an example.
- The treatment of the two disorders is different.
- It is unfair on depressed mothers (most of whom love their infants), already suffering from the stigma of mental illness, to have the additional stigma of bonding disorders.
- This failure to recognize a distinct syndrome, and to focus on it, has put infants at risk and depressed research.

Recognition of this syndrome, independent of depression, and its correct diagnosis is pivotal to recovery and in clinical decision-making. It is interesting that in both these cases, the diagnosis alone was helpful to Luisa and Fabiola.

Management. It is important to restate the precautions set out in *Motherhood and Mental Health* because they have been ignored. The first step is to decide whether or not the mother wants to overcome the problem (because transfer of care is an alternative). If, as in most cases, she opts for treatment, mother and infant are not separated, and treatment is focused on the relationship. But she must always be supported, must be excused the most irksome duties (e.g. calming a screaming infant) and, if there is evidence of anger, must never left alone with the baby. Secondly, it is wise thoroughly to treat depression. Thirdly, treatment is directed to the relationship, for example, with play therapy and baby massage [6].

Research. This description of the syndrome, set out above, has an important weakness: it is subjective, based on the mother's own statements. It needs to be confirmed and complemented by systematic observations of the behaviour of rejecting mothers, compared with normal, anxious and depressed mothers. Such a study should quantify a wide range of other behaviours, such as eye gaze, delay in responding to infant demands, smiling and the mother's facial expression and time spent cuddling and talking to the infant [4] (Brockington 2017, page 140).

In order to prevent this disorder, which is so stressful to mothers and dangerous to infants, it is necessary to clarify its causes. So far, we only have clues from clinical experience, suggesting the paramount importance of depression, and probable role of unwanted pregnancy, and very difficult infants, who scream for hours and are hard to soothe. It will be necessary to conduct controlled cohort studies, following a high-risk group from pregnancy to the first postpartum year and beyond; ideally

the data should be obtained from self-rating, interviews and some method of observation—an expensive study [4].

In this century, however, a new method of studying relationships has become available—f-NMR or other neuroscientific tools revealing the sequence of brain blood flow ("the parental brain"). This is applied to the response to images (photographs or videos) of the infant playing, smiling or crying. These techniques have shown, in normal and depressed mothers, a response that begins with recognition, followed by a warm emotional response and finally the preliminaries of action. Only one study has so far attempted to include "maternal sensitivity" in such studies [7]. Since rejecting mothers often recover completely, either spontaneously or with treatment, it would be possible to compare the emotional response before and after recovery. This requires a link between researchers on "the parental brain" and clinicians capable to diagnosing maternal rejection. It has not so far been achieved; but it would be possible in Lombardy. This investigation has the potential for establishing mother-infant bonding disorders as a brain disease, not just a disputed clinical syndrome.

13.5 Resistance to the Recognition of Maternal Rejection

Some clinicians still do not recognize child rejection as a phenomenon worthy of special attention. This resistance parallels the long delay in recognizing child abuse. But there are indications that bonding disorders are now arousing interest around the world. Clinical studies have shown that they affect mothers of many ethnic groups—Afro-Caribbean, Caucasian, Hindu, Japanese, Mauri, Pakistani and Sikh. The early studies were from Germany and France, but the Japanese are now taking a lead, with research from at least seven different centres [8]. Recent publications have come from ten other nations—Australia [9], Brazil [10], India [11], Iran [12], Italy [13], Malaysia [14], Norway [15], Saudi Arabia [16], Spain [17] and the USA [18]. At the Stafford International Symposium in 2018, verbal presentations are from Egypt, Mexico, Turkey and the UK [19]. Emotional rejection of the infant is becoming recognized as a world-wide human phenomenon.

References

1. Tardieu A. Étude medico-légale sur les sévices et mauvais traitements exercés sur des enfants. Ann Hyg. 1860;15:361–98.
2. Kempe CH, Silverman FN, Steele BF, Droegemuller W, Silver HJ. The battered-child syndrome. J Am Med Assoc. 1962;181:17–24.
3. Orfila MJB. Blessures de la tête: accusation de meurtre d'un enfant par sa mère. Ann Hyg Publique Méd Lég. 1850;43:375–96.
4. Brockington IF. Bonding disorders: emotional rejection of the infant. Bredenbury: Eyry Press; 2018.
5. Brockington IF, Brierley E. Rejection of a child by its mother successfully treated after three years. Br J Psychiatry. 1984;145:316–8.
6. Brockington IF. Motherhood and mental health. Oxford: Oxford University Press; 1996. p. 357–9.

7. Musser ED, Kaiser-Laurent H, Ablow JC. The neural correlates of maternal sensitivity: an fNMR study. Devel Cogn Neurosci. 2012;2:428–36.
8. Kitamura T, Ohashi Y. Perinatal bonding disorders: causes and consequences. Cambridge: Cambridge Scholars Publishing; 2019.
9. Macdonald JA, Youssef GJ, Phillips L, Spry E, Always Y, Patton GC, Olsson CA. The parental bonds of adolescent girls and next-generation maternal infant bonding: findings from the Victorian intergenerational health cohort study. Arch Womens Ment Health. 2018;21:171–80.
10. Faisal-Cury A, Levy RB, Kontos A, Tabb K, Matijasevich A. Postpartum bonding at the beginning of the second year of child's life: the role of postpartum depression and early bonding impairment. J Psychosom Obstet Gynecol. 2020;41(3):224–30. https://doi.org/10.1080/01467482X.2019.1653845.
11. Jose J, Natttala P, Desai G. Effectiveness of a structured teaching program on bonding between mothers with mental illness and their infants. Manipal J Nurs Health Sci. 2018;4:24–9.
12. Tabrizi F, Nournezhad H. Investigating the effect of counseling based on family support on mother-child bonding at 4-6 weeks postpartum in primiparous women: a randomized clinical trial. Int J Pediatr. 2018;6(9):8261–73.
13. Petri E, Palagini L, Bacci O, Borri C, Teresti V, Corezzi C, Faraoni S, Antonelli P, Cargioli C, Banti S, Perugi G, Mauri M. Maternal-foetal attachment independently predicts the quality of maternal-infant bonding and post-partum psychopathology. J Matern Fetal Neonatal Med. 2018;23:3153–9.
14. Fatmawati A, Rachmawati IN, Budiati T. The influence of adolescent postpartum women's psychosocial condition on mother-infant bonding. Enferm Clin. 2018;18(Supplement 1):203–6.
15. Røseth I, Bongaardt R, Lyberg A, Sommerseth E, Dahl B. New mothers' struggles to love their child: an interpretive synthesis of qualitative studies. Int J Qual Stud Health Well Being. 2018;13:1490621.
16. Abbas SI, Turkistani MH, Al-Gamdi AA, Alzahrani SA, Alzahrani AA, Helmy FF. Factors associated with postnatally maternal-infant attachment in Taif, Saudi Arabia. Saudi J Health Sci. 2018;7:127–31.
17. Farré-Sender B, Torres A, Gelabert E, Andrés S, Roca A, Lasheras G, Valdés M, Garcia-Esteve L. Mother-infant bonding in the postpartum period: assessment of the impact of pre-delivery factors in a clinical sample. Arch Womens Ment Health. 2018;21:287–97.
18. Foster DG, Biggs A, Raifman S, Gipson J, Kimport K, Rocca CH. Comparison of health, development, maternal bonding, and poverty among children born after denial of abortion vs after pregnancies subsequent to an abortion. J Am Med Assoc Pediatr. 2019;172:1053–60.
19. Birmingham LB, Bredenbury B. Stafford international symposium. Arch Womens Ment Health. 2020;23:307–15.
20. Brockington I, et al. A screening questionnaire for mother-infant bonding disorders. Arch Womens Ment Health. 2001;3:133–40.

Part II

Prevention, Risk Detection and Treatment

Perinatal Mental Health: Innovative Programmes in Lombardy Region

14

Valeria Brenna, Umberto Mazza, Lorena Vergani, and Mauro Percudani

14.1 Introduction

Perinatal mental health is the discipline that promotes the psychological wellbeing of the mother, father and unborn or newborn child, from conception to, at least, the first year of life, and it is an area in which research and clinical practice can meet, producing a wealth of knowledge that involves different disciplines: psychology, psychiatry, social work, midwifery, nursing, general practice, obstetrics and paediatrics [1].

Coming into the world in western countries occurs in conditions profoundly different from decades ago, both from a social and a family point of view: half of all pregnancies are planned and desired; children, in most cases, will be only children, and this will entail a great concentration of emotions and affectivity and a high level of expectations centred around this life event. Research shows that the risk of incurring in some form of psychological distress, in the stages prior to or following birth, is far from irrelevant [2].

Probably one of the reasons why for years, in spite of high levels of contact with health professionals, both before and after childbirth, disorders were rarely recognised and, even less frequently, appropriate treatment was offered is to be found in

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the difficult integration of all the knowledge gravitating around birth, and that continued to offer a single profile of motherhood and, more generally, of parenthood. This attitude has primarily led to women being precluded from asking for help, and professionals might be deprived of the opportunity to diagnose and treat the disorders which affect the reproductive period.

In recent decades, interest in this field has considerably grown, especially by mental health services, and it has become one of the most challenging and central areas for those involved in the detection, treatment and prevention of psychological distress in human beings. Practitioners are taking care of patients, their partners and their children like never before; those involved can be subjected to, inter alia, relational, psychosocial and genetic risk factors [3].

The focus is worldwide, but while some countries, aside from being pioneers in this field, have progressed both in research and in the organisation of highly specialised services (Australia, the UK, India), others have been devoting themselves to it—within the field of mental health—for a couple of decades, as in Italy.

14.2 Italian Health Services for Expecting Mothers

Italian law recognises the right to health as a fundamental one: expecting mothers are entitled to the national health service, "Servizio Sanitario Nazionale" (SSN), which has an aim of universal coverage, and it is organised by the Ministry of Health and administered by regions. The family advice bureau is a public health and social service offering prevention, information, social, medical and psychological education thanks to specialised professionals. It promotes the physical and mental health of women, couples, adolescents and children and deals with problems concerning contraception, pregnancy, post-birth care and breastfeeding assistance, vaccinations for children, voluntary termination of pregnancy, advice on anonymous childbirth, family mediation in the event of separation or divorce, fertility and sterility, fostering and adoption, psychological problems and legal advice for working women. Maternal and child departments within hospitals provide all women with free specialised health care, including assistance during pregnancy (obstetrical periodic examinations, ultrasounds, instrumental check-ups and tests, childbirth preparation courses) and assistance during labour and childbirth. Before the implementation of specific projects, when mothers showed signs of relevant mental distress, they were referred to general mental health services.

In case the SSN is not the kind of care mothers are looking for or the waiting lists for tests are too long, some of them decide to turn to the private sector [4].

14.3 Perinatal Mental Health Policies in Italy

In order to be organised and to function effectively, public services need social and health policies to pay attention to the users or the stage of the life cycle they address. At a national level, according to the WHO European Ministerial Conference, held

in Minsk in 2015, Italy and other European countries commit to early, appropriate, timely and collective actions with a lifelong approach to public policy and services [5]. The Ministry of Health has set up national actions concerning the perinatal period and addressing both mothers' and children's mental health.

- As early as 2010, the agreement on the "birth pathway" has defined guidelines for the promotion and improvement of quality, safety and appropriateness of care interventions in accompanying birth by the SSN services and has defined a shift in focus from childbirth to the entire pathway, from conception to postpartum [6].
- The National Prevention Plan (NPP, 2014–2019, 2020–2025) strategic guidelines, based on scientific evidence, emphasise the importance of a lifelong approach in community programmes for promotion and equity of health, which begins during pregnancy, continues with the support of breastfeeding and proceeds to the early childhood phase [7].
- LEAs (2017), Essential Levels of Care, are tools that define what healthcare services the public health system is required to provide all citizens; among these are home and territorial assistance, psychological and psychotherapeutic support to parenthood, help to pregnant women and protection of the child's health, courses accompanying the birth in collaboration with hospitals, assistance to puerperium and support in caring for the newborn [8].
- A technical panel operating from 2016 to 2018 issued a ministerial document on the first 1000 days of life, addressed to caregivers, health workers and policymakers; they identified seven periods to undertake preventive and protective actions and interventions to reduce risk factors.
- Among the national surveillance registers, two are relevant to the perinatal sphere: the one on the maternal mortality [9] (this one includes cases of suicide in perinatal period) and the one on the surveillance of children between the ages of 0 and 2, with the detection of actions that, according to scientific evidence, are considered fundamental to children's health (nutrition, vaccinations, reading aloud by caregiver) [10].
- Direct funding of regionally designed projects, dedicated to prevention and early interventions for maternal psychopathology.

14.4 Perinatal Mental Health in Lombardy Region: An Overview

Lombardy is a region in northern Italy where each year more than 73,000 babies are born [11]. Over the last two decades, it has developed outpatient services and screening systems that have assisted, in a more or less harmonious way, the ordinary activity of maternal-infant hospital departments and the family advice bureaus on the territory, usually committed to supporting women in their process of adjusting to pregnancy and postpartum.

In 2004 the Macedonio Melloni-Fatebenefratelli hospital opened a specialised outpatient clinic for treatment, prevention of psychiatric conditions related to the

female life cycle, in view of the bio-hormonal vulnerability to disorders during pregnancy, postpartum, menarche and menopause. Clinical work combined with research and training led, in 2015, to the drafting of "Guidelines for the prevention, diagnosis and treatment of perinatal psychopathology" [12].

Panda Onlus, a non-profit organisation established thanks to private funding, had set a specialist outpatient clinic in 2008 with San Gerardo hospital. It provided free psychological and, if necessary, psychiatric care aimed at preventing and supporting the psychological distress of women in pregnancy and puerperium and supporting parenting. The clinical and prevention activities flanked the training for operators in the maternal-child area.

Other projects, in the Lombardy area, were started to implement the regional plan for mental health: the general health directorate financed activities related to quality, training objectives and services dedicated to specific issues and emerging needs within the population. The focus was on needs documented by epidemiology and on the request to enforce territory services alongside well-established hospital activities. Treviglio hospital has involved depressed women, drawn from a community screening programme for postnatal depression in Bergamo province; this programme was conducted on a group and individual basis following a cognitive-behavioural programme of 10–15 weeks' duration, including at least one session with the partner and adhering to the structured manual of the Milgrom model [13].

The field of perinatal mental health was given a further boost in the city of Milan and its hinterland in 2009 through the so called innovative programmes with the purpose of identification and treatment of postpartum depression (see next section).

In 2017 ATS Milano Metropolitana (the agency for health protection whose function is to govern the social-health network of the metropolitan area) promoted the launch of an action programme for prevention, detection and early intervention of perinatal depression, trying to harmonise the screening procedures for pregnant women within various units: maternal and child health, counselling centres and mental health, with the inclusion of data in a dedicated application. The goal is to define risk profiles based on EPDS for a timely intervention. It is almost natural that the increased number of actors in the perinatal field entails the formalisation of the innovative programmes as second level services, ready to welcome, assess and treat, with specificity and experience, women identified by a more homogeneous screening.

Another essential step in spreading the culture of perinatal mental health was taken with the founding of the Italian regional group of the Marcé Society. The international organisation is dedicated to supporting research and assistance surrounding prenatal and postpartum mental health for mothers, fathers and their babies: it is organised in territorial units to foster territorial cooperation, and it brings together different professionals working in the area. The intense training activity carried out throughout Italy has made it possible to meet the most important national and international experiences and to outline virtuous practices in the field of prevention, diagnosis and treatment.

In the previous paragraphs, it was mentioned that, occasionally, the Ministry of Health directly funds regionally designed projects, dedicated to maternal psychopathology; an example is the executive project "Measures related to prevention, diagnosis, treatment and care of postpartum depressive syndrome", with ten Lombardy hospitals involved and ASST Lecco as the implementing body [14].

The above-mentioned project is based on the programme "Thinking Healthy" (WHO, 2015) which outlines an evidence-based approach, committed to reducing prenatal depression; the focus of the project is on cognitive-behavioural techniques applied at home by midwives. One of the actions implemented was midwives' training for home visits, dedicated to women suffering from perinatal depression because it is a cost-effective intervention of great territorial importance and it involves the integration among services in the territory: maternal and child health and mental health.

The manual has been translated and adapted as part of the project and has been the elective tool for the development of midwifery training; it has also promoted a caring approach to both the physical and mental health of pregnant and postnatal women [15]. Another goal of the project is creating an app for smartphones which allows pregnant women to monitor their own emotional condition (by the EPDS) and allows the link to a website, activated by the project, with information on perinatal mental health. The app is being implemented in the ASST Lecco and will subsequently be made available to all ASSTs participating in the project.

14.5 Innovative Programmes on Prevention and Treatment of Perinatal Disorders in the City of Milan

The mental health departments of some of the major Lombardy hospitals in the city of Milan and its hinterland implemented outpatient clinics dedicated to women's mental health after childbirth, in the framework of the "innovative programmes" funded by Lombardy region. Since then, the metropolitan territory has been characterised by being different from the provincial one in its socio-demographic composition, its offer of services, its own organisation or access methods and its "culture" of intervention, with rich proposals, while other services have no specific initiatives for the puerperium at all. The only common trait was the exclusive focus on the support of the postpartum stage as a central moment of transition in the life cycle, which involves adjustment disorders only. The underlying model appealed to an idea of a maternal instinct which, if properly supported, would certainly lead to the natural establishment of the bond with the infant and the practices of care and dedication. Women who have manifested serious suffering were referred to mental health services, wherewith the maternal and infantile services maintained a dialogue burdened by a feared "psychiatric habit" [16].

The early interest concerned the postpartum period: the detection of the patients took place through a significant screening intervention with the Italian version of EPDS [17], with the goal of identifying at-risk women. After that, an assessment and a possible treatment would be proposed. Innovative programmes have been

renewed over the years; the outpatient clinics continue their activities and expand their scope of intervention: immigrant women, anxiety disorders, support in case of foetal death or admission in neonatal intensive care, PTSD, bonding disorders, psychopathology in fathers and family and couples support.

Conferences are carried out periodically, allowing to raise the awareness of midwives, paediatricians, gynaecologists, GPs, etc. on the subject of perinatal disorders and to intercept women at risk. At the same time, specialists from different contexts can share tools, treatment methods, prevention practices and models of identifying women.

It is possible to define two referral profiles: a *hospital-based* one, typical of the city projects, where the hospital wards are the source of referral and a *territorial-based* one where this role is fulfilled by the services located outside hospitals, such as vaccination centres, family advice bureaus, psychiatric outpatient clinics and paediatricians.

The assessment is carried out by means of a clinical interview, the collection of socio-demographic data (age, marital status, education, employment status and nationality), the migratory history if the woman is a foreigner (date and reasons for immigration, any stressful events during the migratory route), obstetrics and gynaecology data regarding the current and any previous pregnancies and the main risk factors, traditionally associated with the onset of perinatal psychological disorders [16] (previous psychopathological history, familiarity with psychiatric disorders, presence of stressful factors in the previous 6 months of life, etc.).

Also some self-report assessment tools are used:

- Edinburgh Postnatal Depression Scale, EPDS [17, 18].
- Beck Depression Inventory-II (BDI-II) [19, 20].
- State-Trait Anxiety Inventory (STAI-Y) [21].
- Postpartum Bonding Questionnaire (PBQ) [22, 23].
- Clinical Outcomes in Routine Evaluation-Outcome Measure (CORE-OM) [24].
- Social Provisions Scale-10 item (SPS-10), an abbreviated form of the SPS-24 item [25, 26].

If women present a score greater or equal to the cut-off following one or more of the above-mentioned tools, or a positive response to the items related to suicide risk, an evaluation by a psychiatrist is activated.

Through a periodical work of discussion and evaluation by the professional teams of the hospitals involved, a database was shared, in order to collect data on the assessment and treatment pathways of women who come into contact with outpatient clinics. A reference sample of an operative trimester, from June 2018 to October 2018, describes a total of 294 women of women who came into contact with the project: most of the them were of Italian nationality (87%), 58.84% were married and 36.39% are single. The majority of women (88.09%) had a medium-high level of education and a university degree or high school diploma. They were intercepted in pregnancy (60.20%) and 44.50% in postpartum. They were referred by the staff of the Obstetrics and Gynaecology Unit, 11.56%, by psychiatric

services (10.02%) or by family advice bureaus and a very small number by general practitioners (2.38%), while 22% approached perinatal services spontaneously.

55.44% of the screened women began a psychological treatment and 39.9% needed psychiatric consultation. The majority of women in treatment presented with anxiety (53.9%) and mood disorders (26.9%), only a small percentage presented with mental and behavioural disorders associated exclusively with puerperium (11%), personality disorders (7.4%) or psychosis (1.2%) [16]

The experience gained and the research carried out have made it possible to develop a multidisciplinary psychosocial intervention model [27].

Thanks to a collaborative care programme, women presenting for the planned obstetric visits at the beginning of the second or the third trimester of pregnancy were screened and assessed with the above-mentioned tools, searching for risk factors, anxiety or depressive symptoms.

Women were offered different psychosocial interventions, according to the level of risk identified:

- High-risk group: Women with depressive and/or anxiety symptoms and/or suicide risk. They received interpersonal psychotherapy and pharmacological treatment as a second-line treatment.
- Low-risk group: Women without significant symptoms but with a family or a past history of psychiatric disorders and other risk factors. 7/8 sessions of psychosocial counselling were delivered to these women.
- No risk group: During the return of the screening results, a preventive intervention was proposed to help them to recognise symptoms of distress and disorders.

The specific focus on migrant pregnant women led to a research involving the detection and assessment of risk for perinatal disorders [28]: pregnant women were recruited during the scheduled visits or during antenatal classes. The assessment included the collection of socio-demographic information, distressing life events, past psychiatric personal or family history and treatment and the history of migration and pregnancy-related variables. EPDS, Beck Depression Inventory-Short Form (BDI-SF) and the Social Provisions Scale (SPS) were administered in women's mother tongue and with the presence of a cultural mediator, in the event of need. The authors demonstrated that the risk of antenatal depressive symptoms varies between native-born and non-native-born women, living in the city of Milan, and is highest among North African women. They suggested that specific risk factors should be assessed in routine obstetric care to prevent postpartum disorders and its consequences.

14.6 Future Directions

Over the past two decades, Italy has succeeded in promoting a broader culture in the field of perinatal mental health; however there are still challenges Italy needs to face.

First, no nation has come close to meeting the needs of mothers and their infants with perinatal mental health issues: where specialist services exist, only 5% of new

mothers gain access, while many others do not.[3] The problem of barriers to access services is a significant public health concern and it is not solvable only by reinforcing screening procedures. Helthcare providers of specialised services is sometimes the cause of this difficulty, most of the times, the issue is a lack of understanding of perinatal mental health not only among pregnant women or their families but mostly by healthcare providers at any level. Similarly, referral to mental health services is obstructed both by women who are themselves afraid to make a disclosure about their status and by primary care providers, unwilling to refer them. Interdisciplinary communication seems particularly lacking, especially in emergency situations [29].

In second place, although much has been done concerning outpatient activity, these services benefit from the collaboration of a dedicated multidisciplinary team and of a joint care of parents and infants, not only in the treatment approach but also in setting up services. For most mothers with psychiatric disorders related to childbearing, general psychiatric services are the only assistance provided; when emergencies happen, they are admitted to psychiatric wards, separated from their children.

"The mental health services concerned with the pregnant and newly delivered mother have an equal responsibility for the child" [3]: since 1985 psychologists and psychiatrists have been interested in early mother-infant relationships and how perinatal disorders affect children's development. A dual approach—on the specificity of the maternal disorder and the transgenerational risk of the exposed newborn—is the only preventive possibility in predicting adulthood mental health [30].

References

1. Brockington I. Motherhood and mental health. New York: Oxford University Inc.; 1996.
2. Bramante A, Grussu P. Manuale di Psicopatologia Perinatale, Erickson, Trento; 2016:17–18. [publication in Italian].
3. Brockington I, Butterworth R, Glangeaud-Freudenthal N. An international position paper on mother-infant (perinatal) mental health, with guidelines for clinical practice. Arch Womens Ment Health. 2017;20:113–20. https://doi.org/10.1007/s00737-016-0684-7.
4. http://www.salute.gov.it/imgs/C_17_opuscoliPoster_128_allegato.pdf.
5. World Health Organization. The Minsk declaration. The Life-course Approach in the Context of Health 2020; 2015. https://www.euro.who.int/__data/assets/pdf_file/0009/289962/The-Minsk-Declaration-EN-rev1.pdf.
6. Pansieri C, Clavenna A, Pandolfini C, et al. NASCITA Italian birth cohort study: a study protocol. BMC Pediatr. 2020;20:80. https://doi.org/10.1186/s12887-020-1961-1.
7. Mattioli B, Bucciardini R, Falzano L, Bena A, Gilardi L, Capra P, Falcone U, Marra M. A health equity focused National Prevention Plan 2020-2025 and related capacity building (CCM, 201). Eur J Public Heal. 2020;30(Suppl 5):ckaa165.121. https://doi.org/10.1093/eurpub/ckaa165.121.
8. Torbica A, Fattore G. The "essential levels of care" in Italy: when being explicit serves the devolution of powers. Eur J Heal Econ. 2005;6(Suppl 1):46–52. https://doi.org/10.1007/s10198-005-0318-x.
9. Donati S, Maraschini A, Dell'Oro S, Lega I, D'Aloja P, Regional Maternal Mortality Working Group. The way to move beyond the numbers: the lesson learnt from the Italian obstetric

surveillance system. Ann Ist Super Sanita. 2019;55(4):363–70. https://doi.org/10.4415/ANN_19_04_10.
10. Pizzi E, Spinelli A, Battilomo S, Azzarito C, Balducci MT, Bettinelli ME, Campostrini S, Germinario C, Mazzarella G, Mignuoli AD, Morbidoni M, Porchia S, Simeoni L, Speri L, Gruppo sorveglianza bambini 0–2 anni. I determinanti di salute nella prima infanzia: la sperimentazione di un nuovo sistema di sorveglianza in Italia [The health determinants in young children: testing a new surveillance system in Italy]. Epidemiol Prev. 2019;43(1):66–70. [publication in Italian]. https://doi.org/10.19191/EP19.1.P66.022.
11. Istituto Nazionale di Statistica. Bilancio demografico nazionale 2019; 2019. https://www.istat.it/it/files//2020/07/Report_BILANCIO_DEMOGRAFICO_NAZIONALE_2019.pdf.
12. Anniverno R, Bramante A, Petrilli G, Mencacci C. Prevenzione, diagnosi e trattamento della psicopatologia perinatale. [publication in Italian]; 2014. https://www.ondaosservatorio.it/ondauploads/2014/12/Good-clinical-practice.pdf.
13. Piacentini D, Mirabella F, Leveni D, et al. Effectiveness of a manualized cognitive-behavioural intervention for postnatal depression. Riv Psichiatr. 2011;46(3):187–94. https://doi.org/10.1708/889.9809.
14. Regione Lombardia. Progetto esecutivo: misure afferenti alla prevenzione, alla diagnosi, cura e assistenza della sindrome depressiva post-partum. [in Italian]; 2018. http://www.salute.gov.it/imgs/C_17_notizie_3378_listaFile_itemName_7_file.pdf.
15. WHO. Pensare positivo - un manuale per la gestione psicosociale della depressione perinatale. [in Italian]; 2019. https://apps.who.int/iris/bitstream/handle/10665/152936/WHO-MSD-MER-15.1-ita.pdf?ua=1.
16. Brenna V, Cauli G, Corbani I, Corno F, Fisogni A, Gozzini C, Grecchi A, Iapichino E, Pari E, Piccinici G, Puzzini A, Quartieri BM, Scovazzi P, Valentini G, Mazza U, Percudani EM, Toscano M, Vergani L. Programma innovativo: prevenzione e cura dei disturbi psichici per il periodo perinatale. [publication in Italian]. Psichiatria Oggi XXXII. 2019;2:62–9.
17. Benvenuti P, Ferrara M, Niccolai C, Valoriani V, Cox JL. The Edinburgh postnatal depression scale: validation for an Italian sample. J Affect Disord. 1999;53(2):137–41. https://doi.org/10.1016/s0165-0327(98)00102-5.
18. Cox J, Holden J, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150(6):782–6. https://doi.org/10.1192/bjp.150.6.782.
19. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4(6):561–71. https://doi.org/10.1001/archpsyc.1961.01710120031004.
20. Montano A, Flebus GB. Presentazione del Beck Depression Inventory-seconda edizione (BDI-II): conferma della struttura bifattoriale in un campione di popolazione italiana. Psicoterapia Cognitiva Comportamentale. 2006;12:67–82.
21. Spielberger CD. Manual for the state-trait inventory STAI (Form Y). Palo Alto, CA: Mind Garden; 1983.
22. Brockington I, Oates J, George S, et al. A screening questionnaire for mother-infant bonding disorders. Arch Womens Ment Health. 2001;3:133–40. https://doi.org/10.1007/s007370170010.
23. Busonera A, Cataudella S, Lampis J, Tommasi M, Zavattini GC. Psychometric properties of the postpartum bonding questionnaire and correlates of mother-infant bonding impairment in Italian new mothers. Midwifery. 2017;55:15–22. https://doi.org/10.1016/j.midw.2017.08.011. Epub 2017 Sep 1.
24. Palmieri G, Evans C, Hansen V, Brancaleoni G, Ferrari S, Porcelli P, Reitano F, Rigatelli M. Validation of the Italian version of the clinical outcomes in routine evaluation outcome measure (CORE-OM). Clin Psychol Psychother. 2009;16(5):444–9. https://doi.org/10.1002/cpp.646.
25. Cutrona C, Russell D. The provisions of social relationship and adaptation to stress. Adv Pers Relat. 1987;1:37–67.

26. Iapichino E, Rucci P, Corbani IE, Apter G, Quartieri Bollani M, Cauli G, Gala C, Bassi M. Development and validation of an abridged version of the social provisions scale (SPS-10) in Italian. J Psychopath. 2016;22:1–7.
27. Cauli G, Iapichino E, Rucci P, Quartieri Bollani M, Marconi AM, Bassi M, Gala C. Promoting the well-being of mothers with multidisciplinary psychosocial interventions in the perinatal period. J Affect Disord. 2019;246:148–56. https://doi.org/10.1016/j.jad.2018.12.028. Epub 2018 Dec 18.
28. Corbani IE, Rucci P, Iapichino E, Quartieri Bollani M, Cauli G, Ceruti MR, Gala C, Bassi M. Comparing the prevalence and the risk profile for antenatal depressive symptoms across cultures. Int J Soc Psychiatry. 2017;63(7):622–31. https://doi.org/10.1177/0020764017725543. Epub 2017 Aug 14.
29. Sambrook Smith M, Lawrence V, Sadler E, Easter A. Barriers to accessing mental health services for women with perinatal mental illness: systematic review and meta-synthesis of qualitative studies in the UK. BMJ Open. 2019;9(1):e024803. https://doi.org/10.1136/bmjopen-2018-024803. PMID: 30679296; PMCID: PMC6347898.
30. Sutter-Dallay AL, Guedeney N. Introduction: history. In: Sutter-Dallay AL, Glangeaud-Freudenthal NC, Guedeney A, Riecher-Rössler A, editors. Joint Care of Parents and Infants in perinatal psychiatry. Cham: Springer; 2016. https://doi.org/10.1007/978-3-319-21557-0_1.

Screening During Perinatal Period: "SalvagenteMamma," ATS Bergamo

15

Cristina Cattoni, Carmen Rinaldi, and Alessandra Bramante

15.1 Introduction

The birth of a child involves a transition of the role of a woman that includes the creation of a new identity, the maternal identity. In most cases, new mothers gradually adapt to the changes induced by conception and by birth; on some occasions, however, this step can have a different outcome and lead to mental health problems. Depression in the perinatal period, during the period between pregnancy and the first year after birth, is still too often:

- Underestimated.
- Unrecognized.
- Untreated.

In fact, literature tells us that less than 50% of perinatal depressions are identified during routine clinical practices and that only between 12% and 30% of women with perinatal depression receive adequate treatment.

In recent years, the interest in perinatal psychopathology has been progressively increasing, considering implications not only on the mother but also on the health of the children. This kind of psychiatric disorders has been subject of study by the international scientific community: in particular, perinatal depression is considered as a public health problem, due to its high incidence and consequences on women and the quality of mother-child relationships. It is also well known that there are many barriers that prevent women from seeking help for psychological and psychiatric problems during pregnancy and postpartum.

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The National Institute for Health and Care Excellence (NICE 2014–2016) recognizes the importance of early identification of the presence of maternal perinatal psychopathology through screening, for some fundamental reasons [1]:

- Perinatal depression is a common psychopathological condition.
- If left untreated, it can have serious consequences for the woman, the baby, and the entire family.
- Screening is able to recognize cases that would otherwise remain unidentified.
- There are effective treatments for these disorders.

The American Psychiatric Association [2], regarding the use of screening in pregnancy and postpartum, stated that:

- All pregnant women should be screened for the presence or risk of developing a psychiatric disorder.
- All healthcare professionals should provide education to mothers on how to recognize symptoms of depressive, anxiety and psychotic disorders in the perinatal period.
- All psychiatrists should inform their patients about the risks associated with untreated psychiatric illness during pregnancy and breastfeeding and about the risks and benefits for both mother and baby of using psychotropic drugs during pregnancy and/or breastfeeding.

There is scientific evidence that maternal depression can be identified with simple standardized screening tools, quick and easy to administer, and that early treatment improves the prognosis for both the woman and her family. The sooner a woman with perinatal psychopathology is identified, the sooner we can provide adequate treatment.

15.2 "SalvagenteMamma" Screening for Perinatal Disorders

"SalvagenteMamma" started in Bergamo in 2015 thanks to the fundamental contribution of Dr. Alessandra Bramante. Born as a screening project for women in their postpartum, intercepted at vaccination points in the Bergamo geographic area, it grew in 2018 as a screening project also for pregnant women. Its main objectives are:

1. To be able to identify, in the early stage, mothers who present psychological distress or real psychopathologies in pregnancy and postpartum.
2. To investigate the development of the mother-child relationship.

The screening activity has a preventive function and consists of a complex process that includes:

- Identification.
- Rating.

- Involvement.
- Intervention.
- Reduction of symptoms or risk.
- Achievement of functional improvement.

SalvagenteMamma postpartum screening uses two specific tools in order to reduce false positives as much as possible: Cox's Edinburgh Postnatal Depression Scale (EPDS) test and Goldberg's General Health Questionnaire (GHQ-12).

In postpartum screening, questionnaires are distributed by the nurses of the vaccination centers, appropriately trained, to all Italian-speaking mothers, at the first vaccination dose, between the second and third month of the child's life. The screening tools cannot replace an interview or clinical observation and do not represent a diagnostic tool, as no test or questionnaire can provide a diagnosis by itself. However, they are particularly useful in identifying situations at risk or potentially risky.

These are specific tools that require specific skills by adequately trained operators in order to be used correctly both in the application and in the reading of the results.

The most famous screening tool for postpartum depression is the EPDS, a screening tool that identifies the risk of depression. It is the only screening test currently recognized internationally. It is a self-administered questionnaire consisting of ten items that represent.

the psychic state of a woman in the last week, valid for both pregnancy and postpartum (Italian version of the EPDS by Cox and Holden edited by P. Grusso et al.).

The EPDS is not a tool for measuring general psychiatric morbidity and does not detect other common disorders present in the perinatal period; it also does not detect the risk of future depression, so it has no predictive capabilities, but only identifies a risk that can potentially evolve into a condition of greater severity. In administering the test, the woman is asked to mark the answer closest to how she has been feeling in the past 7 days. The cutoff as indicated by the author himself is identified at 12 However a cutoff of 10 allows to identify all cases at risk [3]. Particular attention must be paid to scores greater than 1 in point 10 related to "suicidal ideation." In SalvagenteMamma screening, a "low" cutoff 10 was preferred, although it may include false positives, to be sure not to neglect women at risk of psychopathological evolution.

To avoid the presence of excessive false positives, the 12-Item General Health Questionnaire (GHQ-12) is also used. Mental well-being is an important determinant of health and its social consequences. The GHQ was developed in order to identify two main categories of problems: the inability to perform their normal healthy functions and the appearance of new phenomena of a stressful nature [4]. Specifically, the GHQ allows us to investigate the presence of four elements of discomfort: depression, anxiety, social deterioration and hypochondria (indicated with somatic symptoms). The scale investigates the presence of nonpsychotic psychiatric disorders. The woman is asked to compare her current situation with her usual psychological state, choosing from four different responses: "as usual," "more than usual," "less than usual," and "much less than usual." In this way it is possible to place the subject along a continuum whose extremes are constituted by a condition of psychological well-being, seen as the absence of psychic symptoms, and by a

condition of psychic disorder with different degrees of severity. A cutoff of 4 was chosen; both questionnaires must be positive to be considered indicators of a possible pathology. Following the positivity of the screening questionnaires (cutoff 10 EPDS and cutoff 4 GHQ-12 or positive response to item 10 of the EPDS indicative of suicidal risk), the psychologist offers an in-depth clinical interview in order to assess whether the highlighted psychopathology risk actually corresponds to an ongoing psychic problem, in which case it proposes a free support.

Bergamo family counseling center—postpartum depression screening Vaccinal center of Bergamo and Villa d'Almè years 2016–2019

	2016	2017	2018	2019	Total	%
Number of children vaccinated in the first dose	1656	1564	1535	1480	**6235**	
Distributed questionnaires	1443	1319	1274	1260	**5296**	85%
Collected questionnaires	1235	1063	998	1034	**4330**	82%
Questionnaires of women at psychopathological risk	118	123	100	106	**447**	11%
Contact for consultancy	115	119	94	98	**426**	95%
Consulting carried out	85	65	57	63	**270**	63%
Treated	77	57	50	52	**236**	87%

A screening project in pregnancy was prepared at the end of 2018 considering the results obtained in the 3-year period (2015–2018) in order to identify any psychological distress early. It has been structured as following: with the introduction in January 2019 of the Birth Pathway Agenda, the questions of Whooley and the GAD-2 are asked by the obstetrician staff to every women asking for a consultant for physiological pregnancy. In the case of positivity there is the proposal for an in-depth diagnostic study by the psychology of the family counseling center and a subsequent taking in charge.

The SalvagenteMamma screening in pregnancy also provides that all women who attend the family counseling center for birthing course and who are between the 19th and 38th week of gestation (second and third trimester) are asked to fill in the following three questionnaires:

- EPDS (Edinburgh Postnatal Depression Scale) by Cox et al. [3], in the Italian version of Benvenuti and colleagues from 1999 [5]. Matthey Generic Mood Question (MGMQ) by Matthey et al. [6], Italian translation by A.M. Della Vedova (2014).
- MGMQ [6] was developed to be used in the screening of emotional difficulties of clinical relevance, not just anxiety or depression. It has a few questions and can be administered in minutes. MGMQ has shown a better ability to identify women who meet diagnostic criteria for an anxious disorder and is also superior to other tools commonly used in identifying subjects with high scores on the self-report mood or anxiety scales [6].
- MAAS (Maternal Antenatal Attachment Scale), Italian adaptation partially modified by A.M. Della Vedova in 2016 (unpublished manuscript). The MAAS is a questionnaire consisting of 19 items on a Likert scale of 1–5 aimed at investigat-

ing the development of maternal prenatal attachment. It has good psychometric characteristics, and a recognized factorial structure, also confirmed in the Italian population [5], includes two subscales that specify the intensity and quality of attachment. In agreement with the author, an Italian translation has been prepared which, without making changes to the 19 items, adds 1 final item on possible maternal concern. The administration of this questionnaire allows to compare the results with the Italian validation and to evaluate the characteristics of a 20-item version.

The self-administered questionnaires are delivered to women by properly trained obstetric staff during the birth accompaniment course. The questionnaires are read and signed by the counselor's psychologist, an expert in perinatal psychopathology.

Like all screening methods, EPDS cannot identify all women with anxiety and/or depression; similarly some women with high scores are not clinically depressed. To minimize false positives, a higher cutoff (EPDS $\geq$ 13) was adopted, capable of ensuring a sensitivity of 56%, a specificity of 98%, and a positive predictive value of 83% [3].

The women who are identified at risk are quickly contacted by the counseling psychologist for some in-depth clinical interviews aimed at formulating a diagnosis and subsequent possible treatment.

The call from the psychologist replaces the stressful moment where you recognize that you have a problem and need to ask for help. Moreover when a new mother gets sick, as if the "mother's skills" were taken for granted and not something that is learned with experience. We can therefore assume that these mothers would hardly have taken the initiative to ask for help on their own, if they had not been contacted directly for the results of the screening.

A late or missed diagnosis can expose the woman to the risk of recurrent depression, also as a consequence of the sense of failure felt as a parent, and increases the negative repercussions on the relationship with the newborn. This long-term relationship difficulty can cause cognitive, affective, and attachment disorders in the child's development.

Bergamo family counseling center—screening in pregnancy vaccinal center of Bergamo and Villa d'Almè year 2019

	Pre-natal course	Agenda	Vaccines	Total	%
Collected questionnaires	117	26	136	**279**	
Questionnaires of women at psychopathological risk	13	26	15	**54**	19
Contact for consultancy	12	22	12	**46**	85
Consulting carried out	11	15	5	**31**	67
Treated	11	14	5	**30**	97

The SalvagenteMamma project on perinatal depression therefore arises from the awareness of how important it is to support and be close to women in this particular period of their life during which it is difficult to communicate to others their problems, their sadness, and their anxieties due to a sense of guilt that contrasts strongly with the happy nature of a new birth.

In SalvagenteMamma, the assessment is composed of three tools that allow to investigate all the risk factors of perinatal psychopathology.

Women who have tested positive for screening are given the following tools:

- *The Stafford Interview*, a semi-structured interview (6th Edition 1999), conceived by Prof. Ian Brockington, world-renowned perinatal psychiatrist. It aims to identify women suffering from mental illness in pregnancy and postpartum. The tool is scientifically validated and translated into numerous languages (the Italian translation was edited by Alessandra Bramante). Administration takes about 1.5/2 h.

The prepartum section is divided into four parts:

Introduction contains general questions about the circumstances, the people who will be important in the baby's life, the most important events in the mother's life, and her psychiatric and obstetric history.

The social, psychological, and obstetric background of the pregnancy, the circumstances in which the mother was at the moment of conception; her response, and the response of others to the announcement of pregnancy; a report of each quarter; and questions about all important relationships, lifestyle, sacrifices, and life events.

The unborn child, which includes social and medical concerns and interaction with the fetus.

Prepartum emotional changes and psychiatric disorders. The mother's concerns are explored. General questions are used to explore anxiety, obsessive-compulsive symptoms, irritability, depression, and other psychiatric disorders, including psychosis. Assessments are made with respect to onset and duration, treatment, and role impairment.

The postpartum section is divided into four parts:

Childbirth, which covers the course of obstetric events, mental state during and after birth, and the condition of the newborn.

The social, psychological, and medical background of the puerperium. This is similar to the corresponding prepartum section, but it also covers the mother's reaction to the newborn, breastfeeding, and sleep deprivation.

Postpartum psychiatric disorders. General questions are used to explore anxiety, obsessive-compulsive symptoms, irritability, depression, and other psychiatric disorders, including psychosis.

The mother-child relationship. This section covers the characteristics of the baby and maternal involvement in care, the mother's emotional response to her baby, and various possible manifestations of anger and abuse.

The interview ends with observations, synthesis, diagnosis, and therapeutic plan.

In clinical practice, the 2-h interview is well tolerated by mothers, who appreciate in-depth exploration of their problems. They are able to speak openly on sensitive issues and often find interviews positive and therapeutic.

- *The Postpartum Bonding Questionnaire* (PBQ: [3]), a self-report questionnaire designed to provide early indicators of disturbances in mother-infant interaction. It is composed of 25 items that form four scales (mother-child bonding disorder, severe mother-child relationship disorder, child-focused anxiety, risk of abuse) on a 6-point Likert scale (0–5). The questionnaire gives a total score that allows for the identification of two levels of severity: general bonding disorder and severe relationship disorder. It is a simple administration tool and the time required for compilation is approximately 10 min.
- *The Maternal Aggressive Behaviors Risk Assessment* (MABRA; Bramante, Cutica), an assessment sheet for the risk of self and hetero damaging maternal acts. The tool, built on the basis of the conclusions of a national scientific research, allows to identify women at low, medium, and high risk of self and hetero-harmful acts. It is composed of a personal data sheet and 80 dichotomous items (*yes*/*no*), which investigate individual risk factors (age, sexual abuse in childhood, previous psychopathology, sleep disorders, etc.), risk factors relating to the family of origin (psychiatric familiarity, relationship with parents, witnessed violence, etc.), and situational factors (maternal attitude, relationship with partner, traumatic birth, financial problems, social isolation, recent death of a parent, etc.).

After this diagnostic investigation, the psychologist of the family counseling center decides which path is necessary for that mother. In some cases the in-depth evaluation has proved sufficient to allow the mother to process the emotional difficulties related to her motherhood journey and other times a psychological management project of about 10/15 sessions, and, in the most serious cases, the mother is sent to a psychiatric consultation. Some situations also required the activation of social services.

15.3 Consultation Treatment

The mother-child relationship grows through shared pleasure. The baby has the power to awaken the mother's emotions, so the purpose of the treatment is to create circumstances in which the mother and baby can have fun with each other.

To facilitate all this, a multidisciplinary model of intervention is used in the family counseling center which involves different figures and different therapeutic options:

- Psychoeducation.
- These are interviews aimed at knowing the diagnosis and disorders to allow the woman to acquire self-monitoring of symptoms, aimed at improving awareness of the disease and adherence to treatment.
- It is important to involve the partner as well in psychoeducation:
  - For a greater understanding of the psychopathological condition of women.
  - For a reduction of the risk factors present in the relationship (conflict).
  - For better emotional support.

- Psychological clinical interviews according to the cognitive behavioral approach that focuses on negative thoughts and behaviors that tend to worsen mood. The theory behind cognitive therapy holds that the way you think and perceive the world affects mood and daily functioning. In working with new mothers, it is important to remember that negative perceptions can reduce self-esteem, energy, and motivation, as well as increase the level of stress.

Psychological intervention concerns triggers (such as complications during pregnancy or childbirth), vulnerability factors (such as the presence of a problematic relationship with one's mother or partner), maintenance factors, and aggravating factors (such as negative thoughts and poor social support).

- The newborn massage produces many benefits, some of which have immediate effects: the baby will certainly be more serene and peaceful, will have less difficulty falling asleep, and will almost certainly sleep longer. The neonatal massage can also be used to restore emotional balance with the mother and to help the baby overcome any emotional trauma.
- Play therapy with participatory model (discover and observe laboratory).

In a safe and welcoming environment, the participants share their thoughts and feelings about their new role.

Space is made for the baby during the session, supporting the mother to:

– Notice the child's attempts to connect and communicate.
– Question about the inner life of the child.
– Respond to the needs of the child.

Results include developed maternal sensitivity and increased attuned responses, reduction of self-reported anxiety and depression symptoms, increased parental confidence, and reduced sense of isolation.

A strong point of the intervention in the family counseling center is therefore represented by the psychosocioeducational support, consisting of a network of resources and possibilities: sharing with other people who are going through some important steps in their lives, such as having a child, becomes an opportunity that makes you feel less alone, makes you stronger, and allows for the exchange of skills and personal competences. For this reason, the family counseling center promotes the "Birth Path," through proposals such as the breastfeeding area, the newborn massage course, the "discover and observe" laboratory, the "Bimbo on Board" training course for new parents, etc.

15.4 Intervention in Times of Emergency COVID-19: New Solutions

In the first days of December in Wuhan, China, the first cases of COVID-19 emerged. In a short time, the epidemic advanced taking on the characteristics of a pandemic.

The high number of cases in our region and especially in our province required important restrictions on everyday life and compliance with some rules in order to contain the spread of the virus.

These limitations and rules, linked above all to social relationships, have had an important impact on women peripartum, a period that is already delicate and characterized by anxiety.

Routine checks during pregnancy, the time of delivery, and postpartum have become much more stressful especially for women positive to the virus.

During this emergency, we proceeded to maintain the therapeutic paths in place and accepted the new requests for future mothers by carrying out remote support interviews.

For women who tested positive for COVID-19 in the postpartum period, group courses were started (always remotely) to allow the sharing and processing of anxieties and concerns related to the delicate situation they were experiencing. Quarantine exacerbates loneliness and the lack of reference points amplifies the feelings of uncertainty and anxiety.

The therapeutic group, conducted electronically, worked on two fronts: coping skills and parenting skills. The aims pursued are the support of the woman's decision-making abilities and the promotion of the parental relationship.

15.4.1 Aims

Italian Marcé Society• Promote the state of health and well-being of the woman and the family in the puerperium through information relating to the prevention and containment measures of the coronavirus.

- Recognize the complexity of phenomena that occur with the birth of a child, the symptomatic manifestations, and the various emotional implications.
- Breaking down false myths and evaluating functional relational factors.
- Enhance the maternal skills in the care and relationship with the child.
- Contents.
- The course is divided into four meetings, as specified below:
- Being a parent: learning by trial and error (problem-solving).
- Take care of yourself. Coping with stress (relaxation) nurturing healthy self-esteem.
- A baby is born! Understanding babies (crying, sleeping, feeding, playing).
- Thinking well is good. Irrational ideas, communication, and assertiveness.

15.5 Conclusions

The results of the intervention confirm the importance of early screening and of targeted and timely therapeutic interventions, in the perinatal period, in the significant reduction of the rates of perinatal psychopathology, especially of anxious and depressive symptoms, with a consequent improvement in the quality of life related to health.

In the presence of psychopathology, in addition to the psychologist and psychiatrist, other professionals are involved in the SalvagenteMamma (professional educators, midwives, gynecologists, pediatricians, social workers) who contribute to improving and personalizing the interventions provided. Having a network of professionals around women in need of intervention can be useful in reducing the effects of perinatal psychopathology.

In conclusion, the reliability and importance of early screening are highlighted, which can be concretely used to identify mothers at high risk of developing postpartum psychopathology.

Screening procedures should be performed early even in pregnancy and extend throughout the postpartum period; the professional figures that most frequently gravitate around women in the perinatal period (obstetricians, gynecologists, neonatologists, pediatricians) represent a powerful resource for guaranteeing an early and effective identification of women at risk. Furthermore, the tools used in the SalvagenteMamma (EPDS, GHQ-12) have proven to be valid for perinatal screening.

Early assessment means early recognition, and therefore selectively intervening to prevent or stem as much as possible the negative consequences deriving from perinatal psychopathology, favoring a better overall health status and greater perceptions of well-being to a wider population of mothers, children, and their respective families who will be able to fully live and enjoy a new birth.

References

1. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline CG192; 2014.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edition (DSM-V). Washington, DC: American Psychiatric Association; 2013.
3. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10 items Edinburgh postnatal depression scale. Br J Psychiatry. 2008;150:782–6.
4. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychological Medicine. 1979;9(1):139–45.
5. Bosonera et al. Postpartum Bonding Disorder: Factor Structure, Validity, Reliability and a Model Comparison of the Postnatal Bonding Questionnaire in Japanese Mothers of Infants. Healthcare. 2016;4(3):50.
6. Matthey S, Valenti B, Souter K, Ross-Hamid C. Comparison of four self-report measures and a generic mood question to screen for anxiety during pregnancy in English- speaking women. J Affect Disord. 2013;148:347–51. https://doi.org/10.1016/j.jad.2012.12.022.

Suggested Reading

7. National Collaborating Centre for Mental Health (UK). Antenatal and postnatal mental health: the NICE guideline on clinical management and service guidance. Leicester: British Psychological Society; 2007.

Psychotropic Drugs in Pregnancy and Breastfeeding

16

Laura Orsolini and Cesario Bellantuono

16.1 Introduction: Using Psychotropic Drugs in the Perinatal Period

16.1.1 The Risk Associated with Untreated Mental Illness

The perinatal period, including preconception, pregnancy and postpartum, is considered a high-risk time for women suffering of severe and persistent mental illnesses (SPMI). Several international guidelines, mental health organizations and well-known scientific societies recommended implementing proper screening strategies to early and adequately identify, during the perinatal period, vulnerable women affected by or more prone to develop SPMI and providing timely and evidence-based effective therapeutic interventions, including the prescription of psychotropic drugs (PDs) [1–3]. In fact, it has been well documented that maternal mental illness may be associated with adverse perinatal outcomes, including spontaneous abortion, newborns small for gestational age, low birth weight, foetal distress, preterm delivery, neonatal hypoglycaemia, adverse neurodevelopmental outcomes and changes in the foetus-mother attachment [4]. Pregnant women with untreated mental illness are also more likely to be engaged in high-risk behaviours and unhealthy lifestyles, such as smoking, alcohol drinking and drug abuse and inadequate nutrition and folic acid support. Furthermore, in the perinatal period, the risk of suicide and suicide attempts is not uncommon, since the prevalence rate is

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estimated from 5% to 20% of women [5, 6]. Therefore, a careful assessment and treatment of perinatal mental disorders in clinical settings is essential to ensure better maternal, gestational, obstetrician and foetal outcomes.

16.1.2 The Prescription of Psychotropic Drugs: A Risk-Benefit Approach

Prescribing PD during the perinatal period should be reserved only to women suffering from SPMI or in those clinical cases where non-pharmacological strategies have not been effective. Most available data about the safety of PD in the perinatal period come from longitudinal or retrospective observational studies, national birth registries, systematic reviews and meta-analyses. As *controlled randomized clinical trials* (RCT) are not allowed in pregnancy for ethical and medicolegal issues concerning the foetus/neonatal safety, Wisner [7] properly labelled the pregnant women as "the last therapeutic orphans", and the *perinatal psychiatry* is a relevant topic that should be more deeply investigated.

Overall, considering the literature on the safety of PD during pregnancy and breastfeeding, one could argue how there are several studies published on the same topic, which could report really contrasting and different findings, also in terms of relative risk (RR) and statistical significance. The main reason of such discrepancies could be explained considering the different experimental designs and methodological strategies adopted, as well as the existence of relevant "confounding factors", not adequately controlled when the authors analyse the collected data (e.g. the type and level of severity/intensity of maternal psychopathology, comorbid medical conditions, the use/abuse of alcohol, drugs, nicotine, caffeine, etc.). For this reason, clinicians and mental health professionals working in the field of perinatal psychiatry should own a basic knowledge of medical statistics and clinical epidemiology for a better understanding and interpretation of the findings so far published. For example, an increasing RR for a specific major malformation (MM) needs to be evaluated always along with data of its absolute risk (AR), to allow a better assessment of its clinical and epidemiological relevance. If a study, carried out on newborns exposed to sertraline during early pregnancy, reports a "statistically significant risk" of anal atresia (RR = 4.2), clinician should firstly consider the prevalence of anal atresia in unexposed newborns (0.06%) and then calculates the AR in newborns exposed to sertraline which would be very low (AR = 0.25%). This means that about 99% of newborns exposed to sertraline will not be affected by such malformation [8–10].

Several guidelines and consensus guidance by psychopharmacological societies (e.g. British Association of Psychiatry, BAP) have been produced to provide recommendations for the management of PD usage during the perinatal period [11, 12]. In addition, the development of the *teratogen information service* improved the access of pregnant women and their healthcare providers to data concerning the safety and tolerability of PD use during the perinatal period [13]. However, despite reassuring clinical findings on the safety of most PD during the perinatal time, clinicians are

still fearful to prescribe such medications in pregnancy and/or when a mother wishes to breastfeed her own baby. When PDs need to be prescribed during the first 3 months of pregnancy, this kind of "psychopharmacoteratophobia" among clinicians becomes particularly relevant, due to the risk of inducing birth defects or perinatal complications (PC) [14]. Whilst during the late pregnancy, there is also concern for the risk associated with gestational and neonatal adverse events. Moreover, the uncertainness and worries related to the long-term impact on the infant's behavioural, physical and cognitive neurodevelopment following foetal exposure to PDs, together with the clinicians' poor knowledge about the safety and tolerability of PD in pregnancy and breastfeeding, may negatively influence clinician's prescription choices. However, in the last decade, in some European and Northern American countries, there was a significant increase in PD prescription during pregnancy, mainly antidepressants (ADs) and anxiolytics (AX) [15, 16].

Overall, the management of psychopathological conditions in the perinatal period may indeed represent a challenge for mental health professionals, particularly in those conditions in which the pregnancy is unplanned and the pregnant woman is already affected by a SPMI and is currently taking PDs. In the last case, clinicians should be aware that discontinuing a PD could significantly induce a maternal illness relapse. Therefore, clinicians should properly inform the woman and her partner about the risks and the benefits of a PD therapy in the perinatal period and incentive an adequate and timely planning of conception, pregnancy and pospartum management [17].

16.1.3 Aims of the Review

In the present chapter, we briefly summarized all relevant literature focusing on the safety of the most prescribed PDs during the perinatal period. Original cohort studies, systematic reviews and meta-analyses represent the main sources of data here summarized and discussed. More detailed information on the drug epidemiology, clinical pharmacology and safety of PDs in pregnancy and breastfeeding have been recently published by Uguz and Orsolini (Eds.) in *Perinatal Psychopharmacology* [18].

16.2 Antidepressant Drugs in Pregnancy

ADs, currently prescribed in clinical practice, are considered effective in several psychopathological conditions, such as major depressive disorder (MDD), general anxiety disorder (GAD), panic disorder (PD) and obsessive-compulsive disorder (OCD). Among ADs, *selective serotonin reuptake inhibitors* (SSRIs) are nowadays the most frequently prescribed medications in the perinatal period [19, 20]. Moreover, SSRIs have been also the best investigated class of ADs, as far as the safety in pregnancy and breastfeeding is concerned [11, 12].

MDD, often in comorbidity with anxiety disorders, are quite common in the perinatal period, with prevalence rates ranging between 10% and 20%. It is also

estimated that about 20% of women in childbearing age is affected by depression and up to 15% of them may experience clinically significant depressive symptoms during pregnancy and postpartum [2, 13]. Given the high prevalence of depression and/or anxiety during the perinatal period, prescribing ADs is quite common, but with substantial differences across countries, being documented in about 8% of pregnancies, whilst about 3% of women decide to maintain PD treatment throughout all pregnancy [21, 22]. Moreover, pregnant women who discontinued SSRIs appear to be more likely to experience an illness relapse compared to those women who decide to maintain the treatment during their pregnancy (respectively, 68% versus 26%). Around 50% of pregnant women seem to experience a depressive relapse mainly in the first 10 weeks of gestation [23]. According to recent guidelines and expert opinions, prescribing SSRIs to pregnant women suffering from severe depressive episodes and anxiety disorders should be considered a first-line option [12, 24].

16.2.1 Risk of Major Malformations

Overall, data on the risk of congenital MMs in newborns of women treated with AD in their first trimester of pregnancy are relatively reassuring. The majority of the original investigations, systematic reviews and meta-analytic studies documented that the early antenatal use of such medications, particularly SSRIs and venlafaxine, is not associated with an increased risk of MMs, as the prevalence rate reported in such studies is within the rate observed in newborns of the general population, which is estimated between 2% and 5% [25]. Although some studies have found a small increase in RR for cardiac defects (mainly septal anomalies) in newborns in utero exposed to some ADs, particularly with paroxetine [26, 27], many other studies have not recently confirmed such risk [28–31]. In a study including about 950,000 pregnant women, 6.8% were prescribed an AD during the first trimester. The risk of any cardiac defect in infants exposed to SSRIs, in the preliminary analysis, was relatively small but statistically significant (RR = 1.25). However, after controlling for maternal depression and other confounding factors (i.e. adjusted analysis), no significant increase in RR was observed for cardiac malformations between infants of women who took AD and the control group. Furthermore, in this study no significant increase in the risk of cardiac defects was observed with other ADs (e.g. venlafaxine, bupropion) [32]. This study confirmed how accounting for "confounding factors" is of paramount importance when assessing reproductive outcomes such the birth defects, as this risk can be likely associated more to the underlying maternal disorders, particularly if severe, than simply to the medication exposure [32]. These findings were also confirmed in cohort study in which 5154 and 2776 women were prescribed SSRIs, respectively, before and during pregnancy and 200,213 who did not receive SSRIs during pregnancy: no significant difference in cardiac anomalies was reported in children born to women exposed to prescribing ADs. However, it was found an increased risk of specific cardiac defects in newborns of older women and in those with type 2 diabetes, body mass index (BMI)

above 30 kg/m^2 and with a history of alcohol and/or illicit drug use, independently by AD prescriptions [33].

Overall, reassuring data concerning single SSRI agents have been also reported, even though few studies found a small increased risk of birth defects for some drugs (e.g. paroxetine and fluoxetine), even though without a specific pattern of MMs. However, most of these studies suffer from several methodological flaws and should be interpreted with caution, as in other investigations and critical review, this association was not observed or strongly questioned [34, 35]. Among the class of serotonin noradrenaline reuptake inhibitors (SNRIs), data on the *venlafaxine* and *duloxetine* are rather reassuring, as no risk of birth defects was found in the studies so far published, even though the amount of data concerning these ADs are lesser than those published for SSRIs [36–38]. No information is available on *vortioxetine*. Studies on the foetal safety of other ADs (e.g. tricyclics, mianserin, trazodone, mirtazapine and agomelatine) are lacking, because these drugs have been less frequently prescribed in the perinatal period; therefore, their use should be not recommended in the early pregnancy and during the breastfeeding.

16.2.2 Risk of Adverse Gestational and Neonatal Outcomes

16.2.2.1 Preterm Birth, Spontaneous Abortion and Low Birth Weight

Studies assessing the risk of *preterm birth*, in women exposed to AD during gestation, reported conflicting results [39]. The first investigation was a prospective observational study in which 238 pregnant women were categorized into three mutually exclusive exposure groups: (a) with depression and treated with SSRIs; (b) with depression but untreated; and (c) with no depression and no SSRI treatment. Women with depression treated with SSRIs and those with depression but untreated had higher rates of preterm birth (23% and 21%, respectively), as compared to control group reporting 6% of preterm birth [40]. Different findings have been reported in a study on the risk of SSRIs and perinatal outcomes, including preterm birth. The sampling included 845,345 offspring. All pregnancies included in the analysis were classified as (a) exposed to SSRIs (15,729); (b) unexposed to SSRIs but with a psychiatric diagnosis (9652); and (c) unexposed to drugs and without a psychiatric diagnosis (31,394). SSRI treatment was associated with a significantly lower rate of late and early preterm birth, and caesarean delivery, compared to women affected by psychiatric disorders who were not taking SSRIs. The authors suggest that treating a depression with an AD appears "to be protective of preterm birth" [41].

Therefore, available data are not enough to establish if there is a causal association between exposure to ADs and preterm birth, as such risk could depend upon disentangling contributions from drugs versus exposure to maternal psychopathology. The association between the exposure to an AD and an increased risk of *spontaneous abortion* (SA) has not been still clearly established, as conflicting findings have been reported in the studies published [42–44]. A large population-based study on the risk of SA among depressed pregnant women taking different ADs found a

small increased risk associated with the use of AD during pregnancy (RR = 1.6). According to the authors, the risk was likely "related to the underlying maternal depression or to other factors related to the disorder" [45]. Furthermore, there is also evidence indicating that AD use during pregnancy may be associated with neonatal *low birth weight*, even though further investigations, controlling for potential confounding factors, are needed to confirm such adverse outcome [46].

16.2.2.2 Neonatal Adaptation Syndrome

The neonatal adaptation syndrome (NAS) has been frequently described with the use of most ADs, particularly with SSRIs, during the late pregnancy. The incidence rate was found to affect up to 30% of newborns exposed to serotonin reuptake inhibitors (SRIs), i.e. SSRIs and SNRIs, even though other wide estimations were reported (up to 76%), likely because no standardized measurement tool has been so far utilized in the studies published [47]. The aetiology of NAS is still not well understood. Some authors described the NAS as a "withdrawal or abstinence-like syndrome", whilst others supposed a sort of "toxicity reaction", due to an excessive neonatal serotonin in utero exposure. Symptomatology usually is mild and self-limiting and may include tremors, jitteriness or shivering, irritability, cry, insomnia, altered muscle tone, agitation and restlessness, hypoglycaemia, dysregulation of body temperature and poor feeding difficulties. However, only in rare cases, respiratory distress and convulsions have been observed as well. Generally, symptoms begin within the first 2–4 days after delivery and may last for 1 or 2 weeks. It was suggested to minimize such syndrome, to lower the dosage or even to discontinue the drug treatment some weeks before delivery. This practice, however, is nowadays no longer recommended, as lowering the dose before delivery does not seem to avoid such risk, and, in addition, can make the ongoing treatment ineffective for protecting the mother against an early depressive relapse before delivery or in the postpartum period. In most cases, a careful clinical monitoring of newborn and a supportive treatment like advice about regular feeding (particularly breastfeeding) and reassurance are usually adequate for the management of NAS [48, 49]. Moreover, it was found that concomitant exposure to benzodiazepines (BDZs) and SSRIs in pregnancy may result in a higher likelihood of NAS signs that in some cases may persist up to 30 days post-delivery. However, these findings need to be confirmed by further studies [50].

16.2.2.3 Other Neonatal Adverse Outcomes

The risk of having a newborn affected by a *persistent pulmonary hypertension neonatal* (PPHN), a rare but severe respiratory condition, for women treated with ADs (particularly SSRIs) during pregnancy, is still very controversial, as different studies reported contrasting findings [51–54]. Moreover, the entity of risk found was very small (RR ranging from 1.1 to 2.0), with an incidence rate of 3/1000 live newborns in utero exposed to SSRIs, as compared to 2/1000 in unexposed group [51–53]. Furthermore, also a recent "Drug Safety Communication" from the Food and Drug Administration (FDA) and a review on this topic did not found clear evidence to support such association [54].

Less investigations focused on *long-term neurobehavioral outcomes* in children in utero exposed to ADs. In these studies, it is difficult to disentangle the effects of foetal exposure to ADs (or other drugs) from shared maternal-child genetic susceptibility or postnatal environmental factors, such as maternal depression and/or anxiety disorders and their severity. Neonatal motor and cognitive function delays have been associated with maternal use of ADs. However, a systematic review comparing 280 children exposed to ADs, with 291 who were not exposed, did not find significant differences between the two groups in terms of neurocognitive functions. This review also analysed infant "temperament" vs "behaviour", by reporting no significant differences between these variables [55]. In a recent investigation of 34 studies, a small but statistically significant association between prenatal exposure to ADs and some neurodevelopmental outcomes was reported. However, after considering confounding factors, there were no consistent associations between AD exposure and any of the outcome considered [56]. There have been several studies suggesting an association between prenatal AD exposure and *attention-deficit hyperactivity disorder* (ADHD), even though other studies failed to find such association [12, 39]. For example, findings from a Finland National Register-based study did not report a significant association with exposure to SSRIs and ADHD, after controlling for maternal psychiatric illness [57].

The association between SSRIs and the development of *autism spectrum disorders* (ASD) has been a recent topic of systematic reviews and meta-analyses [39]. Even in this case, the results of different investigations are conflicting, so that no firm conclusion can be drawn on such association [58–61]. We agree with Andrade et al. [62, 63], who recently analysed the most relevant data on this issue, that "AD use during pregnancy is likely to be a marker of more severe illness and that inadequately measured, unmeasured or unknown genetic behavioural and/or environmental confounding factors, associated with more severe illness, may be responsible for the increased risk of ASD, rather than the AD exposure by itself", a conclusion that is widely shared by most experts on this topic, who point out that an association does not necessarily imply a causality [11, 12, 39, 49].

16.3 Benzodiazepines and Z-Drugs in Pregnancy

BDZs and Z-drugs (i.e. *zolpidem*, *zopiclone* and *zaleplon*) represent the most prescribed anxiolytics and hypnotic drugs, widely used in the short-term treatment of acute anxiety and insomnia. Studies investigating the drug utilization found that around from 5% to 15% of general population, particularly women, receives the prescription of such drugs [64]. The current widespread use of these medications also in primary care setting has been associated to their increased and uncontrolled long-term use and misuse. For this reason, BDZs must be used only for short-term periods, with a careful and strict clinical monitoring by the physician prescriber, to avoid the risk of developing dependence and abuse.

Anxiety and insomnia represent one of the most frequently occurring psychopathological conditions during the pregnancy, with a prevalence rate estimated from

8% to 12% [65]. These conditions, particularly if severe and persistent, can lead to relevant distress for the pregnant women and, consequently, can cause adverse gestational and neonatal issues [66]. A survey involving about 15,000 pregnant women in 22 countries showed that BDZs were prescribed to 3.0% of them, even though a great variability between countries in prescription rates was observed [67]. Moreover, it has been also reported that around 64–88% of women experience sleep difficulties during pregnancy, compared to 20–38% of women in general population [68]. As there are no consistent data on the prescription and consumption pattern of BDZs and Z-drugs in the perinatal period, it would be desirable to implement training interventions, concerning an adequate utilization of such drugs in routine clinical practice.

16.3.1 Risk of Major Malformations

Among three of six case-control studies published in the 1990s, foetal exposure to BDZs during the first trimester of pregnancy was associated to an increased risk of inducing MMs, particularly oral cleft or cleft lip. However, three cohort studies published in the same period did not find such congenital anomalies [69, 70]. More recently, original cohort studies and systematic reviews indicate that prescribing BZDs in the early pregnancy should not be considered at risk of inducing MMs, including palate and lip defects [71, 72]. A meta-analysis of 9 cohort studies, with over one million analysed pregnancies, including about 4500 newborns exposed in the early pregnancy, reported that BDZs (as a class) do not increase the teratogenic risk [73]. However, in case-control studies, a small increased risk of oral cleft was observed. Moreover, in this investigation, the case-control studies, addressing the specific risk of cardiac MMs, did not detect any statistical significant association to BZD exposure in utero [73].

A cohort study conducted in the UK on about 2000 pregnant women exposed to BDZs in the first trimester reported reassuring data concerning the risk of teratogenicity. The prevalence rate of MMs was between 2.5% and 2.9% in infants exposed to BDZs and Z-drugs and 2.7% in about 19,000 children whose mothers (affected by depression and/or anxiety) did not receive any drug treatment. Risks of system-specific MMs were generally similar in children exposed and not exposed to BDZs [74]. The "non-teratogenic" effect of BDZs, as a pharmacological class, has been also shared by recent overviews and expert opinions, whilst less information is available for each individual BDZ and/or Z-drugs [75].

16.3.2 Risk of Adverse Gestational and Neonatal Outcomes

Foetal exposure to BDZs during the second and third trimester of pregnancy has been associated with an increased risk of a *neonatal withdrawal syndrome* (NWS), a condition affecting about 25% of newborns BDZ-exposed late in pregnancy. NWS

includes signs such as somnolence, irritability, hypoglycaemia, difficulties with sucking, tremors, tachypnoea, gastrointestinal upset, hypoglycaemia and hyperreflexia. It generally appears within a week after delivery and it may last, in some cases, from few days up to few weeks [76]. Tapering the dose of BZDs some weeks before delivery seems not to be effective to avoid neonatal symptoms, and it can induce a maternal withdrawal reaction, especially among women who have been taking high doses of BZDs for several weeks during gestation. Most newborns presenting only a moderate NWS may spontaneously improve after few days, without any long-lasting sequelae. Using BDZs, especially at high doses (given parenterally or intravenously), just before or during the delivery has been associated to an "infant floppy syndrome", characterized by floppiness or general muscular hypotonia at birth or in early life, affecting the limbs, trunk and the cranial-facial musculature. No clear association has been documented between use of BDZ or Z-drugs and gestational adverse outcomes, such as preterm delivery and SA. Moreover, no long-term neurodevelopment anomalies have been observed in infants in utero exposed to BDZ or Z-drugs [12, 72].

16.4 Antipsychotic Drugs in Pregnancy

Antipsychotic (AP) drugs are generally prescribed in the short- and long-term treatment of psychotic disorders, including bipolar disorder. During the last 15 years, there was an increased AP prescription during the pregnancy, particularly for second-generation APs (SGA), as compared with the first-generation APs (FGA) [77]. Less information on the safety profile in pregnancy is available for ziprasidone, lurasidone and cariprazine and for long-acting AP medications (LAI).

16.4.1 Risk of Major Malformations

All APs cross the placenta and can potentially induce congenital MMs in newborns in utero exposed. The ratio of placental passage was found to be highest for olanzapine (72%), followed by haloperidol (65%), risperidone (49%) and quetiapine (23%) [78]. However, these findings do not seem to be related to the rates of MMs reported with these medications. Recent studies indicate that the early foetal exposure to APs, as a class, should not be considered at risk of MMs. In a sample of 1021 pregnant women treated with AP, the rate of birth defects and other gestational and neonatal complications was found not dissimilar to those observed in a control group [79]. In a systematic review focusing on SGA, the average rate of MMs in newborns exposed was 3.5%, a value not significantly different to that reported in general population [80]. In a meta-analysis of 12 studies including about 1800 cases and more than one million of controls, a small but statically significant risk (OR = 2.0) of MMs was found in newborns of women treated with SGA in the first trimester, even though no specific pattern of defects was identified. The authors,

nevertheless, underlined that "further studies sufficiently controlling for confounding factors are needed to validate these findings" [81]. Data from the *National Register Massachusetts General Hospital* showed no significant statistical difference in the rate of MMs between 214 newborns exposed to SGA and a group of 89 unexposed newborns (1.4% vs 1.2%, respectively) [82]. No statistically significant differences were also found in the rate of MMs in a US study comparing about 9000 newborns exposed during gestation to SGA (4.4%) and about 700 exposed to FGA (3.9%). In the unexposed group, the rate was 3.3% [83]. In a review of 59 studies focusing on the risk-benefit of SGA in pregnant women affected by schizophrenia and bipolar disorder, the authors concluded that SGA, as a class, are not associated with an increased risk of congenital birth defects [84]. These findings have been also shared by the most authoritative experts in the perinatal psychopharmacology [11, 12, 85].

16.4.2 Risk of Adverse Gestational and Neonatal Outcomes

Adverse perinatal outcomes, such as SA, preterm birth, low birth weight, small for gestational age, gestational diabetes mellitus and hypertension, have been reported in some studies evaluating women treated with AP (FGA and SGA) during their pregnancy. However, other investigations that used a control group of pregnant women with mental illness, but unexposed to AP or controlled for confounding factors, reported only few or no associations between AP and such perinatal complications [86–88]. Some studies reported that AP exposure during pregnancy was associated with long-term neurodevelopmental delays. However, such association is to be considered with caution, given the lack of reliable studies published so far on this issue [12].

16.5 Mood Stabilizers in Pregnancy

In this section, we shortly discuss the most relevant data coming from studies on the safety of *mood stabilizers* (MS) more frequently prescribed during pregnancy. The prescriptions of MS in a pregnant woman must be carefully evaluated, considering both the perinatal risks of drug exposure and the risk of an untreated SPMI, such as a *bipolar disorder* (BD). Several investigations have documented that bipolar patients if untreated during pregnancy can be at higher risk to develop adverse perinatal outcomes and relapses compared to treated pregnant bipolar women [89]. A study by Viguera et al. [90] reported a relapse rate of 86% in BD pregnant women who discontinued a MS before pregnancy, as compared to 37% of those who maintained the drug treatment. A recent study reported in BD women a significantly higher postpartum relapse rate among those who did not take any medication during their pregnancy (66%), compared to those who were administered a prophylactic MS treatment (23%) [91].

16.5.1 Lithium

Lithium (Li) remains the "gold standard" treatment for the prevention of recurrences and in manic episode of patients with BD. The efficacy of Li in preventing suicidal behaviour in these patients and in those with MDD has been well documented by several controlled studies. Moreover, consistent evidence supported the effectiveness of augmentation strategy of Li in patients with treatment-resistant unipolar depression (TRD) [92]. Moreover, most authoritative experts recommended Li treatment as first-line choice in the prophylactic treatment of bipolar patients, including in women in their childbearing age [93].

16.5.1.1 Risk of Major Malformations

The use of Li in the early pregnancy has been a cause of clinical concern for several years since its introduction in the psychiatric practice. The main reason was related to its potential teratogenicity, particularly that of inducing severe congenital heart defects, such as the *Ebstein's anomaly*, a rare structural defects of tricuspid valve and right ventricle, whose prevalence is now estimated to be 1 in about 21,000 live births [94, 95]. However, recent original studies reported more reassuring findings concerning the foetal safety of Li exposure. A comprehensive review including nine studies (from 1975 to 2018) has been recently published by Poels et al. [96] to establish the safety of Li during pregnancy; three of such studies, particularly, need to be considered for their clinical implications. The first one was published by Diav-Citrin et al. [97] who did not find any statistically significant differences in congenital birth defects (after excluding anomalies that resolved spontaneously), between newborns exposed to Li and a control unexposed group. In the second study, Patorno et al. [98], using data from 1,325,563 pregnancies (US Medicaid), analysed the outcomes of 663 women who were exposed to Li in the first trimester. The results indicated a dose-dependent association between Li and cardiac MMs. The risk of cardiac defects was higher with Li doses above 900 mg/day (RR = 3.2), as compared to doses between 601 and 900 mg/day (RR = 1.6) and to doses less than 600 mg/day (RR = 1.1); the corresponding prevalence rate (per 100/births) of malformations was, respectively, 4.8, 2.1 and 1.6 [98]. Finally, the third investigation was a meta-analysis of 6 cohort studies including 557 pregnancies. Li-exposed group (in the first trimester) was associated with an increased risk of MMs, as compared to controls (prevalence rate: 7.4% vs 4.3%; RR = 1.7), even though no statistically significant differences were reported for cardiac MMs (prevalence rate: 2.1% vs 1.6%) [99].

Overall, during the pregnancy, women treated with Li must be regularly followed with a close monitoring of blood levels, as Li serum levels change across pregnancy and after delivery; blood levels must be checked every 3 weeks for the first 7–8 months and then weekly until the delivery and the first 2 weeks of postpartum period. Foetal echocardiography and a level 2 ultrasound are strongly recommended at 16–18 weeks' gestation [100].

16.5.1.2 Risk of Adverse Gestational and Neonatal Outcomes

Data concerning the safe use of Li during the second–third trimester of pregnancy produced conflicting findings, so that no firm conclusions can be drawn on the lithium's risk of inducing perinatal complications [12]. Infants exposed to Li plasma concentrations more than 0.70 mEq/L, at the time of delivery, could be at risk for low Apgar scores, longer hospital stays and higher CNS and neuromuscular problems ("infant floppy syndrome"), a condition that can be avoided or mitigated by discontinuing Li 24–48 h before planned deliveries or at the onset of labour in spontaneous deliveries. Some studies have also reported cases of neonatal hypotonia, sedation and respiratory distress. Other rare neonatal complications observed in infants exposed in late pregnancy to Li include diabetes insipidus, hypothyroidism, arrhythmias and nephrotoxicity. Information on the long-term neurodevelopmental outcomes in infants exposed prenatally to Li are poor, even though no cognitive or psychomotor impairment has been so far reported [22].

As general rule, women with BD who need lithium maintenance therapy should always be considered a vulnerable, high-risk obstetric population, who would benefit from preconception counselling, regular antenatal care, delivery with neonatal paediatric support and experienced psychiatric management [101].

16.5.2 Anticonvulsant Drugs

Among anticonvulsant MS most of data concerns medications containing *valproate* (e.g. sodium valproate, valproic acid), *carbamazepine* and *lamotrigine*. Moreover, most clinical information regarding the reproductive safety of these drugs come from studies concerning epileptic patients more than women affected by BD.

16.5.2.1 Risk of Major Malformations

Valproate (VLP). Exposure to VLP in monotherapy during the first trimester of pregnancy was associated with an increased rate of MMs (from 6.6% to 17.4%), according to data published by the *EUROCAT Antiepileptic Working Group* [102]. Among the congenital anomalies identified in the study, the risk of *spina bifida* was particularly high (RR = 12.7), as compared to other MMs, such as *hypospadias* (RR = 4.8), *cleft palate* (RR = 5.2) and *cardiac septal defect* (RR = 2.5).

The prevalence rate of spina bifida was around 13 over 10,000 exposed newborns, as compared to 1 over 10,000 of general population. Data from the *EURAP Study Group* and from a Cochrane systematic review have also reported a dose-dependent risk of MMs for VLP, with a rate ranging from 5.6% at doses <700 mg/day to 24.2% for doses > 1500 mg/day [103, 104]. In a large prospective study by Campbell et al. [105], data from 1290 pregnant women exposed to VLP in monotherapy were analysed, and a clear dose-dependent risk of MMs was confirmed: a low risk (about 5–6%) was reported with doses less than 600 mg/day, whilst the MM rate was higher (about 11–12%) with doses above 1000/1500 mg/day [105]. It has been suggested that high dose of folic acid supplementation, before and during pregnancy, could be protective against the risk of spina bifida associated to VLP

exposure in early pregnancy. However, available evidence coming from *North American Birth Defects Registry* does not support this "protective effect", as about 7% of women taking anticonvulsant (including VP) had a child with MM, including defects of neural tube, with and without prenatal folate administration [106]. Given the well-documented risk of teratogenicity associated with high dose of VLP exposure in pregnancy, many regulatory bodies and guidelines across the world (e.g. National Agency for Safety Medicine in France, NICE in the UK) discouraged and even banned the prescription of medications containing VPL during pregnancy and in women of childbearing age, unless no effective alternative drug treatment is available, or unless a pregnancy prevention programme is implemented [12, 107]. Although there is a general agreement on this recommendation, it should be recognized that in patients on the maintenance treatment with VLP, it should be equally considered and the risk associated to VPL treatment and the risk related to discontinuation balanced. Therefore, a careful evaluation of both the risk of teratogenicity (which is dose-dependent) and the risk of treatment discontinuation needs to be discussed with the pregnant woman and her partner, so that an informed and shared decision can be made [108].

Carbamazepine (CBZ). Foetal exposure to CBZ in early pregnancy has been associated in some studies with a small increased risk of congenital MMs, with a prevalence rate from 3.5% to 5%, even though other studies failed to confirm such data [12]. A moderate dose-dependent risk of MMs was documented also for CBZ, with a prevalence rate of around 5% at dosages more than 1000 mg/day; among birth defects, spina bifida was also found, but the risk was smaller than for VLP [105].

Lamotrigine (LMT). Most studies and guidelines indicated that LMT should not be considered at risk of inducing MMs, as the prevalence rate of birth defects reported in the studies published (2–3%) falls within that of general population [11, 12, 105].

16.5.2.2 Risk of Adverse Gestational and Neonatal Outcomes

Valproate. Limited evidence-based information is available on this issue, most of which were obtained from epileptic patients. Gestational adverse outcomes (e.g. preterm delivery, gestational diabetes, spontaneous abortion) and neonatal complications (e.g. low birth weight, hypoglycaemia, withdrawal symptoms, feeding difficulties, admission to neonatal intensive care unit) have been associated, in some studies, with VLP use during pregnancy. However, Bodén et al. [108] did not find significant differences in such perinatal adverse events between 320 bipolar women who were treated with VLP (and other MS) during pregnancy and 534 untreated bipolar women, even though the risk was higher compared with a control group. A neurodevelopmental delay, reduction of IQ scores and increased impaired language acquisition were also reported in children of epileptic mothers treated with VLP during pregnancy. Such risks, as in case of MMs, seem to be dose-related and more severe when VLP is used in association with other anticonvulsant drugs. A systematic review, focusing on the child development in women taking MS in pregnancy, found a dose-response relationship between doses of VLP above 800/1000 mg/day and poorer global cognitive abilities (worsening of the IQ score by 8–11 points).

This finding was not observed for other anticonvulsant MS [109]. The risk of ASD in infants in utero exposed to VLP has been widely investigated in several studies. However, because of methodological flaws in most of studies, no definite conclusion can be drawn on such risk, and further investigations are needed. In fact, it is well known that some maternal diseases in pregnancy have been associated with ASD (e.g. gestational diabetes mellitus, maternal infections), which cause changes in a variety of inflammatory cytokines. In addition, also SSRIs, BDZs, ethanol, cocaine, heavy smoking and air pollution exposure during pregnancy were associated with ASD [110]. A recent cohort study in Denmark including about 900,000 children of epileptic women (90%) has also reported an increased risk (RR = 1.5) of ADHD in infants in utero exposed to VLP (8.4%), as compared to unexposed group (3.2%), with no statistically significant associations found between ADHD and other antiepileptic drugs [111]. However, these findings need to be interpreted with caution and supported by other studies, before drawing definite conclusions.

Carbamazepine and Lamotrigine. As in case of VLP, no consistent findings have been reported concerning the risk of gestational and neonatal complications in women taking CBZ or LMT during pregnancy, even though some cases of such adverse effects were occasionally observed with high doses (e.g. postpartum haemorrhage, induction of labour, SA) [108]. Available evidence does not indicate that CBZ or LMT are associated with infant poorer cognitive development or IQ reduction, as well as with ASD and ADHD [12, 112].

16.6 Psychotropic Drugs During Lactation

Postpartum is a period of psychopathological vulnerability for women, as in the puerperium, physiological changes in hormonal profile may occur, and the new mother may present a greater emotional reactivity and susceptibility to develop psychopathological disorders or exacerbations of a previously psychiatric illness. Breast milk is the only natural food and the main source of nutrition for the newborn, as it contains all the essential factors to ensure an adequate immune protection [113, 114]. Furthermore, the elements of the first feedings (*colostrum*) provide important protective factors for safeguarding the newborn physical health by protecting him from the risk of infections of the lower respiratory and genitourinary tract, reducing also the risk of mortality [114]. The *World Health Organization* (WHO) recommends exclusive breastfeeding in the first 6 months of the infants' life and its continuation during the entire weaning period [113, 114]. Breastfeeding also benefits the new mother by stimulating natural uterine contraction, reducing the physiological postpartum haemorrhage and allowing the uterus to return to normal size faster. Furthermore, breastfeeding favours the development of an appropriate mother-child attachment.

Considering that PD can be excreted into the breast milk at variable degree, safety data on such medications during lactation is essential to minimize infant exposure and potential adverse effects. A number of compounds within the class of PD are nowadays considered safe during breastfeeding, because their concentration

in breast milk is very low or cannot be determined. It has been proposed to assess an acceptable level of drug into breast milk the *relative infant dose* (RID), which estimates the maximum dose of a drug/kg/day that the newborn would theoretically take during breastfeeding. In general, breastfeeding is considered acceptable when the RID is less than 10%. It has been also suggested, as another safety index, to calculate the ratio between the average concentration of drug in breast milk and that in maternal plasma (*milk/plasma ratio*), whose value less than 1 would qualify a drug as safer and thus is recommended in case of breastfeeding [115]. An international updated source of data on the safety of drugs is represented by the *LactMed US database* (LMD). The LMD contains information on drugs to which breastfeeding mothers may be exposed and on the levels of such substances in breast milk and infant blood, and the possible adverse effects in the nursing infant (http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm). Despite reassuring information available for several PDs, mothers may not be encouraged, or perhaps even discouraged, to breastfeed whilst taking such drugs by medical staff for a variety of reasons, including lack of data, safety concern for infants and/or negative attitudes and bias towards mental illness and psychotropics. However, if the mother wishes to breastfeed her baby, the newborn should be monitored in any cases, for the risk of potential, even not severe, adverse effects, with a careful evaluation of the usual neonatal healthy parameters, such as growth curve, body weight and psychomotor development.

16.6.1 Antidepressant Drugs During Lactation

The SRIs are considered the first-line choice among ADs in the treatment of depressive and anxiety disorders during postpartum period. The data on the safety of SRIs in breastfeeding mainly come from case series or cohort studies conducted on small clinical samples. Even though international guidelines suggested that most PDs are "relatively safe" during breastfeeding, further studies should be carried out, considering more large sample with adequate follow-up of breastfed infants [12]. *Sertraline* and *paroxetine* are considered as first-line drugs in women who need an AD medications during breastfeeding, as no relevant adverse reactions have been reported in most infant exposed during breastfeeding; the RID is calculated around 1–2%. Most authoritative reviewers consider sertraline and paroxetine a preferred AD during breastfeeding; moreover, breastfed infants exposed to such drugs during the third trimester of pregnancy have a lower risk of poor neonatal adaptation syndrome than formula-fed infants. The average amount of *fluoxetine* in breast milk is higher than for other SSRI. The active metabolite, norfluoxetine, is detectable in the serum of most breastfed infants during the first 2 months postpartum. Adverse effects such as colic pain, fussiness, irritability and drowsiness have been reported in some breastfed infants. Decreased infant weight gain was found in some case reports, but not in others. No adverse effects on psychomotor development were found in a few infants followed for up to a year of age. Data concerning *citalopram* and *escitalopram* also report relatively reassuring data. A few cases of minor behavioural side effects such as drowsiness or fussiness have been reported, with citalopram, but no adverse

effects on development have been found in infants followed for up to a year. However, infants exposed in utero can have withdrawal effects in the postpartum period despite breastfeeding. Limited information indicates that maternal doses of escitalopram up to 20 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants. One case of necrotizing enterocolitis was reported in breastfed newborn whose mother was taking escitalopram during pregnancy and lactation, but causality was not established. The RID of the drug and its active metabolite is 5.3%. Limited information is available for *fluvoxamine*, indicating that maternal fluvoxamine doses of up to 300 mg daily produce low levels in breast milk and would not be expected to cause any adverse effects in breastfed infants. Low number of cases have been reported with *venlafaxine*; however, data published on the safety of this SNRI (including its active metabolite) seems reassuring, as its RID varies from 4% to 10%. So far, no consistent data have been reported on the safety of *duloxetine* during breastfeeding. A systematic review of SRIs during breastfeeding has been published by Orsolini and Bellantuono [116]. Data concerning the *tricyclics* (TCA), as a class, are less numerous than those of SRIs. However, data are quite reassuring, particularly for *nortriptyline*, as low levels of nortriptyline have been measured in breast milk; amounts ingested by the infant are small and usually not detected in the serum of the infant. Therefore, nortriptyline is considered, among the TCA, the drug of first choice during breastfeeding [18]. Data on the safety use of other ADs (non-SRIs and non-TCA) during breastfeeding is considered still preliminary, due to the low number of infant exposed, so that their utilization in breastfed infants should be avoided.

16.6.2 Benzodiazepines and Z-Drugs During Lactation

BDZs cross the blood-breast barrier and can be detected in breast milk. The greater is the BDZ half-life (t½), the greater the metabolic effort required by newborn to eliminate the drug and, consequently, the risk of BDZ-related side effects. Therefore, shorter-acting BDZs (such as lorazepam, oxazepam and lormetazepam), which have also the advantage of direct hepatic elimination with glucuronic acid, should be preferred to longer-acting ones (such as diazepam, desmethyldiazepam, flurazepam), which undergo more metabolic stages before being eliminated [18, 72]. In a Mother Risk study, *lorazepam* was the most frequently prescribed BDZ during breastfeeding, being reported in about 53% of all BDZ prescribed to 126 women during breastfeeding. The only adverse reaction reported in the study was "sedation", affecting around 1.6% (two cases) of infant exposed to BDZs [117]. From published data, it can be concluded that the sedative effects reported with BDZ exposure through breast milk (at therapeutic doses) may represent a rare risk in infants exposed to such drugs. However, infant sedation is more likely to occur in mothers taking BDZ at higher doses or concomitant CNS depressant drugs during lactation. There are few data on the safety of *non-benzodiazepine hypnotics* (*Z-drugs*) during breastfeeding. Data on *zolpidem*, *zopiclone* and *zaleplon* shows low drug concentrations in breast milk and neonatal serum. However, the

recommendations from guidelines suggest that infants of mother taking such hypnotics, as well as BDZ, during breastfeeding be monitored for the potential, even uncommon, risk of excessive sedation, hypotonia and respiratory depression [12].

16.6.3 Antipsychotic Drugs During Lactation

Overall, both FGA and SGA are not contraindicated during lactation. Data concerning some FGA like *haloperidol*, *chlorpromazine*, *perphenazine*, *trifluoperazine* and *flupentixol* are reassuring, as the amount of drug detected in serum of breastfed infant is low (RID less than 10%). Also, drugs belonging to the SGA, particularly *olanzapine*, *quetiapine*, *risperidone/paliperidone* and *aripiprazole*, are considered not at risk of inducing relevant infant adverse effects during breastfeeding. Moreover, the concentration of drug in infants is low or undetectable and the milk/plasma ratio is below 0.5%. The RID calculated for SGA widely ranges from 0.1% to 4% for quetiapine and olanzapine whilst from 2% to 9% for aripiprazole and risperidone. *Clozapine* is an exception, because it is considered contraindicated during breastfeeding, due to the risk of infant agranulocytosis and seizure, even though the RID is low (1.4%) [18]. Few case reports observed a neurodevelopmental delay in infants exposed to APs, as a class, during the breastfeeding, but there were no controlled studies, and the impact of underlying maternal disease was not taken into account. In addition, considering the few data published, no firm conclusion can be made on this issue [12]. Overall, according to the recent guidelines, it should be recommended that women who need to be treated during postpartum period with antipsychotic medications should not be discouraged from breastfeeding. As general rule, a clinical monitoring is always recommended in infants breastfed by mothers taking AP medications.

16.6.4 Mood Stabilizers During Lactation

16.6.4.1 Lithium

Li excretion into breast milk and concentrations in infant serum are highly variable; the RID estimates vary, with value of up 42% being reported with Li carbonate. No data are available with lithium one-a-day formulations (“slow release”). Although Li appears on some lists of drugs contraindicated during breastfeeding, many sources do not consider it an absolute contraindication. Several case reports did not document in infants who were breastfed during Li therapy, the emergence of symptoms of toxicity or developmental anomalies. Most infants were breastfed from birth and some continued to nurse for up to 1 year of maternal lithium therapy. However, Li during, in those cases in which there is a renal impairment and/or an impaired Li elimination, such as in neonatal dehydration, infections or prematurity. Occasionally, symptoms like hypothermia, hypotonia, lethargy and T-wave modifications at ECG were observed in infants of mothers taking lithium during postpartum period. On the bases of available evidence, Li (in monotherapy) may be used in

mothers of full-term newborns who are willing and able to monitor their infants. Because maternal Li requirements and dosage may be increased during pregnancy, maternal serum levels should be monitored frequently in the postpartum period and dosage reduced as necessary, to avoid excessive infant exposure via breast milk. It is also recommended, during breastfeeding, a regular monitoring of infant's Li serum levels, creatininemia, blood urea and TSH. A recent overview of Li safety during lactation is reported by Uguz and Orsolini [18].

16.6.4.2 Anticonvulsant Drugs

VLP levels in breast milk are low and infant serum levels range from undetectable to very low. Breastfeeding during VPA monotherapy does not appear to adversely affect infant growth or development, and one study reported that breastfed infants had higher IQs and enhanced verbal abilities than no breastfed infants at 6 years of age. If VLP is required by the mother during puerperium, there is not a reason to discontinue breastfeeding. No definite adverse reactions to VLP in breastfed infants have been reported. It is in any case a good practice that infants should be monitored for jaundice and other signs of liver damage during breastfeeding. Some authors also recommended the monitoring of infant serum VLP levels, platelets and liver enzymes. Treatment with VLP in association with sedating anticonvulsants or PD can result in risk of infant sedation or withdrawal reactions.

CBZ breastfeeding in monotherapy does not appear to adversely affect infant growth or development. Moreover, it has been documented that breastfed infants had higher IQs and enhanced verbal abilities than no breastfed infants at 6 years of age. Generally, if CBZ is required by the mother, there are no reasons to discontinue breastfeeding. However, a few cases of sedation, poor sucking, withdrawal reactions and hepatic dysfunction have been reported. It is also suggested the monitoring of infant serum CBZ levels, liver enzymes and a complete blood count during breastfeeding. Combination of CBZ with other anticonvulsants or PD should be avoided during breastfeeding.

LMT high concentrations are detectable in breast milk few hours after the intake of drug by nursing mother. The maternal serum level of infant exposed via breast milk is approximately around 30–50%. In a study including 30 infants exposed during breastfeeding to CBZ (maternal dose ranging from 50 to 800 mg/day), the mean milk/plasma ratio reported was 41%. However, breastfeeding during LMT monotherapy does not appear to adversely affect infant growth or development, even though some cases of apnoea and CNS depression have been observed. LMT monotherapy may be considered relatively safe during lactation, but a regular monitoring of plasma level and platelet counts of nursing infant is recommended [18].

16.7 Conclusion and Clinical Implications

An early and careful planning for the PD treatment in pregnancy should be made before the women become pregnant. More than 50% of pregnancies are unplanned and, hence, psychiatrists need to make treatment decision for women who are

already pregnant. As general approach, the prescription of PD during pregnancy should take into consideration several factors, such as the patient's psychiatric and psychopharmacological history, the severity of symptoms, the neonatal safety of drug prescribed and the attitude of pregnant women towards PD use. The main priority should be to keep the pregnant women in a good mental health state, as severe psychopathological conditions are a well-established risk factor for the mother, the gestation and the offspring. Nowadays, more accurate information, coming from cohort studies and meta-analyses, are available for clinicians to allow a proper assessment of the safety profile of most commonly prescribed PD during pregnancy [18]. In any cases, the decision to maintain or to start with a new drug treatment must be carefully evaluated by the specialist prescriber and the prescription shared with the pregnant woman and her partner, through a detailed informed consent [17]. Also, during the postpartum period, the decision to start or to maintain a PD treatment needs to be taken on the basis of recent available evidences on the drug safety in breastfeeding, evaluating the available safety parameters. There is some evidence that women very often overestimate PD teratogenic and other perinatal risks and that evidence-based counselling can enable them to restart such drugs, when needed. Thus, it is crucial that mental health professionals, in generic service, need to be trained with to "think family", so that they can deliver care, including drug treatment, with a life course lens, having pregnancy and family in mind [118].

References

1. Biaggi A, Conroy SB, Pawlby S, et al. Identifying the women at risk of antenatal anxiety and depression: A systematic review. J Affect Disord. 2016;191:62–77.
2. ACOG Committee Opinion No. 757. Screening for Perinatal Depression. Obstet Gynecol. 2018;132:e208–12.
3. National Institute of Mental Health (NICE). The perinatal mental health care pathways. National Collaborating Centre for Mental Health London. 2018;
4. Grigoriadis S, Graves L, Peer M, et al. Maternal anxiety during pregnancy and the association with adverse perinatal outcomes: systematic review and meta-analysis. J Clin Psychiatry. 2018;79(5):17r,1201.
5. Orsolini L, Valchera A, Vecchiotti R, et al. Suicide during perinatal period: epidemiology, risk factors, and clinical correlates. Front Psychiatry. 2016;7:138.
6. Gressier F, Guillard V, Cazas O, et al. Risk factors for suicide attempt in pregnancy and the postpartum period in women with serious mental illnesses. J Psychiatr Res. 2017;84:284–91.
7. Wisner KL. The last therapeutic orphan: the pregnant woman. Am J Psychiatry. 2012;169:554–6.
8. Andrade C. A primer on confidence intervals in psychopharmacology. J Clin Psychiatry. 2015;76(2):228–31.
9. Nonacs RM, Cohen L. Challenges in determining outcomes of prenatal exposure to antidepressants. J Clin Psychiatry. 2020;81(3):20com13269.
10. Louik C, Lin AE, Werler MM, Hernández-Díaz S, Mitchell AA. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. N Engl J Med. 2007;356(26):2675–83. Erratum in: N Engl J Med 2015; 373(7): 686
11. Chisolm MS, Payne JL. Management of psychotropic drugs during pregnancy. BMJ. 2016;532:h5918.

12. McAllister-Williams RH, Baldwin DS, Cantwell R., Endorsed by the British Association for Psychopharmacology et al.; British Association for Psychopharmacology (BAP) consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum. J Psychopharmacol 2017; 31(5): 519–552.
13. Alwan S, Bérard A. Chapter 1. Epidemiology of the use of psychotropic drugs in pregnancy and nursing women. In: Uguz F, Orsolini L, editors. Perinatal psychopharmacology. Berlino: Springer; 2019.
14. Ram D, et al. Psychopharmacoteratophobia: excessive fear of malformation associated with prescribing psychotropic drugs during pregnancy: an Indian perspective. Indian J Pharmacol. 2015;47(5):484–90.
15. Huybrechts KF, Palmsten K, Mogun H, Kowal M, Avorn J, Setoguchi-Iwata S, Hernández-Díaz S. National trends in antidepressant medication treatment among publicly insured pregnant women. Gen Hosp Psychiatry. 2013;35:265–71.
16. Shivakumar G, Kroll-Desrosiers AR, Copeland L, Anderson EH, Maydon A, Mattocks K. Patterns of treatment utilization across the perinatal period in the center for maternal and infant outcomes and research in translation (COMFORT) veterans study. J Womens Health (Larchmt). 2020; https://doi.org/10.1089/jwh.2020.8435.
17. Bellantuono C, Martellini M, Orsolini L. Chapter 4. General approach to pharmacological treatment during the perinatal period. In: Uguz F, Orsolini L, editors. Perinatal psychopharmacology. Berlino: Springer; 2019.
18. Uguz F, Orsolini L. Perinatal psychopharmacology. 1st ed. Berlino: Springer; 2019.
19. Molenaar MN, Lambregtse-van den Berg PT, Bonsel GJ. Dispensing patterns of SSRIs before, during and after pregnancy: a 16-year population-based cohort study from the Netherlands. Arch Women's Mental Health. 2020;23(1):71–9.
20. Jimenez-Solem E, Andersen JT, Petersen M, et al. Prevalence of antidepressant use during pregnancy in Denmark, a nation-wide cohort study. PLoS One. 2013;8(4):e63034.
21. Mitchell AA, Gilboa SM, Werler MM, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976–2008. Am J Obstet Gynecol. 2011;205(51):e51–51.e58.
22. Betcher HK, Wisner KL. Psychotropic treatment during pregnancy: research synthesis and clinical care principles. J Womens Health (Larchmt). 2020;29(3):310–8. https://doi.org/10.1089/jwh.2019.778.
23. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006;295:499–507.
24. National Institute for Health and Care Excellence (NICE) 2015 Antenatal and postnatal mental health: Clinical management and service guidance. NICE Guidelines CG192. Available at: https://www.nice.org.uk/guidance/CG192.
25. Centers for Disease Control and Prevention. World birth defects day, 2018. Available at: https://www.cdc.gov/features/birth-defects-day.
26. Kallen BA, Otterblad OP. Maternal use of selective serotonin re-uptake inhibitors in early pregnancy and infant congenital malformations. Birth Defects Res A Clin Mol Teratol. 2007;79:301–8.
27. Reis M, Kallen B. Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data. Psychol Med. 2010;40:1723–33.
28. Jimenez-Solem E, Andersen JT, Petersen M, et al. Exposure to SSRI and risk of MM: a nationwide cohort study. BMJ Open. 2012;2:e001148. https://doi.org/10.1136/bmjopen-2012-0011.
29. Malm H, Artama M, Gissler M, et al. Selective serotonin reuptake inhibitors and risk for major congenital anomalies. Obstet Gynecol. 2011;118:111–20.
30. Ban L, Gibson JE, West J, et al. Maternal depression, antidepressant prescriptions, and congenital anomaly risk in offspring: a population-based cohort study. BJOG. 2014;121(12):1471–81. https://doi.org/10.1111/1471-0528.12682.
31. Wang S, Yang L, Wang L, Gao L, Xu B, Xiong Y. Selective Serotonin Reuptake Inhibitors (SSRIs) and the risk of congenital heart defects: a meta-analysis of prospective cohort studies. J Am Heart Assoc. 2015;4(5):e001681. https://doi.org/10.1161/JAHA.114.001681.

32. Huybrechts KF, Hernandez-Diaz S, Avorn J. Antidepressant use in pregnancy and the risk of cardiac defects. N Engl J Med. 2014;371:1168–9.
33. Petersen I, Evans SJ, Gilbert R, et al. Selective serotonin reuptake inhibitors and congenital heart anomalies: comparative cohort studies of women treated before and during pregnancy and their children. J Clin Psychiatry. 2016;77(1):e36–42.
34. Gentile S, Bellantuono C. Selective serotonin reuptake inhibitor exposure during early pregnancy and the risk of fetal major malformations: focus on paroxetine. J Clin Psychiatry. 2009;70:414–22.
35. Riggin L, Frankel Z, Moretti M, Pupco A, Koren G. The fetal safety of fluoxetine: a systematic review and meta-analysis. J Obstet Gynaecol Can. 2013;35:362–9.
36. Bellantuono C, Vargas M, Mandarelli G, et al. The safety of serotonin-noradrenaline reuptake inhibitors (SNRIs) in pregnancy and breastfeeding: a comprehensive review. Hum Psychopharmacol. 2015;30(3):143–51.
37. Furu K, Kieler H, Haglund B, et al. Selective serotonin reuptake inhibitors and venlafaxine in early pregnancy and risk of birth defects: population based cohort study and sibling design. BMJ. 2015;350:h1798.
38. Lassen D, Ennis ZN, Damkier P. First-trimester pregnancy exposure to venlafaxine or duloxetine and risk of major congenital malformations: a systematic review. Basic Clin Pharmacol Toxicol. 2016;118(1):32–6. https://doi.org/10.1111/bcpt.12497.
39. Grigoriadis S, Peer M. Antidepressants in pregnancy. In: Uguz F, Orsolini L, editors. Perinatal psychopharmacology. Springer; 2019.
40. Wisner KL, Sit DK, Hanusa BH, et al. Major depression and antidepressant treatment: Impact on pregnancy and neonatal outcomes. Am J Psychiatry. 2009;166:557–66.
41. Malm H, Sourander A, Gissler M, et al. Pregnancy complications following prenatal exposure to SSRIs or maternal psychiatric disorders: results from population-based national register data. Am J Psychiatry. 2015;172:1224–32.
42. Nakhai-Pour HR, Broy P, Berard A. Use of antidepressants during pregnancy and the risk of spontaneous abortion. CMAJ. 2010;182:1031–7.
43. Einarson A, Choi J, Einarson TR, Koren G. Rates of spontaneous and therapeutic abortions following use of antidepressants in pregnancy: results from a large prospective database. J Obstet Gynaecol Can. 2009;31:452–6.
44. Einarson A. Antidepressants and pregnancy: complexities of producing evidence-based information. CMAJ. 2010;182:1017–8.
45. Kjaersgaard MI, Parner ET, Vestergaard M, et al. Prenatal antidepressant exposure and risk of spontaneous abortion—a population-based study. PLoS One. 2013;8(8):e72095.
46. Prady SL, Hanlon I, Fraser L, et al. A systematic review of maternal antidepressant use in pregnancy and short- and long-term offspring's outcomes. Arch Women's Mental Health. 2018;21(2):127–40.
47. Galbally M, Spigset O, Johnson AR, Kohan R, Lappas M, Lewis AJ. Neonatal adaptation following intrauterine antidepressant exposure: assessment, drug assay levels, and infant development outcomes. Pediatr Res. 2017;82(5):806–13. https://doi.org/10.1038/pr.2017.156.
48. Grigoriadis S, VonderPorten EH, Mamisashvili L, Eady A, Tomlinson G, Dennis CL, Koren G, Steiner M, Mousmanis P, Cheung A, Ross LE. The effect of prenatal antidepressant exposure on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74:e309–20.
49. Vigod SN, Wilson CA, Howard LM. Depression in pregnancy. BMJ. 2016;352:i1547. https://doi.org/10.1136/bmj.i1547.
50. Salisbury AL, O'Grady KE, Battle CL, et al. The roles of maternal depression, serotonin reuptake inhibitor treatment, and concomitant benzodiazepine use on infant neurobehavioral functioning over the first postnatal month. Am J Psychiatry. 2016;173:147–57.
51. Huybrechts KF, Bateman BT, Palmsten K, Desai RJ, Patorno E, Gopalakrishnan C, Levin R, Mogun H, Hernandez-Diaz S. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. JAMA. 2015;313:2142–51.

52. Andrade SE, McPhillips H, Loren D, et al. Antidepressant medication use and risk of persistent pulmonary hypertension of the newborn. Pharmacoepidemiol Drug Saf. 2009;18(3):246–52.
53. Wilson KL, Zelig CM, Harvey JP, Cunningham BS, Dolinsky BM, Napolitano PG. Persistent pulmonary hypertension of the newborn is associated with mode of delivery and not with maternal use of selective serotonin reuptake inhibitors. Am J Perinatol. 2011;28(1):19–24.
54. Lusskin SI, Khan SJ, Ernst C, Habib S, Fersh ME, Albertini ES. Pharmacotherapy for perinatal depression. Clin Obstet Gynecol. 2018;61(3):544–61. https://doi.org/10.1097/GRF.0000000000000365.
55. Pedersen LH, Henriksen TB, Bech BH, Licht RW, Kjaer D, Olsen J. Prenatal antidepressant exposure and behavioral problems in early childhood--a cohort study. Acta Psychiatr Scand. 2013;127:126–35.
56. Rommel AS, Bergink V, Liu X, Munk-Olsen T, Molenaar NM. Long-term effects of intrauterine exposure to antidepressants on physical, neurodevelopmental, and psychiatric outcomes: a systematic review. J Clin Psychiatry. 2020;81(3):19r12965. https://doi.org/10.4088/JCP.19r12965.
57. Malm H, Brown AS, Gissler M, et al. Gestational exposure to selective serotonin reuptake inhibitors and offspring psychiatric disorders: a national register-based study. J Am Acad Child Adolesc Psychiatry. 2016;55:359–66.
58. Man KK, Tong HH, Wong LY, Chan EW, Simonoff E, Wong IC. Exposure to selective serotonin reuptake inhibitors during pregnancy and risk of autism spectrum disorder in children: a systematic review and meta-analysis of observational studies. Neurosci Biobehav Rev. 2015;49:82–9.
59. Castro VM, Kong SW, Clements CC, et al. Absence of evidence for increase in risk for autism or attention deficit hyperactivity disorder following antidepressant exposure during pregnancy: a replication study. Transl Psychiatry. 2016;6:e708.
60. Andrade C. Antidepressant use in pregnancy and risk of autism spectrum disorders: a critical examination of the evidence. J Clin Psychiatry. 2013;74:940–1.
61. Hagberg KW, Robijn AL, Jick S. Maternal depression and antidepressant use during pregnancy and the risk of autism spectrum disorder in offspring. Clin Epidemiol. 2018;10:1599–612.
62. Andrade C. Antidepressant exposure during pregnancy and risk of autism in the offspring, 2: do the new studies add anything new? J Clin Psychiatry. 2017;78(8):e1052–6.
63. Andrade C. Genes and unmeasured and unknown confounds in studies of neurodevelopmental outcomes after antidepressant prescriptions during pregnancy. J Clin Psych. 2020;81(3):20f13463.
64. Gentile S. Anxiety and sleep disorders, psychopharmacology, and pregnancy. In: Galbally M, Snellen M, editors. Psychopharmacology and pregnancy. Treatment efficacy, risks, and guidelines. Berlin Heidelberg: Springer-Verlag; 2014.
65. Goodman JH, Chenausky KL, Freeman MP. Anxiety disorders during pregnancy: a systematic review. J Clin Psychiatry. 2014;75(10)
66. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Tomlinson G, Vigod SN, Dennis CL, Steiner M, Brown C, Cheung A, Dawson H, Rector NA, Guenette M, Richter M. Maternal anxiety during pregnancy and the association with adverse perinatal outcomes: systematic review and meta-analysis. J Clin Psychiatry. 2018;79(5):17r12011. https://doi.org/10.4088/JCP.17r12011.
67. Bellantuono C, Tofani S, Di Sciascio G, Santone G. Benzodiazepine exposure in pregnancy and risk of major malformations: a critical overview. Gen Hosp Psychiatry. 2013;35:3–8.
68. Ban L, West J, Gibson JE, Fiaschi L, Sokal R, Doyle P, Hubbard R, Smeeth L, Tata LJ. First trimester exposure to anxiolytic and hypnotic drugs and the risks of major congenital anomalies: a United Kingdom population-based cohort study. PLoS One. 2014;9(6):25.
69. Dolovich LR, Addis A, Regis JM, et al. Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case–control studies. BMJ. 1998;317:839–43.
70. Iqbal MM, Sobhan T, Ryals T. Effects of commonly used benzodiazepines on the foetus, the neonate, and the nursing infant. Psychiatr Serv. 2002;53:39–49.

71. Bais B, Molenaar NM, Bijma HH, Hoogendijk WJG, Mulder CL, Luik AI, Lambregtse-van den Berg MP, Kamperman AM. Prevalence of benzodiazepines and benzodiazepine-related drugs exposure before, during and after pregnancy: a systematic review and meta-analysis. J Affect Disord. 2020;269:18–27. https://doi.org/10.1016/j.jad.2020.03.014.
72. Bellantuono C, Martellini M, Orsolini L. Chapter 12. Benzodiazepines and Z-Drugs during pregnancy. In: Uguz F, Orsolini L, editors. Perinatal psychopharmacology. Springer; 2019.
73. Enato E, Moretti M, Koren G. The fetal safety of benzodiazepines: an updated meta-analysis. J Obstet Gynaecol Can. 2011;33(1):46–8.
74. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Ruthirakuhan M, Chan P, Hennawy M, Parikh S, Vigod SN, Dennis CL, Steiner M, Brown C, Cheung A, Dawson H, Rector N, Guenette M, Richter M. Pregnancy and delivery outcomes following benzodiazepine exposure: a systematic review and meta-analysis. Can J Psychiatr. 2020;65(12):821–34. https://doi.org/10.1177/0706743720904860.
75. Wikner BN, Källén B. Are hypnotic benzodiazepine receptor agonists teratogenic in humans? J Clin Psychopharmacol. 2011;31:356–9.
76. Smirk CL, Bowman E, Doyle LW, Kamlin CO. How long should infants at risk of drug withdrawal be monitored after birth? J Paediatr Child Health. 2014;50(5):352–1.
77. Uguz F. Pharmacological prevention of mood episodes in women with bipolar disorder during the perinatal period: a systematic review of current literature. Asian J Psychiatr. 2020;52:102145. https://doi.org/10.1016/j.ajp.2020.102145.
78. Poels EMP, Schrijver L, Kamperman AM, Hillegers MHJ, Hoogendijk WJG, Kushner SA, Roza SJ. Long-term neurodevelopmental consequences of intrauterine exposure to lithium and antipsychotics: a systematic review and meta-analysis. Eur Child Adolesc Psychiatry. 2018;27(9):1209–30. https://doi.org/10.1007/s00787-018-1177-1.
79. Vigod SN, Gomes T, Wilton AS, et al. Antipsychotic drug use in pregnancy: high dimensional, propensity matched, population based cohort study. BMJ. 2015;350:h2298.
80. Ennis ZN, Damkier P. Pregnancy exposure to olanzapine, quetiapine, risperidone, aripiprazole and risk of congenital malformations. A systematic review. Basic Clin Pharmacol Toxicol. 2015;116(4):315–20.
81. Terrana N, Koren G, Pivovarov J, et al. Pregnancy outcomes following in utero exposure to second-generation antipsychotics: a systematic review and meta-analysis. J Clin Psychopharmacol. 2015;35(5):559.
82. Cohen LS, Viguera AC, McInerney KA, Freeman MP, Sosinsky AZ, Moustafa D, Marfurt SP, Kwiatkowski MA, Murphy SK, Farrell AM, Chitayat D, Hernández-Díaz S. Reproductive safety of second-generation antipsychotics: current data from the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics. Am J Psychiatry. 2016;173(3):263–70. https://doi.org/10.1176/appi.ajp.2015.15040506.
83. Huybrechts KF, Hernández-Díaz S, Patorno E, et al. Antipsychotic use in pregnancy and the risk for congenital malformations. JAMA Psychiatry. 2016;73(9):938–46.
84. Tosato S, Albert U, Tomassi S, et al. A systematized review of atypical antipsychotics in pregnant women: Balancing between risks of untreated illness and risks of drug-related adverse effects. J Clin Psychiatry. 2017;78(5):e477–89.
85. Breadon C, Kulkarni J. Antipsychotic in pregnancy. In: Uguz F, Orsolini L, editors. . Perinatal psychopharmacology, Springer; 2019.
86. Bodén R, Lundgren M, Brandt L, et al. Antipsychotics during pregnancy: relation to fetal and maternal metabolic effects. Arch Gen Psychiatry. 2012;69(7):715–21.
87. Lin HC, Chen IJ, Chen YH, et al. Maternal schizophrenia and pregnancy outcome: does the use of antipsychotics make a difference? Schizophr Res. 2010;116(1):55–60.
88. Petersen I, McCrea RL, Sammon CJ, et al. Risks and benefits of psychotropic medication in pregnancy: Cohort studies based on UK electronic primary care health records. Health Technol Assess. 2016;20:1–176.
89. Sharma V, Pope CJ. Pregnancy and bipolar disorder: a systematic review. J Clin Psychiatry. 2012;73(11):1447–55. https://doi.org/10.4088/JCP.11r07499.

90. Viguera AC, Newport DJ, Ritchie J, et al. Lithium in breast milk and nursing infants: clinical implications. Am J Psychiatry. 2007;164:342–5.
91. Wesseloo R, Kamperman AM, Munk-Olsen T, et al. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatry. 2016;173:117–2.
92. Tondo L, Alta M, Bauer M, et al. Clinical use of lithium salts: guide for users and prescribers. Int J Bipolar Disord. 2019;7:16.
93. Bergink V, Kushner SA. Lithium during pregnancy. Am J Psychiatry. 2014;171(7):712–5.
94. Weinstein MR, Goldfield M. Cardiovascular malformations with lithium use during pregnancy. Am J Psychiatry. 1975;132:529–31.
95. Boyle B, Garne E, Loane M, et al. The changing epidemiology of Ebstein's anomaly and its relationship with maternal mental health conditions: a European registry-based study. Cardiol Young. 2017;27(4):677–85.
96. Poels EMP, Bijma HH, Galbally M, Bergink V. Lithium during pregnancy and after delivery: a review. Int J Bipolar Disord. 2018;6(1):26. https://doi.org/10.1186/s40345-018-0135-7.
97. Diav-Citrin O, Shechtman S, Tahover E, et al. Pregnancy outcome following in utero exposure to lithium: a prospective, comparative, observational study. Am J Psychiatry. 2014;171(7):785–94.
98. Patorno E, Huybrechts KF, Hernandez-Diaz S. Lithium use in pregnancy and the risk of cardiac malformations. N Engl J Med. 2017;377(9):893–4. https://doi.org/10.1056/NEJMc1708919.
99. Munk-Olsen T, Liu X, Viktorin A, Brown HK, Di Florio A, D'Onofrio BM, Gomes T, Howard LM, Khalifeh H, Krohn H, Larsson H, Lichtenstein P, Taylor CL, Van Kamp I, Wesseloo R, Meltzer-Brody S, Vigod SN, Bergink V. Maternal and infant outcomes associated with lithium use in pregnancy: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018;5(8):644–52. https://doi.org/10.1016/S2215-0366(18)30180-9.
100. Wesseloo R, Wierdsma A, Hoogendijk WJ, et al. Lithium dosing during pregnancy. Br J Psychiatry. 2017;211:31–6.
101. Frayne J, Nguyen T, Mok T, Hauck Y, Liira H. Lithium exposure during pregnancy: outcomes for women who attended a specialist antenatal clinic. J Psychosomatic Obste Gynecol. 2018;39(3):211–9.
102. Jentink J, Loane MA, Dolk H, Barisic I, Garne E, Morris JK, de Jong-van den Berg LT, EUROCAT Antiepileptic Study Working Group. Valproic acid monotherapy in pregnancy and major congenital malformations. N Engl J Med. 2010;362(23):2185–93.
103. Tomson T, Battino D, Bonizzoni E, EURAP Study Group, et al. Dose-dependent teratogenicity of valproate in mono- and polytherapy: an observational study. Neurology. 2015;85(10):866–72.
104. Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J, Hounsome J, McKay AJ, Tudur Smith C, Marson AG. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. Cochrane Database Syst Rev. 2016;11(11):CD010224. https://doi.org/10.1002/14651858.CD010224.pub2.
105. Campbell E, Kennedy F, Russell A, et al. Malformation risks of antiepileptic drug monotherapies in pregnancy: updated results from the UK and Ireland Epilepsy and Pregnancy Registers. J Neurol Neurosurg Psychiatry. 2014;85(9):1029–34.
106. Patel N, Viguera AC, Baldessarini RJ. Mood-stabilizing anticonvulsants, spina bifida, and folate supplementation: commentary. J Clin Psychopharmacol. 2018;38(1):7–10. https://doi.org/10.1097/JCP.0000000000000813.
107. Andrade C. Valproate in pregnancy. J Clin Psychiatry. 2018;79(3):18f12351.
108. Bodén R, Lundgren M, Brandt L, et al. Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. BMJ. 2012;345:e7085.
109. Haskey C, Galbally M. Mood stabilizers in pregnancy and child developmental outcomes: a systematic review. Aust NZ J Psychiatry. 2017;51(11):1087–97. https://doi.org/10.1177/0004867417726175.

110. Araujo JSA, Delgado IF, Paumgartten FJR. Antenatal exposure to antidepressant drugs and the risk of neurodevelopmental and psychiatric disorders: a systematic review. Cad Saude Publ. 2020;36(2):e00026619. https://doi.org/10.1590/0102-311X00026619.
111. Christensen J, Pedersen L, Sun Y, Dreier JW, Brikell I, Dalsgaard S. Association of prenatal exposure to valproate and other antiepileptic drugs with risk for attention-deficit/hyperactivity disorder in offspring. JAMA Netw Open. 2019;2(1):e186606. https://doi.org/10.1001/jamanetworkopen.2018.6606. Erratum in: JAMA Netw Open. 2019;2(2):e191243
112. McCorry D, Bromley R. Does in utero exposure of antiepileptic drugs lead to failure to reach full cognitive potential? Seizure. 2015;28:51–6.
113. World Health Organization (WHO). Long-term effects of breastfeeding—a systematic review. Geneva: WHO; 2013. Available at: http://apps.who.int/iris/bitstream/10665/79198/1/9789241505307_eng.pdf?ua=1
114. World Health Organization (WHO). Short-term effects of breastfeeding—a systematic review. Geneva: WHO; 2013. Available at: http://apps.who.int/iris/bitstream/10665/79198/1/9789241505307_eng.pdf?ua=1
115. Hale TW, Kendall-Tackett K, Cong Z, Votta R, McCurdy F. Discontinuation syndrome in newborns whose mothers took antidepressants while pregnant or breastfeeding. Breastfeed Med. 2010;5(6):283–8.
116. Orsolini L, Bellantuono C. Serotonin reuptake inhibitors and breastfeeding: a systematic review. Hum Psychopharmacol. 2015;30(1):4–20.
117. Kelly LE, Poon S, Madadi P, Koren G. Neonatal benzodiazepines exposure during breastfeeding. J Pediatr. 2012;161(3):448–51.
118. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry. 2020;19:313–27.

Drugs in Pregnancy and Lactation: The Experience of the Teratology Information Service of Bergamo (Italy)

17

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17.1 The Teratology Information Services Point of View

Teratology Information Services (TIS) provide evidence-based information about the risks and benefits associated with the use of medicines during pregnancy and lactation. These services exist since many years in several countries. They have been shown to be effective in improving maternal and fetal health outcomes: information disseminated by TIS can prevent congenital malformations, unnecessary pregnancy terminations, and occupational risks [1].

In 20 years of activity, the Teratology Information Service of Bergamo (TIS-BG) received 316,834 requests for information about drugs in pregnancy (37%) and lactation (63%). The majority of the callers were the patients themselves (76%) and 98% of the questions were related to drugs.

The most common pharmaceutical exposures during pregnancy and lactation deal with intercurrent, occasional mild diseases requiring treatment, mainly with nonsteroidal anti-inflammatory drugs (NSAIDs) (14%) and/or antibiotics (10.2%). However, in a broader perspective, psychotropic drugs exposure represents the cause that triggers TIS consultation in at least one out of four cases, with anxiolytics (10.9%), antidepressants (7.9%) and antipsychotics (3%) being the drug classes of major subjective concern.

Referral to TIS usually occurs because of (i) the need for a second opinion consulting after a drug prescription made (or an advice given) by a specialist not familial with drug therapy during pregnancy or lactation, (ii) a contradiction between drug leaflet and drug prescription, or (iii) a need to understand drug-related risks and benefits. Last but not least, the possibility to call the TIS represents for the patient an immediate, concrete help in stressful situations like an unplanned

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pregnancy discovered during complex pharmacological treatments or in case of an acute event (e.g., fever, toothache) requiring prompt therapy.

In comparison with other diseases necessitating drug maintenance during pregnancy and lactation (such as hypertension, diabetes, or thyroid dysfunctions), psychiatric disorders pose unique challenges to both the patient and the physician: the disease can be perceived as not life-threatening, erroneously judged as affecting the overall well-being but not the mother and fetus health status, and the proper management may seem not relevant for the pregnancy outcome; as a consequence, the disproportionate subjective balance between the alleged relevant risks of an avoidable pharmacological treatment and the minimal supposed consequences of therapy withdrawal can lead to hasty clinical decisions.

Indeed, the benefits of treating depression during pregnancy far outweigh the consequences that can result from undiagnosed and untreated depression. Rates of depression during pregnancy have been reported to be as high as 15–20% [2–4] . Maternal psychiatric illness is associated with poor prenatal behavior, including low attendance at prenatal checkups and increased substance use [5, 6]; adverse obstetric and neonatal outcomes, such as increased preterm delivery, low birth weight, and admission to neonatal nurseries, have also been linked to depression during pregnancy [7–9].

Moreover, evidence suggests that postpartum depression can be part of a continuum, with onset of illness during pregnancy [2, 10]. If depression persists into the postpartum period, it can have long-term consequences for both the mother and the baby: mothers might go on to develop chronic mood disorders, and untreated postpartum depression can impair mother-infant attachment [11]; moreover, being exposed to a chronically depressed mother can have cognitive, emotional, and behavioral consequences for the child [12].

In this chapter we will present practical, clinical, and pharmacological approaches to pregnant or breastfeeding patients affected by psychiatric diseases, pointing out with several case reports the most frequent issues in the experience of the Teratology Information Service of Bergamo (Italy).

17.2 Pregnancy and Anxiety in COVID-19's Time: Unexpected Psychiatric Disturbances During Pregnancy

- "I find myself in a very stressful period of my life (actually throughout my life I have had quite difficult periods so much that I needed a few drops of citalopram in the past) and I have resumed psychotherapy. However, this is not enough to overcome the anxiety and the deep anguish that have made me to self-isolate and alienate from my whole family for the fear that someone might attack me with COVID or other diseases that could harm the child I'm bearing. The doctor prescribed me citalopram 12 mg per day but… even if I know that citalopram can help me to feel better, I'm sure that it can damage my child, that is small and does not grow as expected."

- These are the words of a 32-year-old pregnant woman, at 34 weeks of her second pregnancy, who called the TIS-BG to discuss the psychiatrist's prescription of 12 mg of citalopram per day for a severe, prolonged anxiety episode, so relevant to have possibly entailed intrauterine growth restriction (IUGR). The TIS-BG reassured the patient about the safety of the drug for the child and asked to be contacted by her gynecologist and her psychiatrist in order coordinate further treatment, with a possible increase of citalopram dose aimed to reach a fully therapeutic, effective dose to be maintained in peripartum and during lactation too, if needed.

Maternal mental disorders during pregnancy are associated with a range of adverse health outcomes for offspring: for instance, a number of studies suggest that cortisol dysregulation associated with maternal distress may play a role in fetal growth restriction [13, 14].

Pregnancy and early parenthood are life-changing periods characterized by intense emotions and a high vulnerability to emotional problems. In the first months of 2020, pregnant and breastfeeding women also needed to face the COVID-19 pandemic, including the fear of infection and the exceptional quarantine measures that disturbed both private and professional life. All together, these troubles might have impacted the emotional well-being of women negatively. As depressive symptoms and anxiety in the pre- and peripartum period have been associated with adverse maternal, neonatal, and infant outcomes, the psychological impact of COVID-19 on pregnant women and new mothers is a cause for concern. Most published studies on COVID-19 in pregnancy have focused on physical effects of the pandemic on infected mothers, as well as on the possibility of vertical transmission: these tend to eclipse the equally relevant maternal mental health needs during these unprecedented times [15, 16].

New onset or relapsing depression and anxiety episodes during pregnancy and lactation may be unrecognized or neglected for quite some time. A study by Marcus et al. (2003) found that among pregnant women screened in an obstetrics setting who reported significant depressive symptoms, 86% of them were not receiving any form of treatment. While most women seek some prenatal care over the course of their pregnancy, they do not seek mental health services due to stigma; thus, antenatal visits to an obstetrician or primary care provider may provide an opportunity for screening and intervention for depression too in this high-risk group [17].

The indications for the pharmacological treatment of depression in pregnancy are the same as for depression occurring at other stages, i.e., moderate to severe depression or persistent mild to moderate depression that did not respond to non-pharmacological interventions. Women can be reassured that the benefits of appropriately prescribed antidepressants generally outweigh the risks [18]. Women with severe or psychotic symptoms should be referred to a secondary mental health service, e.g., if they have thoughts of harm to self or baby, suicide ideation, or a significant recent deterioration in mental state.

The woman's prior pharmacotherapy history should be considered when choosing a medication. Effective prior therapy should be considered carefully. Although many factors influence pharmacotherapy in pregnancy, drugs with fewer metabolites, drug-drug interactions, higher protein binding (preventing placental passage), and lesser teratogenic risk (if known) should be prioritized when possible [19].

17.3 Planning or Discovering a Pregnancy While on Therapy: Different Attitudes to Drug Therapy

A 24-year-old woman with two previous spontaneous abortions was on therapy with sertraline 100 mg/day. She was planning a pregnancy and started 400 mcg of folic acid administration before conception. Solicited by the spouse concerns, they called the TIS-BG in order to be both fully aware of the potential effects of sertraline on the course of pregnancy, partum and lactation. TIS-BG physician explained to the couple the risk-benefit ratio during pregnancy, the possible effects at birth, and the clinical aspects to monitor during the lactation period. The antidepressant treatment was continued during all stages of pregnancy. At 39 weeks of gestation, she delivered a 3100 g healthy boy, with APGAR scores of 10 and 10 at 1 and 5 min, respectively. Seventy-two hours after delivery, they were discharged from hospital. Before discharge, the mother was advised to return in the hospital if any neonatal symptoms should she notice; in particular, she was educated for the neonatal abstinence syndrome occurrence in the next short period. In a phone follow-up 3 months later, the patient reported the appearance, 1 week after discharge, of mild tremors in child upper and lower limbs during breastfeeding that disappeared 3 days later. Knowing the cause of these mild symptoms that were self-limiting, no concern occurred and she did not need to return to the hospital.

The primary care provider should engage in preconception planning with all women of childbearing age who have or are at risk for depressive illness. Treatment planning with regard to the use of pharmacotherapy during conception and the first trimester is among the most important decision points for a woman and her physician. Sometimes, changes in treatment may be recommended before pregnancy or during pregnancy [20].

A study by Barker et al. (2020) found a greater proportion of preconception women than pregnant women who intended to use antidepressants in pregnancy. This result was partially explained by the women's experience with antidepressants: over 85% of preconception participants were taking antidepressant medication (versus 45% of pregnant participants), and a greater proportion of them were well at baseline, suggesting that they were currently benefiting from the medication [21].

Women who are already taking antidepressants and want or plan to conceive would try to make their decision about pharmacological treatment prior to conception. Women making the decision while already pregnant may have had an unexpected pregnancy or a new-onset depressive episode and need to consider antidepressants-related risks and benefits in pregnancy suddenly, thus leading to a more difficult decisional process, as occurred in the next case we present.

17.4 Abrupt Pharmacologic Therapy Stopping: The Wrong Choice due to the Fear

A 32-year-old woman, affected by borderline personality disorder, was being treated with lamotrigine (200 mg/day), lorazepam (7.5 mg/day), mirtazapine (30 mg/day), and flurazepam (15 mg/day). When the patient discovered an unplanned pregnancy at 8 weeks of gestation, she stopped immediately all medicines for the fear of damaging the child. Few days later, a relapse of psychiatric symptoms ensued. The woman called in tears the TIS-BG to receive help and advice, unable to balance her needs and the baby safety. After consulting the TIS-BG, pharmacological treatment as before the pregnancy was proposed. The treatment was reintroduced after repeated calls with the TIS-BG specialist, to achieve complete reassurance. At week 40 of gestation, a healthy female baby was delivered; her weight was 2350 g and APGAR scores at 1 and 5 min were 9 and 9, respectively.

Women diagnosed with depression who have been asymptomatic for over a year may wish to attempt to reduce or discontinue their antidepressants a few months prior to conception and throughout the pregnancy [22]. Abrupt discontinuation of SSRIs (with the exception of fluoxetine, which has a longer half-life) may produce a discontinuation syndrome consisting of nausea, somnolence, and insomnia; therefore, antidepressants should be tapered—if required—over 2 to 4 weeks gradually.

Moreover, stopping medication triggers the return of the symptoms of depression, the so-called relapse. A relapse of depression during pregnancy could increase the risk of pregnancy complications. Therefore, women should be closely monitored for relapse of depressive symptoms.

Overall, relapse rates in pregnant women with a history of recurrent mood disorder are high, at about 50% if both patients who remained on therapy and patients who suspended are considered [23]. Sixty-eight percent of women who discontinued their antidepressants during pregnancy experienced relapse symptoms, compared to 26% of women who continued their medication regimen [23]. Moreover, women who stopped their medications for major depression had a five times greater risk of recurrent relapse during pregnancy compared to pregnant women who stayed on their medications [23].

Einarson et al. reported that the harmful effects of abrupt discontinuation syndrome in pregnancy can be caused by misinformation about fetal safety. Their study also revealed the effectiveness of counseling: reassuring advice from the counselors led many women to restart pharmacotherapy [24]. Restarting the antidepressant medication lowers the chance of a relapse, but it does not completely prevent the relapse in all cases.

A study found that 60% of women taking antidepressants at the time of their baby's conception had depressive symptoms over the course of the pregnancy [25]. In two thirds of the patients, an increase in their daily dose of medication may be required to maintain euthymia, usually in mid-late pregnancy [25].

In conclusion, abrupt discontinuation of psychiatric drug therapy may be associated with deterioration and relapse of the psychiatric disease during pregnancy. Continued medications (with dosage increase, if needed) and careful observation are required for pregnant women complicated by psychiatric disorders; a consensus between obstetricians and psychiatrists is needed, and counseling should be effective in reassuring women to adhere to therapy.

17.5 Antiepileptic Drugs for Psychiatric Illness: Stop, Change, Continue?

A 32-year-old woman with a 4-year history of bipolar disorder type I, presenting severe manic episodes requiring prolonged hospitalizations, was stabilized with valproic acid 1500 mg/day and lorazepam 3 mg/day. She discovered her pregnancy at 7 weeks of gestation. After a deep assessment of treatment options that involved the patient, her psychiatrist, and the TIS-BG, valproic acid was substituted with lithium carbonate therapy, at a dose of 300 mg twice a day; high doses of folic acid were prescribed too. Psychiatric monitoring was careful throughout the pregnancy. High-resolution ultrasound examination and fetal echocardiography were performed at 20 weeks of gestation and they were normal. Ten days before delivery, lithium was decreased to 150 mg once a day to prevent neonatal lithium toxicity. The patient delivered at the 38 weeks of pregnancy a healthy female weighting 2630 g with APGAR scores of 9 and 10 at 1 and 5 min, respectively. No cardiac abnormalities were present in the newborn.

In recent times, many drugs have been evaluated as mood stabilizers. In patients with severe mood disorders, the treatment options include (i) anticonvulsants like valproate, carbamazepine, oxcarbazepine, lamotrigine, topiramate, and gabapentin; (ii) atypical antipsychotic like olanzapine, risperidone, quetiapine, ziprasidone, and aripiprazole; or (iii) lithium.

Major congenital malformation risks in association with gestational exposure to antiepileptic drugs have been extensively studied and are well known. In the last

decade, the use of these drugs in psychiatry is increasing, and clinicians prescribing these medications in women during childbearing years should be aware for the high potential of teratogenic risk. The decision to stop drugs when women with bipolar disorder become pregnant or plan to conceive is difficult: the risk of relapse during pregnancy has been estimated to be 50% or more with recurrence risk reported to be 2.3 times higher after discontinuation of mood stabilizer [26].

The treating clinicians have to take into account various factors like current mental state, longitudinal history of the patient, past history of relapse while off medication, response to medication, and time of pregnancy at which patient presents to the clinician; the choice of the drug should depend on the balance between safety and efficacy profile. In ideal situation, the patient should discuss about her plan of pregnancy and this should be when the patient is euthymic.

Based on the patient's history, decision should be taken about continuation of medication during the period before conception and during the first trimester. If the patient is clinically stable, an attempt to discontinue the mood stabilizer prior to conception should be taken. If on the basis of history the illness is considered to be moderate to severe (i.e., the chances of relapse are high without medication), then the psychiatrist should discuss with the patient and the spouse about continuation of mood stabilizer during the conception period too. In some cases, mood stabilizers could be continued till the confirmation of conception, and then they could be withdrawn cautiously, but close monitoring for relapse should be done. For women with most severe forms of bipolar disorder (i.e., multiple severe episodes, especially with a history of psychotic symptoms and suicidal attempts), maintenance treatment with a mood stabilizer before and during pregnancy may be the safest option. In such a situation, lowest effective dose of a medication must be used and medications which have the least teratogenic potential should be selected.

The drug(s) usually taken by the patient is (are) the second variable to be considered in order to choose the most appropriate clinical approach. If the patient is on lithium, valproate, or carbamazepine before conception, the risk should be discussed with patient and spouse, and wherever possible these drugs should be stopped during the first trimester or replaced by other safer options like atypical antipsychotics. Use of valproate during first trimester is associated with major malformation and long-term sequelae in the form of developmental delay, lower intelligence quotient, and higher risk of development of autism spectrum disorder. Similarly, the use of carbamazepine in first trimester is associated with higher risk of major congenital malformation, and its use in first trimester is contraindicated. Data for lamotrigine appears to be more favorable than other antiepileptics.

The third variable to be considered is time. About 50% of pregnancies in women with bipolar disorders are unplanned and they come to medical attention while on therapy with a confirmed pregnancy. If the patient has not completed the first trimester, the pros and cons about the medication continuation and abrupt stoppage have to be discussed; if the patient is on anticonvulsants, then a higher dose of folic acid should be prescribed; if it is not possible to stop the medication, then an attempt should be made to reduce the dose to minimum. If the patient has completed the first trimester of pregnancy, then the patient and the spouse should be explained about

the pros and cons of continuation of pregnancy, depending on the agent the patient was taking. If the patient is on polypharmacy, then the additional risk should be emphasized. If the decision to continue the pregnancy is made, the decision about the mood stabilizer should consider the past history of response and the risk associated with a particular agent during the second and third trimester. Continuation of the same mood stabilizer with informed consent of the patient and spouse should be preferred. However, some authors suggest that if the woman is on valproate and if there is no history of nonresponse to lithium, the switch to lithium should be considered [27]. Studies have reported that in patients taking lithium, the risk for developing abnormalities is approximately 11%; for presenting a cardiac abnormality, it is close to 8%, and for Ebstein's anomaly it is approximately 2%. Although the teratogenic risk could be significant, it has become apparent over time that alternative pharmacologic treatments for bipolar disorder as acid valproic may exceed the teratogenic risk of lithium monotherapy.

17.6 Poor Neonatal Adaptation Syndrome: Neonatal Drug Toxicity and/or Drug Withdrawal Syndrome

A 3860 g infant boy was delivered by spontaneous vaginal delivery at 40 weeks' gestation. The mother had a positive history of major depression and she had been taking citalopram 20 mg/day until the day of delivery. At birth, the infant had APGAR scores of 8, 8, and 10 at 1, 5, and 10 min, respectively. Ten minutes after birth, the baby became hypertonic. Muscular rigidity attenuated with diazepam 0.8 mg/day. Electroencephalogram and routine laboratory tests were normal. Symptoms resolved over the following 2 days, when the infant was discharged. Citalopram and desmethylcitalopram levels at 31 h of age were 73 ng/ml and 26 ng/ml, respectively (normal adult levels <200 ng/ml). Both drug levels and time-course of symptoms suggest neonatal citalopram toxicity as the most probable diagnosis in this patient.

A 4400 g male infant was born to a 40-year-old female with asthma, anxiety, and depression, at postconception age of 41 weeks and 1 day. At 25 weeks of gestation, her depression symptoms became severe and the patient started therapy with sertraline. Two days after birth, the neonate showed initial signs of withdrawal, including severe irritability, tremulousness, difficulty feeding with emesis after each feed, and difficulty sleeping. Finnegan abstinence scores were as high as 14. A trial of phenobarbital was initiated, with a 10 mg/kg oral load followed by 3 mg/kg/day oral dose divided every 12 h. Within 24 h of initiating the treatment with phenobarbital, the infant's tremor stopped and his irritability improved. Finnegan abstinence scores fell to zero and his appetite improved. A diagnosis of sertraline withdrawal syndrome was made.

Poor neonatal adaptation (PNA) is a syndrome caused by exposure to psychotropic drugs in utero, including antidepressants. It includes symptoms such as jitteriness, tremors, feeding problems, respiratory distress, and hypoglycemia [28]. After exposure to SSRIs and other selective antidepressants in fetal life, 20–30% of infants develop PNA [29]. While the underlying mechanisms remain to be determined, a number of hypotheses have been proposed to account for these symptoms, including a transient increase and/or suppression of monoamine neurotransmitters [30] reflecting a "withdrawal or discontinuation" syndrome or pharmacological toxicity related to increased SSRI levels [31].

Along with anecdotal reports in the last decade describing complications in some babies of mothers who used various antidepressants near term, many studies have described symptoms consistent with neonatal SSRIs withdrawal or with serotonin toxicity syndrome: prospective studies, case series, database analyses, and meta-analyses. In these studies, neonatal symptoms were not universal; serum concentrations of SSRIs after maternal use in late pregnancy have been reported to be high, low, or undetectable, and to be or not correlated with the symptoms.

Some authors consider slowly decreasing the dose of these medications in the third trimester although some warn that the risk of maternal relapse outweighs the risk of discontinuation syndrome [32]. In the TIS-BG experience, in most cases a correct advice to the mother and to the pediatrician can allow proper management of PNA, without the need to modify mother therapy.

17.7 Breastfeeding in Neonatal Intensive Care Unit: A Tailored Approach Can Overcome Pharmacokinetics Concerns

A preterm male baby of 1670 grams born at 31 + 3 weeks of gestation was delivered by a 25-year-old mother through vaginal delivery with history of umbilical cord prolapse. At birth, the neonate was cyanotic and he had no heart rate. He was resuscitated, and after 5 min of neonatal resuscitation, the baby's heart rate reappeared but was only up to 20 beats/min; therefore he underwent intubation, mechanical ventilation, and cardiovascular therapy in neonatal intensive care unit (NICU). The electroencephalogram highlighted a severe hypoxic-ischemic encephalopathy. His mother begun treatment with citalopram 40 mg/d and lorazepam 8 mg/d, and she wanted to give her milk to the neonate, as "it is the only help that I can provide to my baby," she said. In usual situations, the dosages of these drugs are considered too high and affecting negatively the breastfed neonate. In circumstances like in this case, the pharmacokinetic point of view is not the essential concern and the decision was to breastfeed the baby, at least partially.

Feelings of alienation, guilt, and lack of control are recurrent themes among the NICU mothers, and breastfeeding and/or provision of expressed breast milk can take on a whole new meaning within the NICU environment. Breastfeeding builds a bond between mother and child, and their closeness strengthens throughout the breastfeeding relationship; it is not easily lost once breastfeeding ceases. Providing breast milk while the baby is too small or too sick to breastfeed offers to the mother an opportunity to actively take part in the baby's growth and development. Most importantly, it offers an opportunity to share something special that only the mother can provide. A positive emotional experience of breastfeeding may also have implications for outcomes besides duration and exclusivity.

Leff et al. found that maternal enjoyment and attainment of their desired maternal role were identified by mothers as more important for "successful" breastfeeding than duration [33]. Moreover, qualitative researchers found that women who described breastfeeding as pleasurable and enjoyable reported feeling an intimate connection with the infant, maternal confidence, and adequate support [34].

In the neonatal intensive care unit (NICU) usually, breast milk feedings fail to continue until hospital discharge. Fragile, vulnerable, medically compromised infants often cannot eat by mouth initially, and their mothers must regularly express breast milk for gastric feedings while maintaining their milk supply until direct breastfeeding is possible. Also, the NICU is an environment where parents have reported feeling like an outsider and not being able to parent their infant [35]. Through participation in breastfeeding, mothers are given an active and meaningful role in the NICU, which can build confidence and enable parents to handle and care for their infant.

17.8 The Multidisciplinary Approach in Breastfeeding

A 20-day-old, full-term, infant came to the observation of TIS-BG for a weight gain of 150 g per week, considered an acceptable growth but to be kept monitored. The mother's medical history was positive for panic attacks, treated with citalopram 20 mg/day prior pregnancy. Her therapy was suspended when she became pregnant; in the third trimester, given the increase in anxiety, she was prescribed a therapy with bromazepam 0.625 mg three times a day. At the time of the first visit, the patient was experiencing frequent panic attacks and she was afraid to leave the house. She no longer felt comfortable with the psychiatrist who followed her during pregnancy. "Feeling alone with my baby with no help from anybody is more stressful than my panic attacks," the mother said. The patient reported also anhedonia (the inability to experience pleasure), in particular inability to enjoy the baby birth. The patient was provided with clear information on the need to have a trusted professional to follow her for the psychiatric pathology, as well as to contact a professional lactation consultant who could monitor the child's growth and

help her with difficulties during breastfeeding, if any. Moreover, she was advised that bromazepam is not the benzodiazepine of choice in breastfeeding, having a long half-life of 20.6 h, with possible accumulation into breast milk and subsequent sedation of the newborn with poor sucking reflex. At the following follow-ups, the patient reported to be in close contact with a lactation consultant, that a new psychiatrist replaced bromazepam with lorazepam 1 mg every 8 h, and that they started a psychotherapeutic path together. The baby was growing well with about 250 g weekly. After 2 years the baby is growing well and the mother is looking for second pregnancy.

This case report highlights that psychiatric disease management during pregnancy and postpartum is challenging and requires a multidisciplinary approach. In these patients, a close collaboration is mandatory between a series of dedicated physicians that can offer clear advantages for pregnant and breastfeeding women.

Complex pathologies associated with chronic health conditions must be dealt in a coordinated way, and the multidisciplinary team approach represents the most efficacious way of managing these patients. There are many perceived benefits to this approach; it gives a patient access to the right team of healthcare professionals, who work together to plan the most suitable care option, and it allows a full review of all the factors that may affect the treatment and help prevent unexpected problems. Moreover, it may reduce delays in treatment and referral to services and it facilitates transfer of appropriate and consistent information to the patient.

Because management of depression during pregnancy and postpartum also includes care of a growing fetus and the neonate, treatment may be complicated, and primary care providers should consider several disciplines, including an obstetrician, psychiatrist, pharmacologist/toxicologist, and pediatrician to provide optimal care. A multidisciplinary approach can help underserved women overcome obstacles, spend well all time of pregnancy, and obtain the benefits of breastfeeding for themselves and their infants [36]. Developing and implementing a multidisciplinary quality improvement program can address the deficit of depression management in the obstetric setting by identifying early the women at risk for depression during pregnancy and postpartum. It is possible to motivate women with psychiatric disorders, even those who initially seem resistant, to treat the illness, and a multidisciplinary equip can be successful in achieving sobriety and psychiatric stability during pregnancy and postpartum. Fighting the stigma associated with any type of mental illness, they should encourage soon-to-be mothers to reach out for help out of their own initiative. Nevertheless, there should be a protocol agreed upon and in place, and regular meetings should take place to facilitate communication between key professionals involving the mother at early stages.

17.9 Are There Long-Term Consequences?

A 39-year-old patient, gravida 3 para 2, was evaluated at 15 weeks of gestation because of the onset of depressive symptoms during the pregnancy. She had a previous major depressive episode with postpartum onset, 2 years before her current presentation. At that time, she responded to paroxetine, 20 mg/day, but the patient stopped her therapy in the beginning of her third pregnancy. Considering the need of a rapid improvement of depression and according to the TIS-BG advice, the patient started again paroxetine 20 mg/day treatment till the end of pregnancy. The patient gave birth to a healthy female infant at 37 weeks by scheduled cesarean delivery (due to the patient's history of two previous cesarean deliveries) and started breastfeeding her baby. The infant had a normal newborn screen and an unremarkable physical examination. Routine visits indicate that the infant is having a normal development up to date (18 months): she is currently described as a healthy-appearing, interactive, and playful 18-month-old baby with normal weight gain progressing. Language, fine motor, and social development are within normal limits. Physical and neurological examinations at all scheduled visits resulted normal with no developmental delays.

The available literature consists of few studies that demonstrate no impairment of infant neurodevelopment following prenatal and/or postnatal exposure to psychotropic drugs, although the data are partially conflicting.

In a prospective cohort trial, Nulman et al. evaluated IQ, language development, and temperament in children exposed to selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) throughout the pregnancy, compared to infants born to mothers who were not depressed and were not exposed to any known teratogenic medications during pregnancy. Children were evaluated between 16 and 86 months of life with the Bayley Scales of Infant Development or the McCarthy Scales of Children's Abilities and the Reynell Developmental Language Scales. No differences in IQ, language development, or temperament were found in children who were exposed during the first trimester only or throughout the pregnancy [37].

In contrast, Brandlistuen et al. found that prenatal exposure to antidepressants was associated with increased levels of anxiety symptoms in 3-year-old children, after adjusting for maternal familial effects and confounding factors (i.e., maternal depression); anxiety symptoms were not associated with emotional reactivity, somatic complaints, sleep problems, or attention disturbances [38]. Another study found that infants prenatally exposed to antipsychotics showed significantly lower INFANIB scores than those with antidepressant or no psychotropic exposure, after controlling for significant covariates [39]. As maternal depression itself has been associated with a deficient intellectual and language development compared to children of non-depressed mothers, an indication bias cannot be excluded [40].

Nonetheless, it remains unclear whether findings that have been detected represent transient observations or are indicative of subsequent neurobehavioral problems that may be detected at a later age. In a systematic review and Bayesian random-effects network meta-analysis, other authors reported that valproate, oxcarbazepine, and lamotrigine were associated with the greatest odds of adverse neurodevelopmental outcomes and increased occurrence of autism, compared with the control group [41].

Overall, no definitive data are available to date, and further studies are required to better elucidate the effects of gestational psychoactive drugs exposure on fetal brain development and on later life susceptibility to depressive, cognitive, and motor abnormalities. Therefore, even if the current data are not alarming, larger cohort studies designed with an untreated control group for comparison and a longer follow-up period extending into puberty and adolescence are needed to exclude any long-term risk.

17.10 Conclusive Remarks

Treatment of psychiatric diseases during pregnancy requires patients and physicians to make collaborative decisions. Each treatment needs to be chosen on a case-by-case basis. Women with history of recurrent depressive episodes, who are already taking medication at conception, should be encouraged to continue the medication through pregnancy to the postpartum period. If a patient has a history of severe depression and experiences a relapse during her current pregnancy, recommencing treatment with an antidepressant to which she has responded favorably in the past is recommended. For patients who are experiencing an initial depressive episode during pregnancy, treatment with an antidepressant is recommended only if the depression is severe and unlikely to respond to psychotherapy. Finally, the clinical approach must not be drug-based but patient-based.

References

1. Hancock RL, Koren G, Einarson A, Ungar WJ. The effectiveness of Teratology Information Services (TIS). Reprod Toxicol. 2007;23(2):125–32.
2. Gotlib IH, Whiffen VE, Mount JH, Milne K, Cordy NI. Prevalence rates and demographic characteristics associated with depression in pregnancy and the postpartum. J Consult Clin Psychol. 1989;57(2):269–74.
3. Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR. Prevalence of depression during pregnancy: systematic review. Obstet Gynecol. 2004;103(4):698–709. Erratum in Obstet Gynecol. 2004; 103 (6): 1344
4. Yin X, Sun N, Jiang N, Xu X, Gan Y, Zhang J, Qiu L, Yang C, Shi X, Chang J, Gong Y. Prevalence and associated factors of antenatal depression: systematic reviews and meta-analyses. Clin Psychol Rev. 2020;83:101932. (Epub ahead of print)
5. Lindgren K. Relationships among maternal-fetal attachment, prenatal depression, and health practices in pregnancy. Res Nurs Health. 2001;24(3):203–17.

6. Zuckerman B, Amaro H, Bauchner H, Cabral H. Depressive symptoms during pregnancy: relationship to poor health behaviors. Am J Obstet Gynecol. 1989;160(5 Pt 1):1107–11.
7. Chung TK, Lau TK, Yip AS, Chiu HF, Lee DT. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosom Med. 2001;63(5):830–4.
8. Hedegaard M, Henriksen TB, Sabroe S, Secher NJ. Psychological distress in pregnancy and preterm delivery. BMJ. 1993;307(6898):234–9.
9. Dayan J, Creveuil C, Herlicoviez M, Herbel C, Baranger E, Savoye C, Thouin A. Role of anxiety and depression in the onset of spontaneous preterm labor. Am J Epidemiol. 2002;155(4):293–301.
10. Chaudron LH, Klein MH, Remington P, Palta M, Allen C, Essex MJ. Predictors, prodromes and incidence of postpartum depression. J Psychosom Obstet Gynaecol. 2001;22(2):103–12.
11. Edhborg M, Lundh W, Seimyr L, Widström AM. The parent-child relationship in the context of maternal depressive mood. Arch Womens Ment Health. 2003;6(3):211–6.
12. Hay DF, Pawlby S, Angold A, Harold GT, Sharp D. Pathways to violence in the children of mothers who were depressed postpartum. Dev Psychol. 2003;39(6):1083–94.
13. Pinto TM, Caldas F, Nogueira-Silva C, Figueiredo B. Maternal depression and anxiety and fetal-neonatal growth. J Pediatr. 2017;93(5):452–9.
14. Lewis AJ, Austin E, Galbally M. Prenatal maternal mental health and fetal growth restriction: a systematic review. J Dev Orig Health Dis. 2016;7(4):416–28.
15. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. J Affect Disord. 2020;277:5–13.
16. Thapa SB, Mainali A, Schwank SE, Acharya G. Maternal mental health in the time of the COVID-19 pandemic. Acta Obstet Gynecol Scand. 2020;99(7):817–8.
17. Marcus SM, Flynn HA, Blow FC, Barry KL. Depressive symptoms among pregnant women screened in obstetrics settings. J Womens Health (Larchmt). 2003;12(4):373–80.
18. McAllister-Williams RH, Baldwin DS, Cantwell R, Easter A, Gilvarry E, Glover V, Green L, Gregoire A, Howard LM, Jones I, Khalifeh H, Lingford-Hughes A, McDonald E, Micali N, Pariante CM, Peters L, Roberts A, Smith NC, Taylor D, Wieck A, Yates LM, Young AH, Endorsed by the British Association for Psychopharmacology. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017. J Psychopharmacol. 2017;31(5):519–52.
19. American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists number 92, April 2008 (replaces Practice Bulletin number 87, November 2007). Use of psychiatric medications during pregnancy and lactation. Obstet Gynecol. 2008;111(4):1001–20.
20. Hussein N, Kai J, Qureshi N. The effects of preconception interventions on improving reproductive health and pregnancy outcomes in primary care: a systematic review. Eur J Gen Pract. 2016;22(1):42–52.
21. Barker LC, Dennis CL, Hussain-Shamsy N, Stewart DE, Grigoriadis S, Metcalfe K, Oberlander TF, Schram C, Taylor VH, Vigod SN. Decision-making about antidepressant medication use in pregnancy: a comparison between women making the decision in the preconception period versus in pregnancy. BMC Psychiatry. 2020;20(1):54. (1-10)
22. Gonsalves L, Schuermeyer I. Treating depression in pregnancy: practical suggestions. Cleve Clin J Med. 2006;73(12):1098–104.
23. Cohen LS, Altshuler LL, Harlow BL, Nonacs R, Newport DJ, Viguera AC, Suri R, Burt VK, Hendrick V, Reminick AM, Loughead A, Vitonis AF, Stowe ZN. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006;295(5):499–507.
24. Einarson A, Selby P, Koren G. Abrupt discontinuation of psychotropic drugs during pregnancy: fear of teratogenic risk and impact of counselling. J Psychiatry Neurosci. 2001;26(1):44–8.
25. Hostetter A, Stowe ZN, Strader JR Jr, McLaughlin E, Llewellyn A. Dose of selective serotonin uptake inhibitors across pregnancy: clinical implications. Depress Anxiety. 2000;11(2):51–7.

26. Viguera AC, Whitfield T, Baldessarini RJ, Newport DJ, Stowe Z, Reminick A, Zurick A, Cohen LS. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. Am J Psychiatry. 2007;164(12):1817–24.
27. Curtis V. Women are not the same as men: specific clinical issues for female patients with bipolar disorder. Bipolar Disord. 2005;7(Suppl. 1):16–24.
28. Levinson-Castiel R, Merlob P, Linder N, Sirota L, Klinger G. Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term in infants. Arch Pediatr Adolesc Med. 2006;160(2):173–6.
29. Kieviet N, Dolman KM, Honig A. The use of psychotropic medication during pregnancy: how about the newborn? Neuropsychiatr Dis Treat. 2013;9:1257–66.
30. Laine K, Heikkinen T, Ekblad U, Kero P. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. Arch Gen Psychiatry. 2003;60(7):720–76.
31. Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure. J Clin Psychiatry. 2004;65(2):230–7.
32. Yonkers KA, Wisner KL, Stewart DE, Oberlander TF, Dell DL, Stotland N, Ramin S, Chaudron L, Lockwood C. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. Gen Hosp Psychiatry. 2009;31(5):403–13.
33. Leff EW, Gagne MP, Jefferis SC. Maternal perceptions of successful breastfeeding. J Hum Lact. 1994;10(2):99–104.
34. Burns E, Schmied V, Sheehan A, Fenwick J. A meta-ethnographic synthesis of women's experience of breastfeeding. Matern Child Nutr. 2010;6(3):201–19.
35. Aagaard H, Hall EO. Mothers' experiences of having a preterm infant in the neonatal care unit: a meta-synthesis. J Pediatr Nurs. 2008;23(3):e26–36.
36. Webber E, Benedict J. Postpartum depression: A multi-disciplinary approach to screening, management and breastfeeding support. Arch Psychiatr Nurs. 2019;33(3):284–9.
37. Nulman I, Rovet J, Stewart DE, Wolpin J, Pace-Asciak P, Shuhaiber S, Koren G. Child development following exposure to tricyclic antidepressants or fluoxetine throughout fetal life: a prospective, controlled study. Am J Psychiatry. 2002;159(11):1889–95.
38. Brandlistuen RE, Ystrom E, Eberhard-Gran M, Nulman I, Koren G, Nordeng H. Behavioural effects of fetal antidepressant exposure in a Norwegian cohort of discordant siblings. Int J Epidemiol. 2015;44(4):1397–407.
39. Johnson KC, LaPrairie JL, Brennan PA, Stowe ZN, Newport DJ. Prenatal antipsychotic exposure and neuromotor performance during infancy. Arch Gen Psychiatry. 2012;69(8):787–94.
40. Skurtveit S, Selmer R, Roth C, Hernandez-Diaz S, Handal M. Prenatal exposure to antidepressants and language competence at age three: results from a large population-based pregnancy cohort in Norway. BJOG. 2014;121(13):1621–31.
41. Veroniki AA, Rios P, Cogo E, Straus SE, Finkelstein Y, Kealey R, Reynen E, Soobiah C, Thavorn K, Hutton B, Hemmelgarn BR, Yazdi F, D'Souza J, MacDonald H, Tricco AC. Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: a systematic review and network meta-analysis. BMJ Open. 2017;7(7):e017248.

The Influence of Culture on Perinatal Mental Health

18

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18.1 Introduction

The experience of pregnancy and childbirth is deeply influenced by social and cultural factors, and therefore culture plays an important role in the mental health of women in the perinatal period. Culture is known to shape the way one thinks, feels, and behaves and also responds to different life stages. Cultural factors are also known to influence the way one experiences and expresses mental distress and the psychopathology in case of a psychiatric disorder [1]. The influence of culture is also seen in ways in which a society labels a disorder and seeks help.

18.2 Impact of Culture on Perinatal Psychopathology

Like in other mental health conditions, the impact of culture on perinatal psychopathology may be patho-plastic (shaping of symptoms), pathogenic (causation of symptoms), patho-elaborative (exacerbation/exaggeration of symptoms), or patho-facilitative (conferring risk or protection).

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18.2.1 Patho-plastic Influence

Although a wide range of symptoms are shaped by cultural influence, we discuss those where the influence is clinically conspicuous.

18.2.1.1 Somatic Symptoms

While somatic symptoms such as changes in sleep and appetite, and fatigue are innate to the physiological perinatal state, they can be valid indicators for depression. In several situations depressed women are less likely to articulate their problems as "depression" but rather report somatic complaints. Moreover, pregnant women with depressive and anxiety disorders may present with "an amplification of physical symptoms of pregnancy" [2]. These somatic complaints may not only represent a means of culture-specific expression of psychosocial distress but also indicate the presence of an underlying mental disorder. Especially in non-western cultures somatic symptoms are the predominant presentation of distress, and they are indeed considered as a direct manifestation of distress [3].

18.2.1.2 Delusions and Infanticidal Behavior

Culture may strongly influence the theme of delusions in women with postpartum psychosis. A study from India reported many religious themes among women with postpartum psychosis [4]. Women with postpartum psychosis may manifest delusional thoughts of harming the infant [5]. Filicidal behavior among mothers with mental illness usually has an altruistic reason or could arise out of a psychotic experience [6], and there could be an influence of the culture in shaping the filicidal behavior of the mother. Religious delusions, which are strongly pinned to cultural context, are linked to filicidal acts suggesting a dynamic interaction between culture and the filicidal behavior on account of mental illness [7, 8].

18.2.1.3 Dissociation/Conversion

In general, dissociative/conversion disorders, especially those of trance and possession, are fairly common in low- and middle-income countries [9]. Cross-cultural variability in their association with other psychiatric symptoms has led to difficulties in their nomenclature as well, and this has become much more challenging from the perspective of those cultures that are transitioning from orthodoxy to modernization. These challenges are pertinent to perinatal women as well. The experience of labor pain is itself culturally determined—so much so that women belonging to some cultures (such as Ghanaian) deny (or dissociate) labor pain because those who are unable to endure labor pain are labelled emotionally weak [10]. Cultural variations in the experience and report of labor pain have also been reported [11].

18.2.1.4 Catatonia

The prevalence of catatonia during the postpartum period is not infrequent. A prevalence rate of 20% among postpartum women with psychosis has been reported from a Mother-Baby Unit in India [12]. Although some ethnic variation in prevalence of

catatonia among certain cultures is noted [13], broad cultural variation in the presentation of catatonia and specific to postpartum psychosis remains to be explored systematically.

18.2.2 Pathogenic Influence

Mental health illnesses that have direct pathogenic effect of culture are "culture-bound syndromes." Culture-bound syndrome is a condition that is "understood only in certain cultural context" and is labelled based on "the specific ways in which each cultural group understands distress, tension, illness and health" [14]. The *Diagnostic and Statistical Manual of Mental Disorders, fifth edition: DSM-5* uses the terms "cultural syndromes," "cultural concepts of distress," "cultural idioms of distress," and "cultural explanation/perceived causes." Some "cultural syndromes" that are specific to the perinatal women are discussed here.

As most of the cultures are on the crossroads of following traditional customs and of moving on with modernization, these syndromes are important to address. Moreover, the diagnostic challenge posed by these syndromes in psychiatric practice because of the resemblance with many primary axis diagnoses makes their discussion much more relevant. In the community, the symptoms of primary psychiatric disorders are misjudged as culture bound and are considered to have an "external" causality [14] whereas in the clinics, emphasis on the symptoms of primary axis diagnoses is greater, and consequently cultural connotations of these symptoms could be missed.

18.2.2.1 Susto

Susto is a cultural syndrome described in Latin Americans, Central and South Americans, and also in some Asian countries. The other terms that refer to syndromes that are similar to susto are "espanto," "pasmo," and "perdida de sombra." It is "an illness attributed to a *frightening* event that causes the soul to leave the body and results in unhappiness and sickness" [15]. If the event is "anger provoking" instead of "frightening," the illness is termed "Muinas." As "fright" and "anger" are believed to negatively influence the pregnant woman and the in utero baby, the family tries to prevent the pregnant woman from "receiving bad news or from getting them suddenly" as much as possible [14]. Any pregnancy complication (such as diabetes, hypertension) or malformations in the baby are not revealed to the woman. If such news is revealed accidentally or mistakenly and the pregnant woman becomes "frightened," then it is believed that "good fortune or soul" has abandoned the body of the future mother and the baby, and that susto has set in. The susto pregnant woman becomes anxious, restless, unable to sleep, irritable, and emotionally vulnerable, and the susto baby doesn't sleep and eat well, is too sober or anxious, is easily startled, and cries excessively. As a remedy for susto, a curandero (healer) or a shaman will offer special prayers and administer special medicinal potions to the woman and the baby so as to make the "good fortune or soul" return the body [14].

18.2.2.2 Toas

Toas, seen in Cambodia [16], is considered an incurable illness characterized by chronic abdominal pain, weakness, headache, diarrhea, palpitations, weight loss, and poor appetite. Toas, which roughly translates to "conflict," is believed to be caused due to not adhering to customs followed during the postpartum period. Interestingly, a postpartum woman is considered a queen, and the family (and the woman herself) needs to assure adherence to the prescribed customs in order to maintain balance. These customs typically are "ang pleung (warming the mother on a bamboo bed with fire below)," food restrictions, physical activity restrictions, sexual activity restrictions, restrictions on bathing and exposure to rain/dew, and to be free on emotional distress or worry. Five different types of toas, depending on which custom was not adhered to, are described as – toas chamney (eating wrong food); toas sor sai (lifting heavy weight or doing hard work); toas damnek (resuming sexual intercourse before 3 months postpartum); toas tek pleany (exposure to rain/dew or bathing); and toas pruey cet (experiencing emotional distress) [16]. Thematically, toas pruey cet is similar to the concept of susto.

18.2.2.3 Lom pid duan

Lom pid duan is a cultural syndrome prevalent in Thailand. Like toas, it is characterized by body aches and weakness and thought to be caused due to not adhering to a postpartum custom – "yu duan." Yu duan is a 30-day period where postpartum women are cared by female family members and their husbands [17].

18.2.2.4 Aire

Aire, seen in Latin Americans, is a disease that develops as a result of penetration of air into the body. It is believed that if a postpartum woman is exposed to cold air, it shall interrupt the production of milk. There is a great amount of anxiety in the family members to completely wrap the mother and the baby, even to the extent that head of the baby remains covered even in summers so as to prevent air from entering the body by eyes and mouth. A risky tradition termed as "moxibustion," where alcohol is burnt in a glass cup and applied to the "affected area," is followed as a remedy for aire [14].

18.2.2.5 Caida de mollera

Caida de mollera is a syndrome seen in Latin America, where an infant's (anterior) fontanelle is perceived to be sunken or concave (often due to dehydration) and to cause the baby to be listless, less responsive, eating less, intensely crying, and irritable. It is believed to be due to "negative" suction inside the head. The usual remedy is by holding the baby upside down and hitting the soles; this tradition risks the occurrence of the shaken baby syndrome [14].

18.2.2.6 Sanni, Janni, Janni Ekkendi, and Sanni Patam

These are the terms referred to distress and madness during the postpartum period in southern India. While the term "bananti" refers to a woman in her postpartum period, Sanni and Janni are specific terms used to refer to psychosis during the

Table 18.1 Cultural syndromes related to perinatal mental health

S. no.	Cultural syndrome	Description	Region
01	*Susto*	Woman becomes anxious, restless, unable to sleep, irritable, and emotionally vulnerable when she faces a frightening situation. "Frightened" woman's "good fortune or soul" is believed to have abandoned her body	Latin, Central and South America, Some parts of Asia
02	*Toas*	Not adhering to customs followed during the postpartum period leads to an incurable illness characterized by chronic abdominal pain, weakness, headache, diarrhea, palpitations, weight loss, and poor appetite	Cambodia
03	*Lom pid duan*	Not adhering to a postpartum custom – "yu duan" – leads to an illness characterized by body aches and weakness	Thailand
04	*Aire*	An illness characterized by multiple somatic complaints develops as a result of penetration of air into the body	Latin America
05	*Caida de mollera*	"Negative" suction inside the head leads to sunken or concave fontanelle and causes the baby to be listless, less responsive, eating less, intensely crying, and irritable	Latin America
06	*Sanni/ Janni*	Psychosis during the postpartum period	South India

postpartum period. These syndromes are believed to have a supernatural causation and are attributed to ghosts, demons, black magic, "bad breeze," and bad fate [18].

A brief description of the cultural syndromes described in this section is presented in Table 18.1.

18.2.3 Patho-elaborating Influence

In this section, we discuss perinatal problems that might be exaggerated through certain cultural reinforcements.

18.2.3.1 Poor Control Over Contraception due to Lack of Agency or Religious Beliefs

Poor control over contraception mainly has two outcomes pertinent to perinatal mental health – multiparity, and unwanted pregnancy. Cultural context has one of the strongest influences on the acceptance and use of contraception by couples. Different religious backgrounds and different sects within religions influence control over contraception in many distinct ways [19]. While it is important to understand these cultural differences for competently delivering care by healthcare providers, certain beliefs of "prohibition of contraception" among certain masses [20] may have negative influence on the mental health of perinatal women. Women

who have many children have significantly greater concerns regarding lack of financial and social support [21]. Unwanted pregnancy, the other outcome of poor control over contraception, has indeed been directly linked to postpartum depression [22]. Apart from multiparity and unwanted pregnancies, one would assume poor spacing between pregnancies also could negatively affect the mental health of perinatal women. Interestingly, shorter inter-birth spacing has been known to have a negative impact on marital relationships [23], which might mediate its relationship with poor perinatal mental health.

18.2.3.2 Gender Preference

Patriarchal culture has made the male gender the preferred one for the newborn. Unfortunately, "a daughter is pitied at birth and the mother is blamed" [24]. Understandably therefore, the pregnant woman is put under tremendous stress by family as well as herself to give birth to a male child in many cultures like Indian and Chinese. In India, significantly higher number of pregnant women prefer male as the newborn gender; and women who report male gender preference have been found to have higher anxiety and stress [25] and also to be at risk for postnatal depression [26]. This risk, however, does not seem to be present in certain western cultures [27]. Maternal filicide is among most severe consequence related to "birth of non-preferred new born gender" [6]. Also, sex-selective abortions are usually the consequence of preference to infant's male gender adding to a woman's distress.

18.3 Modern Cultural Contexts: Family Structure, Workplace, and Maternity Leave

In many cultures, including traditional societies, more women reside now in nuclear families. Both nuclear and extended families have their advantages and disadvantages in the context of a woman's mental health [28]. One important advantage of living in societies that are socially connected is the availability of social (family) support. Social support is a predictor of antenatal mental well-being. And lack of social support is an important predictor of postpartum distress [29].

Maternal employment and therefore the workplace also add to the social support network. Perhaps, employed status and good support from workplace is associated with lower chances of perinatal psychopathology [30]. Within the context of maternal employment is the important aspect of maternity leaves. Across cultures (North American, European, Australian, and Middle East Asian), longer paid maternity leaves not only translates to improved pregnancy-related outcomes such as breastfeeding but also better maternal mental health [31]. Unfortunately, the access to paid maternity leaves is not straightforward and disparities exist in sanction of such leaves.

With the "cultural change" and the "changing roles of women" that are happening across the globe, there is a likelihood that factors conferring protection against

perinatal mental health problems such as better education, employment, and therefore self-esteem, are likely to improve. While the support structure in the traditional "ethnokinship" cultures is clearly defined, they are mostly dependent on maternity and paternity leaves in modern "technocentric" cultures [32]. Along with the changing roles of women, the social support and its seeking by perinatal women also depends on the deep-rooted distinctive gender roles, both in western societies and traditional ones [33, 34]. Moreover, there is some evidence to suggest that several factors related to the "modern civilization" such as early weaning, low levels of physical activity, and diets deficient in essential fatty acids are also related to postpartum psychopathology [35]. Since these factors vary across cultures, they differentially influence the prevalence of perinatal mental illnesses.

18.3.1 Patho-facilitative Influence

Prevalence of perinatal mental illnesses varies, in fact quite remarkably so, between different regions [36–38]. This remarkable variability, to a large extent attributed could be due to the role of cultural differences across these regions.

Prevalence of antenatal distress (anxiety/depression) varies between 6% and 29% in developed countries and between 20% and 60% in developing countries [38]. Social support (including quality of marital relationship) and a lack of it have been consistently suggested to be protective and risk factor for antenatal distress, respectively. Further, self-confidence has been claimed as another protective factor against antenatal distress in developed countries [38]. Cumulative stressful life events and domestic violence are the other sociocultural determinants that confer risk of antenatal distress.

Prevalence of postpartum depression varies between 0.5% to 63% [36, 37]. Similar to antenatal distress, the prevalence rates of postnatal distress too are higher in developing countries than developed ones [38]. While Pakistan, Guyana, Italy, South Africa, and Korea report high prevalence countires such as Singapore, Denmark, and Malaysia report low rates [36]. In Pakistan, the identified risk factors included low social support, stressful life events, poverty, multiparity, and low education. Birth of a female baby has been found to be a significant risk factor for postpartum depression in India, Turkey, China, and Japan [37]. The single mother status, which is more prevalent in developed countries, has been found to be a risk factor for postpartum depression [38]. The association of antenatal distress with postpartum psychopathology appears to be culture-free (found across nations and cultures) [38]. In South Africa, where the prevalence rates of postpartum depression are high, literacy has been found as the protective factor. Expectedly, good social support is protective across all cultures. Immigrant status, being a homemaker and unemployed, uneducated husband, polygamy, domestic violence, poor living conditions and birth of a female baby are cultural risk factors for postpartum depression in Asian countries [37].

18.4 Influence of Traditional Customs/Rituals on Perinatal Mental Health

The traditional customs and rituals that vary from culture to culture have evolved over years probably with an intention of providing emotional strength support as well as dealing with the unique needs of the motherhood. Organized support and a rest period, which are mostly universal across cultures, appear to provide support to the perinatal woman during her later part of pregnancy and early postpartum [39]. However, the changing role of women might not allow a woman to participate in these rituals for the prescribed time period of rest, which vary from 3 weeks to 10 weeks or even longer across cultures. Apart from the time at disposal, it may not be also feasible many a time for women, especially those from nuclear families, to arrange for availability of required number of female family members for the support [39]. Hence, strictly adhering to these rituals is not possible, and the possible mental health benefits of them (i.e., long needed rest) may not be availed despite being culturally allowed.

Apart from not being able to avail the benefits, the very nature of these customs, i.e., voluntary or forced, and restrictive or flexible, determines the way they influence the mental health of the perinatal women. Voluntary and flexible rituals are likely to have good mental health outcomes, while forced and restrictive ones, due to the resultant tension, stress, and emotional disturbance could lead to perinatal psychopathology [36]. In fact, being in conflict with traditional rituals has been identified as a stressful situation that contributes to occurrence of postpartum distress [37]. There is perhaps an incongruity between the expectation and perception of an "ideal motherhood" role and the realistic nature of the "changed" role, which has "multiple roles and tasks." These "crushed maternal role expectations" and the resultant "going into hiding" and "intense feeling of vulnerability" due to sense of shame, helplessness, and dependency have been included in the qualitative, meta-synthetic, practical life concerns-based theories of postpartum depression [40]. Moreover, as discussed earlier too, the failure to adhere to these traditional customs also has a likelihood of being branded with certain culture-bound syndromes like susto, toas, lom pid duan, aire, etc. [14, 16, 17]

Interestingly and commonly across cultures, foods are idiosyncratically divided into "hot" and "cold." Usually, there is a strict prohibition of "cold" foods and encouragement of consumption of "hot" foods/herbal preparations during the postpartum period since postpartum is considered as a "cold" state [39]. The food prescription for the perinatal women, especially those in their postpartum period, becomes very restrictive. This restriction might have a negative influence on the perinatal woman's "food choice," which is an important component of food security [41].

While adhering to traditional customs seems to offer some protection to perinatal mental women in some cultures, they seem to be "not supportive" in some even when the women has adhered to the cultural prescription of the rituals. While some Taiwanese ("doing the month") and Turkish-Islamic customs were found to be protective for postpartum depression, the Japanese, the Vietnamese, and the Iranians

reported that their respective postpartum rituals (such as "Satogaeribunben," "Zuo Yue Zi," etc.) did not offer any protection [37, 42, 43]. In fact, in Malaysia and Singapore, where the postpartum depression rates are quite low, practicing and adhering to the postnatal rituals ("Pantang" and Singaporean confinement, respectively) was rather associated with more negative mental health consequences [37]. Whether or not such negative mental health consequences are associated with other idiosyncratic rituals and practices related to "hygiene and physical warmth" such as the Islamic—"ghusl"—and the Thai, "kao krachome" and "yu fai" [39] remains to be specifically assessed. Further, there is a stark contrast in the nature of these rituals—while baths are restricted in some cultures like Mexican and Chinese, they are acceptable and encouraged in Malaysian, Indian, and Thai cultures [39]. Apart from being idiosyncratic, certain rituals, especially those related to breastfeeding and infant feeding, may contradict the scientifically undermined essential medical advice. Breastfeeding, medically recommended to be initiated within the first hour of birth, is delayed for 2–3 days or even till the sixth day "Chatti" in some parts of India. In fact, colostrum, which is considered as an immune booster, is perceived as "dirty" and indigestible in South Asian and Guatemalan cultures [39]. The contrast between medical advice and characteristics of traditional rituals is likely to result in stress among perinatal women [37].

Although linked to religion, afore discussed traditional customs and rituals commonly cut across various religions. Interestingly, studies have found that religiosity and participation in organized religious participation is indeed protective for perinatal women [44]. Negative religious coping appears to be associated with higher levels of perinatal psychopathology. Intriguingly, certain religious practices also tend to have negative effects on antenatal as well as postnatal psychopathology. One such interesting practice is that of "Marianismo." Marianismo is an orthodox Christianity-based self-sacrificing and subordination idealism followed in Latina women, where they assume "a role of virtue, passivity and priority to others over oneself." Marianismo is found to be significantly associated with postpartum depression, although the association of antenatal depression is not consistent. Several negative cognitive-emotional factors and poor mental healthcare seeking have also been associated with the practice of Marianismo [45].

18.5 Migration, Culture, and Postpartum Mental Health

Feelings of loneliness among migrant women may worsen during the perinatal period especially during the postpartum. Few stressors associated with migration such as leaving behind one's social network and having to face unfamiliar circumstances and uncertainties about income, healthcare access, and residential status exacerbate the sense of solitude among women and more so if a woman is depressed. Migrant women with PPD have fears about accessing healthcare, worries about being labelled, and fear of losing children to state care on being perceived as incompetent. Mothers who had migrated and had postpartum depression reported a crushed maternal role, disruption in sense of self, vulnerable feelings such as

helplessness, and daily practical concerns [40]. Expectations about being a good mother and perceptions about availability of support can vary in the new country and can be stressful to the immigrant mothers. Further, societal expectations that a new mother has to be happy all the time contrast with the maternal experiences of adjusting to the challenges of motherhood in a new country.

Migration within the country is also associated with challenges for women during perinatal period, and factors such as poor income, low social support, and disrupted marital relationships are associated with perinatal depression [46]. Immigrant women are particularly at risk for postpartum depression [47].

Research examining the role of specific cultural aspects such as degree of acculturation and religiosity in the manifestation of perinatal depression has remained inconclusive.

In a Canadian setting, the prevalence of PPD among immigrants was similar to the local population. Poor social support, lesser duration of stay in Canada, poor physical health and mental well-being, living among immigrant communities, and financial constraints appear to have a more bearing on PPD than acculturation alone [48].

Migrant mothers with PPD often do not speak about their problems for fear of stigma. The feeling of fear, shame, and guilt that accompany PPD often leads to a position wherein the mother thinks that she should cope on her own. Further, some women may not be even aware of their depressed state being as a problem and could deny the existence of depression during postpartum period. They tend to "suffer in silence" for fear of being labelled, being prescribed medications, and being diagnosed with severe mental illness at a later point of time. Hence, perinatal depression remains an invisible illness. Disruption in rituals due to migration could be a source of stress due to perceived guilt of missing the rituals. Often, the distress associated with PPD is shaped by cultural context and beliefs—e.g., exposure to cold and water in a Canadian migrant women of Asian descent. Further, while depressed they are more likely to voice concern about settlement, social isolation, gainful employment, being lonely, and having no one around to help during the adverse times. Some women of Asian origin may also have to face the aspirations for a male baby from the families despite moving to a new culture where there is not much emphasis on gender of infant.

Migrant women from certain cultures may not have a cultural equivalent to describe their postpartum depressed state in a western healthcare setting and may attribute the distress to practical issues such as being busy with household responsibilities with no time to rest. Depressive symptoms are also attributed to economic factors—as poor income—and social factors such as family problems.

The barriers to healthcare access among migrants with PPD include the fear of stigma and alienation on being diagnosed with a clinical condition from the healthcare system in the new country [49]. The barriers to access of care include lack of therapists who are tuned to cultural nuances, perception that one may not get access to healthcare system, transportation, care of the child, unemployment and language incompatibility. Migrant women may downplay their emotional problems because

of the likelihood being prescribed pills on disclosing emotional distress to a health-care provider and may prefer counselling and non-pharmacological measure.

18.6 Cultural Formulation in Perinatal Psychiatry

Popular methods for forming a cultural formulation include the Explanatory Model Interview Catalogue (EMIC) for cultural epidemiological studies, the Short Explanatory Model Interview (SEMI), and the Cultural Formulation Interview (CFI) of the American Psychiatric Association (APA). The CFI-APA involves interviewing patient and reliable informants in order to understand the cultural aspects of the individual's problem [50]. The salient points of the CFI are mentioned in Table 18.2.

CFI may be helpful in evaluating perinatal women who are from a different cultural background. In some cultures, the presence of relatives during an interview with a woman could interfere with the responses [51]. Hence, it would be worthwhile to interview caregivers and the woman separately.

Formulating a cultural formulation in perinatal mental health may involve asking open-ended questions during the beginning of a clinical interview which include the following:

- What brings you here?
- How would you explain your problem?

Table 18.2 A perinatal mental health cultural formulation interview

Definition of the problem – Explore the woman's view of the problems with a focus on the perinatal context, and her current social situation
Perception of cause, context, and supports – Focus on the woman's ideas and of those in her family about the possible causes of her problems – Explore regarding her support systems and ongoing stressors, if any – Assess the woman's background and cultural identity that could be either ameliorating or worsening the problems; explore for the role of discrimination due to migration, race/ethnicity, or gender; conflicts in the family arising out of migration, and any feelings of isolation
Help-seeking – Gather information on how the woman and her family have handled the problem so far – Explore the sources of help sought by the individual for resolution of the problems including traditional healers – Explore the usefulness of the sources if help in reducing the problem – Examine the barriers that prevented an individual to seek help and care from a mental health facility
Present help-seeking – Ask the current needs and expectations regarding the help; help from the social network – Examine if the individual has concerns about clinician-patient relationship due to differences in ethnicity, language, or cultural differences and any ideas about she can resolve them

- How would you describe your problem to family/friends?
- Among the described problems, which one bothers you most?
- What is your understanding about how your current problem is related to your pregnancy or the postpartum period?

Later, the interview could be more explorative by asking the below questions:

- What do you think are the causes of your problems? Specific questions about the meaning of motherhood in that culture and rituals that are known to be protective and practices that are known to be harmful can be explored.
- According to your family/friends, what are the possible causes of your problem? Explore factors such as diet, black magic, postpartum rituals, not resting, and cold food.
- Could you tell me about the factors that worsen/make better the problems you are going through?
- What have you done from your end to overcome these problems?
- Could you tell me the details of help sought by you for your problems? Specifically, it may be important to ask about the use of alternative and complementary methods. Most women prefer not to use modern medicine (pharmacological) during pregnancy or postpartum thinking that it might cause harm to the fetus or infant. Use of other methods of healing needs to be explored.
- To examine for barriers of care questions—such as "Has anything prevented you from accessing help to overcome the problems?"—may be useful.
- Questions for their expectations from care and satisfaction in relation to their explanatory models need to be explored with questions such as "What kind of care did you expect?" and "What types of care are likely to be most useful?".
- Has anyone else known to you suggested other types of care?
- Explore the role of the infant: How do you feel about the infant? Are there expectations from the family about your infant that you would like to talk about? Are their concerns about an evil eye on the infant, the infant bringing you good or bad luck, rituals, and traditions related to the infant?
- About breastfeeding: What are the attitudes to whether you can or cannot feed your infant because of the problems you are facing?

A well-conducted interview with the woman and her caregivers will help in developing a cultural formulation that can be extremely beneficial in management, and facilitate better communication between the treatment team and the woman.

18.7 Cultural Competence in Perinatal Mental Health Services

Enhancement of cultural competence among healthcare providers when working with mothers with mental health problems is very important especially if the health provider and the woman come from different cultures. One must remember that

many times these differences may be evident even within the same culture because of religious differences or urban-rural and educational variations.

A culturally sensitive training program for perinatal healthcare providers should consider the needs and viewpoints of local population as well as that of healthcare providers. The framework for a training program should include consideration for therapist gender preferences of mothers with illness, local language compatibility and availability of interpreters, understanding of metaphorical expressions, as well as a curiosity to understand the illness from the mother's cultural viewpoint.

Psychosocial interventions also need to be tailored to the cultural characteristics of the target group [52]. Bernal and Sáez-Santiago [53] provide a framework for culturally sensitive psychosocial interventions—language adaptations of the interventions should include local expressions or idioms of distress instead of technical terminology. Further, a provider who could share experiences and also is aware of local culture would be of most help in delivery of interventions. Incorporation of local stories, characters similar to patient's psychosocial environment, and the use of metaphors and symbols help to understand and quantify distress of patients. Addressing the local customs prevalent in the community is likely to improve the acceptability of the psychosocial interventions [54].

18.8 Conclusions

Culture is important in shaping how mental health problems are perceived, experienced, labelled, and handled. This is even more relevant for mental health problems in pregnancy and the postpartum where traditions, rituals, and practices are closely linked with both the physical and emotional health of the mother-fetus-infant dyad. A good understanding of a woman's cultural background, her beliefs, and how she experiences her mental health condition is an important aspect of providing care. While it may not be realistic for mental health professionals to be aware of all the possible cultural aspects, developing cultural competence will lead to pregnant and postpartum women feeling better understood at this vulnerable time of their lives.

References

1. Moleiro C. Culture and psychopathology: new perspectives on research, practice, and clinical training in a globalized world. Front Psychiatry. 2018;9:366. https://doi.org/10.3389/fpsyt.2018.00366.
2. Kelly RH, Russo J, Katon W. Somatic complaints among pregnant women cared for in obstetrics: normal pregnancy or depressive and anxiety symptom amplification revisited? Gen Hosp Psychiatry. 2001;23:107–13. https://doi.org/10.1016/s0163-8343(01)00129-3.
3. Isaac M, Janca A, Burke KC, e Silva JA, Acuda SW, Altamura AC, et al. Medically unexplained somatic symptoms in different cultures. A preliminary report from phase I of the World Health Organization International Study of Somatoform Disorders. Psychother Psychosom. 1995;64:88–93. https://doi.org/10.1159/000288996.

4. Chandra PS, Bhargavaraman RP, Raghunandan VN, Shaligram D. Delusions related to infant and their association with mother-infant interactions in postpartum psychotic disorders. Arch Womens Ment Health. 2006;9:285–8. https://doi.org/10.1007/s00737-006-0147-7.
5. Kumar R, Marks M, Platz C, Yoshida K. Clinical survey of a psychiatric mother and baby unit: characteristics of 100 consecutive admissions. J Affect Disord. 1995;33:11–22. https://doi.org/10.1016/0165-0327(94)00067-j.
6. Hatters Friedman S, Resnick PJ. Child murder by mothers: patterns and prevention. World Psychiatry. 2007;6:137–41.
7. Knabb JJ, Welsh RK, Graham-Howard ML. Religious delusions and filicide: a psychodynamic model. Ment Health Relig Cult. 2012;15:529–49. https://doi.org/10.1080/13674676.2011.594998.
8. Spinelli M. A systematic investigation of 16 cases of neonaticide. Am J Psychiatry. 2001;158:811.
9. Bhavsar V, Ventriglio A, Bhugra D. Dissociative trance and spirit possession: challenges for cultures in transition. Psychiatry Clin Neurosci. 2016;70:551–9. https://doi.org/10.1111/pcn.12425.
10. Aziato L, Acheampong AK, Umoar KL. Labour pain experiences and perceptions: a qualitative study among post-partum women in Ghana. BMC Pregnancy Childbirth. 2017;17:73. https://doi.org/10.1186/s12884-017-1248-1.
11. Weisenberg M, Caspi Z. Cultural and educational influences on pain of childbirth. J Pain Symptom Manag. 1989;4:13–9. https://doi.org/10.1016/0885-3924(89)90059-6.
12. Nahar A, Kondapuram N, Desai G, Chandra PS. Catatonia among women with postpartum psychosis in a Mother-Baby inpatient psychiatry unit. Gen Hosp Psychiatry. 2017;45:40–3. https://doi.org/10.1016/j.genhosppsych.2016.12.010.
13. Mustafa M, Bassim R, Meguid M, Sultan M, Al Dardiry M. Ethnic differences in the prevalence of catatonia among hospitalized psychiatric patients in Kuwait. Middle East Curr Psychiatry. 2012;19:214–21.
14. Maldonado-Duran JM, Manguia-Wellman M, Lubin S, Lartigue T. Latino Families in the perinatal period: cultural issues in dealing with the health-care system. Gt Plains Res. 2002;596:75–100. Available at: https://core.ac.uk/download/pdf/188043656.pdf
15. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.
16. Tea J. Cambodian perinatal culture-bound syndromes: Providing care to Cambodian women with toas. University of Washington; 2010. Available at: https://ethnomed.org/resource/cambodian-perinatal-culture-bound-syndromes-providing-care-to-cambodian-women-with-toas/
17. Liamputtong P. Yu Duan practices as embodying tradition, modernity and social change in Chiang Mai, Northern Thailand. Women Health. 2004;40:79–99. https://doi.org/10.1300/J013v40n01_05.
18. Thippeswamy H, Dahale A, Desai G, Chandra PS. What is in a name? Causative explanatory models of postpartum psychosis among patients and caregivers in India. Int J Soc Psychiatry. 2015;61:818–23. https://doi.org/10.1177/0020764015597016.
19. Pinter B, Hakim M, Seidman DS, Kubba A, Kishen M, Di Carlo C. Religion and family planning. Eur J Contracept Reprod Health Care. 2016;21:486–95. https://doi.org/10.1080/13625187.2016.1237631.
20. Atighetchi D. The position of Islamic tradition on contraception. Med Law. 1994;13:717–25.
21. Hung CH. The psychosocial consequences for primiparas and multiparas. Kaohsiung J Med Sci. 2007;23:352–60. https://doi.org/10.1016/S1607-551X(09)70421-8.
22. Shitu S, Geda B, Dheresa M. Postpartum depression and associated factors among mothers who gave birth in the last twelve months in Ankesha district, Awi zone, North West Ethiopia. BMC Pregnancy Childbirth. 2019;19:435. https://doi.org/10.1186/s12884-019-2594-y.
23. Berg V, Miettinen A, Jokela M, Rotkirch A. Shorter birth intervals between siblings are associated with increased risk of parental divorce. PLoS One. 2020;15:e0228237. https://doi.org/10.1371/journal.pone.0228237.

24. Mojumdar M. The girl child and the family. Yojana. 1990;34:13–4.
25. Supraja TA, Varghese M, Desai G, Chandra PS. The relationship of gender preference to anxiety, stress and family violence among pregnant women in urban India. Int J Cult Ment Health. 2016;9:356–63. https://doi.org/10.1080/17542863.2016.1205114.
26. Patel V, Rodrigues M, DeSouza N. Gender, poverty, and postnatal depression: a study of mothers in Goa. India Am J Psychiatry. 2002;159:43–7. https://doi.org/10.1176/appi.ajp.159.1.43.
27. Sylvén SM, Papadopoulos FC, Mpazakidis V, Ekselius L, Sundström-Poromaa I, Skalkidou A. Newborn gender as a predictor of postpartum mood disturbances in a sample of Swedish women. Arch Womens Ment Health. 2011;14:195–201. https://doi.org/10.1007/s00737-011-0211-9.
28. Allendorf K. Going nuclear? Family structure and young women's health in India, 1992–2006. Demography. 2013;50:853–80. https://doi.org/10.1007/s13524-012-0173-1.
29. Milgrom J, Hirshler Y, Reece J, Holt C, Gemmill AW. Social support—a protective factor for depressed perinatal women? Int J Environ Res Public Health. 2019;16:1426. https://doi.org/10.3390/ijerph16081426.
30. Gjerdingen D, McGovern P, Attanasio L, Johnson PJ, Kozhimannil KB. Maternal depressive symptoms, employment, and social support. J Am Board Fam Med. 2014;27:87–96. https://doi.org/10.3122/jabfm.2014.01.130126.
31. Andres E, Baird S, Bingenheimer JB, Markus AR. Maternity leave access and health: a systematic narrative review and conceptual framework development. Matern Child Health J. 2016;20:1178–92. https://doi.org/10.1007/s10995-015-1905-9.
32. Posmontier B, Horowitz JA. Postpartum practices and depression prevalences: technocentric and ethnokinship cultural perspectives. J Transcult Nurs. 2004;15:34–43. https://doi.org/10.1177/1043659603260032.
33. Tang L, Zhu R, Zhang X. Postpartum depression and social support in China: a cultural perspective. J Health Commun. 2016;21:1055–61. https://doi.org/10.1080/10810730.2016.1204384.
34. Albuja AF, Lara MA, Navarrete L, Nieto L. Social support and postpartum depression revisited: the traditional female role as moderator among Mexican women. Sex Roles. 2017;77:209–20. https://doi.org/10.1007/s11199-016-0705-z.
35. Hahn-Holbrook J, Haselton M. Is postpartum depression a disease of modern civilization? Curr Dir Psychol Sci. 2014;23:395–400. https://doi.org/10.1177/0963721414547736.
36. Abdollahi F, Lye MS, Md Zain A, Shariff Ghazali S, Zarghami M. Postnatal depression and its associated factors in women from different cultures. Iran J Psychiatry Behav Sci. 2011;5:5–11.
37. Klainin P, Arthur DG. Postpartum depression in Asian cultures: a literature review. Int J Nurs Stud. 2009;46:1355–73. https://doi.org/10.1016/j.ijnurstu.2009.02.012.
38. Satyanarayana VA, Lukose A, Srinivasan K. Maternal mental health in pregnancy and child behavior. Indian J Psychiatry. 2011;53:351–61. https://doi.org/10.4103/0019-5545.91911.
39. Dennis CL, Fung K, Grigoriadis S, Robinson GE, Romans S, Ross L. Traditional postpartum practices and rituals: a qualitative systematic review. Womens Health. 2007;3:487–502. https://doi.org/10.2217/17455057.3.4.487.
40. Mollard EK. A qualitative meta-synthesis and theory of postpartum depression. Issues Ment Health Nurs. 2014;35:656–63. https://doi.org/10.3109/01612840.2014.893044.
41. Alonso EB, Cockx L, Swinnen J. Culture and food security. Glob Food Secur. 2018;17:113–27.
42. Demirel G, Egri G, Yesildag B, Doganer A. Effects of traditional practices in the postpartum period on postpartum depression. Health Care Women Int. 2018;39:65–78. https://doi.org/10.1080/07399332.2017.1370469.
43. Abdollahi F, Etemadinezhad S, Lye MS. Postpartum mental health in relation to sociocultural practices. Taiwan J Obstet Gynecol. 2016;55:76–80. https://doi.org/10.1016/j.tjog.2015.12.008.
44. Mann JR, McKeown RE, Bacon J, Vesselinov R, Bush F. Do antenatal religious and spiritual factors impact the risk of postpartum depressive symptoms? J Women's Health. 2008;17:745–55. https://doi.org/10.1089/jwh.2007.0627.

45. Nuñez A, González P, Talavera GA, Sanchez-Johnsen L, Roesch SC, Davis SM, et al. Machismo, Marianismo, and negative cognitive-emotional factors: findings from the Hispanic Community Health Study/Study of Latinos Sociocultural Ancillary Study. J Lat Psychol. 2016;4:202–17. https://doi.org/10.1037/lat0000050.
46. Xiong R, Deng A. Prevalence and associated factors of postpartum depression among immigrant women in Guangzhou, China. BMC Pregnancy Childbirth. 2020;20:247. https://doi.org/10.1186/s12884-020-02946-4.
47. Falah-Hassani K, Shiri R, Vigod S, Dennis CL. Prevalence of postpartum depression among immigrant women: a systematic review and meta-analysis. J Psychiatr Res. 2015;70:67–82. https://doi.org/10.1016/j.jpsychires.2015.08.010.
48. Ganann R, Sword W, Thabane L, Newbold B, Black M. Predictors of postpartum depression among immigrant women in the year after childbirth. J Women's Heal. 2016;25:155–65. https://doi.org/10.1089/jwh.2015.5292.
49. Tobin CL, Di Napoli P, Beck CT. Refugee and immigrant women's experience of postpartum depression: a meta-synthesis. J Transcult Nurs Soc. 2018;29:84–100. https://doi.org/10.1177/1043659616686167.
50. Aggarwal NK, Jarvis GE, Gómez-Carrillo A, Kirmayer LJ, Lewis-Fernández R. The Cultural Formulation Interview since DSM-5: prospects for training, research, and clinical practice. Transcult Psychiatry. 57:496–514. https://doi.org/10.1177/1363461520940481.
51. Paralikar VP, Sarmukaddam SB, Patil KV, Nulkar AD, Weiss MG. Clinical value of the cultural formulation interview in Pune, India. Indian J Psychiatry. 2015;57:59–67. https://doi.org/10.4103/0019-5545.148524.
52. Nyatsanza M, Schneider M, Davies T, Lund C. Filling the treatment gap: developing a task sharing counselling intervention for perinatal depression in Khayelitsha, South Africa. BMC Psychiatry. 2016;16 https://doi.org/10.1186/s12888-016-0873-y.
53. Bernal G, Sáez-Santiago E. Culturally centered psychosocial interventions. J Community Psychol. 2006;34:121–32. https://doi.org/10.1002/jcop.20096.
54. Rodrigues M, Patel V, Jaswal S, De Souza N. Listening to mothers: qualitative studies on motherhood and depression from Goa, India. Soc Sci Med. 2003;57:1797–806. https://doi.org/10.1016/s0277-9536(03)00062-5.

Prevention and Treatment of Perinatal Mental Disorders in Migrant Women

19

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19.1 Introduction

Perinatal mental health is an important public health and mental health issue. Women during the perinatal period are at higher risk of mental illness. This has implications for the women themselves, infant development and the wider society [1]. Migrants and refugee women make up a highly vulnerable sub-group with high rates of physical and mental health illness. As such, it is necessary to understand the migratory contributors and unique stressors facing this population. This will aid diagnosis and management during the perinatal period.

In this chapter, we use the term migrant to denote all individuals living outside of their country of birth, including economic migrants, refugees, asylum seekers and those who hold other legal statuses.

19.2 Migratory Patterns

According to 2019 estimates from the United Nations, the number of migrants worldwide is 272 million, representing 3.5% of the world's population [2]. Women accounted for 47.9% of all migrants worldwide (ibid.). The percentage of women migrants varies between nations, with highest proportional levels in North America and Europe at 51.8% and 51.4%, respectively (ibid.).

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It is also to be noted that official government data regarding the number of migrants typically refers to those who are officially residents in host countries. As such, the data is likely to underestimate the considerable number of female migrants who are undocumented.

Migratory patterns often follow an unequal geographical distribution within counties. Therefore, perinatal challenges related to migrant populations are likely to be concentrated in particular regions. This has implications for the local health systems in responding to the needs of this population and may guide where preventative efforts and resources should be targeted. Further, the declining birth rates in regions such as Europe, combined with increased levels of migration, indicate that the proportion of migrant births is likely to be increasing [2].

19.3 Prevalence

Migrant women are thought to have high rates of depressive symptoms in the perinatal period. A systematic review and meta-analysis (n = 40 studies; representing 18,783 women) that specifically considered migrant women from low- and middle-income countries (LMICs) found pooled prevalence rates of 31% for any depressive disorder and 17% for major depressive disorder [3]. With a few exceptions, they noted that most studies showed that migrant women had higher rates of depression compared to host populations.

A different systematic review and meta-analysis (n = 50 studies) found elevated levels of depressive symptoms during pregnancy and post-partum [4]. They did not find a statistically significant overall increase when compared to nonmigrant women; however they issued a strong note of caution in interpretation of this given the heterogeneity in migrant and nonmigrant groups and contexts between studies. For example, they found elevated levels amongst migrant women in studies undertaken in Canada but did not find this to be the case in the United State of America. Interestingly, different literature reviews have found that postnatal depression affects up to 42% of migrant women, and this was significantly higher than 10–15% noted in native/host country-born women [5, 6].

With regard to other mental health conditions such as anxiety, post-traumatic stress disorder and psychosis, there is limited information in comparative rates during the perinatal period. This exemplifies the research gap for this particular population. An Australian study found that there were greater levels of anxiety 6 months post-partum in migrant women who were of non-English-speaking background. Interestingly, the level was the same as host populations amongst those who were English speaking [7].

Finally, whilst the above prevalence data is related to individuals migrating to high-income countries, there is very little evidence related to migratory impact of those moving to middle- or low-income settings [3]. This is an important and large migrant group in whom prevalence estimates are not well understood.

19.4 Risk Factors, Identification and Diagnostic Assessment

When considering migratory patterns and risk factors, it is necessary to recognise the immense heterogeneity within this group. This had been dubbed as 'super-diversity' [8]. In addition to the country of origin, the complex push and pull factors leading to migration are also varied. For example, push factors for migration could include the threats of persecution or natural disasters; and pull factors often cited include better educational or employment opportunities. As such, whilst recognising the systemic challenges and risks faced by migrant populations, an individualised culturally competent approach is necessary to better understand which factors may be contributing to an individual's presentation.

Migrant women face a number of risk factors for perinatal mental disorders [9]. Firstly, they may share some of the risk factors faced by maternal women from the host population, such as lack of social support, socio-economic status, stress and minority ethnic status. In addition to these shared risk factors, migrant women face unique risk factors; these include host country language proficiency, legal status (particularly women who are refugees/asylum seekers), access to social institutions including education and health, employment rights and time period spent in the host country. Further, migrants' health experience is also shaped by their own personal health history, which is intrinsically linked to and influenced by their pre-migratory circumstances, for example, their individual socio-economic status prior to migration, level of education, disease burden and quality of care received in country of origin and/or transit. As such, an intersectional approach is helpful in understanding how gender, ethnicity, nationality/citizenship status, religion, socio-economic status, pre-migratory circumstances and the migratory journey interact to make a woman more or less vulnerable.

Barriers faced by migrant women can be classified as 'practical' or 'cultural' [10]. Practical barriers include language difficulties, and access to health care—due to a lack of familiarity and knowledge of the local healthcare system. Cultural barriers relate to limited awareness of Western explanatory models of distress (i.e. diagnosis of postpartum depression), fear of stigma, fear of impacting family reputation or harmony, limited family support, discriminatory practice from staff or fear that the child might be taken away from the mother by social services (ibid.).

The incidence of perinatal depression is notably higher amongst those lacking social support [3]. This is particularly important for those women who hail from sociocentric cultures (e.g. Africa, Asia and the Middle East) where considerable emphasis is placed on the maternal wellbeing with related social support rituals. Often this support is physical rather than technological and is felt to be central in providing safety for the postpartum mother [11]. Conversely, technocentric cultures (e.g. Europe and North America) place greater importance in conventional healthcare systems and technological approaches in helping a postpartum mother (ibid.).

Studies also show that women from non-Western cultures such as Asia, Africa or Latin America may express symptoms of postpartum depression psychosomatically [12]. Often in such cultures, there is no mind-body dualism which characterises Western cultures.

19.5 Prevention, Support and Treatment

19.5.1 Primary Prevention

Primary prevention for migrant women relates to the steps taken to reduce the risk of developing mental health conditions before the onset of the disorder [13]. Various interventions can assist with this, for example, ensuring that all written information is translated and provided in the woman's native language and adapting services such as wellbeing tips for newly pregnant women and prenatal support meetings to be more culturally and linguistically inclusive.

Beyond women who are already pregnant, there may also be a role for seeking to improve the wider social determinants of health facing migrant women of childbearing age and widening access to appropriate services/social support during the migratory process. Strategies to help with martial difficulties, family conflict, social isolation, socio-economic difficulty and management of pre-existing mental health disorders also minimise the vulnerability to mental health conditions during the perinatal period [14, 15]. In particular, social support has been found to be an important protective factor [3].

Another important aspect to consider is the acculturation process that migrant women undergo. Acculturation refers to the way in which an individual assimilates to a different culture. During acculturation, migrant women may have to adapt to a new language, value systems, behaviours and customs, norms and mores and laws [16]. For many migrant women, this acculturation process moves beyond assimilation or integration and may result in either giving up their own ethnic identity and accepting the host culture, or marginalisation should they refuse to do so. As such, the acculturation process may be a significant threat to self-identity and lead to depressive symptoms [17]. Promoting protective contact with others and activities that improve wellbeing such as those related to employment, leisure/social activities and physical exercise are needed to support people during this difficult process [18]. Such activities could be addressed at various sectors such as through education in schools, via social and healthcare institutions (particularly those in community/primary and maternal care) and through the wider mass media, including television shows and popular culture.

19.5.2 Secondary Prevention

Secondary prevention relates to early symptom identification and diagnosis [13]. This approach aims to reduce the time between onset of symptoms and significant consequences. Early identification, particularly by considering changes and trends, can be undertaken through use of screening scales such as the Edinburgh Postnatal Depression Scale [19]. It is important to note that the cultural adaptability of these scales, particularly when administered in English through an interpreter when a woman does not speak the language, may itself pose significant challenges and lack cultural congruence [20]. As such, other signs and symptoms during clinical

interactions such as presence of somatic symptoms should be used as prompts to undertake a more detailed exploration. Collateral history may also be of help in such situations. In a high-income country context, there may be multiple opportunities for such screening given that a large percentage of perinatal migrant women will be attending health checks, ultrasounds and other appointments. For healthcare workers to be better able to undertake secondary prevention, they would benefit from cultural competency training particularly around the cultural mediators, idioms of distress and varied nature of mental health presentations.

Further, services may benefit from ensuring that migrant populations are informed of the social and health care available to them, and the pathways to access such care. Local stakeholder mapping and co-development may allow for further determination of specific barriers and facilitators.

19.5.3 Tertiary Prevention

Tertiary prevention relates to the point at which a woman is suffering from symptoms of mental health illness such as depression, and the related use of a therapeutic intervention [13]. Given the disease burden, some individuals may benefit from psychological and/or pharmacological therapy, for example, when depressive symptoms are having a significant functional impact during and after pregnancy. It is important to recognise that this complex decision-making process in management must involve the woman, her family (if the woman is wishing to be involved) and her mental health specialist.

With regard to psychological therapy, appropriate language and cultural adaptations may be needed, including reassurance regarding anonymity [14]. Some may also benefit from group rather than individual therapy due to cultural beliefs, expressions of distress and personal preference.

Where medication is advised, there is need to provide up to date information regarding the safety profile and risks of using psychoactive drugs. These considerations should be clearly explained as related to both the mother and child. Such explanations will again need to be undertaken in a culturally appropriate way, with an understanding of potential varied pre-existing health beliefs and explanatory models. Healthcare providers may benefit from emphasising recent studies which suggest that psychotropic medications are relatively safe and are of benefit depending on disease severity. Follow-up for depressive and other mental health symptoms would be of great benefit during pregnancy, and the postpartum period. This would allow for establishment of a therapeutic relationship and better collaborative working and, at times, dissuade notions that individuals may have that mental health care is entirely coercive. This is particularly important given the risk of relapse associated with some perinatal mental health disorders.

When considering medication, there may benefit in taking into account ethnopharmacological evidence. Factors that contribute to the antidepressant therapy can be related to age, gender and ethnic background [21]. Specific pharmacogenetic factors that influence response include enzymatic and receptor differences as well as

those related to transporters. Dietary habits can also affect the response to antidepressants, for example, related use of natural and herbal remedies, body fat and weight.

19.6 Conclusion

Pregnant and postpartum migrant women are vulnerable to mental health disorders and are noted to have high rates. This vulnerability is related to an intersectionality of factors around gender, ethnicity, nationality/citizenship status, religion, socioeconomic status, pre-migratory circumstances and their migratory journey. Across assessment, prevention and management, a culturally trained health workforce is crucial. In particular, it is necessary to have an understanding of cultural expressions of illness which may include somatisation, expectations and conceptualisation of pregnancy, childbirth and the postpartum period, and what is considered as good maternal and mental health care. It is also necessary to consider the social determinants of health especially in primary and secondary preventative strategies. Finally, it is crucial that steps are taken to address the research gap in the perinatal mental health of migrants.

References

1. Bauer, A. Estimating the costs of perinatal mental health problems; 2015.
2. United Nations, D. O. E. A. S. A., Population Division. International Migration 2019: Report, 2019.
3. Fellmeth G, Fazel M, Plugge E. Migration and perinatal mental health in women from low-and middle-income countries: a systematic review and meta-analysis. BJOG Int J Obstet Gynaecol. 2017;124:742–52.
4. Anderson FM, Hatch SL, Comacchio C, Howard LM. Prevalence and risk of mental disorders in the perinatal period among migrant women: a systematic review and meta-analysis. Arch Womens Ment Health. 2017;20:449–62.
5. Collins CH, Zimmerman C, Howard LM. Refugee, asylum seeker, immigrant women and postnatal depression: rates and risk factors. Arch Womens Ment Health. 2011;14:3–11.
6. Miszkurka M, Goulet L, Zunzunegui MV. Antenatal depressive symptoms among Canadian-born and immigrant women in Quebec: differential exposure and vulnerability to contextual risk factors. Soc Psychiatry Psychiatr Epidemiol. 2012;47:1639–48.
7. Yelland J, Sutherland G, Brown SJ. Postpartum anxiety, depression and social health: findings from a population-based survey of Australian women. BMC Public Health. 2010;10:1–11.
8. Vertovec S. Super-diversity and its implications. Ethn Racial Stud. 2007;30:1024–54.
9. Corbani IE, Rucci P, Iapichino E, Quartieri Bollani M, Cauli G, Ceruti MR, Gala C, Bassi M. Comparing the prevalence and the risk profile for antenatal depressive symptoms across cultures. Int J Soc Psychiatry. 2017;63(7):622–31.
10. Lati Z. Better health briefing: the maternal mental health of migrant women. Race Equality Foundation; 2014.
11. Posmontier B, Horowitz JA. Postpartum practices and depression prevalences: technocentric and ethnokinship cultural perspectives. J Transcult Nurs. 2004;15:34–43.
12. Bashiri N, Spielvogel AM. Postpartum depression: a cross-cultural perspective. Primary Care Update OB/GYNS. 1999;6:82–7.

13. Shah CP. Public health and preventive medicine in Canada. Saunders; 2003.
14. Dennis CL, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. Cochrane Database Syst Rev. 2013;
15. Elliott SA, Leverton TJ, Sanjack M, Turner H, Cowmeadow P, Hopkins J, Bushnell D. Promoting mental health after childbirth: a controlled trial of primary prevention of postnatal depression. Br J Clin Psychol. 2000;39:223–41.
16. Bhugra D, Watson C, Ventriglio A. Migration, cultural capital and acculturation. Int Rev Psychiatry. 2020:1–6.
17. Davila M, McFall SL, Cheng D. Acculturation and depressive symptoms among pregnant and postpartum Latinas. Matern Child Health J. 2009;13:318–25.
18. Loh MI, Klug J. Voices of migrant women: the mediating role of resilience on the relationship between acculturation and psychological distress, 2012.
19. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150:782–6.
20. Zubaran C, Schumacher M, Roxo M, Foresti K. Screening tools for postpartum depression: validity and cultural dimensions. Afr J Psychiatry. 2010;13(5):357–65.
21. Ng CH, Klimidis S. Cultural factors and the use of psychotropic medications; 2008.

Prevention and Treatment in Peripartum: The Multicentric Observatory for Perinatal Depression

20

Cinzia Niolu, Franca Aceti, Gloria Angeletti, Nicoletta Giacchetti, and Ilaria Adulti

20.1 Introduction

Interest in perinatal mental distress has been increasing in recent years. The publication in 2015 of data on maternal perinatal mortality (i.e., between 42 days and 1 year after birth) in the UK showed that around a quarter of perinatal deaths were caused by mental health problems; in particular, one in seven cases resulted in suicide. These data make the need for early and adequate interventions in this field dramatically evident. In Italy, since 2012, the Istituto Superiore di Sanità (ISS) has been coordinating the monitoring of maternal perinatal mortality, by collating data from ten Italian regions (Piedmont, Lombardy, Friuli Venezia Giulia, Emilia-Romagna, Tuscany, Lazio, Campania, Apulia, Sicily, and Sardinia), covering 77% of national births. This monitoring revealed that, for every 100,000 live births, there were 2.1

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maternal deaths due to post-partum haemorrhage, while there were 2 deaths due to suicide, mainly occurring in a violent manner such as by hanging or jumping from a height. Due to these dramatic observations, 16 regional projects dedicated to the prevention and early recognition of perinatal mental distress were approved in 2018. In 2016, the project "Intervention for the recognition of perinatal psychological distress and support for fragile motherhood and fatherhood" had already started. This project is promoted by the network of services of the birth path and primary care, coordinated by the Emilia-Romagna region in collaboration with the National Centre for Disease Prevention and Control (CCM) and with the involvement of five other Italian regions: Piedmont, Tuscany, Lazio, Campania, and Sicily.

The UK guideline on Antenatal and Postnatal Health calls on maternity professionals, who are, often exclusively, focused on physical health, to carefully assess the woman's psychological conditions "empathically", thereby detecting information considered fundamental to the identification of women at risk of developing perinatal psychological distress: both the woman's and the couple's attitude towards pregnancy, the presence of a social and family network, the abuse of alcohol or other substances , the quality of the woman's interpersonal relationships, any conditions of social and housing isolation, domestic abuse and violence, employment, and economic and migration conditions. As far as the anamnestic assessment is concerned, the ISS-CCM project suggests collecting, as part of the first clinical interview during pregnancy or after childbirth, information on conditions, which would necessitate the involvement of a specialist mental health service, i.e. current or previous serious mental disorders, current or previous treatment for mental disorders, close family history of serious psychological distress after childbirth, use of alcohol and drugs, eating disorders, and advises the use of screening tests. Also in 2018, the Ministry of Health funded the project "Measures pertaining to the prevention, diagnosis, treatment and care of postpartum depressive syndrome", which involved the territorial services dedicated to primary care throughout the country. In the same period, a collaboration between the Perinatal Psychopathology Centres of three University Policlinics in Rome (Policlinico Tor Vergata, Policlinico Umberto I—Sapienza 1, Azienda Ospedaliera S. Andrea—Sapienza 2) led to the establishment of a Multicentric Observatory for Perinatal Depression (OMPD), supported by the association "Volontari per il Policlinico Tor Vergata o.n.l.u.s" with the patronage of the Italian Society of Psychiatry (SIP) Lazio regional section.

20.2 The Multicentric Observatory for Perinatal Depression—OMDP

The purpose of the Multicentric Observatory for Perinatal Depression (OMDP) is to conduct an extensive and precocious screening programme for perinatal depression with a uniform and standardised criterion, which will lead, in the future, to the creation of a prophylactic and therapeutic network, offering the most effective and the safest therapeutic pathways.

Therefore, the OMDP programme entails the following activities:

- Screening programme for women from the first trimester of pregnancy
- Identification of social and psychiatric predictors of perinatal depression
- Assessment of the risk and diagnosis of any disorders from the first trimester of pregnancy, so that early intervention can be established to reduce foetal damage in the early stages of pregnancy
- Prospective re-evaluation during the whole peripartum period: second and third pregnancy trimester, 1 and 6 months after childbirth, 1 year after delivery, to facilitate early identification of new cases and protect the mental health of both of woman and child

OMDP oversees the participation of several universities and territorial structures located in central, southern, and northern Italy.

Currently the OMDP centres are the following:

Local Health Districts: Departments of Mental Health of Rome and Lazio and Psychiatric Service of the Health District of Bolzano

University Facilities: University of Rome "Tor Vergata", University of Rome "La Sapienza" (Policlinico Umberto I and Azienda Ospedaliera Sant'Andrea), Catholic University of the Sacred Heart of Rome, University "Gabriele d'Annunzio" Chieti-Pescara, University of Foggia, University of L'Aquila, University of Campania "Luigi Vanvitelli", University of Catania, University of Palermo, and Polytechnic University of Marche

Since December 2018, the screening programme promoted by the OMDP has taken the form of a research project in collaboration with the three Roman centres and the Italian Society of Psychiatry (SIP), Lazio regional section, promoted by the Association "Volunteers for the Policlinico Tor Vergata o.n.l.u.s". The scientific managers of the project are Prof. Cinzia Niolu, Prof. Franca Aceti, and Prof. Gloria Angeletti. Among the collaborators of the scientific committee are Dr. Emanuela Bianciardi, Dr. Giulia Lisi, Dr. Nicoletta Giacchetti, Dr. Ilaria Adulti, Dr. Lavinia De Chiara, and Dr. Alexia Koukopoulos. The coordinator of OMDP is Prof. Alberto De Stefano, President of "Policlinico Tor Vergata Onlus". The study is still in progress at all the centres, with the aim of collecting as much data as possible, which will be analysed from a dynamic and longitudinal point of view, to allow an accurate assessment, over time, of all the variables examined. Therefore, the aims of the OMDP can be summarised as the intention to implement a screening programme with a shared and uniformly applied criteria, in line with national and international programmes promoting women's mental health, as well as studying the role and distribution of the psycho-socio-demographic factors most associated with maternal depression, in order to identify risk factors at an early stage. In this way, we try to highlight the need to create, in the near future, a network of preventions and treatment valid in all regions, including homogeneous therapeutic strategies.

A specific inter-university working group has been created to coordinate the project in order to:

1. Integrate and systematise data collection from the different centres.
2. Organise periodic meetings to update on the activities.
3. Organise training activities (congresses, seminars, CME courses, masters of perinatal psychopathology, FAD courses, dedicated lectures, internships) aimed at professionals involved in patient and group/family management: doctors, psychologists, psychiatric rehabilitation technicians, nurses, midwives, and assistants. The training courses have been carried out both in-person (at the different university sites and at the local centres) and via virtual connection during the pandemic.
4. Establishing and maintaining a periodic discussion on gender psychiatry issues and perinatal health with the regional mental health authorities, in particular with the Regional Consultation and the Mental Health Commission of the Medical Association, the ISS, and the Ministry of Health.

Study subjects are women over 18 years old in pregnancy or during the postpartum period, able to understand the purpose and procedures of the study and to give their written informed consent. The exclusion criteria considered are as follows: (a) diagnosis of mental retardation/intellectual disability; (b) diagnosis of autism spectrum disorder; and (c) inability to give written informed consent.

After signing the informed consent to participate in the study, women are required to fill out a data sheet that investigates the following anamnestic data: personal data, level of education, occupation, presence or absence of a stable relationship, information regarding the current pregnancy, and stressful life events that occurred in the 12 months prior to pregnancy.

Participants are also asked to complete the EPDS (Edinburgh Perinatal Depression Scale). The EPDS excludes somatic symptoms (e.g. changes in appetite and sleep) that are very common in women during the perinatal period. Item 10 investigates thoughts of self-harm and suicidal tendencies. Final score reaches a maximum of 30. Cut-off for a positive screening is, generally, applied at 13. In a summary of over 40 studies using EPDS, Hewitt et al. have, instead, adopted 12 as the cut-off for major depression and 10 for a combination of major and minor depression. Recent review work shows that both sensitivity and specificity of EPDS range from 80 to 90%, considering the most common cut-offs applied, but there is a considerable variability between studies in terms of setting, population, and screening threshold. In addition to identifying a condition of possible depression, three EPDS sections investigate the anxiety element arising in the prenatal and postnatal population. EPDS is available in many different languages other than English. In fact, for South Tyrolean patients whose mother tongue was German, we translated the informed consent and the data sheet into German and used EPDS validated in Germany. The evaluation is repeated in the three quarters of the pregnancy and at 1 month, 6 months, and 1 year after childbirth.

In the results presented below, when considering EPDS, a minimum cut-off of 9 was used. It was, also, useful to propose a subdivision of the scores obtained into ranges:

A score from 9 to 11 is an indication of a possibility of depression.

A score higher than 12 correlates with a greater probability of depression.

Certainly, in accordance with the most recent literature and with the DSM V, the EPDS cannot be used as the sole tool for diagnosing perinatal depression, as it, always, requires clinical confirmation by a psychodiagnostic interview, but it provides a concrete indication of the need for in-depth clinical investigation in a specialist setting. Health professionals, subsequently, contacted each patient found to be at risk of perinatal depression, to investigate the presence of possible pathology.

20.3 Data Analysis: Big Data and Machine Learning

We have chosen to analyse and process the preliminary data collected from the various participating centres using machine learning tools that allow us to analyse as many variables as possible, thereby giving us a point of reference for the future.

In particular, we refer to the Bayesian network, a machine learning tool, which "learns" from past data, relying on previously collected data and the associated evolution, to make predictions from input of new data.

The tool has a solid scientific basis, utilising the Bayes theorem, which manages the calculation of conditional probabilities. The idea is to build a network between variables (graph) in which the available data are connected by "cause-effect" relationships, with scientifically verified reliability.

Therefore, the potential of this tool is, easily, understood, when applied to the characteristics investigated in our patients. Basically, from the data provided at the first evaluation, the Bayesian network is able to calculate, in the first trimester, the individual risk of developing post-partum depression or, at least, of experiencing an increase in EPDS scores after childbirth.

Thus, the Bayesian network offers a completely transparent analysis tool, capable of calculating and providing the relationships between specific variables and able to easily identify the individual relative weight. It is an easy-to-use system, quick to activate, since a few hundred historical data are generally sufficient to build a training dataset in preparation for learning. Finally, as well as a screening and projection tool for individual patient, it can also be used to outline the most incisive risk factors and to identify the most exposed profiles for depression.

Access to such an innovative calculation tool was guaranteed by the profitable collaboration with KPMG ("Klynveld Peat Marwick Goerdeler"), a network of independent companies that deals with the provision of professional services to companies, active in more than 150 countries. In particular, KPMG in the healthcare sector is recognised by the market as a centre of absolute excellence, thanks to a portfolio of best practices and integrated services able to support the evolution of the national, regional, and local health service. KPMG has, freely, made available to

the OMDP the activity of expert consultants in the field of big data, for the creation of a Bayesian network demo, in which the data coming from the following centres have converged:

LAZIO: University of Rome "Tor Vergata", University of Rome "La Sapienza" (Policlinico Umberto I and Azienda Ospedaliera Sant'Andrea), and Catholic University of the Sacred Heart of Rome

ABRUZZO: University "d'Annunzio" Chieti-Pescara and University of L'Aquila

CAMPANIA: University of Campania "Luigi Vanvitelli"

PUGLIA: University of Foggia

SICILY: University of Palermo

TRENTINO ALTO ADIGE: Psychiatric Service of the Health District of Bolzano

The data collection period stops to the immediate pre-pandemic, February 2020. The lockdown situation, with the consequent remodelling of the afferent to perinatal mental health services, resulted in a prolonged stop to OMDP activity, with most centres active only for emergencies and different procedures for routine visits. Later, we will discuss the new approaches used during the pandemic, which the OMDP shared with the working group of the Istituto Superiore di Sanità in the ISS report COVID-19 n 44/2020 [1].

The data refer to a total of 1294 assessments of which 907 were performed in the *pre-partum* period and 387 in the *post-partum* period.

The first waffle chart shows the prevalence by trimester of pregnancy and by region, considering the cut-off at EPDS $\geq$ 12 (Fig. 20.1). There is considerable heterogeneity between regions in the prevalence estimates. This is due to regional differences in the organisation of perinatal health that make it difficult, for example, in some centres, to recruit patients in the first trimester. In the first trimester, the prevalence is higher in Campania, while in the third trimester, the highest prevalence is found in Abruzzo.

The waffle chart in Fig. 20.2 shows the prevalence of perinatal depression post-partum divided by follow-up period and by region. The data for Sicily and Trentino Alto Adige are not yet available. The number for Puglia is very small. In Lazio there is a particularly high prevalence in all follow-up periods. By the way, data from Lazio are pooled from three centres, Tor Vergata, Sapienza 1 and 2, and Sacred Heart Universities. We would like to specify that the entry of the University of Foggia into the study was, despite their best efforts, delayed by bureaucratic constraints. This explains the lack of data collected by this centre at the time of the statistical evaluation. The Apulian centre is rapidly coming into line with the sample size.

The variables considered and investigated, especially from the biographical data sheet, are extremely useful in defining clinical risk variability. The aim of the OMDP is to overcome these regional differences, providing valid instruments for conducting standardised screening in the general population. Although the administration of the EPDS, alone, is useful for this purpose, it is clear that this instrument may be incomplete and undoubtedly reductive, given the complexity of psychiatric pathology which is ill-suited to objective and binary measurements and moreover considering the huge organising inequalities in mental health facilities in different regions in our country. This is even more true regarding depression during pregnancy, when, at more than any other time of life, biology is intertwined with numerous other social, psychological, and environmental factors.

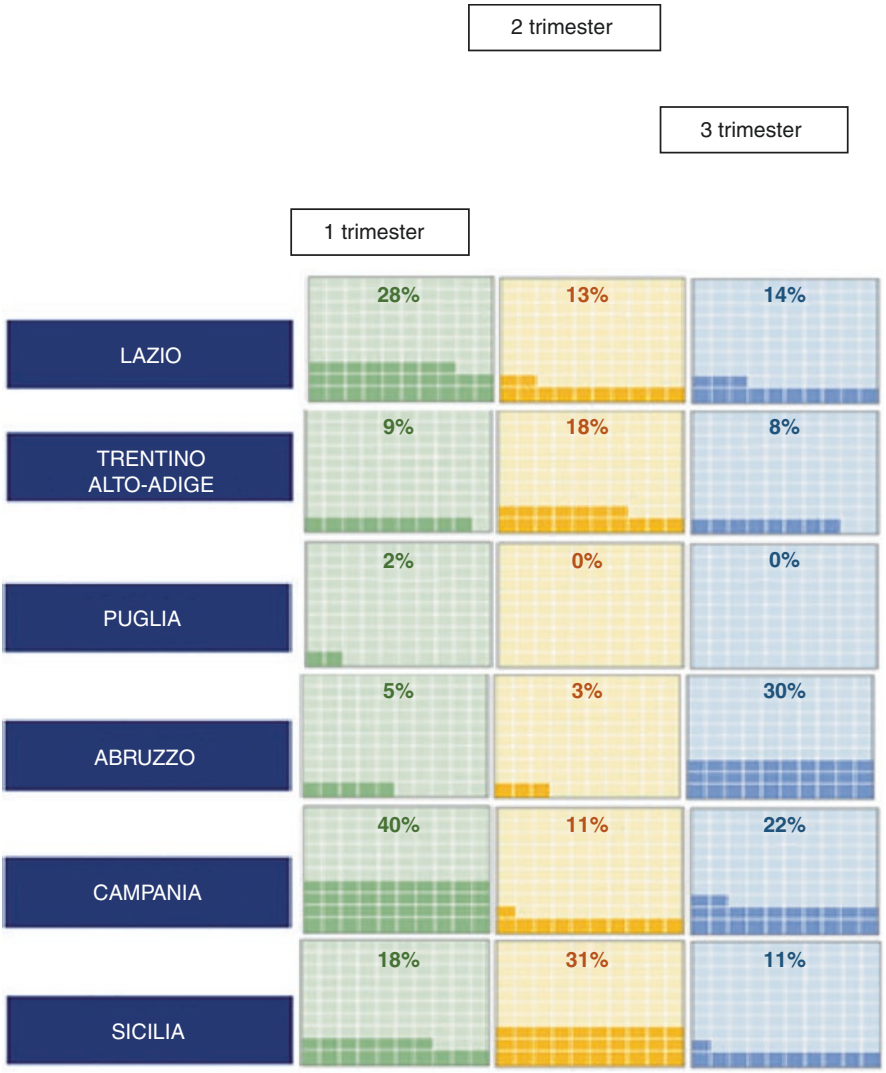

Fig. 20.1 Pregnancy

In light of these reflections, there is an urgent need to resort to new calculation tools, capable of functioning in a big data mining system, with machine learning software being the only ones able to respond to one of the specific and perhaps most pressing needs we have in psychiatry, that is, the need for personalisation, precision psychiatry, and patient-tailored treatment strategies.

For decades, we have been working on group averages and statistics that examine general populations with only diagnostic homogeneity, but which are insufficient to respond to the needs and complex individuality of the single patient. Machine learning will allow us to make individualised predictions, with an accuracy

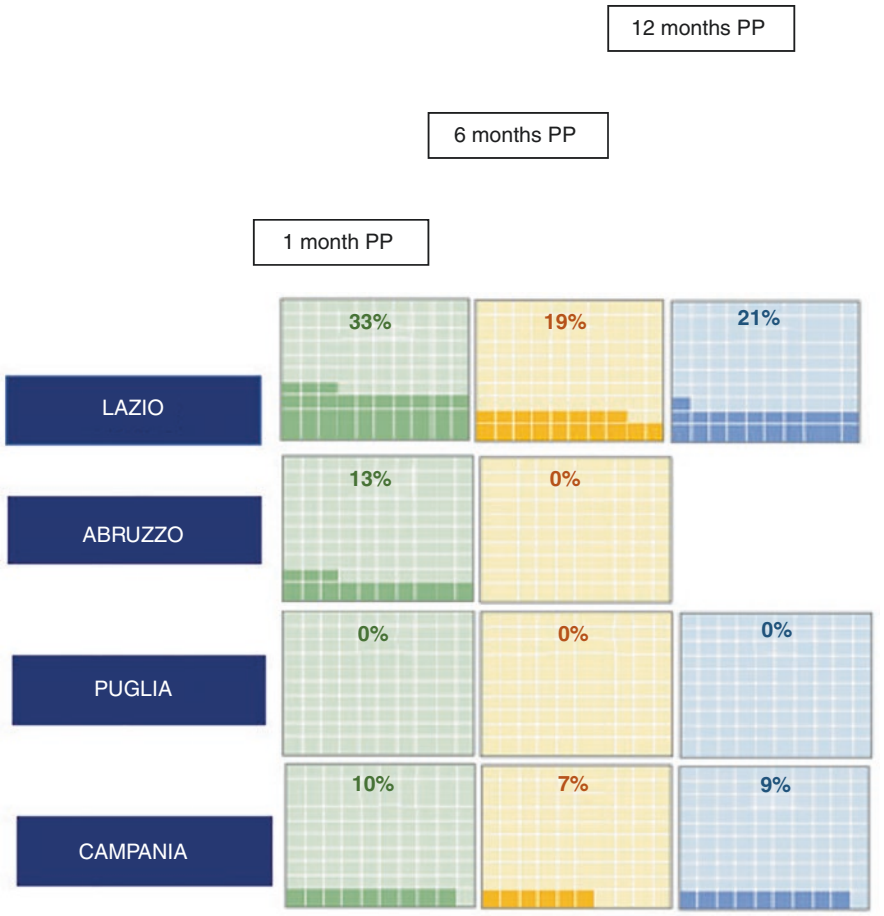

Fig. 20.2 Post partum

that psychiatric medicine has never been capable of, leading to the common goal of precision psychiatry and hoping that this tool will be extended to our entire field of research and clinical practice.

20.4 Notes on the First Multicentre Experience

The OMDP project aims to analyse the perinatal period from the very beginning, i.e. from the first trimester of gestation. From the data collected so far, the importance of investigating symptoms and pre-morbid characteristics, from the very first moments of pregnancy, is highlighted for predicting the possible development and evolution of perinatal depression.

In this first multicentric experience, we have noticed a certain rate of non-participation in the study mainly due to the lack of interest in the topic and the belief in the low relevance of the problem. The number of women who dropped out of the current study was approaching half of the initial participating sample. We have, also, identified the cause as the stigma that still surrounds the concept of mental illness, and especially perinatal mental illness, added to the lack of knowledge of the pathology. Many women were surprised and put off by the proposal to administer the test during pregnancy, as they were unaware that depression could occur even before birth and not only post-partum. Other women felt it necessary to specify that the pregnancy was planned and experienced with extreme joy, ascribing peripartum depression to unwanted pregnancies only. The women who were most enthusiastic about participating in the project were those who were, already, well informed about the topic or who reported personal experiences, direct or indirect, of perinatal depression or psychiatric disorders in general.

A truly decisive factor in promoting the adherence of the participants was the collaboration of the gynaecologists and midwives, who, in several cases, were personally involved in proposing the study in advance, during routine visits. So, it was possible to include the questionnaire in the classic gynaecological pathway followed by all pregnant women, and in these cases, we have been able to ascertain a greater ease and immediacy of proposal and higher rates of adherence to the project. The data obtained for this sample, which we can probably consider representative of the entire population, also show the unfortunately well-rooted presence of stigma, which continues to affect psychiatric pathology. Similarly, our data seem to carry with them the solution to the problem. They show us the clear and incontrovertible need for collaboration between specialists in order to spread correct knowledge of the illness and the need for screening. Only if doctors begin to consider psychiatric pathology in the same way as other complications that can affect pregnancy, can we, really, envisage active and effective prevention of peripartum depression.

Considering the current data in our possession and the experiences of the clinicians involved in the OMDP project, there is a need to structure national screening programmes that can reach the entire population from the first trimester. The identification of a disorder that is so widespread and so sadly fraught with complications cannot be left to chance or to the good sense of gynaecologists, but requires regulation and clear guidelines. Complications due to perinatal depression can be avoided, or at least improved, through early identification and care of the mother. With the OMDP project, we propose to implement a standardised, efficient, and functionally economical screening programme, demonstrating the real feasibility of such a project, which, without burdening health budgets, would reach all pregnant women in a widespread and early way, thus enabling real prevention.

Unfortunately, many women are still unaware of the importance of perinatal depression for themselves, for the child, and for the whole family, but what is most shocking is the refusal to cooperate, albeit fortunately, in only a few cases, by professionals who should follow women at all stages of their lives, especially the most delicate and fragile one, namely, reproduction.

The hope for the future is that, through close coordination between psychiatrists, obstetricians, gynaecologists, and paediatricians, an adequate level of awareness and knowledge of the disease can be achieved and that screening can be included as a routine examination, to be carried out directly in the obstetrical environment and then assessed in the psychiatric setting. The questionnaires for perinatal depression *must* be included in the routine medical records of the pregnant woman, in the same way as all other specialist examinations and tests carried out to ensure the well-being of the maternal-foetal dyad. This is one specific target of OMDP program, which we submitted to the Regional Council of Lazio, to the Minister of Health Beatrice Lorenzin during the third day for Woman's Health in April 2018, and to the Health Councilor of Lazio in 2019.

It is essential that a proper screening programme starts as soon as the woman becomes aware of her pregnancy, because the first trimester is actually a time of great psychological (A), endocrine (B), and immunological (C) upheaval (A) [2]; (B) [3]; (C) [4]; [5, 6]. These changes lead to a significantly increased risk of developing depression and anxiety. This is also a crucial period for foetal development, so early intervention improves obstetric and neonatal outcomes [7].

The effects of perinatal depression on the child have as yet not been fully clarified and undoubtedly need further study and investigation to extend knowledge to neonatology, paediatrics, and child neuropsychiatry and, why not, to adult psychiatry, because, after all, "there is no health without perinatal mental health". In fact, the increasing amount of data in the literature shows that the length of the study of peripartum should be extended up to 1 year after delivery, because throughout this period the probability of the onset of the disease remains constantly high and, therefore, prevention must continue well after discharge from the obstetric ward.

Another important factor highlighted in the context of the OMDP is the importance of administering not only an EPDS questionnaire but also a comprehensive data sheet that collects all the information needed to stratify the population into risk classes and direct prevention interventions towards the most vulnerable groups. Prevention should also include fathers, who play an important role in perinatal care and can act as both a protective and risk factor in the development of perinatal depression, as well as being affected by their partner's mental health status and needing support themselves.

Working on the prejudice that, unfortunately, still surrounds this pathology, improving coordination between maternal and neonatal health specialists and promoting the spread of adequate longitudinal perinatal screening programmes, means protecting the health of the whole family and, in particular, permitting the healthiest possible development of the foetus and the newborn. This will be achieved thanks to the activity that therapy for depression has, indirectly, on the uterine environment in which the foetus grows, by decreasing the impact of all the neurohormonal and inflammatory factors on epigenetic mechanisms. In addition, achieving maternal psychopathological compensation promotes a correct and healthy way of interacting with the newborn and thus the creation of the attachment bond after birth. This

makes it possible to interrupt the chain of intergenerational transmission of mental disorders and, more generally, of pathology and distress in the newborn, as well as in the future adolescent and adult.

20.5 OMDP in the Lockdown and New Challenges in Perinatal Mental Health

The COVID-19 pandemic has been and continues to be in its various waves, an element that has profoundly modified the content and manifestations of mental health, in general, and of perinatal health in particular.

While we are starting to collect the first data on the short-term effects, we still do not know what the medium- and long-term effects will be on the psyche of women who experienced pregnancy during the first lockdown.

The November 2020 [8] review and meta-analysis by Hessami et al., for example, show evidence of an increased risk of mental disorders, such as depression and anxiety, in women in the perinatal period, due to the restrictions associated with the COVID-19 pandemic. Eight studies reporting depressive and anxiety states of 7750 women, either pregnant or post-partum, were included. The overall pooled EPDS score was higher among women during the pandemic (SMD = 0.40, 95% CI: −0.05 to 0.86, $p = .083$) compared to previous non-pandemic times, without reaching a statistically significant difference. However, the overall pooled STAI score was significantly higher during the pandemic (SMD = 0.82, 95% CI: 0.49–1.16, $p < .001$).

In order to investigate the presence of peripartum anxious and depressive symptoms, during the SARS-Co-V2 pandemic, and in an attempt to highlight any existing relationships between the COVID-19 worry and psychopathological or sociodemographic variables, the OMDP conducted a study on a sample of 100 women in pregnancy and post-partum. The study (Noos et al.; [9]) was born from the collaboration between the Policlinico Tor Vergata and the territorial service of the ASL of Latina. The subjects were administered:

- EPDS
- PSS (Perceived Stress Scale)
- DES-T (Dissociative Experience Scale)
- DASS-21 (Depression, Anxiety, Stress Scales)
- PHQ-9 (Patient Health Questionnaire)
- Questionnaire on the Degree of Preoccupation About Virus COVID-19 Contagion [10]

From the analysis of the data collected, it emerged that 11% ($n = 11$) of the women had a minor depressive disorder, having obtained an EPDS score between 9 and 11, while 24% ($n = 24$) had an overt perinatal depression, having obtained values greater than or equal to 12 (Figs. 20.3 and 20.4). In addition, 7% of the sample had mild symptoms of anxiety, 8% had moderate symptoms, 6% had severe

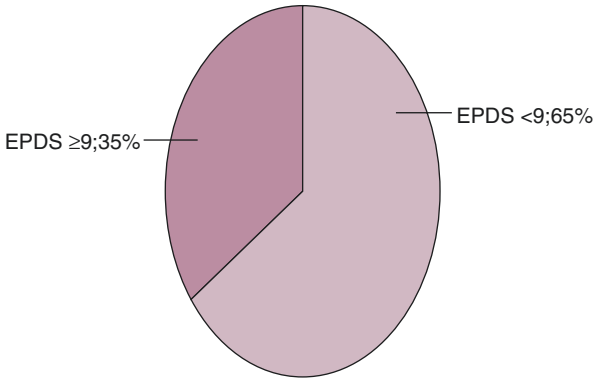

Fig. 20.3 Proportion of EPDS with a cut off of 9

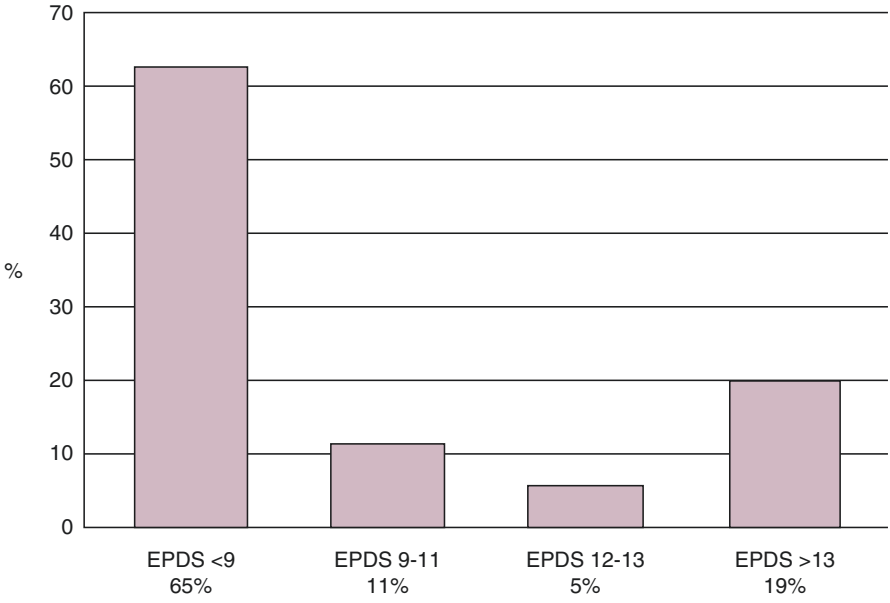

Fig. 20.4 EPDS scoring

symptoms, and 1% had severe symptoms of anxiety. Finally, 84% of the sample scored between 5 and 9 on the PHQ-9, indicating the presence of subthreshold depression.

With regard to the items and instruments most closely related to stress and its COVID-related consequences, at the PSS 24% of the sample scored between 11 and 14, indicating the presence of stressful events but a good coping capacity, able to ensure the maintenance of a good level of well-being. 27% had a score between 15 and 18, a medium-high result that indicates the possibility that, although unconscious, the accumulated stress is already affecting the body, thoughts, emotions, and behaviour. 22% scored above 19, indicating a state of suffering experienced by both

Table 20.1 Analysis of the responses to questionnaire about COVID-19 concern

	Absent	Mild	Moderate	Severe
What is your level of concern about the situation?	4%	41%	45%	10%
How afraid are you of becoming infected?	10%	51%	32%	7%
How worried are you about your family members?	4%	32%	47%	17%
How often do you experience anxiety related to infection?	38%	37%	20%	5%
How much the quality of your sleep has changed?	44%	36%	17%	3%
How much has your life changed?	18%	36%	33%	13%
How satisfied are you with the security measures taken so far?	9%	31%	51%	9%
How influential is the information disseminated by the media?	10%	24%	43%	23%
How worried are you at home?	35%	41%	18%	6%
How worried are you at work?	53%	28%	13%	6%

body and mind in response to high levels of potentially harmful stress in the medium to long term.

Finally, analysis of the responses to the questionnaire on concern about COVID-19 infection showed that 84% of the sample had at least a mild-to-moderate degree of concern. Specific data are presented in Table 20.1.

Preliminary results showed a statistically significant relationship between scores obtained in the EPDS, DASS21, PHQ-9, and PSS psychometric scales and the degree of worry about COVID-19 infection. On the other hand, as regards the linear relationship between dissociative symptomatology, age of the sample, and preoccupation with contagion, a trend was observed without reaching a statistical significance. Figure 20.5 below summarises the results of the various relationships measured.

The overview described in the previous paragraphs highlights the urgency and importance of promoting and supporting research concerning the impact of the pandemic and its psychopathological influences in such a delicate period as the peripartum.

The result of the OMDP Lazio study is greater than that described by the previous case studies: 35% of the sample presented depressive symptoms (also subthreshold symptoms) with an EPDS score > or equal to 9.

The psychopathological variables investigated (depression, anxiety, stress) were found to be correlated with the dimension "COVID-19 worry". In the sample recruited, age does not influence the degree of COVID-19 worry; however, the sample has a limited age range (women of childbearing age between 21 and 44 years with an average age of 33 years) which does not allow the results to be extended to the general population. Furthermore, there is no relationship between the level of concern by COVID-19 and the carrying out of a working activity in the week preceding data collection. It is also clear that the presence of material socio-economic determinants (the presence or absence of employment) is not a variable that influences COVID-19 anxiety and distress. As widely demonstrated in the literature,

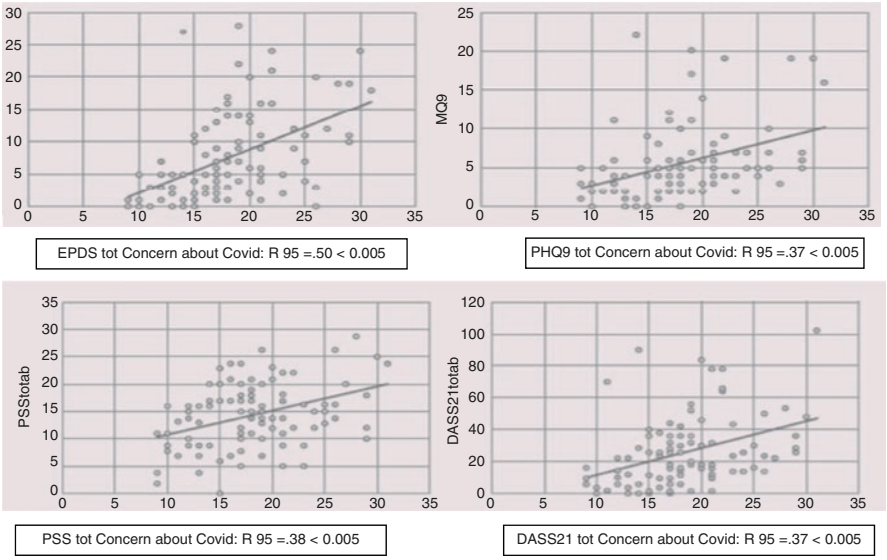

Fig. 20.5 Statistics relationships

there are psycho-social determinants of mental health that are not strictly related to a concrete economic-employment condition, but are more inherent to an existential condition of "vital poverty".

Among the risk factors specifically linked to the pandemic, loneliness and isolation stand out. Norms for social distancing have made it impossible for fathers to access both pregnancy check-ups and the delivery room itself. The distancing of the partner from these shared procedures not only creates discomfort for the latter, which is likely to increase the already large number of paternal perinatal depressions, but also increases the woman's sense of isolation and perceived loneliness, with a consequent increase in the risk of depressive experiences of loneliness, helplessness, and inability. By the same token, with estrangement from extended family members, mother and mother-in-law, especially in the post-partum period, the woman finds herself alone and facing a new and potentially destabilising situation, unable to "lean on" her own attachment figures. Therefore, women find themselves in a state of loneliness, at just the moment when, more than any other, they have need of support. This has, inevitably, generated a strong concern and anxiety in facing the whole peripartum period. Loneliness can be defined as "a psychological condition arising from the lack of meaningful interpersonal relationships or from the discrepancy between the human relationships a subject wishes to have and those he actually has. They may be unsatisfactory by their nature, their number, or the subject's inability to establish or maintain positive and meaningful relationships with others" [11, 12]. As a reminder of how this is a significant risk factor for women's psychological and physical well-being, the World Health Organisation emphasises the right of all women to a positive birth experience, regardless of COVID-19

infection. The presence of the father, or of a person of the woman's choice (chaperone), during labour, birth, and hospitalisation is an organisational aspect that falls within the competence of individual healthcare facilities. At present, there is a great deal of variability between healthcare facilities, even within the same regions, although the evidence on the positive effects (well-being and safety of the woman) of having a trusted person present during childbirth is now well established. The indications, therefore, recommend the presence of a person of the woman's choice during labour and childbirth, as an essential element for her well-being. In addition to setting up perinatal mental health screening programmes as early as the first trimester of pregnancy, there is a particularly urgent need to set up programmes to monitor the psychological conditions of women facing motherhood at this sensitive time [13]. This is also aimed at preventing psychophysical damage to the foetus and repercussions for the development of the mother-child relationship linked to the conditions described above. Dedicated applications (app) can be made available for use by the mother on her smartphone, with the aim of collecting the emotional diary, the online appointment diary, and the weekly EPDS. This practice was carried out by the SOS Mamma service, implemented during the COVID-19 emergency by the Policlinico di Tor Vergata in Rome and by many other centres belonging to the Multicentric Observatory for Perinatal Depression.

In May 2020, just at the end of the first lockdown, the staff of OMDP collaborated with the ISS working group Mental Health and Emergency to the writing of Report no. 44/2020 of the Istituto Superiore di Sanità. This document, among other detailed recommendations and suggestions on dealing with perinatal mental health and pandemic, establishes that the screening programme can also be presented by means of information material (containing complete information for contacting operators by telephone or email) on occasions when contact with the healthcare facility is maintained by necessity: routine visits during pregnancy in consulting rooms or hospital wards; at the time of delivery and, in any case, before the woman and child are discharged from the hospital ward; during post-delivery visits, in particular those with the midwife, gynaecologist, and free-choice paediatrician; and the child's first vaccination at vaccination points. A basic requirement of the programme is the signing of the privacy policy and the informed consent, which can be sent by e-mail to the address the woman provided at the first telephone contact. As a second option, for women who do not have an email address, confirmed adherence via the functions of a smartphone may be sufficient.

After screening, it is also possible to offer an in-person interview, given the willingness to come to the facility, to women with high EPDS scores and who are assumed to have a high level of depression or anxiety. In this case the recommended measures to limit the spread of the epidemic should be respected. Meetings in the facility should be conducted according to current recommendations: face-to-face interviews should be conducted with the necessary PPE (mask), maintaining a safe distance of at least 1 m between the user and the operator. Interviews should be staggered to avoid crowding, and waiting rooms should be reorganised: fewer chairs should be provided and spaced out, and magazines and newspapers should be removed. In addition, carers should be asked to wait outside.

In any case, whatever the method chosen by health professionals, it is highly desirable, in the current emergency scenario, that the monitoring of women's psychological well-being in the postnatal period be maintained by means of attentive follow-ups, in order to intercept any forms of psychological distress linked to the experience of the epidemic that might also manifest themselves at a later date.

References

1. ISS Report COVID-19, n. 44/2020. Indications of an intervention plan for the management of perinatal anxiety and depression in COVID-19 emergency and post-emergency phase. Version of May 31, 2020. ISS Working Group Mental Health and Emergency Covid-19-2020
2. Stewart DE. Clinical practice. Depression during pregnancy. N Engl J Med. 2011;365(17):1605–11.
3. Sacher J, et al. The peripartum human brain: current understanding and future perspectives. Front Neuroendocrinol. 2020:100859.
4. Mellor, A. L., & Munn, D. H. Extinguishing maternal immune responses during pregnancy: implications for immunosuppression. In: Seminars in immunology, vol. 13(4), pp. 213–218, 2001, Academic Press
5. Trowsdale J, Betz AG. Mother's little helpers: mechanisms of maternal-fetal tolerance. Nat Immunol. 2006;7(3):241–6.
6. Molendijk ML, et al. Serum BDNF concentrations as peripheral manifestations of depression: evidence from a systematic review and meta-analyses on 179 associations (*N* = 9484). Mol Psychiatry. 2014;19(7):791–800.
7. Rosenberg MD. Baby brains reflect maternal inflammation. Nat Neurosci. 2018;21(5):651–3.
8. Hessami K, et al. COVID-19 pandemic and maternal mental health: a systematic review and meta-analysis. J Mater Fetal Neonatal Med. 2020:1–8.
9. Zerbin F, Lisi G, Siracusano A, Niolu C. Salute mentale perinatale e Covid 19. Noos. 2020;26(2):97–107.
10. Lisi G, Ribolsi M, Siracusano A, Niolu C. Maternal vitamin D and its role in determining fetal origins of mental health. Curr Pharm Des. 2020;26(21):2497–509.
11. Van Amelsvoort TAMJ. Eenzaamheid is ongezond [Loneliness is unhealthy]. Tijdschr Psychiatr. 2020;62(10):824–5.
12. Giacchetti N, Roma P, Pancheri C, Williams R, Meuti V, Aceti F. Personality traits in a sample of Italian filicide mothers. Rivista di Psichiatria. 2019;54(2):67–74.
13. Giacchetti N, Pancheri C, Williams R, Marconi M, Magistro R, Pozzuoli S, Aceti F. Violence and motherhood: a case study about the personality profile and attachment style of a Filicide woman. Deviant Behav. 2020a;41(5):607–18.

"Oramamma": A Volunteer Association for Maternal Mental Health

21

Susanna Banti, Camilla Corezzi, and Mauro Mauri

21.1 Introduction

Oramamma is an association of mental health professionals who provide free outpatient's care to women during their pregnancy and the first year after delivery.

Originally funded in Florence in 2015, an association with social intent and a no-profit status, by Dr. Camilla Corezzi, a psychologist with specific experience in perinatal psychopathology, and others, in 2016 was reallocated in Pisa, where a group from the Perinatal Depression Research and Screening Unit (PND-ReScU®) team of the University of Pisa-Italy decided to participate to the project and joined the association.

21.2 History

The PND-ReScU® team was created as a spin-off group in a wider project dedicated to mood and anxiety psychopathology.

In fact, at the beginning of the 1990s, in an attempt to define "soft indicators of bipolarity," the focus was shifted on affective temperaments. Over the following years, clinicians and researchers of the University of Pisa (Italy) and of the Universities of Pittsburgh, Columbia (New York), and California (San Diego) promoted the "Spectrum Project Collaborative Group" (SPCG) whose aim was to create and validate instruments able to recognize the wide halo of phenomenology surrounding the "core" features of each DSM mood and anxiety diagnosis and overcome the classic categories adding a dimensional approach.

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21.3 Studies

The PND- ReScU® team has been involved in perinatal psychopathology since the first 2000 years and has been dedicated to research and patient's care within the activities of the Psychiatry Unit of the University and Community Hospital of Pisa (AOUP, Italy).

21.4 First Study: Assessment of Perinatal Depression

The primary aim of the PND-ReScU® was to evaluate the effectiveness of screening for early identification and planning of intervention strategies to reduce mood disorders in the perinatal period. Furthermore, the PND-ReScU® team aimed to define a battery of instruments that could be easily administered in a primary prevention setting. As a first step, and in order to evaluate the entity of the phenomenon, women presenting at the obstetrics/gynecology department for the first ultrasound examination (between the 12th and the 15th gestational weeks) were recruited for the first study in the years between 2004 and 2007. This study covered the period from first trimester of pregnancy to first year postpartum, with multiple assessment sessions and instruments to evaluate psychopathology, risk factors, and impairment. Central to our plan was a letter given to each pregnant woman who presented to the local health service to collect the booklet of information, prepared by the health services of the region of Tuscany, describing various aspects of pregnancy and maternal health, the schedule of future obstetrical visits, and the other evaluations patients were going to be submitted during their pregnancy. Our letter, enclosed within the booklet, provided a very brief description of perinatal depression (PND) and informed the woman of the possibility to participate in a study on mood and anxiety symptoms and disorders.

21.5 First Study: Relation Between Anxiety Disorders and Perinatal Depression

Another aim of the study was to evaluate the role of anxiety diagnoses during pregnancy as predictors of different conceptualizations of postpartum distress. Overall, anxiety in pregnancy was deemed to be associated with a substantially increased likelihood of postnatal distress outcomes, even after controlling for established risk factors assessed, in this case, with Postpartum Depression Predictors Inventory-Revised (PDPI-R). The main finding of the study was that different anxiety diagnoses had a specific predictive role on the different conceptualizations of postnatal distress and that, in general, the effect size of a predictor decreased from the first month point prevalence to the 1-year period prevalence. Anxiety symptoms are frequently reported by pregnant women and are often considered as part of the normal psychic experiences of pregnancy, especially if they are focused on the baby's

health or on maternal competencies. Many panic symptoms can be attributed to the mental state of the new mother, rather than to the panic disorder (PD) itself. The findings of the study revealed that anxiety symptoms should not be too hastily considered as a normal adaptive process to pregnancy, but should be further investigated to exclude the presence of a PD diagnosis, given its significant association with the development of subsequent postpartum depression (PPD). To our knowledge, no studies have examined the predictive role of PD in postpartum depression, although previous studies have evaluated the predictive role of anxiety symptoms and anxiety disorders in general. Our study suggested that PD as present in patient's history or in the family history is an independent risk factor for PPD. Women with PD had a significantly greater risk of developing PPD than those without PD, and women with PD during the early phase of pregnancy were 4.2 times more likely to have PPD than those without PD, even after controlling for the risk factors for PPD or the presence of previous or current depression. Moreover, our findings pointed out that women who had both a previous history of PD and a family history for PD were, respectively, 2.5 and 2.1 times more likely to develop PPD, independently of lifetime comorbidity of minor and major depression (mMD) and the presence of risk factors for PPD.

21.6 Further Research Studies and Patient's Care Activities

Subsequent studies dealt, besides mood disorders, with anxiety disorders, impact of risk factors, and suicidality.

The project had an optimal resonance and helped to establish a valid functional collaboration with the health providers involved in this specific field from nurses to midwives, gynecologists, neonatologists, pediatricians, and social workers.

Furthermore, the group has published a number of papers in scientific journals concerning research in the field and involving approximately 3000–4000 women during their pregnancy and first year after delivery, the largest Italian sample so far in the literature [1–5].

Moreover, a full-time out- and inpatient's care was provided for women in need, accessing the hospital with psychological and psychopathological complaints concerning the perinatal period and other significant issues such as abortion, assisted fertility programs, and pre-adoption concerns.

21.7 Founding of Oramamma

It was than only natural that some of the professionals, involved in this activity, decided to join into Oramamma as the association had similar goals and clinical approach to perinatal issues.

According to the founding chart, Oramamma is a no-profit association dedicated to the social promotion of significant action in the field of maternity and parenthood

in extent. In particular, the association tends to develop projects aimed to prevention, support, and research, by spreading of information, improving general population awareness, and providing adjournment for the involved mental health professionals.

21.8 Oramamma's Activities

In order to accomplish the aims of the founding chart, a series of activities and programs have been organized and planned.

An out-patient service has been dedicated to accept women, and their partners, so to give information concerning the perinatal period and the possible onset or recurrence of mood and anxiety symptoms. This setting provides medical and psychological care, both as individual and as group counselling and treatment. Special attention is given to risk factors assessment, prevention of depression, and evaluation of anxiety-inducing issues, during pregnancy and the first year after delivery.

Similar attention and care are provided to partners, in order to offer information and support to fathers who may request it, or need it, and, above all, to improve parental setting.

Another service, including medical and psychological counselling, is offered to couples undergoing, or planning to, a course of assisted reproductive technology. Different approaches are provided both for successful and for failed attempts.

Planning and support self-help groups are among the proposals for future activities of the association that can be achieved by supporting an educational program for group management.

The association is also dedicated to information spreading and formation programs among and for professionals involved with the perinatal period, with special focus on early recognition of risk factors for pregnancy and postpartum depression.

An effort has been made to create information channels with national and local associations and agencies similarly involved in perinatal care and support. A network has been established in particular with ONDA (National Observatory for Women Health), Italian Marcé Society, and Regional Register for Social Support Associations, sector family aid.

As a work in progress project, the association is involved in the production and distribution of articles, pamphlets, and presentations aimed to different subjects, from patients themselves to professionals and general population. An effort has been made to present previous PND-ReScU® research and actual Oramamma activities to create an evident link between research, clinical experience, and everyday care application. So, most of the association professionals have been involved in congress, meetings, masters' lectures, and webinars dealing with the various aspects of perinatal psychopathology diagnosis and treatment.

In line with the past of the association and the attitude of its founding members, research is still carried on, collecting available data from the women and their partners, with the aim of creating a new database relative to perinatal psychopathology in subjects followed in a free access out-patient's ambulatory.

21.9 Oramamma's Members and Fund Raising

A mention must be made about members and fund raising. Members dedicate their time and professional skills with no economical retribution and save for expense reimbursement. As an example, a free Pilates course is provided during and after pregnancy by a gym owner associate (Ms M. Minuti).

Fund raising is supported by membership fees, donations, payment for third-party services, and contributions from private and public groups and agencies. Recently, a concert has been organized to raise funds, and, as a collaborative activity, a children books editor is giving part of the profits to the association from the selling of a new series of books on the infancy of famous Pisa citizens (*Bimbi Ganzi* by Elledibook Edizioni).

21.10 Oramamma's No-Profit Out-Patient's Care

As mentioned above, Oramamma operates in Pisa, through an out-patients' ambulatory, where women are followed from the beginning of pregnancy up to the first year after delivery on a free care service plan.

Initial assessment is provided by a psychiatrist and/or a psychologist, and a course of action is established. Individual and group counselling and therapy are the standard of care available, and, when needed, pharmacological treatment is prescribed and monitored.

Special attention is devoted to lactation, through specific counselling and monitoring of mother and child condition.

An assessment is also done of the couple relationship, and fathers are included in the treatment plan, both as a support to the mothers and whenever they need psychological and psychiatric therapy.

In the initial phase of the association life, namely, the first 3 years, approximately 50 women have been followed through pregnancy and first year after delivery (an average of 15–20 per year). The requests are growing as the association becomes known in the area, and more specialists are willing to give their contribution to this initiative.

21.11 Mental Illness and the Perinatal Period

Mental illness during the perinatal period is socially unacceptable, due to the belief that women should "bloom" during pregnancy and that they "must be happy" for the imminent motherhood. However, childbearing is one of the most important and significant events in human life; pregnant women and mothers who delivered recently are generally more prone to be affected by the full range of psychiatric disorders. Even though Marcé had long ago shown the importance of mental disorders during pregnancy, research has been mainly focused on postpartum mental disorders. Consequently, little is known about mood and anxiety disorders during

pregnancy, despite a growing body of evidence underlines their epidemiological and clinical relevance. Recent literature suggests that perinatal mood and anxiety disorders are not culturally bound: they affect women in every society and from every socioeconomic background. The prevalence rates of clinical depression in the perinatal period are comparable to those seen in non-childbearing groups; however, rates of subclinical symptoms of depression reported at this time are higher than expected.

For some women, the risk for depression is increased by major negative life events. Traumatic experiences play a significant role and increase risk for major depression in women as compared to men. Thus, early traumas, such as parental loss, as well as more proximal events such as divorce, separation, marital discord, severe illness, assault, loss of a job, or the death or serious illness of a close relative all appear to contribute to the preponderance of depression in women. As noted, females are much more vulnerable to a lack of social support than their male twin siblings. It is not surprising that increased childbearing responsibilities and little social support are among the factors that increase the risk for postpartum depression. Clinically, this can be seen in young mothers who have little support when pregnant and in the postpartum, leaving them to shoulder the burden of childbearing responsibilities. Special attention should be devoted to the impact of untreated perinatal depression and anxiety. Although untreated perinatal mental disorders may have severe obstetrical and psychiatric short- and long-term consequences, not only for the woman (i.e., suicide, reduced self-care, substance abuse) but also for her family and mostly for the newborn baby, only a very small number of mentally ill pregnant women receive any kind of treatment, including psychological support, so that, in high-risk pregnant women, only a minority of women with a prenatal diagnosis of major depressive disorder (MDD) are treated and current MDD is not always predictive of treatment use, suggesting the need for improved detection of depression. Another significant issue is the consequences of untreated anxiety disorders on the well-being of mothers; anxiety during pregnancy is often linked to negative expectations about motherhood, difficulties adjusting to the demands of the maternal role, and the development of other forms of distress, particularly postnatal depression. So, it has become recognized that a prenatal anxiety disorder should be considered one of the strongest risk factors for developing postnatal depression.

21.12 Conclusions and Take-Home Message

One of the take-home messages of Oramamma is that “you become a mother, you are not born one.” A common perspective is that becoming a mother is an easy and absolutely normal process, like eating or sleeping, always related to, or full of, emotions such as joy and serenity. All women must feel gratified, and fully accomplished, by bearing children, growing them, and caring for them. A woman who feels sad or shows any psychological distress during pregnancy, or after delivery, must therefore be considered weak, and not a good mother.

There is no common path already established to become an ideal mother, and probably there is not an ideal mother. Each woman has her own way to face this significant life event, and every child has his own peculiar way of behaving. Therefore, becoming a mother is the result of a mutual knowing process that starts during pregnancy and follows subsequent steps, involving a cognitive and emotional course of growth.

In Oramamma, women find a place where their emotions can be expressed, without fear of being judged and where they can feel free to talk about their doubts about their role as mothers, their attitude toward the baby, and their future as women.

It is a place where negative emotions can be talked about and strategies found to cope with them.

Negative emotions may include ambivalent feelings concerning pregnancy and/or the baby, lack of empathic bonding with the newborn, anger when required to fulfill the child's needs, and feelings of guilt for all of this. It may happen also that new mothers feel frustrated and sometimes disoriented, failing to recognize themselves in this perceived inability to accept their new role.

The association was established to offer a free space where these feelings could become manifest and shared among women during pregnancy and up to the first year postpartum. During this period, a specific counselling approach is given, and, when needed, a psychological and psychiatric treatment is made available by experienced professionals.

Fathers are also included in the project, since it is now common knowledge that their role is equally important for a healthy couple and for the development of the child.

However, it is often difficult to accept the evolution from partner to father. During pregnancy, the father should have the time to review his attitude or doubts concerning this step in his life, including the coming presence of a new individual in the couple, the assessment of his resources facing the responsibility of caring for a newborn, and sometimes the fear of being not ready, or inadequate, for it. Moreover, after the birth, the new father may have the feeling of being excluded from the mother and child relation, with consequences that may range from reduced self-esteem to total detachment from the baby or depression, anger, increased work involvement, and substance abuse.

On the other hand, the presence of the father during pregnancy and postpartum is definitely relevant for the mother, who needs full support in this significant life event. Doubts and difficulties can be shared and faced much more effectively by the couple, more so than by the single individual. This is true during pregnancy, for the need of helping each other in evaluating and accepting their new role as parents, but is also definitely important after birth, when the presence and effective help given by the father are fundamental to create a safe and sane approach to parenthood.

Fathers may be able to adjust rapidly to their new role, but sometimes they may develop anxiety and mood symptoms, or disorders; therefore support must be available for them and Oramamma provides psychological and psychiatric assessment and treatment for them also.

The life of the association is hopefully going to grow in the future, but so far it has provided an appreciated service to couples in need of support, through the dedication of its members and the help of supporters.

References

1. Banti S, MauriM OA, et al. From the 3rd month of pregnancy to 1 year postpartum. Prevalence, incidence, recurrence and new onset of depression. Results from the perinatal depression-research & screening unit study. Compr Psychiatry. 2011;52(4):343–51.
2. Borri C, Mauri M, Oppo A, et al. Axis-I psychopathology and functional impairment at the 3rd month of pregnancy. Results from the Perinatal Depression-Research & Screening Unit (PND-ReScU) study. J Clin Psychiatry. 2008;69(10):1617–24.
3. Rambelli C, Montagnani MS, Oppo A, Mauri M, Banti S, Borri C, et al. Panic disorder as a risk factor for postpartum depression. Results from the Perinatal Depression-Research & Screening Unit (PND-ReScU) study. J Affect Disord. 2010;122:139–43.
4. Oppo A, Mauri M, Ramacciotti D, Camilleri V, BantiS BC, et al. Risk factors for postpartum depression: the role of the Postpartum Depression Predictors Inventory-Revised (PDPI-R). Results from the Perinatal Depression—Research & Screening Unit (PND-ReScU) study. Arch Womens Ment Health. 2009;12:239–49.
5. Mauri M, Oppo A, Montagnani MS, Borri C, Banti C, Camilleri V, et al. Beyond "postpartum depressions": specific anxiety diagnoses during pregnancy predict different outcomes Results from PND-ReScU. J Affect Disord. 2010;127:177–84.

22 A Perinatal Psychiatry Service in Bangalore, India: Structure and Function

Vandita Shanbhag, Manisha Murugesan, Sachin Nagendrappa, and Prabha S. Chandra

22.1 Introduction

Lower- and middle-income (LAMI) countries have a higher prevalence of perinatal mental health (PMH) problems when compared to high-income countries [1], and maternal suicide is also a concern in many countries [2]. LAMI countries have very few dedicated PMH services available, most of which are concentrated in the urban areas. High-income countries offer PMH services through dedicated perinatal psychiatry services which provide both outpatient and inpatient PMH to pregnant and postpartum women. These services are run in liaison with obstetricians, NGOs, community health workers and families of patient [3]. Several countries such as France, the UK, Australia and New Zealand have dedicated inpatient mother-baby psychiatry units (MBU) for women with perinatal psychiatric illnesses [4, 5].

Providing PMH services requires additional knowledge, specialized skills and proficiency to meet the specific demands of the mother during pregnancy and postpartum in addition to addressing concerns about foetal development and infant health [6]. Several LAMI countries still face challenges such as high prevalence of nutritional deficiencies in mothers, poor access and availability of hospital deliveries as well as high maternal and infant mortality rates. Therefore, reproductive and child health programmes in the LAMI countries predominantly focus on improving these parameters, and mental health is not prioritized [7]. Lack of awareness on mental health issues, stigma related to mental illnesses, higher prevalence of poverty and domestic violence, lower literacy rates and limited resources allocated to mental health delivery are some of the barriers to access mental healthcare in the LAMI countries [8]. In resource-limited regions of South Asian countries, a stepped

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care approach by up-skilling the community healthcare workers and primary care doctors has been tried successfully. This includes sensitization and training of obstetricians, mid-wives and auxiliary nurse midwife (ANMs) and up-skilling of mental health professionals to handle PMH disorders [9].

Further, in most South Asian countries, due to lack of specialized MBUs, inpatient perinatal mental health care is offered through general hospital psychiatric units or adult psychiatry units. This may lead to difficulty in admitting the baby along with the mother, leading to baby being admitted under paediatric services or being sent back home. The other challenge includes the lack of simple screening tools, as the available screening tools developed in the west maybe too complex for women with low literacy and often do not translate easily to vernacular languages. In addition, research focussing on the magnitude, extent and determinants of perinatal mental health problems from the LAMI countries is limited. Studying the barriers and facilitators for accessing maternal mental health services including the cultural factors will enable these countries in establishing perinatal health services tailored to their needs [10].

Understanding the felt need for a specialized PMH service, the Perinatal Psychiatric Service was established in 2004 at the National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, in a LAMI country, India. This is an inpatient and outpatient service in a clinical hospital setting. We describe this service in the current chapter.

22.2 Perinatal Psychiatry Services

Currently, the PMH services provided at NIMHANS include outpatient services through the perinatal psychiatric clinic, inpatient services through the mother-baby unit and a perinatal mental helpline service. Our perinatal psychiatry outpatient clinic was the first clinic of its kind in Asia and was started in 2004 at NIMHANS, Bengaluru. Its founder, Professor Prabha Chandra who currently heads the perinatal psychiatric services, was inspired and mentored by Professor Ian Brockington and also derived inspiration from other services in the UK. The service while based on western models was customized to meet the local cultural and resource needs. The inpatient service and mother-baby unit was started in 2009, at NIMHANS [11].

Services are delivered by a multidisciplinary team comprising of psychiatrists, a post-doctoral fellow in women's mental health, clinical psychologists, psychiatric social workers, infant development assessment team, nursing staff, health assistants and administrative staff who work to provide holistic perinatal psychiatric care to women. We also liaise actively with obstetricians and gynaecologists, paediatricians and lactation specialists to offer comprehensive care.

22.3 The Perinatal Team

The psychiatry team comprises of psychiatry post-graduate trainees posted in the perinatal clinic and inpatient services who do a detailed evaluation of the mental health problems using a structured proforma developed for the purpose and

a detailed physical examination under the supervision of the senior residents. Each case is discussed with the psychiatry consultant, and a management plan is made involving the patient and caregivers. Emphasis is laid on preconception counselling in women planning for pregnancy, regular antenatal check-ups including the necessary ultrasound scans in pregnancy and preparing the parents for delivery and parenthood in the postpartum period. In addition, lactation advice, developmental and maternal-infant bonding assessment and contraception advice are provided.

The **psychiatric social work team** evaluate and educate the family. They also explore the psychosocial issues such as social support, intimate partner violence, stigma and cultural practices and offer necessary intervention. Follow-up calls are made to women to address ongoing psychosocial issues, reduce drug defaults, maintain the treatment loop and encourage regular follow-ups. Partner groups and grandmother groups are also held at every clinic.

Clinical psychologists perform personality assessments and IQ assessments and provide psychotherapy for women with personality disorders or mother-infant bonding disorders, mild to moderate forms of anxiety and depression, grief and perinatal loss and coping with infertility. Developmental assessment of infants is done by qualified developmental psychologists to pick up development delays as early as possible. Case-based inputs are provided to family, and appropriate referrals to child psychiatry team or paediatricians are made.

Nurses, in addition to offering nursing care, discuss issues related to breastfeeding, bonding and side effects of medications. To overcome the shortage of nurses, we have skilled and trained **health assistants** who help the mother with activities such as infant care and hygiene and breastfeeding. They also maintain cleanliness of the ward, assist in making baby feeds, accompany mothers during electroconvulsive therapies and make referrals for immunization for baby along with providing support to the mother and the caregiver.

The clinic also has **administrative staff** who manage appointments, record-keeping and referrals.

22.4 The Perinatal Psychiatry Outpatient Clinic: Structure and Function

The perinatal psychiatry clinic functions once a week every Friday and offers evaluation and treatment for psychiatric problems to women who are planning pregnancy, are pregnant and are in postpartum period (up to 2 years postpartum). The clinic is housed in a separate airy and well-lit building away from the main psychiatric outpatient to ensure privacy and provide a safe space for perinatal women and infants. The clinic is equipped with basic amenities such as access to safe drinking water, toilets, diaper changing room and a separate room for breastfeeding. This clinic runs in liaison with general adult psychiatry services within and outside NIMHANS, other mental health professionals, obstetricians and paediatricians for referrals. Patients can attend the clinic through prior appointments or walk-ins, and average time taken for completing a consult is around 90–120 min.

Structured proformas specifically developed for detailed evaluation of mental health, pregnancy and postpartum-related factors, risk assessments and mother-infant bonding assessments are used in the clinic. Information and educational materials such as booklets and pamphlets about mental health care in pregnancy and postpartum, stress reduction and physical exercise are made available in the perinatal clinic for patients and caregivers. A structured care plan for communication to obstetrician and paediatrician is also available.

The clinic also maintains registers on antenatal exposure to psychotropic drugs and reasons for referrals.

22.5 The Inpatient Mother-Baby Unit

22.5.1 MBU Structure

India's first exclusive inpatient mother-baby unit was started in 2009, at NIMHANS, Bengaluru, enabling the joint admission of mother-baby dyad. Our MBU setup includes the main components of an ideal MBU such as having a dedicated multi-disciplinary team caring for the mother and infant and is staffed 24 h a day, 7 days a week [11]. India's current legislation, the Mental Health Care Act (2017), mandates a child under the age of 3 years of a woman receiving care, treatment or rehabilitation at a mental health establishment to ordinarily not be separated from her during her stay in such establishment [12]. However, our current MBU setup like other traditional MBUs has facilities to admit babies up to 1 year of age as joint admission with the mother.

Our five-bedded MBU has been set up in a relatively quieter part of the inpatient psychiatric block, on a ground floor of a building, away and separate from other wards with all safety precautions. The ward has ample space for mothers to move around with an outdoor play area and garden for infants. Adequate care has been taken for ventilation and to keep it pest-free. The indoor areas include a small kitchenette with an area for milk preparation, facilities for sterilizing the vessels and common dining area which also doubles as an entertainment area.

In the Indian culture, family plays an important role in decision-making and caregiving especially in the postpartum period. Family members are often reluctant to admit the mother alone in the hospital during the postpartum. Keeping this in mind, we have provisions for a caregiver to stay with the dyad, often the woman's mother or mother-in-law (sometimes the spouse), to stay with the patient during inpatient care. This provides additional support to women, ensures safe bonding with the baby and offers us with an opportunity to work with the family members. Along with a bed for mother and a crib for the baby, we provide an additional bed for the female caregiver. Ours is a collectivistic culture which encourages interaction between families. Our MBU provides a shared but comfortable space, with beds separated by curtains to ensure privacy for breastfeeding while allowing interaction and support between families.

We have a separate infant bathing space where traditional ways of bathing the babies are encouraged. Additionally, we have physical space for infant intervention,

mother-baby bonding intervention and clinical rounds. The common areas have a closed circuit TV monitoring to ensure safety. We also maintain a stock of toys and baby clothes (often donated by philanthropists) to provide for the families.

22.5.2 Admission Procedures

Pregnant and postpartum women with mental illness are admitted from the perinatal clinic or the psychiatry emergency after being evaluated by the perinatal psychiatry team. While the MBU mainly admits women with babies, we also offer inpatient care for pregnant women in the general psychiatry female wards. If risk of harm to herself or the infant is high or if the woman requires more intensive monitoring in cases like pregnancy with complications, she is admitted to a high monitoring ward such as FICU (female intensive care unit). Paediatrician referrals are done routinely for every infant to assess the general health, feeding and immunization of the baby while admitting in the MBU. We have the advantage of having a well-known children's hospital at walking distance from the unit; hence this arrangement works efficiently. If the mother is very disturbed or significant risk of harm to infant is noted on initial assessment, we consider a temporary separation of mother and baby. The mother's condition is assessed daily, and all efforts are made to ensure that baby is brought back to stay with the mother as early as possible. Mothers are closely monitored by relatives and nursing staff, while feeding the infant and leaving the mother alone with the infant is avoided especially in the early days of admission.

22.6 Assessments and Management

22.6.1 Handling of Risks

The presence of suicidal ideation or attempts warrants high-risk suicidal precautions in the ward, such as continuous monitoring by nursing staff and making sure that the patient does not have access to ropes and sharp objects. Depending on the clinical picture, electroconvulsive therapy (ECT) is considered if there are no contraindications. The underlying psychiatric illness that leads to suicidality is treated aggressively. If the mother is found to have a poor oral intake, an input/output chart is maintained by the nursing staff. Adequate hydration is prioritized and the mother is given intravenous fluids, if necessary. Considering the need for risk assessment in perinatal settings and the paucity of data in this population, doctors and nurses of the MBU at NIMHANS developed a 15-item tool for risk assessment based on data from 200 admissions, which was later modified to include 17 items. This tool called the Formal Initial Risk Assessment for Mothers and Babies (FIRST-MB) has been immensely useful in the NIMHANS MBU in assessing and managing risks [13]. FIRST-MB form includes the assessment of risk to self, risk to others, risk to infant and infant health. The risk assessment is done before the admission to triage the patients and to plan the management accordingly. Risk assessment is repeated at the

ward immediately after the mother gets admitted and after 6 hours by the resident. Further, risk assessment is continued daily until the mother gets discharge.

A systematic assessment of risk is important, as it picks up the risks higher than routine assessments. In a study done on 58 mother-infant dyads at our MBU, formal risk assessment using FIRST-MB was found to be superior to routine risk assessment for picking up suicidal ideas, suicidal attempts, physical harm to the infant and poor self-care [14].

22.7 Electroconvulsive Therapy (ECT)

Both pregnant and postpartum women with severe illness needing augmentation of pharmacotherapy, suicidality or catatonia are considered for ECTs. Generally, bitemporal ECT is the therapy provided. In the case of pregnant women, clearance is obtained from obstetrician before proceeding. The risks involved with ECT during pregnancy are explained in detail to the patient and caregivers before consent is obtained. The ECT team includes experienced personnel in providing ECT treatment for pregnant women. The foetal heart rate is recorded at baseline, before and after the procedure at the ECT suite. In the case of lactating postpartum woman, care is taken to not disrupt the feeding due to the ECT procedure. Expression of breast milk prior to receiving ECT is encouraged, so that the infant can be fed while the mother is in an overnight fasting state before the procedure or drowsy after receiving ECT.

In a naturalistic study of 78 women with postpartum psychosis admitted in our inpatient service, 43.6% received ECT. Presence of catatonia, augmentation of medications and suicidality were common indications for ECT. Catatonic symptoms were significantly higher among women who received ECT. Transient side effects to ECT were observed in few women, with no adverse effects noted in infants who were breastfed. Hence ECTs appear to be a safe treatment option in the case of postpartum psychosis [15]. Bifrontal ECTs have also been given to some of our patients. In a study conducted in our centre of comparison of bifrontal and bitemporal ECT, analysis of 13 postpartum women who received bifrontal ECTs were found to have significantly more improvement (as shown by lower scores on the Edinburgh Postnatal Depression Scale, compared to 18 mothers who received bitemporal ECTs [16].

22.7.1 Clinical Assessments

Other than the risk assessment, the mother's assessment also includes rating them using standardized instruments including Edinburgh Postnatal Depression Scale, Young's Mania Rating Scale, Brief Psychiatric Rating Scale, Bush-Francis Catatonia Rating Scale and Yale-Brown Obsession and Compulsion Scale as well as the Clinical Global Improvement (CGI) scale. The ratings are done at the time of admission and then weekly until the mother gets discharged.

A detailed interpersonal trauma interview is also done with the mother when she is cooperative for the same. Items from the Stafford Interview have been included as part of clinical assessment. We have now developed an electronic database to ensure efficient capturing of data.

22.7.2 Infant Assessment

A detailed general physical examination is done at admission. Weight is measured weekly. Infant sleep and rhythms are also monitored. An infant behaviour questionnaire is used to for infants, 3 months or older. Daily monitoring of infants is done for early detection of any lactation-related side effects of psychotropic drugs. A study done in our MBU among infants who were being breastfed by mothers receiving psychotropic drugs found only minimal side effects and no major developmental problems in the infants during follow-up [17].

22.7.3 Infant Feeding

The various myths and misconceptions of patients and families regarding breastfeeding are assessed and addressed accordingly. In a low-income setting like ours, women are encouraged to breastfeed to meet the nutritional demands of the baby and prevent diarrhoeal illnesses except in conditions when breastfeeding is contraindicated due to the mother being on specific medications such as lithium or clozapine. However, in cases when the mother is unable to breastfeed due to sedation, agitation or when they receive ECTs, breast milk is expressed with electronic or manual breast pumps, stored in a hygienic manner and fed using a "pallada" – wide-mouth spoon which is the local practice. Advice from a lactation expert is sought for women who have severe lactation difficulties. Successful restitution of breastfeeding after disruption due to illness and separation of mother and infant has been done in several cases in our MBU. If the mother has lactation problems despite intervention and is very disturbed and unable to feed or there are medication-related contraindications, formula feeds are provided under safe and hygienic conditions.

22.7.4 Mother-Infant Bonding

Maternal-infant bonding can be affected by pre-existing mental illness, personality issues, emotional dysregulation or mental health issues developing during pregnancy and postpartum [18, 19]. We use clinical tools such as the *Kannada* (local language) version of the Postpartum Bonding Questionnaire [20], the Stafford Interview sixth edition of the Birmingham Interview for Maternal Mental Health 2015 [21] and the NIMHANS Maternal Behaviour Scale (NIMBUS). NIMBUS scale was developed by our team for the assessment of a mother's behaviour towards an infant that can be used easily without formal training and hence is ideal for use in low-resource

settings. This 16-item scale was developed by assessment of 100 mother-baby dyads. The NIMBUS is rated based on observations and information from caregivers, health assistants and nurses. The scale has six domains with adequate inter-rater and test-retest reliability (Cohen's kappa >0.81). The Cronbach's alpha for internal consistency was 0.94, and it showed adequate external validity when used with the Bethlem Mother-Infant Interaction Scale ($R = 0.947$, $p = 0.000$) and PBQ [22].

22.7.5 Video Feedback Sessions to Improve Mother-Infant Interaction

We use video feedback sessions to assess and promote mother-infant bonding once the mother is clinically stable. In a 15–20-min play interaction, the mother is instructed to interact with her infant being as natural as possible. No suggestions or interruptions are made by the observer during the recording. The recording is then viewed with the mother on a laptop computer, and she is encouraged to identify areas which she did well and where it can be improved. Mothers are often able to identify several areas which need improvement. Mother is provided skills and support to improve her bonding with the infant based on the video feedback. Similar video feedback sessions are repeated with the mother every week till she is discharged, and she is encouraged to practice these skills in between sessions [23]. While assessing for maternal-infant bonding, we observe the pattern of communication, the interaction between the mother and the baby, eye-to-eye contact, cooing, smiling and singing lullabies, gentle touch and response to cues and needs of the baby. The immediate caregiver account is also taken into consideration. Grandmothers are often co-therapists for this intervention and act as good role models.

22.7.6 Interventions to Improve Mother-Infant Bonding

The specific interventions carried out include encouraging touch and holding, encouraging attention towards infant during breastfeeding, infant massage to promote physical contact between mother and baby and emphasizing the need for face-to-face and eye-to-eye contact between mother and baby. Mothers are also encouraged to speak to baby, play with the baby, sing to the baby, tell stories to the baby and mimic baby's sound and facial expressions. The nurses also help in the process by involving the mothers gently in the process. In mothers with fears of rejection and attachment issues, individual psychotherapy and mother-infant psychotherapy are provided.

22.7.7 Infant Development Assessment

Infants of mothers with psychiatric problems are vulnerable to developmental issues. This could be due to poor stimulation, poor bonding and attachment, neglect

due to the family's preoccupation with the mother's illness and exposure to psychotropic medication if the mother was ill during pregnancy.

All the infants admitted to the MBU are screened for developmental issues. This is done by observation of the infant in a well-ventilated spacious room, and non-toxic bright toys and other common household items such as cups, boxes, bells and strings are used for assessment. This is followed by a detailed assessment of development done by the certified clinical psychologist, and appropriate interventions are offered.

The strengths of the infant and family are emphasized. The dynamic nature of development and scope of improvement with early interventions are explained. The family members are explained about the importance of play and the need for their active involvement in their infant's play.

22.7.8 Contraception Counselling

To avoid unplanned pregnancies and the risk of foetal exposure to psychotropics, contraception counselling is provided. Safe methods of contraception, how and when to plan the next pregnancy, are some of the important issues which are discussed with both patient and the spouse.

22.7.9 Additional Services

22.7.9.1 Liaison Services

Liaison with obstetricians and paediatricians is integral in effective functioning of the perinatal services. All referrals to obstetrician for pregnant women include a care plan for management of pregnancy and psychiatric illness. In case a pregnant women needs ECT, obstetrician opinion is sought before the procedure. Gynaecological problems such as discharge per vagina, menstrual irregularities, pelvic pain, etc. that require an evaluation are also referred. All babies admitted to the MBU are evaluated by a paediatrician for health concerns. Referrals are also made for purpose of immunization or in view of poor weight gain or feeding difficulties. When latching-related difficulties are observed, referral to a lactation consultant is considered.

In addition to active liaison with obstetricians and paediatricians, we also liaise with the neurology team. In the case of suspected organicity or a neurological cause for the presentation of illness, neurology referral is done before admitting the patient in the psychiatry ward. In such cases neuroimaging if indicated is obtained and discussed with the radiologist. We have higher rates of acute psychosis in the postpartum period when compared to the West, possibly due to organic factors. Patients presenting with atypical features or catatonia need investigations to assess for organic causes. Liaison with neurologists has facilitated timely referrals, early detection and management of organic conditions such as autoimmune encephalitis [24–26].

We also offer mother-infant yoga services at the NIMHANS Integrated Centre for Yoga (NICY). The yoga team also conducts mother-baby yoga sessions which promote bonding between mother and infant after women are clinically stable and able to follow instructions.

22.7.9.2 Support for Caregivers

Support from the family is essential during this period in terms of providing care to the mother, helping her develop a bond with the baby, taking care of her baby when she is unable to, supervising her medication and providing emotional, physical and practical support. The spouse, maternal family and in-laws are educated about the illness and its management. They are involved from the outset which helps in enhancing the support to the mother and baby. The various issues for which the family is assisted with include expressed emotions, violence against mother and baby, emotional and psychiatric problem in spouse, socio-cultural practices related to pregnancy, childbirth and postnatal care. Knowledge, attitude and practices regarding breastfeeding and illness are assessed and enhanced.

22.7.9.3 Special Focus on Spouses

Traditionally, husbands in India receive little attention from health systems during the perinatal period. So their involvement may be limited. This in turn may adversely affect the mother and baby. Spouses' groups are held regularly in our service to help them support each other and also express and share their own emotional concerns. This helps them in handling stress and decreasing caregiver burden.

22.7.9.4 Special Focus on Grandmothers

In our MBU, patients are frequently accompanied by their mothers or mothers-in-law during inpatient care. Taking care of the patient as well as the baby during the acute period often causes added stress and caregiver burden. Sometimes grandmothers themselves have been subject to domestic violence; hence we routinely assess the caregivers for their mental and physical health and offer support.

22.7.9.5 Cultural Sensitivity in Providing Perinatal Psychiatric Service

In different parts of the world, women and their families have their unique explanations and beliefs for the occurrence of postpartum disorders [27]. Understanding their belief systems and explanatory models is therefore essential in making services user-friendly and removing barriers of help-seeking. There are unique nuances and a diverse array of birthing rituals and practices. Some of the common practices that we have come across in our region include a belief that the new mother should remain in a state of "hot and cold" balance during the postpartum period because of which the mother is made to wear warm clothes, eat hot food, drink warm water and bathe in hot water in a belief that a state of "cold" will lead to lactation failure or even postpartum illnesses. A deep embedded preference for a male child by family members can lead to emotional and physical violence on the mother if she has only a girl children. A woman may feel a range of emotions if she does not give birth to

Table 22.1 Number of new registrations and follow-ups made in perinatal clinic and MBU 2012–2020

Year	2012–2013	2013–2014	2014–2015	2015–2016	2016–2017	2017–2018	2018–2019	2019–2020
New registrations	114	109	104	238	203	216	146	231
Follow-ups	471	496	672	799	1037	1619	1541	1490
Admissions to MBU	76	69	74	58	66	74	68	71

the son her family desires. There are other range of rituals performed to ward off evil during the postpartum period for the safety and well-being of the infant. As healthcare providers, we believe that the more one educates themselves about various cultural practices and the meaning of these practices, the more they can advocate for diverse patient populations.

Initial assessment of the patient and family includes a detailed assessment of their knowledge about the illness and their explanatory models and beliefs surrounding treatment and care. The mother is supported if she faces stress and discrimination from the family due to gender preference of the child. A flexible approach is taken while providing treatment. The families may conduct traditional practices or rituals which do not cause harm to the mother or infant and those which do not hamper treatment. This helps in building trust with the families.

22.7.9.6 Reach of Our Services

The numbers of outpatient registrations and inpatient admissions over 8 years has been depicted in Table 22.1 indicating a steady increase in women and families availing the service. The MBU admissions range from 60 to 75 every year.

22.8 Clinical Profile of Women Admitted to MBU

Analysis of the profile of 252 patients admitted in our MBU from 2016 to 2020 shows that 76.6% of women were admitted during their postpartum period and the rest were pregnant women. The majority belonged to a lower socioeconomic status (67.5%), and to rural areas (36.5%). The mean age of admitted women was 26.72 ± 5.03 years, and most were married. Diagnoses ranged from bipolar affective disorder (36.7%), unspecified nonorganic psychosis (18.5%), severe depression (17.4%), acute and transient psychotic disorder (13.2%), schizophrenia (9.5%), schizoaffective disorder (2.4%), organic psychosis (2.3%). In a retrospective analysis of 200 women with postpartum psychosis admitted in our MBU, it was seen that 20% ($n = 40$) presented, with catatonia of whom 19 required ECT as a treatment modality [26]. Higher rates of catatonia seen in our centre might be due to comorbid medical illness or nutritional deficiencies.

Majority of infants admitted were less than 8 weeks of age, similar to other MBUs across the world. Although duration of admission, good clinical outcomes

and lesser readmission rates are similar to other MBUs, there are some notable differences in the nature of illness occurring in this region. Considering the sparse research in the field of PMH from LAMI countries, our team strives to undertake research activities to highlight unique challenges faced and serviced provided.

22.8.1 Perinatal Helpline Services

For women who find it difficult to access healthcare services, especially during the COVID 19 pandemic, telephonic helpline services are a better alternative, especially in LAMI countries. Through helplines, women can access information, identify and manage symptoms and seek help when necessary. We offer a 24-h perinatal mental health helpline service for women in the perinatal period including post-discharge care. Women across all states in the country access the helpline. The Perinatal Mental Health helpline service has been found it to be useful in addressing a wide range of concerns about medications, symptom exacerbation, suicidal ideations, planning for pregnancy, breastfeeding and seeking appointments [28].

22.9 Conclusion

This chapter provides details about the various services provided by the perinatal psychiatric team in Bangalore, South India, including a dedicated outpatient perinatal psychiatry service and an inpatient mother-baby unit. The range of services provided have been developed over time based on a combination of evidence-based practices worldwide [29] and culturally appropriate adaptations. Based on this model, similar clinical services maybe developed in other lower- and middle-income countries as well to care for mothers with mental illness and their infants.

References

1. Fisher J, Mello MC, Patel V, Rahman A, Tran T, Holton S, Holmes W. Prevalence and determinants of common perinatal mental disorders in women in low-and lower-middle-income countries: a systematic review. Bull World Health Organ. 2012;90:139–49.
2. Supraja TA, Thennarasu K, Satyanarayana VA, Seena TK, Desai G, Jangam KV, et al. Suicidality in early pregnancy among antepartum mothers in urban India. Arch Womens Ment Health. 2016;19(6):1101–8. https://doi.org/10.1007/s00737-016-0660-2. Epub 2016 Aug 26.
3. Royal college of Psychiatrists. Perinatal mental health services: Recommendations for the provision of services for childbearing women [Internet]. 2015. Available from: https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr197.pdf?sfvrsn=57766e79_2.
4. Elkin A, Gilburt H, Slade M, Lloyd-Evans B, Gregoire A, Johnson S, Howard LM. A national survey of psychiatric mother and baby units in England. Psychiatr Serv. 2009;60(5):629–33.
5. Glangeaud-Freudenthal NC. Mother-Baby psychiatric units (MBUs): national data collection in France and in Belgium (1999–2000). Arch Womens Ment Health. 2004;7(1):59–64.

6. National Collaborating Centre for Mental Health. The Perinatal Mental Health Care Pathways. [Internet] London; 2018. Available from: https://www.rcpsych.ac.uk/docs/default-source/improving-care/nccmh/perinatal/nccmh-the-perinatal-mental-health-care-pathways-full-implementation-guidance.pdf?sfvrsn=73c19277_2.
7. Bagadia A, Chandra PS. Starting the conversation-Integrating mental health into maternal health care in India. Indian J Med Res. 2017;145(3):267.
8. Maitra S, Brault MA, Schensul SL, Schensul JJ, Nastasi BK, Verma RK, Burleson JA. An approach to mental health in low-and middle-income countries: a case example from urban India. Int J Ment Health. 2015;44(3):215–30.
9. Mendenhall E, De Silva MJ, Hanlon C, Petersen I, Shidhaye R, Jordans M, et al. Acceptability and feasibility of using non-specialist health workers to deliver mental health care: stakeholder perceptions from the PRIME district sites in Ethiopia, India, Nepal, South Africa, and Uganda. Soc Sci Med. 2014;118:33–42.
10. Ganjekar S, Thekkethayyil AV, Chandra PS. Perinatal mental health around the world: priorities for research and service development in India. BJPsych Int. 2020;17(1):2–5.
11. Chandra PS, Desai G, Reddy D, Thippeswamy H, Saraf G. The establishment of a mother-baby inpatient psychiatry unit in India: adaptation of a Western model to meet local cultural and resource needs. Indian J Psychiatry. 2015;57(3):290.
12. The Mental Healthcare Act, 2017. Ministry of Law and Justice, India [Internet]. Available from: http://egazette.nic.in/WriteReadData/2017/175248.pdf.
13. Chandra PS, Saraf G, Desai G, Harish T, Reddy DGS. Detecting and managing risk to mother and infant in a mother-baby unit in India using a tool—the FIRST MB (formal initial risk assessment for mothers and babies). Arch Womens Ment Heal. 2015.
14. Saraf G, Chandra P, Desai G, Thippeswamy H. Systematic risk assessment in a mother-baby unit (MBU)—importance for maternal and infant safety. Eur Psychiatry. 2017;41(S1):S363.
15. Babu GN, Thippeswamy H, Chandra PS. Use of electroconvulsive therapy (ECT) in postpartum psychosis—a naturalistic prospective study. Arch Womens Ment Health. 2013;16(3):247–51.
16. Raghuraman BS, Varshney P, Sinha P, Ganjekar S, Desai G, Chandra PS. Electroconvulsive therapy (ECT) for severe mental illness (SMI) during perinatal period: the role of bifrontal (BF) ECT. Brain Stimul. 2019;12(2):388.
17. Sinha S, Kishore M, Thippeswamy H, Kommu J, Chandra P. Adverse effects and short-term developmental outcomes of infants exposed to atypical antipsychotics during breastfeeding. Indian J Psychiatry. 2021;63(1):52–7. Available from: https://www.indianjpsychiatry.org/article.asp?issn=0019-5545.
18. Nakano M, Upadhyaya S, Chudal R, Skokauskas N, Luntamo T, Sourander A, et al. Risk factors for impaired maternal bonding when infants are 3 months old: a longitudinal population based study from Japan. BMC Psychiatry. 2019;19(1):1–9.
19. McNamara J, Townsend ML, Herbert JS. A systemic review of maternal wellbeing and its relationship with maternal fetal attachment and early postpartum bonding. PLoS One [Internet]. 2019;14(7):e0220032. https://doi.org/10.1371/journal.pone.0220032.
20. Brockington IF, Oates J, George S, Turner D, Vostanis P, Sullivan M, et al. A screening questionnaire for mother-infant bonding disorders. Arch Womens Ment Health. 2001;3:133–40.
21. Brockington I, Chandra P, Bramante A, et al. The Stafford interview: a comprehensive interview for mother-infant psychiatry. Arch Womens Ment Health. 2017;20(1):107–12. https://doi.org/10.1007/s00737-016-0683-8.
22. Ganjekar S, Prakash A, Thippeswamy H, Desai G, Chandra PS. The NIMHANS (National Institute of Mental Health and Neuro Sciences) Maternal Behaviour Scale (NIMBUS): Development and validation of a scale for assessment of maternal behaviour among mothers with postpartum severe mental illness in low resource setting. Asian J Psychiatr. 2020;47:101872.
23. Reddy PD, Desai G, Hamza A, Karthik S, Ananthanpillai ST, Chandra PS. Enhancing mother infant interactions through video feedback enabled interventions in women with schizophrenia: a single subject research design study. Indian J Psychol Med. 2014;36:373–7.

24. Dahale AB, Chandra PS, Sherine L, Thippeswamy H, Desai G, Reddy D. Postpartum psychosis in a woman with Graves' disease: a case report. Gen Hosp Psychiatry. 2014;36(6):761.e7–8.
25. Reddy MSS, Thippeswamy H, Ganjekar S, Nagappa M, Mahadevan A, Arvinda HR, et al. Anti-NMDA receptor encephalitis presenting as postpartum psychosis-a clinical description and review. Arch Womens Ment Health. 2018;21(4):465–9.
26. Nahar A, Kondapuram N, Desai G, Chandra PS. Catatonia among women with postpartum psychosis in a Mother-Baby inpatient psychiatry unit. Gen Hosp Psychiatry. 2017;45:40–3.
27. Thippeswamy H, Dahale A, Desai G, Chandra PS. What is in a name? Causative explanatory models of postpartum psychosis among patients and caregivers in India. Int J Soc Psychiatry. 2015;61(8):818–23. https://doi.org/10.1177/0020764015597016. Epub 2015 Aug 3.
28. Ragesh G, Ganjekar S, Thippeswamy H, Desai G, Hamza A, Chandra PS. Feasibility, acceptability and usage patterns of a 24-hour mobile phone helpline service for women discharged from a mother-baby psychiatry unit (MBU) in India. Indian J Psychol Med. 2020;42(6):530–4.
29. Antenatal and postnatal mental health: clinical management and services guidelines. National Institute of Health and Care Excellence. 2020 Feb. Available from: https://www.nice.org.uk/guidance/cg192.

A Day Hospital Service for Mothers and Babies: Barcelona as a Model for Southern Europe

23

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23.1 Introduction

Perinatal mental disorders (PMD) are considered a public health problem because of the impact they have on both women and children's health. 20% of women will suffer from a mental disorder throughout gestation and/or postpartum [1–3]. The perinatal period is a moment of greater complexity for women with a mental disorder because of the impact of mental illness and exposure to psychopharmacs. It is estimated that the cost of untreated PMD is more than EUR 9 billion per year, with 72% of it attributable to the child's consequences [4].

For more than a decade, international organizations have pointed the need to improve the detection, prevention, and specialized treatment of PMD with the development of devices that integrate dyadic care by professionals specialized in perinatal mental health. Until now, there were no specific mental health programs in Spain that offered integrated and intensive care to women in the perinatal stage. In line with the recommendations of the International Clinical Guidelines on Perinatal Mental Health [5–7], during 2018, the first Mother-Baby Day Hospital (MBDH) in Spain was developed and implemented at the Hospital Clínic from Barcelona.

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23.2 History of the Perinatal Mental Health Program of Hospital Clinic Barcelona

The Perinatal Mental Health Program of Hospital Clínic from Barcelona was initiated in 1988 with one psychiatry consultant (Dra Garcia-Esteve) as a small outpatient consultation of perinatal mental health. This program was located adjacent to Obstetrical and Neonatological Service on the campus of the Maternitat and depends on the Psychiatry and Clinical Psychology Service of the Neuroscience Clínic Institute.

Many years later, this program expanded with another psychiatrist and one clinical psychologist, and the first Spanish program of perinatal psychiatry was developed. In this program we attended women with mental disorders during their pregnancy and postpartum periods. Also, we established a pregnancy planning consultation for women with mental disorders and psychopharmacological treatment who wanted to become a mother. Collaboratively with the Obstetric Service, we developed a consultation for perinatal grief and a liaison consultation for inpatient pregnant or postpartum women.

Later, in the presence of improved mother-baby bonding, a child psychologist was included in the program, and mother-baby groups have been developed.

For years, awareness campaigns were carried out with the Catalan administration, and in December 2017 the Catalan Government financed what was the first Perinatal Mental Health Unit, the unique mother-baby services in Spain. This unit is compounded of an outpatient consultation and the Mother-Baby Day Hospital (MBDH) for postpartum women with mental disorder and their babies.

The Perinatal Mental Health Unit CLINIC-BCN is composed of a community perinatal mental team, who serve half of the city of Barcelona (10,000 births a year), and the MBDH offers suprasectorial attention to region of Catalonia (60,600 births a year). The unit offers diagnostic evaluation and psychotherapy, both individualized and group, and has specific programs for perinatal mental disorders such as postpartum depression, bipolarity, and puerperal psychosis, as well as bonding disorders. Sensitive maternal behavior is promoted, and the mothers are offered assistance, attention, care, and accompaniment in order to improve their mental health and their maternal function.

The risks and benefits decision-making process is carried out together with the mother, and different therapeutic options are evaluated, including psychopharmacology treatments that are compatible with breastfeeding. Likewise, evaluations of the newborns are carried out for early detection of neurodevelopment disorders.

The MBDH has been inspired by two baby-mother units in England, the Channi Kumar Mother and Baby Unit in the Royal Bethlem Hospital of London and the Brockington Mother and Baby Unit of Stafford. The MBHD was intended as a partial hospital model of care due to the difficulties implied in the establishment of a fully serviced mother-baby unit. The budget available was 300.000 euros a fraction of the budget that we initially requested. In the second stage, we wanted to create a full mother-baby unit (MBU).

23.3 Description of Mother-Baby Day Hospital (MBDH)

The Mother-Baby Day Hospital was officially opened on March 20, 2018. The MBDH utilizes a partial hospital model of care and thus provides intensive services during the day to patients who require a higher level of care than traditional outpatient services, due to high level of symptoms and/or substantial functional impairment interfering with their daily activities. Staffing includes a multidisciplinary team of perinatal psychiatrist, perinatal clinical psychologist (adult and child), nurse specialists (mental health and pediatrics), and social worker. Moreover, the MBDH is a frequent training site for residents in psychiatry, psychology, or nurses, as well as master's practices or specialization course for mental health professionals.

The sessions take place from Monday to Friday from 9:30 a.m. to 16:00 p.m. and include psychopharmacological, psychological, nursing, and social interventions. The service offers intensive and specific therapies during the first year following birth to improve the severe perinatal mental disorders. Mothers come with their baby and take care of them with a higher or lower level of nursing supervision, depending on their abilities and level of autonomy.

The objective of MBHD is to improve the prevention, detection, and intervention of severe mental disorders during the first postpartum year through the use of specialized treatment. Treatments are based on multidisciplinary interventions to promote maternal breastfeeding and enhance mother-baby relationship, as well as positive parenting. The day hospital has 10 places for mothers and 10–12 for babies with the possibility to stay for 3 months or during 60 sessions (one session × 1 day). The frequency of intervention is established according to the clinical condition of women and their accessibility.

23.3.1 Patient Population

MBHD is focused on women's care during the first postpartum year. However, pregnancy programs are also carried out for women at high risk of relapse such as mothers with bipolar disorder and/or a history of puerperal psychosis.

The MBDH is useful for:

- Women with acute mental disorder in postpartum period which requires semi-intensive, multidisciplinary, and complex interventions. This may be due to the mother's pathology or to its interference in the ability to care the baby.
- Women with mental disorder at high risk for relapse in postpartum period (bipolar disorder, previous puerperal psychosis, previous severe postpartum depression).
- Women with difficulties in bonding to the baby due to maternal mental pathology.
- Women who require a psychiatric hospitalization during perinatal period, especially in postpartum. In Spain there is no MBU, so psychiatric hospitalization involves the separation of mother and baby. The MBH could be usefull for recovery not only of mother's psychopathology also bonding with the baby.

Women who pose an immediate risk to themselves or someone else or with dependence of substance are not appropriate for partial hospital level of care and are referred for admission to an inpatient psychiatric unit or specific units. Neither recommends admission to MBDH in those mothers with chronic mental disorders without a minimum of personal self-sufficiency and/or capacity to care for their baby, who are not expected to benefit from the type of care provided by the day hospital.

23.4 Objectives of Mother-Baby Day Hospital

MBDH offers an intensive and multidisciplinary care and treatment model for mental disorders from childbirth to 12 months postpartum, which ensures early intervention and continuity of care focused on mother-baby dyad and promotes mental health and maternal functioning recovery processes, as well as maternal bonding and parenting. The main objectives of the MBDH are:

- **Design and apply a personalized intervention plan** evidence-based and mother's needs-based that incorporates the dyad, taking into account the specific period for the choice of psychopharmaceuticals and their clinical safety and a shared decision-making model.
- **Reduce the impact of maternal mental illness on the child** through early and intensive intervention on maternal psychopathology, incorporating the baby into treatments and evaluating early signs of neurodevelopment disturbance.
- **Evaluate the mother-baby relationship and develop specific treatments** for bonding disorders, with the aim of training the mother in her competencies by enhancing maternal sensitivity and responsiveness and thus preventing situations of abuse, neglect, neglect, or filicide.
- **Develop group interventions** aimed at improving psychopathology and knowledge of maternal disease and its consequences at this period and promoting breastfeeding, bonding, and positive parenting.
- Develop and implement **specific interventions for perinatal mental disorders** like perinatal OCD and/or thoughts of harming the baby, postpartum depression, and perinatal post-traumatic stress disorder.
- **Develop specific programs to decrease the risk of relapse** in women with high-risk mental pathology like bipolar disorder and/or previous puerperal psychosis or severe postpartum depression.
- **Increase awareness** of maternal disease and diminish self-stigma and social stigma.
- Train the mother in her **maternal skills** and optimize her skills modeling by enhancing maternal sensitivity and responsiveness.

23.5 Evaluation and Interventions

The MBDH_Protocol evaluation includes maternal psychopathological status and maternal care behaviors, mother-baby relationship, and baby neurodevelopmental and health status (see Table 23.1).

Table 23.1 Maternal psychopathological status and care behaviors

Maternal psychopathological evaluation
Edinburgh Postnatal Depression Scale [15, 16]
State-Trait Anxiety Disorder Inventory [17]
Marital Adjustment Test [18]
Insomnia Severity Index [19]
Early Trauma Inventory—Short Form [20, 21]
Health of the Nation Outcome Scales [22]
Mini-international Neuropsychiatric Interview [23]
Mother–baby relationship
Stafford Clinical Interview for Maternal Mental Health [10]
Postpartum Bonding Questionnaire [8, 24, 25]
CARE-Index [26]
Baby neurodevelopmental and health status
Escala para la evaluación del comportamiento neonatal [27]
Escalas Bayley de desarrollo infantil-III [28]
Alarm Distress Baby Scale [29]
Communication and Symbolic Behavior Scales Developmental Profile [30]

At admission all patients perform a protocol evaluation that includes maternal psychopathological evaluation with MINI and battery of scales and mother-baby relationship evaluation. All babies are evaluated at admission for both neurodevelopment and health aspects. At the beginning of MBDH, the level of maternal capacity for basic care is determined by a scale developed by our team based on maternal behavior observation. At discharge, assessments are administered again: maternal psychopathological status and mother-baby relationship. Neurodevelopment of all babies is retested at 12 months.

During their stay at MBHD, all women carry out the psychosocial risk assessment, thus ensuring a holistic vision with community and family interventions if necessary. Specific evaluation and intervention protocols have been developed in the case of detection of traumatic events (current or past) and/or partner violence during the perinatal period.

Our team developed a specific protocol evaluation for mother-baby relationship (VINCLINIC_BCN Protocol) based on three tools with a final diagnosis using the Brockington criteria [8] exposed at the Stafford Symposium in 2018 [9]. We used the autoadministered Postpartum Bonding Questionnaire (PBQ), the Care-Index Videotape evaluation for mother-baby interaction, and the Stafford Clinical Interview for Maternal Mental Health [10].

The Stafford Clinical Interview for Maternal Mental Health is a clinical instrument designed to explore the social, psychological, and psychiatric course of pregnancy, parturition, and puerperium. In our protocol we employ the section exploring the mother-infant relationship for diagnosis of bonding disorder, and some other probes from the earlier sections exploring psychiatric and obstetric history, pregnancy, parturition, puerperium, and postpartum (response to conception, well-being of the fetus, the newborn, early postpartum events, and the focus of anxiety and worrying) are added. A team of clinical psychologists used the interview and case

records to diagnose various forms and degrees of bonding disorders: mild disorder, threatened or established rejection, infant-focused anxiety, over-involvement, and pathological anger.

Taking into account the specific characteristics of this service, treatments and interventions for perinatal mental disorders have been developed and/or adapted considering the inclusion of the baby and aspects related to maternal care. Activities are mainly carried out in a group to facilitate modeling and improve stigma. All patients attend at least two psychological intervention groups according to their needs (transdiagnosis group based on the Barlow Unified Protocol [11]; emotional regulation group; postpartum depression group based on the Milgrom Protocol [12]; mother-baby bonding group). In addition, specialized nurses hold massage groups, psychofitness, psychoeducation, relaxation, art therapy, and baby care information workshops.

All patients are visited by perinatal psychiatrist who evaluates the diagnosis of acute episode, medical, and psychiatric comorbidities and carries out risk assessment (substance use, relationship with the partner, suicidal ideation, risky behaviors with the baby, and others). Also, perinatal psychiatrist carried out the risk-benefit assessment of psychopharmacological treatment as well as the control of plasma levels of those drugs that require it during lactation with monitoring of results and possible adverse effects. Specialized individual psychological interventions are also performed for perinatal OCD and/or baby harm phobias based on cognitive behavioral therapy (CBT) and post-traumatic stress disorder related to perinatal trauma with eye movement desensitization and reprocessing (EMDR).

For some patients with mother-baby interaction disturbance, videofeedback interventions are performed by perinatal psychologist. In addition, a structured experience group of positive parenting based on the online course "Ganar salud y bienestar de 0 a 3 años" [13] is offered to all families at the time of discharge.

23.6 Description of Mothers Attended at MBDH

Since 2018, we treated 128 mothers and their babies. 64.1% of these were referred by psychiatric services, while 35.9% were referred by community services. Mean age at admission was 34y (20–47) for mothers and 3.6 months (0–12) for babies. Most of them had a partner (89%), 30% were migrant, half had university studies, and one-third report financial problems. Regarding obstetrical data 74% were primiparous, 62% had an unplanned pregnancy, 44.1% had a cesarean delivery, and 41.9% were breastfeeding at admission. From a clinical point of view, it is to be noted that 79% had a personal psychiatric history, and 28.6% had a previous psychiatric admission.

The most frequent diagnosis was perinatal depression (46.1%) (most of them started at postpartum period), followed by bipolar disorder (14.1%), psychotic disorder (12.5%), and obsessive-compulsive disorder (10.2%), and 17.1% had other diagnosis (panic disorder, post-traumatic stress disorder, borderline disorder, eating disorders, autism spectrum disorder). Three-quarters had some comorbidity according to MINI.

Almost all mothers received pharmacological treatment, and 30.5% two or more drugs (not anxiolytics considered). The risks and benefits decision-making process

is carried out together with the mother, and different therapeutic options are evaluated. 71.1% of mothers had started exclusive breastfeeding after childbirth. At the time of admission, 41.9% of the mothers were breastfeeding and continued to do so, until the time of discharge, combining it with pharmacological treatment.

The mean EPDS score was 16.8 (SD 6.79), 73.6% had EPDS ≥13, and 47.1% had thoughts of harming themselves (10 items of EPDS). Also we found 36% of suicidal ideation during clinical interview, and 10.2% had attempted suicide during the current episode prior to admission. When the risk of suicide is identified, an action plan is carried out by a psychiatrist and a nurse from the MBDH consisting of these three steps: First is identification of suicide risk. Then, using Columbia Suicide Severity Scale [14], we prepare, together with the patient, several measures. And finally, we consider admission to the psychiatric acute care which entails separation of mother and baby.

When we assessed the maternal bonding, we found that the mean PBQ score was 27.4 (SD 19), 67.4% had PBQ ≥ 18, and 70% had a diagnosis of mother-baby relationship disorder according to the Brockington criteria.

In summary, we have found that the Mother-Baby Day Hospital is a good model for treatment of severe mental disorders during the first postpartum year. Our specialized and multidisciplinary interventions facilitate psychiatric and psychological treatment, maternal breastfeeding, sensitive mother-baby relationship, as well as positive parenting. This type of approach will benefit an increasing number of mothers and babies and also a diversity of perinatal mental conditions. It also encompasses an increase in the types of therapies and support.

23.7 Conclusions

MBDH allows us intensive and multidisciplinary care to mothers with a perinatal mental disorder with good results and possibility of containment risky behaviors and can avoid psychiatry hospitalization that involves the mother-baby separation. More specifically, it allows us to observe the mother and baby relationship as well as maternal care behaviors, enabling direct intervention through observational learning (modeling) processes, support in breastfeeding, and accompaniment in respectful parenting. This type of device with a model focused on the dyad (mother and baby), considering the participation of the patient in decision-making process and with multidisciplinary interventions, allows us the comprehensive evaluation and detection of complex disorders as well as the possibility of integrated actions. We have also identified the need of including babies as risky subjects that require early evaluations and specific interventions in some cases. Maternal mental health affects not only women but also their offspring, partner, family, and society.

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References

1. Navarro P, García-Esteve L, Ascaso C, Aguado J, Gelabert E, Martín-Santos R. Non-psychotic psychiatric disorders after childbirth: prevalence and comorbidity in a community sample. J Affect Disord. 2008;109(1–2):171–6.
2. Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry. 2008;65(7):805–15.
3. Borri C, Mauri M, Oppo A, Banti S, Rambelli C, Ramacciotti D, et al. Axis I psychopathology and functional impairment at the third month of pregnancy: results from the Perinatal Depression-Research and Screening Unit (PND-ReScU) study. J Clin Psychiatry. 2008;69(10):1617–24.
4. Bauer A, Parsonage M, Knapp M, Iemmi V, Adelaja B. Costs of perinatal mental health problems. London: Centre for Mental Health; 2014. [cited 2021 Apr 20]. Available from: https://www.centreformentalhealth.org.uk/costs-of-perinatal-mh-problems.
5. Scottish Intercollegiate Guidelines Network. SIGN 127—Management of perinatal mood disorders. 2012 [cited 2021 Apr 20]; (March):1–54. Available from: www.sign.ac.uk.
6. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance | Guidance | NICE [Internet]. NICE; 2014 [cited 2020 Jun 25]. Available from: https://www.nice.org.uk/guidance/cg192.
7. Austin M, Highet N, and the Expert Working Group. Mental Health Care in the perinatal period: Australian Clinical Practice Guideline. Aust Clin Pract Guidel [Internet]. 2017. [cited 2021 Apr 20]; (October):1–121. Available from: https://cope.org.au/wp-content/uploads/2017/10/Final-COPE-Perinatal-Mental-Health-Guideline.pdf%0A, http://cope.org.au/about/review-of-new-perinatal-mental-health-guidelines/.
8. Brockington IF, Fraser C, Wilson D. The postpartum bonding questionnaire: a validation. Arch Womens Ment Health. 2006;9(5):233–42.
9. Ian Brockington A, Öngel Atar A, Aydin N, Bharadwaj B, Bramante A, Chandra P, et al. Stafford international symposium. Arch Womens Ment Health. 2020;23(2):307–15.
10. Brockington I, Chandra P, Bramante A, Dubow H, Fakher W, Garcia-Esteve LL, et al. The Stafford interview: a comprehensive interview for mother-infant psychiatry. Arch Womens Ment Health. 2017;20(1):107–12.
11. Ellard KK, Fairholme CP, Boisseau CL, Farchione TJ, Barlow DH. Unified protocol for the transdiagnostic treatment of emotional disorders: protocol development and initial outcome data. Cogn Behav Pract. 2010;17(1):88–101.
12. Milgrom J, Martin PR, Negri LM. Treating postnatal depression: a psychological approach for health care practitioners. Chichester, UK: John Wiley & Sons; 1999. p. 265.
13. Rodrigo López MJ, Martín Quintana JC, Máiquez Chaves ML. Parentalidad Positiva: Ganar Salud y Bienestar de 0-3 Años. Ministerio de Sanidad Servicios Sociales e Igualdad. Familias en positivo [Internet]. 2017 [cited 2021 Apr 20]. Available from: https://familiasenpositivo.org/.
14. Posner BL, Gould S, Brown F, et al. Columbia-Suicide Severity Rating Scale (C-Ssrs): risk assessment (Lifeline crisis center version). Res Found Ment Hyg. 2014; [cited 2021 Apr 20];1–2. Available from: http://c-ssrs.trainingcampus.net/.
15. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150:782–6.
16. Garcia-Esteve L, Ascaso C, Ojuel J, Navarro P. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in Spanish mothers. J Affect Disord. 2003;75(1):71–6.
17. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the state-trait anxiety inventory. Palo Alto, CA: Consulting Psychologist Press; 1983.
18. Locke HJ, Wallace KM. Short marital-adjustment and prediction tests: their reliability and validity. Marriage Fam Living. 1959;21(3):251.
19. Bastien CH, Vallières A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. Sleep Med. 2001;2(4):297–307.

20. Bremner JD, Bolus R, Mayer EA. Psychometric properties of the early trauma inventory-self report. J Nerv Ment Dis. 2007;159(3):211–8.
21. Plaza A, Torres A, Martin-Santos R, Gelabert E, Imaz ML, Navarro P, et al. Validation and test-retest reliability of early trauma inventory in Spanish postpartum women. J Nerv Ment Dis. 2011;199(4).
22. Wing JK, Curtis RH, Beevor AS. Health of the Nation Outcome Scales (HoNOS). In: A compendium of tests, scales and questionnaires; 2020. p. 635–42.
23. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59(Suppl. 20):22–33.
24. Brockington IF, Oates J, George S, Turner D, Vostanis P, Sullivan M, et al. A screening questionnaire for mother-infant bonding disorders. Arch Womens Ment Health. 2001;3(4):133–40.
25. Garcia-Esteve L, Torres A, Lasheras G, Palacios-Hernández B, Farré-Sender B, Subirà S, et al. Assessment of psychometric properties of the Postpartum Bonding Questionnaire (PBQ) in Spanish mothers. Arch Womens Ment Health. 2016;19(2):385–94.
26. Crittenden PM. CARE-Index: coding manual. Miami, FL; 2004.
27. Brazelton TB, Nugent JK Escala para la evaluación del comportamiento neonatal. Ed. Paidós. Barcelona, 1997.
28. Bayley N. Bayley-III, Escalas Bayley de desarrollo infantil-III. Madrid: Pearson; 2015.
29. Guedeney A, Matthey PK. Social withdrawal behavior in infancy: a history of the concept and a review of published studies using the Alarm Distress Baby Scale. Infant Mental Health J. 2013;34(6):516–31.
30. Wetherby AM, Prizant BM. CSBS DP manual: communication and symbolic behavior scales developmental profile. Baltimore, MD: Paul H. Brookes Pub; 2002.

Perinatal Depression and Mother-Infant Interventions: A Literature Review

24

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24.1 Introduction

Perinatal depression is a mood disorder that can affect women during pregnancy and after childbirth. The word 'perinatal' refers to the time before and after the birth of a child: depression that occurs during pregnancy is referred to as antenatal (AND), and depression occurring after childbirth is described as postpartum depression (PND). This mood disorder is one of the most common complications of the antenatal and postpartum periods [1]: AND affects approximately 7–12% of women, and PND affects 10–15% of women, with even higher rates among low-income populations [2–4] and ethnic minority groups [5]. Furthermore, women who experience perinatal depressive episodes are at increased risk for subsequent episodes of both postpartum and non-postpartum depression [6]. In terms of major risk factors for perinatal depression, they include a history of depression and/or anxiety, bipolar disorder, unintended pregnancy, life stress, history of sexual abuse, domestic violence, low social support, and poor relationship quality [7–9].

Perinatal depression not only has implications for maternal mental health and wellbeing [10], which includes depressed mood, anxiety, compulsive thoughts, loss of control, feelings of inadequacy, inability to cope, irrational fears, fatigue, and despair [11], but also for decreased quality of interactions between mothers and their children [12], higher levels of psychiatric disturbances among children [13], and greater child insecurity in attachment relationships [14]. Some studies have underlined that poor perinatal attachment until 15 months postpartum, reduced medical check-ups, low foetal development, preterm deliveries, and low care of the infant are often associated with prenatal depressive symptoms [15–17]. Moreover, a

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child's behavioural, cognitive, linguistic, and emotional problems can persist into school age as a long-term effect of a mother's perinatal depression [18, 19]. Evidence shows that problems can recur also into adulthood. In a study conducted with the aim to study whether the adult offspring of antenatally depressed mothers were at an elevated risk of developing a mental health disorder (i.e. psychoses, depression, bipolar disorder, antisocial and borderline personality disorder, and schizotypal and affective traits), results showed that adult offspring of antenatally depressed mothers had an increased risk of depression, and the male offspring for antisocial personality disorder, compared to cohort members without antenatally depressed mothers [20].

24.2 Mother-Infant Interaction

During mother-infant interactions, depressed mothers usually interact less with their infant and are more withdrawn [21, 22] and less responsive to infant cues, leading to greater incidences of insensitive caregiving [23, 24]. Maternal sensitivity is highly predictive of infant secure attachment [25], which has long been linked to optimal developmental outcomes including offspring mental health [26]. Depressive mothers also develop a less-intense relationship with their children, experience more stress, perceive their children in a more negative way, and may assess them as less securely attached than non-depressive mothers [27]. Some mothers experience lowered maternal instinct, as well as greater hostility and aggressive impulses, and a feeling of rejection towards their own children [28]. Moreover, depressed mothers are less likely to mentalize appropriately with their infants [29]. As babies learn from the outside in, through the mind of another person, they learn how to regulate their behaviours from the responses of their mothers. In the context of depression, which often combines elevated stress levels with low emotional arousal, it can be difficult for a mother to recognize and perceive her own and her child's needs and emotions: this can have consequences on the ability to feel what they are thinking and to think about what they are feeling in order to appropriately interact with their infant. Consequently, children may tend to mirror this behaviour by disengaging and adopting a passive behavioural style [21].

24.2.1 Attachment

The infant's extreme dependency on their caregiver, their sensitivity to interpersonal contacts [30], and the fact that, in the great majority of cases, the mother constitutes the infant's primary environment in the first postnatal months make the question of the impact of depression one of particular importance. According to John Bowlby [31], humans are born with a predisposition to become attached to caregivers, and attachment is one specific and circumscribed aspect of the relationship between a child and caregiver that involves with making the child feel safe, secure, and protected. In addition, attachment is a mechanism where the child uses the primary

caregiver as a secure base from which to explore and, when necessary, as a haven of safety and a source of comfort [32], and it is a powerful predictor of a child's later social and emotional outcome [33]. Many studies have suggested that the influence of a mother's depressive disorder on the way the mother and child interact can be linked to the subsequent emotional disturbance of the child [34] and to the insecure infant attachment [35–37].

Most of the assessments of the quality of infant attachment have been made using the Ainsworth's Strange Situation procedure [38]: in a study conducted with children aged two to three, it was found that insecure attachment was more frequent in children whose mothers had a history of major depression than in those whose mothers had no such history, and the evidence for insecure attachment was the child's avoidance of and resistance to the mother when reunited with her after a brief separation [39]. Another study conducted by Lyons-Ruth and colleagues using the Strange Situation found an association between insecure attachment at 12 months and high levels of maternal depression [35]. Similarly, Lynne Murray [36] found a significant association between the occurrence of depression in the postnatal period and insecurity of attachment at 18 months postpartum, with avoidance being the prominent insecure attachment profile. In addition, the author found insecure attachment, behaviour problems, and poorer cognitive outcome associated with the occurrence of postnatal depression to obtain in infants of 18 months even though, in the great majority of cases, the mother's depression had remitted by around 6–8 months postpartum.

24.2.2 Mentalization

Mentalization has been defined as the mental ability to recognize and interpret one's own and others' behaviour in the context of underlying mental processes such as needs, feelings, thoughts, beliefs, and desires, and it is central for the affect regulation, interpersonal relationships, and social functioning [40]. As Peter Fonagy [41] underlines, mentalizing is something we do interactively: while interacting, each person remains attentive to mental states, holding the other person's mind in mind as well as their own. Additionally, we aspire to understand each other as autonomous persons and to influence each other on the basis of our understanding.

It is well known that mentalization is a developmental achievement that emerges in the attachment context of the early infant-caregiver interaction: during the first years of life, the primary caregiver's appropriate mirroring of the infant's needs and emotions—and the infant's exposure to it—is essential to the development of an adequate intersubjectivity [42] and mentalizing models [43]. An adequate interaction context then, where the caregiver shows interest in the infant's mental state, can be expected to facilitate secure attachment and advance the development of mentalization [44, 45]. Furthermore, mentalizing is proposed as one of the mechanisms that utilize its influence on child's attachment security and socio-cognitive development [46].

Mentalizing is not only something mothers do but also something they can fail to do. Although just few studies have investigated maternal mentalization in the context of perinatal depression during mother-infant interaction, depressed mood is hypothesized to lead to increased arousal and stress levels, resulting in impairments and distortions in mentalization, which in turn may cause a loss of resilience in the face of stress, adding to a vicious cycle of increasingly depressed mood [47]. Murray et al. [48] have reported that depressed mothers are less likely to acknowledge infant intentions and agency, compared with non-depressed mothers. Similarly, Herrera et al. [49] found that mothers with depression made fewer references to their infants' emotional and cognitive experience in their speech, and, finally, another study of in-patients found that depressed mothers, compared with healthy controls, were marginally less likely to comment on their infants' mental state [29].

In women who experience mental problems shortly after birth, impaired mentalization may have negative consequences for the mother's ability to provide sensitive caregiving for her child [50]. A study conducted with depressed fathers and their 3-month-old infants showed that not only depressed fathers were more negative about themselves and their infants compared with non-depressed fathers but depression was also associated with speech that was more focused on the paternal experience and less on the infant's experience [51]. Levy and Truman [52] suggested that when caregivers are not able to reflect on their own mental states, their ability to be sensitive and emotionally responsive to their children is restricted. In fact, it has been underlined that the ability to mentalize is a key aspect of maternal sensitivity [45], which is one of the most important predictors of child socioemotional development [53].

24.2.3 Maternal Sensitivity

Maternal sensitivity includes a variety of interrelated affective and behavioural caregiving attributes. It is defined as the quality of a mother's behaviours that are based on her abilities to perceive and interpret her infant's cues and respond to them appropriately, and it is a dynamic process which accompanies the adaptation and changeability [54]. Maternal sensitivity is an important aspect and a key indicator of the quality of early mother-infant interactions. As caregivers are critical to the development of the offspring, maternal sensitivity can affect an infant's behaviour and development [55]. Particularly, during the first year of life, sensitive mothering is considered to be the most important precursor of the secure attachment relationship that influences an infant's physical, psychological, and cognitive development [56, 57]. Indeed, decreased maternal sensitivity is associated with poor mother-child interaction quality and, ultimately, insecure infant attachment.

It is largely demonstrated that maternal depression, both during and after pregnancy, is associated with decreased maternal sensitivity and less responsiveness to infants [58–60]. Mothers who suffer from depression are more susceptible to cognitive deficits and appear biased when processing emotional events [61]. Distorted maternal cognitions, driven by depressive symptoms, may lead to a mother-centred,

rather than infant-centred, approach to caregiving, such as attending to their own needs before attending to infant signals, and this may result in less sensitive caregiving, particularly when infants are in distress [62, 63]. Moreover, they are more likely to have a negative view about themselves and the world and therefore may tend to have a negative view about their infants. Some studies have shown that the effects of depression during the perinatal period on early childhood outcomes can also have an impact on child language development, cognitive functioning, and increased risk of socioemotional difficulties [64–66], and these effects are thought to be, in part, related to decreased maternal sensitivity towards the infant and young child.

24.3 Mother-Infant Interventions

Although the perinatal period is considered a very delicate and sensitive phase for both mothers and infants, there are still many critical obstacles in the way of treatment for maternal perinatal depression. Since having a baby is generally considered to be a joyous event, perinatal depressive symptoms may be particularly susceptible to stigma, and women may be especially reluctant to talk about depression during the prenatal and postpartum period [67]. New mothers may tend to avoid, and not to communicate and elaborate, negative effects and thoughts related to childbirth, which could lead them to express and value openly only the positive aspects of childbirth. Negative or upsetting events that are kept secret or silent are more likely to result in health problems than those that could be spoken about more openly or, better, expressed in a written language that demands more integration and structure than spoken language [68]. Expressive writing could represent a low-cost early intervention to prevent or reduce the development of postpartum distress in new mothers [69].

A study that explored pregnant women's barriers to mental health care found that although women with severe depression were generally willing to seek mental health care, they identified multiple barriers such as cost, lack of insurance, lack of transportation, long waits for treatment, previous bad experience with mental health care, and not knowing where to go for treatment [70]. Increasing the options for effective treatment of perinatal depression with the aim of improving mother-infant relationship remains a critical public health goal. The first year of the infant's life is considered a crucial moment for the development of their self-regulatory skills [71, 72]: mother's perinatal depression may have implications for the development of those important skills, making the infant more vulnerable to later psychopathology. In reviewing mediating factors between postnatal depression and adverse child outcomes, Murray and Cooper [73] stress early maternal interactional style, secondary to exposure to depression/social adversity, as critical in contributing to adverse outcomes. Thus, early interventions to improve mother-infant interaction are highly recommended in order to protect offspring future development.

There is growing evidence demonstrating that perinatal depression impacts a mother's ability to properly interact with her baby. But treating maternal mood alone is not sufficient for improving mother-infant relationship difficulties [74].

Evidence-based individual psychotherapies, such as interpersonal psychotherapy and cognitive behavioural therapy, have demonstrated efficacy in reducing mothers' depressive symptoms during the perinatal period [75], with overall depression remission rates similar to that of anti-depressants [76]. Evidence indicates that treating postpartum depression alone may not be sufficient in protecting children against long-term poor outcomes [27, 77]. In addition to reducing depressive symptoms, optimal perinatal depression interventions should address impaired caregiving to improve interaction quality and, in turn, enhance infants' developmental outcomes [78, 79].

Mother-infant interventions may be an important complement to individual approaches, optimizing both maternal, infant, and relationship outcomes [80]. Evidence suggests that dyadically based postpartum interventions are more efficacious than individual psychotherapy for enhancing parenting and improving outcomes for infants of depressed mothers. These relationship-based treatments may be short or long term, and many of them are rooted in psychodynamic and attachment theories [81, 82]. Finally, some reviews [83, 84] have emphasized that interventions, mainly focused on the mother-infant relationship, have the best chance of improving outcomes for the children of depressed mothers, as well as reducing maternal depression.

24.3.1 Dyadic Psychotherapy

Child-parent psychotherapy (CPP) is an attachment theory-informed intervention intended to enhance the quality of the parent-child relationship and foster secure attachment, in which the primary focus is on the relationship between parent and child, rather than on each as individuals. Mothers and their children are seen in conjoint therapy sessions: through the use of observation and empathic comments, the therapist works towards assisting the mother in recognizing how she experiences and perceives her infant and herself, thereby allowing for correction of distorted perceptions and alterations in how the infant and the self are experienced. The therapist also attends to the nature of the interactions that occur between the mother and her child [85].

CPP has also been specifically examined within the context of maternal depression. CPP can protect cognitive development, and it increases rates of secure attachment among children of mothers with depression [86]. A recent study has shown that children of mothers with depression who received CPP attained significantly higher rates of secure attachment post-intervention than children of mothers with depression who received no intervention [87]. The follow-up study with the same sample reported evidence of the long-term effect of CPP: participation in CPP is associated with increased maternal warmth and decreased child anger/behavioural problems when children are 9 years old through its effect on attachment security at 36 months [87]. These results indicate that CPP continues to have positive indirect effects on both caregivers and children as far as 6 or more years post-intervention. The longitudinal findings from the study suggest that participation in CPP may have

fostered positive maternal behaviour (i.e., maternal warmth) that improved attachment security and that this change in maternal behaviour is stable over time.

However, a pilot study conducted in 2014 did not confirm the same positive efficacy of mother-infant psychotherapy in the improvement of mother-infant interaction in the context of perinatal depression [88]. The study tested the perinatal dyadic psychotherapy (PDP), a dual-focused mother-infant intervention to prevent/decrease maternal postpartum depression and improve aspects of the mother-infant relationship related to child development. Forty-two depressed first-time mothers and their 6-week-old infants were enrolled and randomized to receive the PDP intervention or usual care. The intervention consisted of eight home-based, nurse-delivered mother-infant sessions consisting of a supportive, relationship-based, mother-infant psychotherapy and a developmentally based infant-oriented component focused on promoting positive mother-infant interactions. Results showed that depression and anxiety symptoms and diagnoses decreased significantly, and maternal self-esteem increased significantly across the study time frame. However, there were no significant differences between groups on parenting stress or mother-infant interaction at post-intervention and follow-up. Further research is needed to explore using low-intensity interventions as a first step in a stepped care approach.

24.3.2 Video Feedback Intervention

Video feedback is an effective technique used in early interventions which include video recording sessions of the mother and the baby playing together for 15–20 min [89]. Afterwards, the recorded scenes are analysed, and certain sequences are selected to work on with the mother. Video feedback technique can reveal important details of the mother-baby interaction: analysing the video recorded makes it possible to focus on specific aspects, which provides an opportunity to process and reflect on successful and difficult moments of the interaction [90]. Moreover, this allows mothers to identify emotions and reorganize their mental representations of themselves and the baby [91]. Then, with the therapist's help, these images are shown to the mother in order to foster her reflection on her baby's physical and verbal cues, as well as on her own representational models and bonding experiences [89]. According to Beebe [92], video feedback allows parents to learn about their babies' non-verbal language, thus promoting new forms of interaction. The objective is to provide parents with a new perspective on the child's non-verbal language and his/her skills and behaviours [93].

In the specific case of perinatal depression, evidence indicates that after a video feedback intervention, mothers discover a more positive image of themselves and increase their enjoyment of the time they spend with their children, which has a positive impact on their interaction [94]. A study conducted in 2015 [95] assessed a brief intervention for mother-infant dyads with mothers suffering from depressive symptomatology using the video feedback technique. The results of the intervention confirmed the effectiveness of early video feedback interventions in dyads with maternal depressive symptomatology and relationship difficulties. Results showed

a significant increase in maternal sensitivity and child cooperativeness in the intervened dyads: the mothers in the experimental group display an increased ability to read children's signals, interpret them adequately, and respond suitably and in accordance with their needs, alongside a decrease in their hostile behaviour, in terms of overt or concealed anger, which can be manifested through incongruity in maternal behaviour or direct intrusions.

In concordance to these findings, another pilot study conducted in 2020 [96] has confirmed the efficacy of video feedback technique intervention in the context of perinatal depression. The pilot study was designed to improve maternal-infant interaction, depressive symptoms, and cortisol patterns of depressed mothers and their infants. The results showed that there were significant differences favouring the group who received the intervention compared with the control group regarding the quality of maternal-infant interaction, particularly with maternal sensitivity and cognitive growth fostering activities and reduced infant diurnal cortisol. Thus, video feedback intervention appears to support improvements in interactions between depressed mothers and their infants and optimize infants' diurnal cortisol patterns.

24.3.3 Group-Based Interventions

Mother-child group therapy interventions refer to a format of the dyads taking part in a psychological intervention aimed at helping them change or deal with problems they are encountering, guided by a therapist or counsellor. The advantages of group over individual interventions include learning by observing others (i.e. vicarious learning), knowing and being comforted by the fact that others share one's difficulties, and practising in a safe environment constructive solution for interpersonal problems [97]. A recent pilot study showed the efficacy of a group-based perinatal depression intervention on depressive symptomatology, maternal-foetal attachment, and maternal sensitivity delivered with pregnant women with moderate to severe depressive symptoms. The pilot study findings provided preliminary support for the benefits of a perinatal depression intervention, delivered in a group setting, on reducing depressive symptomatology and improving maternal-foetal attachment and maternal sensitivity. Results also suggested that a group-based intervention, targeting depressive symptoms, delivered during pregnancy may have enduring effects on maternal sensitivity.

Ponteri [98] conducted a mixed-method study to investigate the effectiveness of group art therapy for depressed mothers and their children. Four mother-child pairs attended 8 weeks of 90-min group art therapy sessions. A video of 20 min of a play session was recorded to assess mother–child interaction. The findings revealed that mothers who participated in the group art therapy reported higher levels of self-esteem and a more positive self-image following treatment. Participants mentioned in their post-interview that the group art therapy helped them to recognize their strengths as a person. Group art therapy with mothers and their babies provided a safe, therapeutic forum for women to explore issues such as self-esteem, competency, and a new identity as a mother and fostered a positive social and learning

environment for the child. Thus, art therapy showed the potential for dual benefits: improving mother's self-image and decreasing of depressive symptoms and improving the quality of interactions between her and her baby.

Many mothers engage in community group activities with their babies, as they are found to be effective at relaxing mothers, providing good sources of social interaction, decreasing the monotony of each day, and a sense of personal fulfilment for mothers [99]. Specifically, there is a growing body of evidence demonstrating the effects of community group singing on both maternal and children's mental health [83, 100]. Research has demonstrated valuable benefits of singing to new-borns, such as improving mother-infant interaction and reducing infant distress [101, 102]. Listening to music during pregnancy is also associated with greater maternal wellbeing and reduced depressive symptoms in the first 3 months post-birth, while daily singing to babies is associated with fewer symptoms of depression and increased maternal wellbeing, self-esteem, and perceived mother-infant bond [103]. A study conducted in 2018 showed that new mothers involved in 10-week programme of singing group had a significantly faster decrease in their depressive symptoms compared with mothers that participated to play groups [104]. Overall, the study suggested that a programme of group singing workshops could help speed the recovery from symptoms of PND among new mothers. Based on these results with a group of 134 women, a new randomized clinical trial (SHAPER-PND[1]) aims to establish effectiveness of a 10-week singing intervention in a larger sample of 400 participants [105]. Mothers and their babies will be assigned to either a 10-week singing intervention or a 10-week active waiting-list control group, where they will be encouraged to attend community mother-baby activities. Early remission from PND has been associated with reduced effects on both mother and baby [106]. Thus, evidence that singing interventions can speed the rate of recovery in women affected by symptoms of PND could have clinical relevance.

24.4 Conclusion

It is well known that perinatal depression not only has implications for maternal mental health and wellbeing but also for decreased quality of interactions between mothers and their children, which has long been linked to negative developmental outcomes including offspring mental health. A systematic review from 2017 aimed to examine which among AND and PND treatment interventions are most efficacious in improving parenting and/or child development and underlined that, although promising findings exist for interpersonal psychotherapy, cognitive behavioural therapy, maternal child interaction guidance, and other interventions including massage and psychotherapeutic group support, it is difficult to draw any definitive conclusions regarding any one treatment that shows the most potential to influence maternal and infant outcomes [79]. Currently, there is not sufficient evidence

[1] Scaling-up Health-Arts Programmes: the largest study in the world bringing arts-based mental health interventions into a national health service.

available to make practice recommendations for a universal intervention, and further research in this area is recommended. On another note, given the evidence that perinatal depression impacts a mother's ability to properly interact with her baby, and treating maternal mood alone is not sufficient for improving mother-infant relationship difficulties, there is growing evidence demonstrating interventions that focus on addressing mother-infant interaction appear to be benefit to both mothers and their children.

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References

1. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. Obstet Gynecol. 2005;106(5 Part 1):1071–83.
2. Campbell SB, Cohn JF. The timing and chronicity of postpartum depression: implications for infant development. In: Murray L, Cooper PJ, editors. Postpartum depression and child development. Guilford Press; 1997. p. 165–97.
3. Muñoz RF, Le H-N, Ippen CG, Diaz MA, Urizar GG Jr, Soto J, Mendelson T, Delucchi K, Lieberman AF. Prevention of postpartum depression in low-income women: development of the Mamás y Bebés/mothers and babies course. Cogn Behav Pract. 2007;14(1):70–83.
4. Murray L, Cooper P. Intergenerational transmission of affective and cognitive processes associated with depression: infancy and the preschool years. In: Goodyer IM, editor. Unipolar depression: a lifespan perspective. Oxford University Press; 2003.
5. Robinson AM, Benzies KM, Cairns SL, Fung T, Tough SC. Who is distressed? A comparison of psychosocial stress in pregnancy across seven ethnicities. BMC Pregnancy Childbirth. 2016;16(1):1–11.
6. Cooper PJ, Murray L. Course and recurrence of postnatal depression: evidence for the specificity of the diagnostic concept. Br J Psychiatry. 1995;166(2):191–5.
7. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. Lancet. 2014;384(9956):1775–88.
8. Norhayati MN, Hazlina NHN, Asrenee AR, Emilin WMAW. Magnitude and risk factors for postpartum symptoms: a literature review. J Affect Disord. 2015;175:34–52.
9. Verreault N, Da Costa D, Marchand A, Ireland K, Dritsa M, Khalifé S. Rates and risk factors associated with depressive symptoms during pregnancy and with postpartum onset. J Psychosom Obstet Gynecol. 2014;35(3):84–91.
10. Murray L, Fearon P, Cooper P. Postnatal depression, mother-infant interactions, and child development: prospects for screening and treatment. In: Identifying perinatal depression and anxiety: evidence-based practice in screening, psychosocial assessment, and management. Wiley-Blackwell; 2015. p. 139–64.
11. Sichel D. Postpartum psychiatric disorders. In: Dunitz M, editor. Mood disorders in women; 2000. p. 313–28.
12. Stein A, Gath DH, Bucher J, Bond A, Day A, Cooper PJ. The relationship between post-natal depression and mother–child interaction. Br J Psychiatry. 1991;158(1):46–52.
13. Murray L, Stein A. 13 The effects of postnatal depression on the infant. Baillieres Clin Obstet Gynaecol. 1989;3(4):921–33.

14. Marmorstein NR, Malone SM, Iacono WG. Psychiatric disorders among offspring of depressed mothers: associations with paternal psychopathology. Am J Psychiatr. 2004;161(9):1588–94.
15. Cataudella S, Lampis J, Busonera A, Marino L, Zavattini GC (2016) From parental-fetal attachment to a parent-infant relationship: a systematic review about prenatal protective and risk factors.
16. Hazell Raine K, Nath S, Howard LM, Cockshaw W, Boyce P, Sawyer E, Thorpe K. Associations between prenatal maternal mental health indices and mother–infant relationship quality 6 to 18 months' postpartum: a systematic review. Infant Ment Health J. 2020;41(1):24–39.
17. Smorti M, Ponti L, Tani F. Maternal depressive symptomatology during pregnancy is a risk factor affecting newborn's health: a longitudinal study. J Reprod Infant Psychol. 2019;37(4):444–52.
18. Goodman JH. Perinatal depression and infant mental health. Arch Psychiatr Nurs. 2019;33(3):217–24.
19. Waters CS, Hay DF, Simmonds JR, van Goozen SHM. Antenatal depression and children's developmental outcomes: potential mechanisms and treatment options. Eur Child Adolesc Psychiatry. 2014;23(10):957–71.
20. Taka-Eilola T, Veijola J, Murray GK, Koskela J, Mäki P. Severe mood disorders and schizophrenia in the adult offspring of antenatally depressed mothers in the Northern Finland 1966 Birth Cohort: relationship to parental severe mental disorder. J Affect Disord. 2019;249:63–72.
21. Field T. Maternal depression effects on infants and early interventions. Prev Med. 1998;27(2):200–3.
22. Field T, Healy BT, Goldstein S, Guthertz M. Behavior-state matching and synchrony in mother-infant interactions of nondepressed versus depressed dyads. Dev Psychol. 1990;26(1):7.
23. Jones NA, Field T, Hart S, Lundy B, Davalos M. Maternal self-perceptions and reactions to infant crying among intrusive and withdrawn depressed mothers. Infant Mental Health J. 2001;22(5):576–86.
24. Murray L, Fiori-Cowley A, Hooper R, Cooper P. The impact of postnatal depression and associated adversity on early mother-infant interactions and later infant outcome. Child Dev. 1996;67(5):2512–26.
25. Campbell SB, Brownell CA, Hungerford A, Spieker SJ, Mohan R, Blessing JS. The course of maternal depressive symptoms and maternal sensitivity as predictors of attachment security at 36 months. Dev Psychopathol. 2004;16(2):231–52.
26. DeKlyen M, Greenberg MT. Attachment and psychopathology in childhood. In: Handbook of attachment: theory, research, and clinical applications. The Guilford Press; 2008. p. 637–65.
27. Forman DR, O'hara MW, Stuart S, Gorman LL, Larsen KE, Coy KC. Effective treatment for postpartum depression is not sufficient to improve the developing mother–child relationship. Dev Psychopathol. 2007;19(2):585–602.
28. Klier CM. Mother–infant bonding disorders in patients with postnatal depression: the postpartum bonding questionnaire in clinical practice. Arch Womens Ment Health. 2006;9(5):289–91.
29. Pawlby S, Fernyhough C, Meins E, Pariante CM, Seneviratne G, Bentall RP. Mind-mindedness and maternal responsiveness in infant–mother interactions in mothers with severe mental illness. Psychol Med. 2010;40(11):1861–9.
30. Murray L. Effects of postnatal depression on infant development: direct studies of early mother-infant interactions. In: Kumar R, Brockington I, editors. Motherhood and mental illness, vol. 2. Butterworths; 1988. p. 159–90.
31. Bowlby J. Attachment and loss: retrospect and prospect. Am J Orthopsychiatry. 1982;52(4):664.
32. Waters E, Cummings EM. A secure base from which to explore close relationships. Child Dev. 2000;71(1):164–72.
33. Benoit D. Infant-parent attachment: definition, types, antecedents, measurement and outcome. Paediatr Child Health. 2004;9(8):541–5.
34. Rutter M, Quinton D. Parental psychiatric disorder: effects on children. Psychol Med. 1984;14(4):853–80.

35. Lyons-Ruth K, Zoll D, Connell D, Grunebaum HU. The depressed mother and her one-year-old infant: environment, interaction, attachment, and infant development. In: Tronick EZ, editor. Maternal depression and infant disturbance. New directions for child development: Jossey-Bass; 1986.
36. Murray L. The impact of postnatal depression on infant development. Child Psychol Psychiatry Allied Discipl. 1992;
37. Teti DM, Gelfand DM, Messinger DS, Isabella R. Maternal depression and the quality of early attachment: an examination of infants, preschoolers, and their mothers. Dev Psychol. 1995;31(3):364.
38. Ainsworth MD, Wittig BA. Attachment and exploratory behaviour in one-year-olds in a strange situation. In: Floss BM, editor. Determinants of infant behaviour. London: Methuen; 1969.
39. Radke-Yarrow M, Cummings EM, Kuczynski L, Chapman M. Patterns of attachment in two- and three-year-olds in normal families and families with parental depression. Child Dev. 1985:884–93.
40. Fonagy P, Gergely G, Jurist EL. Affect regulation, mentalization and the development of the self. Routledge; 2018.
41. Fonagy P. Mentalizing in practice. In: Allen JG, Fonagy P, editors. Handbook of mentalization-based treatment. John Wiley & Sons; 2006. p. 3–30.
42. Fischer-Kern M, Tmej A. Mentalization and depression: theoretical concepts, treatment approaches and empirical studies—an overview. Z Psychosom Med Psychother. 2019;65(2):162–77.
43. Bateman AW, Fonagy PE. Mentalizing and borderline personality disorder. In: Allen G, Fonagy P, editors. Handbook of mentalizing in mental health practice. John Wiley & Sons; 2006. p. 185–200.
44. Sharp C, Fonagy P, Goodyer IM. Imagining your child's mind: psychosocial adjustment and mothers' ability to predict their children's attributional response styles. Br J Dev Psychol. 2006;24(1):197–214.
45. Slade A. Parental reflective functioning: an introduction. Attach Hum Dev. 2005;7(3):269–81.
46. Sharp C, Fonagy P. The parent's capacity to treat the child as a psychological agent: Constructs, measures and implications for developmental psychopathology. Soc Dev. 2008;17(3):737–54.
47. Bateman A, Fonagy P. Mentalizing in mental health practice. In: Bateman P, Fonagy A, editors. Handbook of mentalizing in mental health practice. Arlington, VA: American Psychiatric Publishing Inc.; 2012. p. 3–42.
48. Murray L, Kempton C, Woolgar M, Hooper R. Depressed mothers' speech to their infants and its relation to infant gender and cognitive development. J Child Psychol Psychiatry. 1993;34(7):1083–101.
49. Herrera E, Reissland N, Shepherd J. Maternal touch and maternal child-directed speech: effects of depressed mood in the postnatal period. J Affect Disord. 2004;81(1):29–39.
50. Vliegen N, Casalin S, Luyten P. The course of postpartum depression: a review of longitudinal studies. Harv Rev Psychiatry. 2014;22(1):1–22.
51. Sethna V, Murray L, Ramchandani PG. Depressed fathers' speech to their 3-month-old infants: a study of cognitive and mentalizing features in paternal speech. Psychol Med. 2012;42(11):2361–71.
52. Levy DW, Truman S. Reflective functioning as mediator between drug use, parenting stress and child behavior. College on Problems of Drug Dependence Annual Meeting, Quebec, 2002.
53. De Wolff MS, Van Ijzendoorn MH. Sensitivity and attachment: a meta-analysis on parental antecedents of infant attachment. Child Dev. 1997;68(4):571–91.
54. Shin H, Park Y, Ryu H, Seomun G. Maternal sensitivity: a concept analysis. J Adv Nurs. 2008;64(3):304–14.
55. Crittenden PM, Bonvillian JD. The relationship between maternal risk status and maternal sensitivity. Am J Orthopsychiatry. 1984;54(2):250.

56. Drake EE, Humenick SS, Amankwaa L, Younger J, Roux G. Predictors of maternal responsiveness. J Nurs Scholarsh. 2007;39(2):119–25.
57. Meins E, Fernyhough C, Fradley E, Tuckey M. Rethinking maternal sensitivity: mothers' comments on infants' mental processes predict security of attachment at 12 months. J Child Psychol Psychiatry. 2001;42(5):637–48.
58. Bind RH, Biaggi A, Bairead A, Du Preez A, Hazelgrove K, Waites F, Conroy S, Dazzan P, Osborne S, Pawlby S, Sethna V, Pariante C. Mother-infant interaction in women depressed in pregnancy and in women with a history of depression in the Psychiatry Research and Motherhood – Depression (PRAM-D) study. BJPsych Open; 2021. In Press
59. Lefkovics E, Baji I, Rigó J. Impact of maternal depression on pregnancies and on early attachment. Infant Ment Health J. 2014;35(4):354–65.
60. Parsons CE, Young KS, Rochat TJ, Kringelbach ML, Stein A. Postnatal depression and its effects on child development: a review of evidence from low-and middle-income countries. Br Med Bull. 2012;101(1):57–79.
61. Girgus JS, Nolen-Hoeksema S. Cognition and depression. In: Keys CLM, Goodman SH, editors. Women and depression: a handbook for the social, behavioral, and biomedical sciences. Cambridge University Press; 2006.
62. Cicchetti D. Developmental psychology. In: Lamb RMME, Freund AM, Lerner M, editors. The handbook of life-span development, Social and emotional development, vol. 2. Hoboken, NJ: John Wiley & Sons Inc.; 2010. p. 511–89.
63. Dix T, Moed A, Anderson ER. Mothers' depressive symptoms predict both increased and reduced negative reactivity: aversion sensitivity and the regulation of emotion. Psychol Sci. 2014;25(7):1353–61.
64. Giallo R, Cooklin A, Wade C, D'Esposito F, Nicholson JM. Maternal postnatal mental health and later emotional–behavioural development of children: the mediating role of parenting behaviour. Child Care Health Dev. 2014;40(3):327–36.
65. Jensen SKG, Dumontheil I, Barker ED. Developmental inter-relations between early maternal depression, contextual risks, and interpersonal stress, and their effect on later child cognitive functioning. Depress Anxiety. 2014;31(7):599–607.
66. Pearson RM, Evans J, Kounali D, Lewis G, Heron J, Ramchandani PG, O'Connor TG, Stein A. Maternal depression during pregnancy and the postnatal period: risks and possible mechanisms for offspring depression at age 18 years. JAMA Psychiatry. 2013;70(12):1312–9.
67. Goodman JH. Women's attitudes, preferences, and perceived barriers to treatment for perinatal depression. Birth. 2009;36(1):60–9.
68. Pennebaker JW, Susman JR. Disclosure of traumas and psychosomatic processes. Soc Sci Med. 1988;26(3):327–32.
69. Rebecchini, L. (2019). Using expressive writing to cope with childbirth. https://www.inspirethemind.org/blog/2019/06/26/using-expressive-writing-to-cope-with-the-childbirth?rq=lavinia.
70. Kopelman RC, Moel J, Mertens C, Stuart S, Arndt S, O'Hara MW. Barriers to care for antenatal depression. Psychiatr Serv. 2008;59(4):429–32.
71. Tronick E, Reck C. Infants of depressed mothers. Harv Rev Psychiatry. 2009;17(2):147–56.
72. Tronick EZ, Weinberg MK. Depressed mothers and infants: failure to form dyadic states of consciousness. In: Murray CP, editor. Postpartum depression and child development. Guilford Press; 1997. p. 54–81.
73. Murray L, Cooper PJ. Postpartum depression and child development. Psychol Med. 1997;27(2):253–60.
74. Milgrom J, McCloud P. Parenting stress and postnatal depression. Stress Med. 1996;12(3):177–86.
75. Kopelman R, Stuart S. Psychological treatments for postpartum depression. NJ: SLACK Incorporated Thorofare; 2005.
76. DeRubeis RJ, Hollon SD, Amsterdam JD, Shelton RC, Young PR, Salomon RM, O'Reardon JP, Lovett ML, Gladis MM, Brown LL. Cognitive therapy vs medications in the treatment of moderate to severe depression. Arch Gen Psychiatry. 2005;62(4):409–16.

77. Cooper PJ, Murray L, Wilson A, Romaniuk H. Controlled trial of the short-and long-term effect of psychological treatment of post-partum depression: I. Impact on maternal mood. Br J Psychiatry. 2003;182(5):412–9.
78. Field T. Postpartum depression effects on early interactions, parenting, and safety practices: a review. Infant Behav Dev. 2010;33(1):1–6.
79. Letourneau NL, Dennis C, Cosic N, Linder J. The effect of perinatal depression treatment for mothers on parenting and child development: a systematic review. Depress Anxiety. 2017;34(10):928–66.
80. Muzik M, Marcus SM, Flynn HA. Psychotherapeutic treatment options for perinatal depression: emphasis on maternal-infant dyadic outcomes. J Clin Psychiatry. 2009;70(9):1318–9.
81. Cohen NJ, Muir E, Lojkasek M, Muir R, Parker CJ, Barwick M, Brown M. Watch, wait, and wonder: testing the effectiveness of a new approach to mother–infant psychotherapy. Infant Mental Health J. 1999;20(4):429–51.
82. Fraiberg S, Adelson E, S. V. A psychoanalytic approach to the problems of impaired infant-mother relationships. In: Fraiberg L, editor. Selected writings of Selma Fraiberg. Ohio State University Press; 1987. p. 100–36.
83. Nylen KJ, Moran TE, Franklin CL, O'hara, M. W. Maternal depression: a review of relevant treatment approaches for mothers and infants. Infant Ment Health J. 2006;27(4):327–43.
84. Poobalan AS, Aucott LS, Ross L, Smith WCS, Helms PJ, Williams JHG. Effects of treating postnatal depression on mother-infant interaction and child development: systematic review. Br J Psychiatry. 2007;191(5):378–86.
85. Guild DJ, Alto ME, Handley ED, Rogosch F, Cicchetti D, Toth SL. Attachment and affect between mothers with depression and their children: longitudinal outcomes of child parent psychotherapy. Res Child Adolesc Psychopathol. 2021:1–15.
86. Cicchetti D, Rogosch FA, Toth SL. The efficacy of toddler-parent psychotherapy for fostering cognitive development in offspring of depressed mothers. J Abnorm Child Psychol. 2000;28(2):135–48.
87. Toth SL, Rogosch FA, Manly JT, Cicchetti D. The efficacy of toddler-parent psychotherapy to reorganize attachment in the young offspring of mothers with major depressive disorder: a randomized preventive trial. J Consult Clin Psychol. 2006;74(6):1006.
88. Goodman JH, Prager J, Goldstein R, Freeman M. Perinatal dyadic psychotherapy for postpartum depression: a randomized controlled pilot trial. Arch Womens Ment Health. 2015;18(3):493–506.
89. Rusconi-Serpa S, Rossignol AS, McDonough SC. Video feedback in parent-infant treatments. Child Adolesc Psychiatric Clin. 2009;18(3):735–51.
90. Fonagy P. Affect regulation, mentalization, and the development of the self, vol. 2002. New York (Other Press); 2002.
91. Beebe B. Brief mother–infant treatment: psychoanalytically informed video feedback. Infant Mental Health J. 2003;24(1):24–52.
92. Beebe B. My journey in infant research and psychoanalysis: microanalysis, a social microscope. Psychoanal Psychol. 2014;31(1):4.
93. Beebe B. Mother–infant research informs mother–infant treatment. Clin Soc Work J. 2010;38(1):17–36.
94. Vik K, Braten S. Video interaction guidance inviting transcendence of postpartum depressed mothers' self-centered state and holding behavior. Infant Ment Health J. 2009;30(3):287–300.
95. Olhaberry M, León MJ, Seguel M, Mena C. Video-feedback intervention in mother-baby dyads with depressive symptomatology and relationship difficulties. Res Psychother: Psychopathol Process Outcome. 2015;
96. Tryphonopoulos PD, Letourneau N. Promising results from a video-feedback interaction guidance intervention for improving maternal–infant interaction quality of depressed mothers: a feasibility pilot study. Can J Nurs Res. 2020;52(2):74–87.
97. Gidron Y. Group therapy/intervention. In: Gellman MD, Turner JR, editors. Encyclopedia of behavioral medicine. Springer; 2013.

98. Ponteri AK. The effect of group art therapy on depressed mothers and their children. Art Ther. 2001;18(3):148–57.
99. Gelfand DM, Teti DM, Seiner SA, Jameson PB. Helping mothers fight depression: evaluation of a home-based intervention program for depressed mothers and their infants. J Clin Child Psychol. 1996;25(4):406–22.
100. Clift S, Morrison I. Group singing fosters mental health and wellbeing: findings from the East Kent "singing for health" network project. Ment Health Soc Incl. 2011;
101. Coulton S, Clift S, Skingley A, Rodriguez J. Effectiveness and cost-effectiveness of community singing on mental health-related quality of life of older people: randomised controlled trial. Br J Psychiatry. 2015;207(3):250–5.
102. Nakata T, Trehub SE. Infants' responsiveness to maternal speech and singing. Infant Behav Dev. 2004;27(4):455–64.
103. Vlismas W, Malloch S, Burnham D. The effects of music and movement on mother–infant interactions. Early Child Dev Care. 2013;183(11):1669–88.
104. Fancourt D, Perkins R. Effect of singing interventions on symptoms of postnatal depression: three-arm randomised controlled trial. Br J Psychiatry. 2018;212(2):119–21.
105. Estevao C, Fancourt D, Dazzan P, Chaudhuri KR, Sevdalis N, Woods A, Crane N, Bind R, Sawyer K, Rebecchini L, Hazelgrove K, Manoharan M, Burton A, Dye H, Osborn T, Jarrett L, Ward N, Jones F, Podlewska A, et al. Scaling-up Health-Arts Programmes: the largest study in the world bringing arts-based mental health interventions into a national health service. BJ Psych Bull. 2021;45(1):32–9. https://doi.org/10.1192/bjb.2020.122.
106. Harris B, Huckle P, Thomas R, Johns S, Fung H. The use of rating scales to identify postnatal depression. Br J Psychiatry. 1989;154(6):813–7.

Part III

Research and Peripartum

Research Topics in Perinatal Mental Health: The Current State of the Art

25

Carlotta Cogoni, Valeria Brenna, Alessandra Bramante, and Mauro Percudani

25.1 Introduction

Perinatal mental health is a relatively new area of knowledge developed in recent decades. The Perinatal Section of the UK's Royal College of Psychiatrists, for example, emerged in 1996 and became a faculty in June 2014 [1].

Perinatal period was traditionally considered as a period of well-being for women, in general, and a period of relative stability for those suffering from mental disorders, but evidence has shown that mental disorders occurring in pregnancy and postnatal period are far from uncommon. The repercussions are evident both in the field of diagnosis and treatment: the consequences of unaddressed perinatal mental illnesses can be acute and chronic, with suicide remaining the leading cause of indirect maternal mortality [2].

Yet the specificity of the perinatal mental area remains controversial. The question concerns whether these disorders are unique in regard to causes and psychopathology or the same as mental disorders occurring during other periods in life [3].

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Initially, the focus was on the postpartum period, but now it has been expanded to include not only diverse clinical conditions (i.e., postpartum psychosis, OCD, bonding disorders among others) but also the period of pregnancy, given the infant's risks of developing pathologies from exposure to the mother's illness. However, treatment of psychiatric disorders in women during the reproductive years is complex because a pharmacological treatment exposes a developing child to the mother's medications, and it has to adjust to the significant hormonal shifts women experience during their lifetime. The perinatal research perspective is increasingly complex, and it is moving toward reproductive psychiatry which is focused on the psychiatric disorders' treatments during reproductive years [4].

Drawing conclusions from the sparse available evidence is not an easy task, especially for clinicians. Communication between researchers and clinicians is pivotal for the latter to identify women at risk of developing illnesses and help them to make adequate treatment choices.

25.2 A Little History

In a position paper on mother-infant mental health, Brockington et al. [5] trace the origin of this field back to three important personalities. One of them is Jean-Étienne-Dominique Esquirol [6], a French physician, who dealt with mental illnesses and who painstakingly described the conditions of women admitted to the Salpêtrière Hospital in Paris, immediately after giving birth.

The first systematic description of mental illness occurring in the perinatal period, the "Treatise on Insanity in Pregnant, Postpartum, and Lactating Women," was written by Louis Victor Marcé [7]. He was the first to suggest that the physiological changes of the puerperium might influence the mental functioning of the mother. His pioneering single case studies in pregnancy and after childbirth amassed detailed information regarding the patient's family history, psychological elements, social circumstances, and medical assessments. The first international scientific society, dedicated to perinatal mental health, recognizes his central role and names after Marcé.

Finally, Ambroise Tardieu [8] is remembered for the great attention he paid, as a criminologist, to the phenomenon of child abuse, of which he described many cases and their effects.

25.3 From an Atypical Depression to the Postnatal Triad

In the 1970s Brice Pitt [9] found a significant disparity in perinatal hospitalizations between men and women, an increase in female hospitalizations in the 3 months after childbirth, a lower level of well-being in the children of mothers with postnatal depression, and a condition of mild, transient mood swings in the immediate postnatal period, seen as a frequent occurrence. He described an atypical postnatal depression that differed from the classic ones for the presence of great anxiety, irritability, a feeling of inability, and increased suffering at the end of the day. Meanwhile, in the USA, the focus was on the phenomenon of infanticide: Resnick [10] coined the term neonaticide to describe the murder of an infant within the first

24 hours of life. He made a review [11] of the world psychiatric literature on maternal filicide and found filicidal mothers to have frequent depression, psychosis, prior mental health treatment, and suicidal thoughts.

The foundation of the International Marcé Society for Perinatal Mental Health [12] marked another important step. It was formed at an international conference in 1980 and brought together high-profile perinatal personalities, including Ian Brockington, Channi Kumar, James Hamilton, Ralph Paffenbarger, George Winokur, and Robert Kendell. Its purpose was to establish a forum to discuss puerperal mental illness in its broadest sense and to create a multidisciplinary community that supports the aim of the society [13].

In the USA, O'Hara [14] conceptualized the psychopathology in the perinatal period as the triad of maternity blues, postpartum depression, and puerperal psychosis. The mild affective anguish after childbirth was regarded as common and generally explained by the variations in hormone levels. Postpartum depression (which appeared to resemble depression occurring at other moments in life) lasted for several months and impaired the woman's ability to function. Postpartum psychosis was considered the rarest but highly disabling disorder. Differential levels of treatment were proposed, from an inpatient basis to mild support.

All these studies pointed to the existence of widespread distress in the postpartum period, but the results of all these investigations were difficult to compare due to the lack of common instruments.

It was 1987 when John Cox, Jenifer Holden, and Ruth Sagovsky [15] developed a 10-item self-report scale, the Edinburgh Postnatal Depression Scale (EPDS), to assist health professionals in detecting mothers suffering from postnatal depression. The EPDS was found to have satisfactory sensitivity and specificity and was also sensitive to change in the severity of symptoms over time. It has been translated into over 60 languages and validated in most counties. EPDS has provided a common language for clinicians and researchers, but some precautions must be considered in its use. EPDS is not a diagnostic panacea for detecting all disorders occurring in the perinatal period [16].

25.4 Beyond Postpartum Depression

In the 1990s, the availability of standardized tools has refreshed research in the area with important contributions. For example, qualitative studies were conducted to find perspectives involved in postpartum depression [17]. The strand of risk factors began to emerge, and the study of pregnant women revealed that the strongest predictors of postpartum depression were history of psychopathology and distress during pregnancy, poor marital relationship, stressful life events, and low social support [18, 19].

The more in-depth study of the perinatal period and the emergence of its specificity leads to the exploration of other clinical manifestations. Alongside anxiety [20–22] and obsessive-compulsive disorders [23, 24], studies on puerperal psychosis increased [25, 26], as well as on bonding disorders [27–29]. Also, the transcultural approach began to emerge as a unique opportunity to test hypotheses about social and cultural contributions to the etiology of psychotic and non-psychotic reactions to childbirth, but also to study how social factors can influence the evolution of psychopathology [30].

These are also the years when "a wealth of knowledge has accumulated in literature of many lands," leading to the publication of *Motherhood and Mental Health* [27], a landmark of perinatal mental health research, where Prof. Ian Brockington reviewed and made available research and clinical cases, from infertility to infanticide.

25.5 Psychological Treatment

In terms of treatment options, perinatal research has focused on pharmacotherapy and psychological interventions. The prominent concern examining the use of drugs in the perinatal period covered both pregnancy and lactation periods [31, 32]. Regarding psychological treatments, cognitive-behavioral and interpersonal models have been explored in the perinatal setting. An Australian group, headed by Prof. Jeanette Milgrom, began experimenting with the principles of Beck's cognitive therapy for depression, adapting it to the perinatal period based on available research [33]. Results were encouraging, hinting that a group program was an effective treatment for depression in the postpartum period and resulted in the world's best-known manualized treatment [34]. Margaret Spinelli has adapted Klerman and Weissman's interpersonal psychotherapy to antenatal depression [35], and several clinical trials [36–38] have demonstrated its efficacy for postpartum depression.

Flexibility in the delivery of interventions seems to be crucial to address maternal problems: telephone-based peer support has been evaluated and was effective and highly accepted in decreasing depressive symptomatology among new mothers [39]. Also, Internet-based support has been increasingly implemented and seems very suitable to overcome main barriers to treatment, stigma, and lack of services. Milgrom and colleagues have developed an online cognitive-behavioral therapy intervention – MumMoodBooster [40]—for treating postnatal depression. It is an adapted form of the *Getting Ahead of Postnatal Depression treatment program* [33, 34], and it allows individuals to customize their own intervention. On top of emergency treatments, the efficacy of various approaches to guarantee a prolonged alleviation of mental health symptoms should be investigated. Experimental research is exploring the use of user-friendly technologies like smartphone-based intervention for this purpose, with some already succeeding in reducing postnatal depression [41]. However, in the aforementioned case, the efficacy of the intervention had been checked only up until 4 weeks postpartum, which represents a short postpartum period.

Specific treatments are required to focus on bonding disorders: they have the aim to promote the relationship between mother and infant through behavioral training implying a physical contact (i.e., a massage to the baby) and via video feedback interventions [42, 43]. A study using video feedback intervention [44] showed how maternal bonding was increased among healthy women. This particularly effective technique has been also used with women with severe psychiatric symptomatology and relationship disorders and has shown to be effective in improving sensitivity, cooperativeness, and responsiveness in the dyads [45].

25.6 Into the New Millennium

The new millennium has dawned with the foundation of *Beyond blue*, an independent, not-for-profit national initiative funded by the Commonwealth and Victorian State governments. This experience brought together perinatal mental health experts from all the territory, established the National Postnatal Depression Program, and implemented screening and early intervention programs for perinatal depression. Over 5 years, 160,000 women and many health professionals were involved. A National Action Plan was formulated with recommendations about the operational resources and political structures essential for the implementation of perinatal screening, psychosocial assessment, training and staff development for healthcare professionals, and the delivery of quality pathways to care. It supported the development of the first Australian Clinical Practice Guidelines for Depression and Related Disorders in the Perinatal Period—they were updated in 2017 [46] which played a central role in directing best practice for universal screening and pathways to care to reduce maternal mental health morbidity.

Prevention seems to be the preferred route, and its effectiveness is facilitated by the fact that pregnant women seem to be highly motivated to take care of all aspects that may concern their children [43] and by an antenatal screening of specific anxiety diagnoses, for example [47].

A paradigm shift, consistent with clinical and empirical evidence, has included fathers in perinatal assessment. From a focus on women after childbirth and women with pre-existing psychiatric disorders, it has expanded to a broader family perspective. Taking into account the fathering role and the perinatal paternal mental illness is part of the preventive approach: fathers can not only experience distress after the birth of their child like mothers do, but such distress has been strongly linked to maternal depression and child outcomes [48].

25.7 Innovation and Future Perspective in Research

25.7.1 The Biomarkers of Postpartum Depression and Psychosis

During the last decades, rather than investigating the underlying causes of perinatal disorders, researchers have begun to investigate disorder's predictive factors, with a specific focus on biomarkers [49]. A biomarker has been defined as a measured indicator of normal biological processes able to predict specific clinical outcomes [50].

Several biomarkers have been proposed as useful identifiers for patients at risk for perinatal mental disorders: genetic, epigenetic, neuroendocrine, and neuroinflammatory. However, this section will focus only on biomarkers implicated specifically in recent perinatal disorders research, and we do not intend to provide an extensive literature review of all of them.

25.7.1.1 Endocrinological and Immunological Markers

The most recent biomarkers discoveries regard two main disorders of the perinatal area: puerperal psychosis (PP) and the postpartum depression (PPD).

Puerperal psychosis, often referred to as postpartum psychosis (PPP), is a disabling psychiatric disorder that occurs in the first few weeks after delivery [26]. It is considered a rare condition with an incidence of 1–2 every 1000 childbearing women [51], with potentially devastating consequences for both mother and child. The symptoms include paranoid delusions, hallucinations, confused thinking, and/or mood swings (depression, mania, or a combination of both), which increase the risk for maternal suicide and infanticide [52]. Due to an abrupt onset of psychotic symptoms often in women that do not have a previous history of mental disorders [53, 54] and its progressive course, this disease is approached as an emergency [55].

The etiopathology of PPP is still unknown, but several risk factors have been identified. The risk of developing PPP significantly increases with a personal or familiar history of bipolar disorder, as well as a prior episode of PPP [56]. Even though 40–50% of PPP cases appear to cluster within families [52, 56], it has been equally found in primiparous women without a previous personal or familial psychiatric history [54]. Hence, it is necessary to understand why only some women develop PPP while others do not. Because the PPP incidence rate is similar across countries and cultures [57], the hypothesis that biological factors could crucially influence the susceptibility to the disease cannot be excluded. While several psychosocial risks for PPP have been identified, the biological contributors are assuming increasing roles as potential determinants in the etiology of PPP [58].

Stress response abnormalities are important risk factors for psychosis, and they could also be a pathophysiological mechanism in the onset of PPP in vulnerable women. To identify the women that are most at risk of developing the PPP, the experimental research has been recently focusing on the investigation of the biological response to stress with the two main stress-response systems of the body, the hypothalamic-pituitary-adrenal (HPA) axis and the immune system. The HPA axis dysfunction may alter the response to stressful events (i.e., environmental factors) for some individuals, facilitating the occurrence of psychotic events, as suggested by the vulnerability-stress model [59]. Importantly, stress-related illnesses are thought to be caused by an upregulation of the stress hormone system, i.e., the HPA, as well as the inflammatory arm of the immune system [60].

The HPA activity is usually estimated from salivary samples by measuring the cortisol fluctuations at several time points during the day. On the other hand, the immune markers can be evaluated from peripheral blood samples, and they include high sensitivity C-reactive protein (hs-CRP), interleukin (IL)-1a, IL-1b, IL-2, IL-4, IL-6, IL-8, IL-10, tumor necrosis factor (TNFa), vascular endothelial growth factor (VEGF), interferon-gamma (INFγ), monocyte chemoattractant protein 1 (MCP-1), and epidermal growth factor (EGF) [61].

Corroborating evidence, even if not directly related to the perinatal research, can support the interplay between the stress hormone system and the inflammatory one in PPP. First, C-reactive protein (CRP) and IL-6 levels might play a role in the pathophysiology of depression [62, 63], and stressful events have been shown to

impair response to antidepressants via HPA axis and immune system activation [64]. Second, an HPA axis dysfunction can be present in the illness onset stage in patients with first-episode psychosis [65], pointing at the possibility of its role in preceding the symptoms' onset. Third, first-episode psychoses are characterized, together with HPA axis abnormalities [66], by dysfunction of the immune system, evidenced by increased inflammatory markers (i.e., three proinflammatory (hs-CRP, TNFa, lL-6) and one anti-inflammatory cytokine (IL-4)) [67, 68]. Fourth, the concomitant activation of the immune system together with an inability to suppress the HPA axis has been linked to antenatal and postnatal depression not related to the puerperium [69, 70].

Research on the PPP is a growing field and presents significant challenges, given that the HPA axis is normally suppressed from pregnancy to the postpartum period. Nevertheless, promising preliminary evidence points toward a possible immune-HPA system dysregulation in women with PPP. For instance, PPP women showed an upregulation of the immune system-related gene expression profile and a reduced T cell elevation which is usually characteristic in the postpartum period [71, 72]. In addition, it has been recently found that IL- 6 is elevated in women with PPP [73]. These findings are in line with a recent report of immune system anomalies, such as the elevated levels of hs-CRP, observed in women with PPP [61]. Given that high cortisol is responsible for downregulating the immune system, but women with PPP have elevated hs-CRP in conjunction with elevated cortisol levels, these results might indicate that PPP women present steroid resistance. In other words, their cortisol levels are not able to decrease the immune response. Subsequently, the PPP onset might be triggered by an imbalance between proinflammatory and immunosuppressive cells in the postpartum period [74], possibly because of their interaction with several neuroendocrine pathways [75]. It is worth noting that cytokines communicate information regarding immune activity to the brain and neuroendocrine system [76]. However, the exact biological mechanisms mediating the onset of PPP after the immune system dysregulation remain unclear. Research in this direction would point to the use of pharmacological interventions targeting the HPA axis and the immune system to reduce the risk of PPP in vulnerable women.

An interplay of the stress hormone and the inflammatory systems could be also hypothesized to contribute to the development of the PPD. This is derived from the evidence that the hypothalamic-pituitary-adrenal dysregulation, genetic vulnerability, and inflammatory processes represent major biological predictors of major depression [77].

With regard to the PPD, a psychoneuroimmunology model has been hypothesized to explain the role of immune system alterations (i.e., through micronutrient deficiencies) in contributing to PPD onset [78]. Firstly, prolonged or excessive proinflammatory immune system activation (IL-1, IL-6, and TNF-α) has been established as one of the mechanisms involved in perinatal depressive episodes [79], but also in postpartum depressive episodes [80]. Secondly, a dysfunctional HPA axis, as indicated by high levels of cortisol, has been frequently found in pregnant women affected by MDD [81]. Furthermore, different findings seem to agree on the role of

IL-6 as a reliable and useful biomarker of risk in perinatal depression (see [82] for a review).

Altogether, the above evidence points to the concomitant role of the HPA axis and inflammatory system as biomarkers of the PPP and PPD. However, further research should explore their separate and conjunct role in the development of perinatal disorders.

25.7.1.2 Epigenetic Biomarkers

Pioneering research has been conducted to develop PPD prediction models able to identify pregnant women at risk of PPD [83]. Biomarkers such as DNA methylation of the TC9B and HP1BP3 genes can predict which women will develop PPD with ~80% accuracy. The analysis can be done on data derived from a simple blood test. If conducted during pregnancy, it would potentially allow for early intervention with appropriate psychological and psychiatric treatment in the postpartum period.

25.7.1.3 Microbiota

Current research focuses on the poorly understood microbiota-gut-brain axis, a bidirectional communication between the microbiota (i.e., bacteria, viruses, fungi present in the intestine) and the brain [84, 85]. This relationship is critically mediated by stress responses. Specifically, stress may lead to a deviation of the microbial composition causing microbial dysbiosis [84, 86]. Dysbiosis is in turn associated with psychological disorders such as anxiety and MDD [85, 87]. The microbiota investigation is extremely important in the understanding of the development of depression and anxiety mood disorders during pregnancy and the postpartum period. This is because the interrelationship of the immune system, microbiota, and neuroendocrine system potentially induces or exacerbates perinatal mental illness. Although research in this area has focused on identifying microbiota's compositional differences in clinical as compared to healthy perinatal populations, investigating the basis of these differences represents the next step in this fast-moving area of biomarker research. In line with this, a correlation between gut microbiota and PPD has been recently shown [88]. Specifically, *Faecalibacterium*, *Phascolarctobacterium*, and *Butyricicoccus* were found to be significantly lower in patients with PPD as compared to the healthy controls. In addition, antenatal depression was recently found to be associated with altered gut microbial (i.e., enriched *Paraprevotella* and depleted *Faecalibacterium* and *Lactobacillus* in women with antenatal depression vs controls) and immune system, revealing its usefulness in detecting antenatal depression in clinical settings [89]. This was further supported by finding that administration of probiotic *Lactobacillus rhamnosus* HN001 vs placebo during perinatal (i.e., from early pregnancy to 6 months after delivery) resulted in improved depression and anxiety symptoms [90].

These results are not conclusive but indicate that research on the microbiota-gut-brain axis in perinatal mental disorder is still germinal but worth to be explored. Early identification of gut microbiota-based biomarkers (such as bacterial communities) will lead to not only identifying women at risk but also sharpening the diagnostic criteria, in the spirit of precision medicine approach [91].

In summary, deepening the understanding of the etiology, development, and management of maternal distress is an urgent need and should be a priority in the nearest future. The association between maternal stress and mental disorders to alterations of microbiota and in utero neurodevelopment may explain the transmission of maternal mental illness to following generations (see the section "Offspring outcomes"). Therefore, an evaluation of the clinical utility of perinatal disorder biomarkers is fundamental to reduce treatment latency.

25.7.2 Perinatal Disorders Influence Offspring Outcomes: Several Methodologies

Mental disorders during the perinatal period are associated with an increased risk of psychological and neurodevelopmental disturbances in children at different ages [23, 92]. The evaluation of the relationship between perinatal mental disorders and child neurodevelopment has the purpose of understanding what may confer risk in offspring and consequently define preventive strategies.

Some studies pointed out how inflammation in early pregnancy can affect fetal brain development. Specifically, the synthesis of inflammatory cytokines can be induced in the placenta due to maternal bacterial infection creating placental dysfunction [93]. This can in turn induce different developmental abnormalities of the fetus that are not necessarily fatal but whose consequences might appear later during the child's development. The research on the impact of neuroinflammation and cytokines on Parkinson's disorder, autism spectrum disorder, and infertility is ongoing but mostly conducted on animal models [94], while research on humans is still at an embryonal stage. Although the underlying biological mechanisms for mothers' mental disorders leading to changes at the offspring brain level are not fully understood, endocrine, inflammation, epigenetic, and genetic pathways have been indicated as those most probably involved [95]. Results of structural and functional imaging studies identified connectivity changed in the offspring whose mother had antenatal depression. These changes mostly targeted brain areas belonging to the salience network and the default mode network whose dysfunctions have been observed in various psychiatric disorders including anxiety disorders, depression, and post-traumatic stress disorder [96].

Zooming into one specific case of perinatal disorder, few studies have prospectively traced the maternal depression course in relation to adolescent offspring depression, from pregnancy to the following 16 years. It was shown that the risk of depression was 4.7 times higher for the progeny exposed to maternal prenatal depression than for offspring not exposed to it and that the effect was mediated by repeated episodes of motherly mood disorder [97].

One of the most important longitudinal studies is the South London Child Development Study (SLCDS) on women's mental health recruited in pregnancy in 1986 and its impact on the children. Exposure to maternal prenatal depression predicted behavioral and emotional problems such as antisocial attitudes and acts of violence, while maternal postpartum depression was linked to cognitive outcomes

in children such as low IQ, difficulties in reading comprehension, and mathematical reasoning [98, 99].

Other research showed how maternal antenatal depression might be a risk factor for offspring psychotic experiences, ranging from borderline personality features in childhood to antisocial, criminal, and violent behavior in adolescence [100].

Follow-up studies are also fundamental to understand the long-term consequences of the pharmacological treatment related to the mother's mental disorder, during pregnancy and postpartum, on their offspring's mental health.

A follow-up study interviewed mother-child dyads previously recruited for the "Thinking Healthy Programme," a WHO project aimed at reducing prenatal depression through cognitive-behavioral interventions delivered by community health workers in several home visits [101]. The follow-up study was conducted 7 years later and included mothers who, after depression treatment, showed significantly reduced depression levels 12 months postpartum, as compared to those who did not receive the treatment. Results revealed that the reduced depression levels previously found in those mothers were not sustained long term. Moreover, prenatally depressed mothers' children who received the treatment show worse socioemotional outcomes than the children not receiving the treatment. Both groups of children (treated and untreated) displayed worse overall outcomes when compared to the children of healthy mothers [102]. Another study with an increased follow-up time highlighted how high vs low perinatal depressive symptoms increase the likeliness of psychotic experiences in the offspring at 18 years of age [103]. To the author's knowledge, one of the first follow-up studies on the offspring of antenatally depressed mothers until middle adulthood was conducted on a Northern Finland 1966 Birth Cohort [104]. Results showed that these mothers' adult offspring did not show any higher risk of developing borderline personality disorder (BPD). However, the sons, as compared to the daughters, had an increased risk for antisocial personality disorder (ASPD). This study highlights that early diagnosis and interventions provided to depressed mothers will have long-term consequences for reducing the risk of antisocial personality disorder in the offspring.

Overall, these findings clearly show the need for long-term assessments of the efficacy of interventions aimed to promote maternal and child well-being.

25.7.3 Research on Mother-Infant Bonding

Perinatal disorders have consequences that are not restricted to the mother but affect the entire family and might represent a risk factor for poor maternal-infant bonding [105]. Bonding is defined as the emotional connection experienced by a mother toward her children. Occasionally, the bonding process can fail [106, 107] with an incidence of 10% of sub-optimal bonding cases in the general population [108]. As a consequence mothers experience ambivalent emotions, lack of affection, and, in extreme cases, feeling of rejection toward the infant which can culminate in aggressive impulses [109]. Impaired bonding can occur in psychologically healthy mothers, but it is particularly observed in those with postpartum depression [110]. In

both cases, the maternal-infant relationship is formed prenatally [111], at a stage when it is known as maternal-fetal attachment, and those feelings developed during pregnancy supposedly continue after birth [112, 113]. Increasing evidence is pointing to the necessity of performing early preventive assessments and interventions during the pregnancy mainly to promote the relationship with the fetus in utero, but also postnatally [114]. Hence, the enhancement of fetal bonding can be already planned during the pregnancy period through new advanced technologies. The enrichment of the ultrasonography with the fetal facial 3D models has been found to increase maternal-fetal attachment [115], delineating future perspectives into the use of this new technology as a facilitator of bonding in mothers already at risk for bonding impairments.

In addition to the treatments described above, imaging research has been moving forward in the development of new tools for the use of perinatal mental health treatments. It was already established that attachment and bonding behaviors rely, on a neural level, on the dopamine-mediated reward system, with the ventral striatum and the nucleus accumbens areas primarily responsible for the process [116]. Several findings indicate that striatal reward areas of mothers with postpartum depression are less responsive to stimuli that depict their children [117, 118]. Using this knowledge, a recently proposed protocol using the neurofeedback (NFB) technique has been suggested to investigate whether training mothers to increase the activity of the ventral striatum can improve maternal bonding [119]. NFB is a novel method that allows individuals to regulate their brain activation through visualizing them in real time ([120] but see [121] for a review). The regulation of the specific brain areas aims at therapeutically improving mental symptoms. Exploring the use of video feedback interventions and training interventions with NFB techniques seems to be the most promising line of research so far to improve mother-infant bonding.

25.7.4 Next-Generation Pharmacological Interventions

The peripartum period is characterized by fluctuations in steroid hormonal levels and, crucially, in allopregnanolone levels [122, 123]. It has been hypothesized that perinatal mood disorders can arise because of the decline of these hormonal levels in the postpartum period (for a review, see [124]). Research is mostly focusing on the allopregnanolone hormone (for a review, see [83]), given that it dramatically decreases following delivery and it is seen as a potential mediator of major depression [125]. In favor of this theory, allopregnanolone levels have been found to increase following antidepressant treatments [126]. However, until recently, no specific antidepressants were developed or received regulatory approval for the treatment of postpartum depression [127].

New clinical findings highlighted the use of brexanolone, a synthetic allopregnanolone analog that has been recently approved by the US Food and Drug Administration. This allopregnanolone-based compound showed rapid robust antidepressant effects for the treatment of postpartum depression [128, 129], with effects prolonged to the month after the cessation of treatment.

Even though it has already been commercialized, its mechanism of action as an antidepressant is still not well understood. Furthermore, its future widespread use might present some limitations due to its cost, administration modality (i.e., a 60-h continuous intravenous infusion), and the requirement of continuous patient monitoring by the healthcare provider. To overcome these limitations, zuranolone, a new synthetic allopregnanolone analog, chemically modified to increase its oral bioavailability and administered at bedtime, is currently being tested in clinical trials [130, 131]. Preliminary results indicate that it is well tolerated and passed the first and second endpoints of the studies, efficiently improving postpartum depression in adult women diagnosed with severe PPD. To date, zuranolone and brexanolone are the only two new-generation drugs that have been selectively tested to treat mental disorders of the perinatal period.

In sum, recent pharmacological interventions have mainly centered around postpartum depression, with relatively little research for other perinatal mental disorders such as psychosis, bipolar disorder, and so on. Given the complexity of the perinatal mental symptomatology, further research should aim to develop pharmacological treatments specifically selective for the wide range of perinatal disorders.

References

1. Humphreys J, Obeney-Williams J, Cheung RW, Shah N. Perinatal psychiatry: a new specialty or everyone's business? BJPsych Adv. 2016;22:363–72. https://doi.org/10.1192/apt.bp.115.014548.
2. Oates M. Suicide: the leading cause of maternal death. Br J Psychiatry. 2003:279–81. https://doi.org/10.1192/bjp.183.4.279.
3. Howard LM, Khalifeh H. Perinatal mental health: a review of progress and challenges. World Psychiatry. 2020;19:313–27. https://doi.org/10.1002/wps.20769.
4. Payne JL. Reproductive psychiatry: giving birth to a new subspecialty. Int Rev Psychiatry. 2019:207–9. https://doi.org/10.1080/09540261.2018.1579991. Taylor and Francis Ltd.
5. Brockington I, Butterworth R, Glangeaud-Freudenthal N. An international position paper on mother-infant (perinatal) mental health, with guidelines for clinical practice. Arch Women's Mental Health. 2017;20:113–20. https://doi.org/10.1007/s00737-016-0684-7.
6. Esquirol JED. De l'Aliénation Mentale des Nouvelles Accouchées et des Nourrices. In: Annuaires médicales-chirurgiques des hôpitaux de Paris, editor. Annuaire Médico-Chirurgical des Hôpitaux de Paris. Patrick Pollak Rare Books ABA ILAB; 1819. pp. 600–632.
7. Marcé L-V (1828–1864). A du texte. Traité de la folie des femmes enceintes, des nouvelles accouchées et des nourrices: et considérations médico-légales qui se rattachent à ce sujet/par le Dr L.-V. Marcé,... 1858.
8. Tardieu A. Étude médico-légale sur les sévices et mauvais traitements exercés sur des enfants. Enfances Psy. 2008;39:174. https://doi.org/10.3917/ep.039.0174.
9. Pitt B. "Atypical" depression following childbirth. Br J Psychiatry. 1968;114:1325–35. https://doi.org/10.1192/bjp.114.516.1325.
10. Resnick PJ. Murder of the newborn: a psychiatric review of neonaticide. Am J Psychiatry. 1970;126:1414–20. https://doi.org/10.1176/ajp.126.10.1414.
11. Resnick PJ. Child murder by parents: a psychiatric review of filicide. Am J Psychiatry. 1969;126:325–34. https://doi.org/10.1176/ajp.126.3.325.
12. Cox JL, Wisner KL. Recollections on the early days of the Marcé Society for Perinatal Mental Health from Professor John Cox. Arch Women's Mental Health. 2016;19:197–200. https://doi.org/10.1007/s00737-015-0569-1.

13. Hamilton JA. Postpartum psychiatric syndromes. Psychiatric Clin N Am. 1989;12:89–103. https://doi.org/10.1016/S0193-953X(18)30453-2.
14. O'hara MW. Post-partum "blues," depression, and psychosis: a review. J Psychosom Obstet Gynecol. 1987;7(3):205–27. https://doi.org/10.3109/01674828709040280. Informa Healthcare
15. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150:782–6. https://doi.org/10.1192/bjp.150.6.782.
16. Cox J. Use and misuse of the Edinburgh Postnatal Depression Scale (EPDS): a ten point 'survival analysis'. Arch Women's Mental Health. 2017;20(6):789–90. https://doi.org/10.1007/s00737-017-0789-7. Springer-Verlag Wien
17. Beck CT. Postpartum depression: a metasynthesis. Qual Health Res. 2002;12:453–72. https://doi.org/10.1177/1049732202129120016.
18. O'Hara MW, Swain AM. Rates and risk of postpartum depression: a meta-analysis. Int Rev Psychiatry. 1996;8:37–54. https://doi.org/10.3109/09540269609037816.
19. Boyce P, Hickie I, Gordon P. Parents, partners or personality? Risk factors for post-natal depression. J Affect Disord. 1991;21:245–55. https://doi.org/10.1016/0165-0327(91)90004-C.
20. Glover V. Maternal stress or anxiety during pregnancy and the development of the baby. Pract Midwife. 1999;2(5):20–2.
21. Hundley V, Gurney E, Graham W, Rennie AM. Can anxiety in pregnant women be measured using the State-Trait Anxiety Inventory. Midwifery. 1998;14:118–21. https://doi.org/10.1016/S0266-6138(98)90009-2.
22. Stuart S, Couser G, Schilder K, O'Hara MW, Gorman L. Postpartum anxiety and depression: Onset and comorbidity in a community sample. J Nerv Ment Dis. 1998;186:420–4. https://doi.org/10.1097/00005053-199807000-00006.
23. Maina G, Albert U, Bogetto F, Vaschetto P, Ravizza L. Recent life events and obsessive-compulsive disorder (OCD): the role of pregnancy/delivery. Psychiatry Res. 1999;89:49–58. https://doi.org/10.1016/S0165-1781(99)00090-6.
24. Stein DJ, Hollander E, Simeon D, Cohen L, Hwang M, Neziroglu FA, et al. Pregnancy and obsessive-compulsive disorder. Am J Psychiatry. 1993;150(7):1131–2. https://doi.org/10.1176/ajp.150.7.1131-a.
25. Brockington IF, Meakin CJ. Clinical clues to the aetiology of puerperal psychosis. Prog Neuro-Psychopharmacol Biol Psychiatry. 1994;18:417–29. https://doi.org/10.1016/0278-5846(94)90001-9.
26. Brockington IF, Cernik KF, Schofield EM, Downing AR, Francis AF, Keelan C. Puerperal psychosis: phenomena and diagnosis. Arch Gen Psychiatry. 1981;38:829–33. https://doi.org/10.1001/archpsyc.1981.01780320109013.
27. Brockington I, Guedeney A. Motherhood and mental health. Infant Observ. 1999;2:116–7. https://doi.org/10.1080/13698039908400552.
28. Kumar RC. "Anybody's child": severe disorders of mother-to-infant bonding. Br J Psychiatry. 1997;171:175–81. https://doi.org/10.1192/bjp.171.2.175.
29. Brockington IF. Disorders of the mother-infant relationship. Br J Psychiatry. 1997;171(5):486. https://doi.org/10.1192/bjp.171.5.486c.
30. Kumar R. Postnatal mental illness: a transcultural perspective. Soc Psychiatry Psychiatric Epidemiol. 1994;29:250–64. https://doi.org/10.1007/BF00802048.
31. Wisner KL, Perel JM, Findling RL. Antidepressant treatment during breast-feeding. Am J Psychiatry. 1996;153(9):1132–7. https://doi.org/10.1176/ajp.153.9.1132. American Psychiatric Association
32. Wisner KL, Gelenberg AJ, Leonard H, Zarin D, Frank E. Pharmacologic treatment of depression during pregnancy. J Am Med Assoc. 1999;282(13):1264–9. https://doi.org/10.1001/jama.282.13.1264.
33. Meager I, Milgrom J. Group treatment for postpartum depression: a pilot study. Aust New Zealand J Psychiatry. 1996;30:852–60. https://doi.org/10.3109/00048679609065055.

34. Milgrom J, Martin PR, Negri LM. Treating postnatal depression: a psychological approach for health care practitioners. Wiley; 1999.
35. Spinelli MG. Interpersonal psychotherapy for depressed antepartum women: a pilot study. Am J Psychiatry. 1997;154:1028–30. https://doi.org/10.1176/ajp.154.7.1028.
36. Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. Am J Psychiatry. 2003;160:555–62. https://doi.org/10.1176/appi.ajp.160.3.555.
37. Stuart S. Interpersonal psychotherapy for postpartum depression: a treatment program. J Psychother Pract Res. 1995;4(1):18.
38. O'Hara MW, Scott S, Gorman Laura L, Amy W. Efficacy of interpersonal psychotherapy for postpartum depression. Arch Gen Psychiatry. 2000;57:1039–45. https://doi.org/10.1001/archpsyc.57.11.1039.
39. Dennis CL. The effect of peer support on postpartum depression: a pilot randomized controlled trial. Can J Psychiatr. 2003;48:115–24. https://doi.org/10.1177/070674370304800209.
40. Danaher BG, Milgrom J, Seeley JR, Stuart S, Schembri C, Tyler MS, et al. MomMoodBooster web-based intervention for postpartum depression: feasibility trial results. J Med Internet Res. 2013;15 https://doi.org/10.2196/jmir.2876.
41. Chan KL, Leung WC, Tiwari A, Or KL, Ip P. Using smartphone-based psychoeducation to reduce postnatal depression among first-time mothers: randomized controlled trial. JMIR Mhealth Uhealth. 2019;7:e12794. https://doi.org/10.2196/12794.
42. Bakermans-Kranenburg MJ, Van IJzendoorn MH. Sniffing around oxytocin: review and meta-analyses of trials in healthy and clinical groups with implications for pharmacotherapy. Transl Psychiatry. 2013;3(5):1–14. https://doi.org/10.1038/tp.2013.34.
43. Kalinauskiene L, Cekuoliene D, van Ijzendoorn MH, Bakermans-Kranenburg MJ, Juffer F, Kusakovskaja I. Supporting insensitive mothers: the Vilnius randomized control trial of video-feedback intervention to promote maternal sensitivity and infant attachment security. Child Care Health Dev. 2009;35:613–23. https://doi.org/10.1111/j.1365-2214.2009.00962.x.
44. Hoffenkamp HN, Tooten A, Hall RAS, Braeken J, Eliëns MPJ, Vingerhoets AJJM, et al. Effectiveness of hospital-based video interaction guidance on parental interactive behavior, bonding, and stress after preterm birth: a randomized controlled trial. J Consult Clin Psychol. 2015;83:416–29. https://doi.org/10.1037/a0038401.
45. Kenny M, Conroy S, Pariante CM, Seneviratne G, Pawlby S. Mother-infant interaction in mother and baby unit patients: before and after treatment. J Psychiatr Res. 2013;47:1192–8. https://doi.org/10.1016/j.jpsychires.2013.05.012.
46. National Perinatal Mental Health Guideline—COPE. [cited 6 Apr 2021]. Available: https://www.cope.org.au/health-professionals/health-professionals-3/review-of-new-perinatal-mental-health-guidelines/
47. Mauri M, Oppo A, Montagnani MS, Borri C, Banti S, Camilleri V, et al. Beyond "postpartum depressions": specific anxiety diagnoses during pregnancy predict different outcomes: results from PND-ReScU. J Affect Disord. 2010;127:177–84. https://doi.org/10.1016/j.jad.2010.05.015.
48. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression: a meta-analysis. J Am Med Assoc. 2010;303(19):1961–9. https://doi.org/10.1001/jama.2010.605.
49. Gururajan A, Clarke G, Dinan TG, Cryan JF. Molecular biomarkers of depression. Neurosci Biobehav Rev. 2016;64:101–33. https://doi.org/10.1016/j.neubiorev.2016.02.011. Elsevier Ltd.
50. Strimbu K, Tavel JA. What are biomarkers? Current opinion in HIV and AIDS. Curr Opin HIV AIDS. 2010;5(6):463–6. https://doi.org/10.1097/COH.0b013e32833ed177.
51. Davies W. Understanding the pathophysiology of postpartum psychosis: challenges and new approaches. World J Biol Psychiatry. 2017;7(2):77–88. https://doi.org/10.5498/wjp.v7.i2.77. Taylor and Francis Ltd.
52. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. J Women's Health. 2006;15(4):352–68. https://doi.org/10.1089/jwh.2006.15.352.

53. Di Florio A, Gordon-Smith K, Forty L, Kosorok MR, Fraser C, Perry A, et al. Stratification of the risk of bipolar disorder recurrences in pregnancy and postpartum. Br J Psychiatry. 2018;213:542–7. https://doi.org/10.1192/bjp.2018.92.
54. Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB. New parents and mental disorders: a population-based register study. J Am Med Assoc. 2006;296:2582–9. https://doi.org/10.1001/jama.296.21.2582.
55. Johannsen BMW, Larsen JT, Laursen TM, Bergink V, Meltzer-Brody S, Munk-Olsen T. All-cause mortality in women with severe postpartum psychiatric disorders. Am J Psychiatry. 2016;173:635–42. https://doi.org/10.1176/appi.ajp.2015.14121510.
56. Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJM, Kushner SA, Bergink V. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatry. 2016:117–27. https://doi.org/10.1176/appi.ajp.2015.15010124. American Psychiatric Association
57. VanderKruik R, Barreix M, Chou D, Allen T, Say L, Cohen LS. The global prevalence of postpartum psychosis: a systematic review. BMC Psychiatry. 2017;17:272. https://doi.org/10.1186/s12888-017-1427-7.
58. Bloch M, Rotenberg N, Koren D, Klein E. Risk factors for early postpartum depressive symptoms. Gen Hosp Psychiatry. 2006;28:3–8. https://doi.org/10.1016/j.genhosppsych.2005.08.006.
59. Zubin J, Spring B. Vulnerability: a new view of schizophrenia. J Abnormal Psychol. 1977;86:103–26. https://doi.org/10.1037/0021-843X.86.2.103.
60. McEwen BS. The brain on stress: toward an integrative approach to brain, body, and behavior. Perspect Psychol Sci. 2013;8:673–5. https://doi.org/10.1177/1745691613506907.
61. Aas M, Vecchio C, Pauls A, Mehta M, Williams S, Hazelgrove K, et al. Biological stress response in women at risk of postpartum psychosis: the role of life events and inflammation. Psychoneuroendocrinology. 2020;113:104558. https://doi.org/10.1016/j.psyneuen.2019.104558.
62. Marques AH, Cizza G, Sternberg E. Brain-immune interactions and implications in psychiatric disorders. Braz J Psychiatry. 2007;29:s27–32. https://doi.org/10.1590/S1516-44462007000500006.
63. Valkanova V, Ebmeier KP, Allan CL. CRP, IL-6 and depression: a systematic review and meta-analysis of longitudinal studies. J Affect Disord. 2013;150(3):736–44. https://doi.org/10.1016/j.jad.2013.06.004. Elsevier B.V.
64. Menke A, Nitschke F, Hellmuth A, Helmel J, Wurst C, Stonawski S, et al. Stress impairs response to antidepressants via HPA axis and immune system activation. Brain Behav Immunity. 2021;93:132–40. https://doi.org/10.1016/j.bbi.2020.12.033.
65. Pruessner M, Bechard-Evans L, Pira S, Joober R, Collins DL, Pruessner JC, et al. Interplay of hippocampal volume and hypothalamus-pituitary-adrenal axis function as markers of stress vulnerability in men at ultra-high risk for psychosis. Psychol Med. 2017;47:471–83. https://doi.org/10.1017/S0033291716002658.
66. Hope S, Melle I, Aukrust P, Steen NE, Birkenaes AB, Lorentzen S, et al. Similar immune profile in bipolar disorder and schizophrenia: selective increase in soluble tumor necrosis factor receptor I and von Willebrand factor. Bipolar Disord. 2009;11:726–34. https://doi.org/10.1111/j.1399-5618.2009.00757.x.
67. Leboyer M, Oliveira J, Tamouza R, Groc L. Is it time for immunopsychiatry in psychotic disorders? Psychopharmacology. 2016;233(9):1651–60. https://doi.org/10.1007/s00213-016-4266-1. Springer Verlag
68. Mørch RH, Dieset I, Færden A, Hope S, Aas M, Nerhus M, et al. Inflammatory evidence for the psychosis continuum model. Psychoneuroendocrinology. 2016;67:189–97. https://doi.org/10.1016/j.psyneuen.2016.02.011.
69. Melón LC, Hooper A, Yang X, Moss SJ, Maguire J. Inability to suppress the stress-induced activation of the HPA axis during the peripartum period engenders deficits in postpartum behaviors in mice. Psychoneuroendocrinology. 2018;90:182–93. https://doi.org/10.1016/j.psyneuen.2017.12.003.

70. Osborne S, Biaggi A, Chua TE, Du Preez A, Hazelgrove K, Nikkheslat N, et al. Antenatal depression programs cortisol stress reactivity in offspring through increased maternal inflammation and cortisol in pregnancy: The Psychiatry Research and Motherhood—Depression (PRAM-D) Study. Psychoneuroendocrinology. 2018;98:211–21. https://doi.org/10.1016/j.psyneuen.2018.06.017.
71. Bergink V, Burgerhout KM, Weigelt K, Pop VJ, De Wit H, Drexhage RC, et al. Immune system dysregulation in first-onset postpartum psychosis. Biol Psychiatry. 2013;73:1000–7. https://doi.org/10.1016/j.biopsych.2012.11.006.
72. Kumar MM, Venkataswamy MM, Sathyanarayanan G, Thippeswamy H, Chandra PS, Mani RS. Immune system aberrations in postpartum psychosis: an immunophenotyping study from a tertiary care neuropsychiatric hospital in India. J Neuroimmunol. 2017;310:8–13. https://doi.org/10.1016/j.jneuroim.2017.06.002.
73. Sathyanarayanan G, Thippeswamy H, Mani R, Venkataswamy M, Kumar M, Philip M, et al. Cytokine alterations in first-onset postpartum psychosis-clues for underlying immune dysregulation. Asian J Psychiatry. 2019;42:74–8. https://doi.org/10.1016/j.ajp.2019.03.012.
74. Dazzan P, Fusté M, Davies W. Do defective immune system-mediated myelination processes increase postpartum psychosis risk? Trends Mol Med. 2018:942–9. https://doi.org/10.1016/j.molmed.2018.09.002. Elsevier Ltd
75. Mondelli V, Howes O. Inflammation: its role in schizophrenia and the potential anti-inflammatory effects of antipsychotics. Psychopharmacology. 2014:317–8. https://doi.org/10.1007/s00213-013-3383-3.
76. Epstein FH, Reichlin S. Neuroendocrine-immune interactions. N Engl J Med. 1993;329:1246–53. https://doi.org/10.1056/nejm199310213291708.
77. Yim IS, Tanner Stapleton LR, Guardino CM, Hahn-Holbrook J, Dunkel Schetter C. Biological and psychosocial predictors of postpartum depression: systematic review and call for integration. Ann Rev Clin Psychol. 2015;11:99–137. https://doi.org/10.1146/annurev-clinpsy-101414-020426.
78. Ellsworth-Bowers ER, Corwin EJ. Nutrition and the psychoneuroimmunology of postpartum depression. Nutr Res Rev. 2012;25(1):180–92. https://doi.org/10.1017/S0954422412000091.
79. Osborne LM, Monk C. Perinatal depression: the fourth inflammatory morbidity of pregnancy? Theory and literature review. Psychoneuroendocrinology. 2013;38(10):1929–52. https://doi.org/10.1016/j.psyneuen.2013.03.019.
80. Scrandis DA, Langenberg P, Tonelli LH, Sheikh TM, Manogura AC, Alberico LA, et al. Prepartum depressive symptoms correlate positively with C-reactive protein levels and negatively with tryptophan levels: a preliminary report. Int J Child Health Hum Dev. 2008;1:167–74.
81. O'Connor TG, Tang W, Gilchrist MA, Moynihan JA, Pressman EK, Blackmore ER. Diurnal cortisol patterns and psychiatric symptoms in pregnancy: short-term longitudinal study. Biol Psychol. 2014;96:35–41. https://doi.org/10.1016/j.biopsycho.2013.11.002.
82. Serati M, Redaelli M, Buoli M, Altamura AC. Perinatal major depression biomarkers: a systematic review. J Affect Disord. 2016;193:391–404. https://doi.org/10.1016/j.jad.2016.01.027. Elsevier B.V.
83. Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019;52:165–80. https://doi.org/10.1016/j.yfrne.2018.12.001. Academic Press Inc.
84. Rackers HS, Thomas S, Williamson K, Posey R, Kimmel MC. Emerging literature in the microbiota-brain axis and perinatal mood and anxiety disorders. Psychoneuroendocrinology. 2018:86–96. https://doi.org/10.1016/j.psyneuen.2018.05.020. Elsevier Ltd.
85. Jiang H, Ling Z, Zhang Y, Mao H, Ma Z, Yin Y, et al. Altered fecal microbiota composition in patients with major depressive disorder. Brain Behav Immunity. 2015;48:186–94. https://doi.org/10.1016/j.bbi.2015.03.016.
86. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006;444:1027–31. https://doi.org/10.1038/nature05414.

87. Dinan TG, Cryan JF. Microbes immunity and behavior: psychoneuroimmunology meets the microbiome. Neuropsychopharmacology. 2017:178–92. https://doi.org/10.1038/npp.2016.103. Nature Publishing Group
88. Zhou Y, Chen C, Yu H, Yang Z. Fecal microbiota changes in patients with postpartum depressive disorder. Front Cell Infect Microbiol. 2020;10:567268. https://doi.org/10.3389/fcimb.2020.567268.
89. Penalver Bernabe B, Dowty S, Pezley L, Goel N, Hill E, Gibbons R, et al. Depression during pregnancy is associated with an altered gut microbiome in an Urban Diverse Population. Biol Psychiatry. 2020;87:S36. https://doi.org/10.1016/j.biopsych.2020.02.114.
90. Slykerman RF, Hood F, Wickens K, Thompson JMD, Barthow C, Murphy R, et al. Effect of Lactobacillus rhamnosus HN001 in pregnancy on postpartum symptoms of depression and anxiety: a randomised double-blind Placebo-controlled trial. EBioMedicine. 2017;24:159–65. https://doi.org/10.1016/j.ebiom.2017.09.013.
91. Hayes CL, Peters BJ, Foster JA. Microbes and mental health: can the microbiome help explain clinical heterogeneity in psychiatry? Front Neuroendocrinol. 2020; https://doi.org/10.1016/j.yfrne.2020.100849. Academic Press Inc.
92. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. Lancet. 2014:1800–19. https://doi.org/10.1016/S0140-6736(14)61277-0. Lancet Publishing Group
93. Lye P, Bloise E, Javam M, Gibb W, Lye SJ, Matthews SG. Impact of bacterial and viral challenge on multidrug resistance in first- and third-trimester human placenta. Am J Pathol. 2015;185:1666–75. https://doi.org/10.1016/j.ajpath.2015.02.013.
94. Izvolskaia M, Sharova V, Zakharova L. Perinatal inflammation reprograms neuroendocrine, immune, and reproductive functions: profile of cytokine biomarkers. Inflammation. 2020:1175–83. https://doi.org/10.1007/s10753-020-01220-1. Springer
95. Duan C, Hare MM, Staring M, Deligiannidis KM. Examining the relationship between perinatal depression and neurodevelopment in infants and children through structural and functional neuroimaging research. Int Rev Psychiatry. 2019;31(3):264–79. https://doi.org/10.1080/09540261.2018.1527759. Taylor and Francis Ltd.
96. Sha Z, Wager TD, Mechelli A, He Y. Common dysfunction of large-scale neurocognitive networks across psychiatric disorders. Biol Psychiatry. 2019;85:379–88. https://doi.org/10.1016/j.biopsych.2018.11.011.
97. Pawlby S, Hay DF, Sharp D, Waters CS, O'Keane V. Antenatal depression predicts depression in adolescent offspring: prospective longitudinal community-based study. J Affect Disord. 2009;113:236–43. https://doi.org/10.1016/j.jad.2008.05.018.
98. Hay DF, Pawlby S, Waters CS, Perra O, Sharp D. Mothers' antenatal depression and their children's antisocial outcomes. Child Dev. 2010;81:149–65. https://doi.org/10.1111/j.1467-8624.2009.01386.x.
99. Hay DF, Pawlby S, Waters CS, Sharp D. Antepartum and postpartum exposure to maternal depression: different effects on different adolescent outcomes. J Child Psychol Psychiatry Allied Discipl. 2008;49:1079–88. https://doi.org/10.1111/j.1469-7610.2008.01959.x.
100. Taka-Eilola T, Veijola J, Miettunen J, Koskela J, Kantojärvi L, Mäki P. Antisocial and borderline personality disorders in the offspring of antenatally depressed mothers—a follow-up until mid-adulthood in the Northern Finland 1966 birth cohort. Nordic J Psychiatry. 2020;74:138–46. https://doi.org/10.1080/08039488.2019.1681508.
101. Rahman A, Malik A, Sikander S, Roberts C, Creed F. Cognitive behaviour therapy-based intervention by community health workers for mothers with depression and their infants in rural Pakistan: a cluster-randomised controlled trial. Lancet. 2008;372:902–9. https://doi.org/10.1016/S0140-6736(08)61400-2.
102. Maselko J, Sikander S, Bhalotra S, Bangash O, Ganga N, Mukherjee S, et al. Effect of an early perinatal depression intervention on long-term child development outcomes: follow-up of the Thinking Healthy Programme randomised controlled trial. Lancet Psychiatry. 2015;2:609–17. https://doi.org/10.1016/S2215-0366(15)00109-1.

103. Srinivasan R, Pearson RM, Johnson S, Lewis G, Lewis G. Maternal perinatal depressive symptoms and offspring psychotic experiences at 18 years of age: a longitudinal study. Lancet Psychiatry. 2020;7:431–40. https://doi.org/10.1016/S2215-0366(20)30132-2.
104. Mäki P, Riekki T, Miettunen J, Isohanni M, Jones PB, Murray GK, et al. Schizophrenia in the offspring of antenatally depressed mothers in the Northern Finland 1966 birth cohort: relationship to family history of psychosis. Am J Psychiatry. 2010;167:70–7. https://doi.org/10.1176/appi.ajp.2009.09010133.
105. Dubber S, Reck C, Müller M, Gawlik S. Postpartum bonding: the role of perinatal depression, anxiety and maternal–fetal bonding during pregnancy. Arch Women's Mental Health. 2015;18:187–95. https://doi.org/10.1007/s00737-014-0445-4.
106. Reck C, Klier CM, Pabst K, Stehle E, Steffenelli U, Struben K, et al. The German version of the postpartum bonding instrument: psychometric properties and association with postpartum depression. Arch Women's Mental Health. 2006;9:265–71. https://doi.org/10.1007/s00737-006-0144-x.
107. Brockington IF, Aucamp HM, Fraser C. Severe disorders of the mother-infant relationship: definitions and frequency. Arch Women's Mental Health. 2006;9:243–51. https://doi.org/10.1007/s00737-006-0133-0.
108. O'Higgins M, Roberts ISJ, Glover V, Taylor A. Mother-child bonding at 1 year; associations with symptoms of postnatal depression and bonding in the first few weeks. Arch Women's Mental Health. 2013;16:381–9. https://doi.org/10.1007/s00737-013-0354-y.
109. Brockington I. Postpartum psychiatric disorders. Lancet. 2004;363(9405):303–10. https://doi.org/10.1016/S0140-6736(03)15390-1. Elsevier B.V.
110. Reck C, Zietlow AL, Müller M, Dubber S. Perceived parenting stress in the course of postpartum depression: the buffering effect of maternal bonding. Arch Women's Mental Health. 2016;19:473–82. https://doi.org/10.1007/s00737-015-0590-4.
111. Trombetta T, Giordano M, Santoniccolo F, Vismara L, Della Vedova AM, Rollè L. Prenatal attachment and parent-to-infant attachment: a systematic review. Front Psychol. 2021;12:620942. https://doi.org/10.3389/fpsyg.2021.620942.
112. de Cock ESA, Henrichs J, Vreeswijk CMJM, Maas AJBM, Rijk CHAM, van Bakel HJA. Continuous feelings of love? The parental bond from pregnancy to toddlerhood. J Fam Psychol. 2016;30:125–34. https://doi.org/10.1037/fam0000138.
113. Rossen L, Mattick RP, Wilson J, Clare PJ, Burns L, Allsop S, et al. Mother–infant bonding and emotional availability at 12-months of age: the role of early postnatal bonding, maternal substance use and mental health. Mater Child Health J. 2019;23:1686–98. https://doi.org/10.1007/s10995-019-02809-1.
114. Branjerdporn G, Meredith P, Wilson T, Strong J. Prenatal predictors of maternal-infant attachment. Can J Occup Ther. 2020;87:265–77. https://doi.org/10.1177/0008417420941781.
115. Coté JJ, Badura-Brack AS, Walters RW, Dubay NG, Bredehoeft MR. Randomized controlled trial of the effects of 3D-printed models and 3D ultrasonography on maternal–fetal attachment. J Obstet Gynecol Neonatal Nurs. 2020;49:190–9. https://doi.org/10.1016/j.jogn.2020.01.003.
116. Daniel R, Pollmann S. A universal role of the ventral striatum in reward-based learning: evidence from human studies. Neurobiol Learn Memory. 2014:90–100. https://doi.org/10.1016/j.nlm.2014.05.002. Academic Press Inc.
117. Laurent HK, Ablow JC. A face a mother could love: depression-related maternal neural responses to infant emotion faces. Soc Neurosci. 2013;8:228–39. https://doi.org/10.1080/17470919.2012.762039.
118. Wonch KE, de Medeiros CB, Barrett JA, Dudin A, Cunningham WA, Hall GB, et al. Postpartum depression and brain response to infants: differential amygdala response and connectivity. Soc Neurosci. 2016;11:600–17. https://doi.org/10.1080/17470919.2015.1131193.
119. Eckstein M, Zietlow AL, Gerchen MF, Schmitgen MM, Ashcroft-Jones S, Kirsch P, et al. The NeMo real-time fMRI neurofeedback study: protocol of a randomised controlled clinical intervention trial in the neural foundations of mother-infant bonding. BMJ Open. 2019;9:e027747. https://doi.org/10.1136/bmjopen-2018-027747.

120. Thibault RT, MacPherson A, Lifshitz M, Roth RR, Raz A. Neurofeedback with fMRI: a critical systematic review. NeuroImage. 2018;172:786–807. https://doi.org/10.1016/j.neuroimage.2017.12.071. Academic Press Inc.
121. Sulzer J, Haller S, Scharnowski F, Weiskopf N, Birbaumer N, Blefari ML, et al. Real-time fMRI neurofeedback: progress and challenges. NeuroImage. 2013;76:386–99. https://doi.org/10.1016/j.neuroimage.2013.03.033. Academic Press Inc.
122. Mastorakos G, Ilias I. Maternal and fetal hypothalamic-pituitary-adrenal axes during pregnancy and postpartum. Ann N Y Acad Sci. 2003;997:136–49. https://doi.org/10.1196/annals.1290.016.
123. Bloch M, Daly RC, Rubinow DR. Endocrine factors in the etiology of postpartum depression. Compr Psychiatry. 2003;44(3):234–46. https://doi.org/10.1016/S0010-440X(03)00034-8. W.B. Saunders
124. Meltzer-Brody S, Stuebe A, Dole N, Savitz D, Rubinow D, Thorp J. Elevated Corticotropin Releasing Hormone (CRH) during Pregnancy and Risk of Postpartum Depression (PPD). J Clin Endocrinol Metab. 2011;96:E40–7. https://doi.org/10.1210/jc.2010-0978.
125. Schüle C, Nothdurfter C, Rupprecht R. The role of allopregnanolone in depression and anxiety. Prog Neurobiol. 2014;113:79–87. https://doi.org/10.1016/j.pneurobio.2013.09.003. Elsevier Ltd.
126. Schüle C, Eser D, Baghai TC, Nothdurfter C, Kessler JS, Rupprecht R. Neuroactive steroids in affective disorders: target for novel antidepressant or anxiolytic drugs? Neuroscience. 2011;191:55–77. https://doi.org/10.1016/j.neuroscience.2011.03.025. Pergamon
127. Faden J, Citrome L. Intravenous brexanolone for postpartum depression: what it is, how well does it work, and will it be used? Ther Adv Psychopharmacol. 2020;10:2045125320968658. https://doi.org/10.1177/2045125320968658.
128. Meltzer-Brody S, Colquhoun H, Riesenberg R, Epperson CN, Deligiannidis KM, Rubinow DR, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet. 2018;392:1058–70. https://doi.org/10.1016/S0140-6736(18)31551-4.
129. Kanes S, Colquhoun H, Gunduz-Bruce H, Raines S, Arnold R, Schacterle A, et al. Brexanolone (SAGE-547 injection) in post-partum depression: a randomised controlled trial. Lancet. 2017;390:480–9. https://doi.org/10.1016/S0140-6736(17)31264-3.
130. Hoffmann E, Nomikos GG, Kaul I, Raines S, Wald J, Bullock A, et al. SAGE-217, A Novel GABAA receptor positive allosteric modulator: clinical pharmacology and tolerability in randomized phase I dose-finding studies. Clin Pharmacokinetics. 2020;59:111–20. https://doi.org/10.1007/s40262-019-00801-0.
131. Walton N, Maguire J. Allopregnanolone-based treatments for postpartum depression: why/how do they work? Neurobiol Stress. 2019;11:100198. https://doi.org/10.1016/j.ynstr.2019.100198.

Biomarkers, Between Diagnosis and Prognosis

26

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26.1 Perinatal Depression

26.1.1 Introduction

The *Diagnostic and Statistical Manual of Mental Disorders* fifth edition (DSM-5) defines a major depressive episode with onset in the peripartum as an episode that occurs during pregnancy or within 4 weeks after delivery [1]. In clinical practice this period is usually extended to up to 1 year postpartum [2] and can involve 13% of pregnant women, having a complex aetiology, including psychological, social and biological factors, in addition to genetic and environmental background [3–7]. Perinatal depression (PD) is a heterogeneous disorder with differences in depression timing onset, influencing symptomology, severity and treatment efficacy [8]. Nowadays, the early individuation of mental health disease in women is mandatory to prevent a long duration of untreated illness, widely recognized as a negative factor associated to poor outcome in psychiatric disorders, for which a specific training is required [9, 10]. Moreover, a mental disease in women during peripartum can

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increase obstetric complication risks such as preterm birth and low birth weight [11–13]. Intrauterine signals can affect fetal growth and act in "program" tissue differentiation predisposing to later illness onset as outlined in the *Developmental Origins of Health and Disease* [14]. Several studies have shown that PD has long-term consequences on offspring's behavior in later childhood and adolescence, including increased vulnerability to psychopathology and increased reactivity in the stress response [15–18]. WHO considers PD a global problem, including maternal health effects in terms of mortality and morbidity, on the newborn [19]. In 2015, the American College of Obstetrics and Gynecology (ACOG) included in their guidelines the indication to screen mothers for depressive and anxiety symptoms during perinatal period; screening recommended also by the American Academy of Pediatrics (AAP) during visits to the newborn in the first 4 months of life and by the US Preventive Services Task Force, for women at increased risk of PD [20]. Recently paternal PD has been understudy with a 10% of prevalence, however available studies are limited [21, 22].

Several biomarkers have been linked to PD onset: hormonal factors (oxytocin, vitamin D, hypothalamic-pituitary-adrenal axis-HPA dysregulation) and immunological factors (particularly interleukin-6 increase and dysregulation of innate immunity) [23, 24]. A biomarker has been defined by the National Institutes of Health Biomarkers Definitions Working Group as "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, that has to be reproducible and objective in indicating a medical state observed and has to repeatedly show to correctly predict clinical outcomes" [25]. As reported by Aronson [26], biomarkers can be used in disease screening, diagnosis, characterization, and monitoring as prognostic indicators. Moreover, to understand the value of a biomarker, it is necessary to know the pathophysiological relationship between the biomarker and the relevant clinical endpoint [27]. Nowadays, no specific biomarkers have been identified for PD: clinical screening in cooperation between gynecologists and psychiatrists is one of the major tools to identify women at risk [28–30]. Research is ongoing to find specific biomarkers in order to early detect PD and treat it: the aim of this chapter is to outline the actual state of the art on biomarkers in PD, although being not comprehensive of all available data in literature.

26.2 Hormones

Estrogen levels are fundamental for women's mental health, having neuromodulation properties, being a trigger for changes in gene expression [3]. During pregnancy estrogen rises progressively and falls at birth, returning to their normal levels during postpartum period, being PD more frequent when estrogen levels are progressively changing [31]. Two studies suggested that postpartum depression risk could be mediated by an increased sensitivity to estrogen-mediated epigenetic reprogramming [32]. The estrogen receptor alpha gene (ESR1) is a candidate gene in mediating hormonal differences during pregnancy and the postpartum period, through serotonin modulation signaling [33].

Neuroactive steroids in PD concern allopregnanolone: some studies found a direct correlation between lower allopregnanolone levels and increased depressive symptoms, but other studies did not [34].

HPA axis alterations are considered as a robust biomarker of anxiety and depression: mid-pregnancy depression has been significantly associated with increased cortisol levels [35]. In a prospective study by Glynn and Sandman [36], depressive symptoms at 3-month postpartum were associated with elevated midgestational placental CRH (pCRH), whereas pCRH was not predictive of PD symptoms at 6-month postpartum, and prepartum cortisol/corticotrophin levels did not increase the risk of developing PD. Meltzer-Brody [37] failed to find an association between midpregnancy pCRH levels and risk of PD, as Zaconeta and colleagues [38] in cerebrospinal fluid. Previously, a prospective study evaluated maternal self-report psychosocial distress at mid-and late gestation: cortisol levels were found to be directly correlated with maternal depression, anxiety, and stress [39]. Stress and depression in pregnancy can affect placental expression of enzymes regulating cortisol levels and methylation status of stress-related genes with an impact on brain development [40, 41]; cortisol hypersecretion contributes to activate microglia, with neuronal circuitry functional abnormalities [42]. In a recent study by Apter-Levy and colleagues [43], maternal diurnal cortisol and dehydroepiandrosterone (DHEA) were assessed: depressed mothers had lower levels of DHEA, flattened DHEA diurnal variability, and smaller DHEA-to-CT ratio. The increased risk of MDD during pregnancy has been explained not only as the consequence of sex hormone excess but also as the result of an increase of corticotropin-releasing hormone (CRH) and testosterone [44]. In a prospective longitudinal study on MDD in pregnancy, inflammatory and cortisol biomarkers and offspring stress response were evaluated: women with MDD had raised interleukin IL-6, IL-10, tumor necrosis factor alpha, and vascular endothelial growth factor, together with raised diurnal cortisol secretion, raised evening cortisol and blunted cortisol awakening response, and an 8-day shorter length of gestation. Moreover, they had neonates with suboptimal neurobehavioral function in four out of five NBAS clusters measured and increased cortisol response to stress at 1 year of age [45].

26.2.1 BDNF

The gene encoding BDNF is a strong candidate for PD pathogenesis: its polymorphism (Val66Met) alters the regulated protein secretion (the methionine variant is associated with insufficient secretion compared to the valine variant). Figueira and colleagues [46] evaluated BDNF geneVal66Met polymorphism and the association with PD, reporting no difference. A case-control study evaluated whether functional polymorphic variants, BDNF Val66Met, 5-HTTLPR, or Period 2(PER2) SNP10870, were associated with PD symptoms without revealing any statistically significant association between such polymorphisms and PD symptoms. Interestingly, a significant association between BDNFMet66 carrier status and development of PD symptoms was found at 6 weeks postpartum among mothers delivering during

autumn/winter [47]. Maternal BDNF serum levels were markedly decreased, both before and after childbirth, being correlated with 5-HT decreased levels in a study by Lommatzsch [48]. Maternal early pregnancy serum BDNF levels were significantly lower in women with antepartum depression compared to women without depression; lower BDNF levels were associated with increased odds of maternal antepartum depression. In particular, women whose serum BDNF levels were in the lowest three quartiles had 1.61-fold increased odds of antepartum depression compared with women whose BDNF levels were in the highest quartile [49]. Fung [50] found lower maternal serum BDNF levels in early pregnancy associated with antepartum depression. Decreased BDNF concentrations in perinatal depressive disorders have been reported in a recent review [51].

26.2.2 Cytokines

During depressive episodes, a glucocorticoid resistance has been observed, explaining innate immunity activation and the consequent inflammatory dysregulation typical of depressed patients [52]. During pregnancy increased inflammation has been reported to contribute to MDD susceptibility, particularly in the third trimester [53]. On the other hand, Simpson and colleagues [54] found no significant association between depressive symptoms and IL-6, IL-10, TNF-α, and CRP levels during pregnancy, at 12 weeks postpartum, or over time. CRP was not associated with depressive symptoms nor response to treatment in a secondary analysis of a trial of PPD treatment conducted by Miller and colleagues [55]. Depression and inflammation have been associated with poorer birth outcomes: a study with African-American women reported higher levels of some inflammatory biomarkers (IL-6, IL-1), which were directly associated with more depressive symptoms and a disparate burden of poorer birth outcomes [56]. Similar results were reported by Azar and Mercer [57].

A study examined biomarker trends with EPDS score in the third trimester of pregnancy and 3 and 6 months postpartum: elevated serum TNF-α was associated with lower EPDS total score, and IL-6, CRP, and IL-1β did not demonstrate significant associations with depressive symptoms [58]. A prospective, observational study enrolled women undergoing a scheduled cesarean delivery, and maternal plasma and cerebrospinal fluid were collected preoperatively: no significant associations were found between any of the plasma cytokines and PD, whereas higher cerebrospinal fluid, interleukin-1β, interleukin-23, and interleukin-3 were significantly associated with increased odds of PD [59]. As recently reported by Brann and colleagues [60] from pregnancy to postpartum, there is a tremendous change in the immune system with several proteins with anti-inflammatory and immune modulatory properties being higher in pregnancy, promoting pregnancy progress. This group previously reported that inflammation markers in a late pregnancy plasma sample can predict depressive symptoms at 8 weeks postpartum [61]. A recent study

evaluated mean counts of T cells (all CD3+ T cells), T helper cells, (CD3 + CD4+ T cells), and T cytotoxic cells (CD3 + CD8+ T cells) finding increased levels in healthy postpartum women compared to healthy non-postpartum controls, but not in women with PPD, confirming that the postpartum period in healthy women is a time of enhanced T cell activity, whereas women with postpartum depression failed to show physiological enhanced T cell activity postpartum [62].

26.2.3 Oxytocin

A prospective perinatal cohort study tested associations between OT levels during breastfeeding and stress reactivity: in breastfeeding women with PPD, a positive correlation was found between oxytocin AUC and cortisol, whereas a negative correlation was reported among asymptomatic women [63]. Higher oxytocin levels were associated with lower depressive symptoms in a review by Moura and colleagues [64]. In our study subjects with lower oxytocin plasma levels, independently from the presence of preeclampsia or an affective/anxiety disorder, showed worse EPDS and STAI-S scores than women with higher hormone levels [65]. In a previous study, OXT during pregnancy was negatively associated with a EPDS $\geq$ 10, indicating a higher risk for the development of PD. This suggests an increased occurrence of depressive symptoms in the first 2 weeks after delivery in individuals with low plasma OXT concentrations during pregnancy [66]. A recent review evaluated literature on potential relationships between OT and PD: of the 12 studies focused on endogenous oxytocin, 8 studies suggested an inverse relationship between plasma OT levels and depressive symptoms [67].

26.2.4 Vitamin D

Vitamin D has regulatory functions in the immune system, acting as a potential neurosteroid. Both vitamin D receptors and 1α-hydroxylase have been found in the brain, which suggests that low 25OHD levels may be linked to neuropathology [68]. In animal models there is evidence that developmental vitamin D deficiency can lead to brain abnormalities which mimic those in schizophrenic patients (e.g., enlarged ventricles), demonstrating that vitamin D may be critical for normal cognitive development and function. In addition to its role in neurological function, vitamin D has important implications for the immune system. Pregnancy may represent a stress test [69] in women, explaining why vitamin D deficiency in pregnancy may reveal depression, leading to potential negative sequelae for the maternal infant dyad. Inactive precursor 25(OH)D readily crosses the tissue to the fetal compartment, besides the kidneys, the placenta can potentially activate 25(OH)D, through 1-α-hydroxylase enzyme producing 1,25(OH)2D [70]. A vitamin D levels

regulation in the placental tissue may modulate anti-inflammatory effects and influence pregnancy development and/or perinatal outcome.

Moreover, the active form of vitamin D regulates tyrosine hydroxylase gene transcription, a key enzyme for catecholamine synthesis. Vitamin D deficiency in pregnancy has important maternal and fetal implications, with increased risk of developing gestational diabetes, preeclampsia, preterm birth, and small for gestational age birth weight. In the first stage of pregnancy, vitamin D (mainly Vitamin D3, the predominant form in the maternal blood) is involved in cytokine metabolism regulation and in the modulation of the immune system, thereby contributing to the embryo implantation and regulating the secretion of several hormones. Actually, there is no homogeneous consensus on vitamin D recommended intakes, in Italy, a recent consensus document published by the Societies of Pediatrics emphasizes the high prevalence of deficiency and the importance of prophylaxis also during pregnancy and breastfeeding.

Low vitamin D levels have been associated with a greater vulnerability to depressive symptoms onset [71]. In 2010 Murphy and colleagues [72] postulated that there may be a negative correlation between vitamin D levels and PD, being women with lower vitamin levels at higher risk of depression. A significant negative correlation between vitamin D levels in the first trimester of pregnancy and depressive symptoms in the second trimester was later reported in two different studies [73, 74]. Gur and colleagues [75] pointed out that lower maternal25-hydroxyvitaminD3 levels during the second trimester of pregnancy were associated with higher levels PD, data confirmed in a prospective cohort by Robinson et al. [76]. A cross-sectional study, by Miyake et al. [77], found that higher dietary vitamin D intake was significantly associated with a lower prevalence of depressive symptoms during pregnancy. A recent prospective study reported, among women with higher levels of inflammatory markers, an association between lower prenatal log25(OH)D and significantly higher PD symptoms [78]. In a study by Lamb [79] exploring relationships between maternal and cord blood vitamin D levels and maternal depressive symptoms, a significant inverse relationship between vitamin D status and depressive symptoms was observed. In particular, low cord blood 25OHD levels were inversely associated with higher EPDS scores in the third trimester. A review reported an association of PD with lower levels of folate, vitamin D, Fe, Se, Zn, and fats and fatty acids, while two studies found associations between PD and higher nutrient levels, and eight studies found no evidence of an association [80].

Prenatal vitamin D deficiency increased risk for adverse perinatal outcomes (DAVID study): this relative risk increased as the woman reached her delivery (RR = 3.43 at 14 weeks gestation; RR = 5.14 at the time of delivery). In the same sample, 19% of women were considered at risk for minor depression with a cutoff of EPDS > 10. When women were both above this minor depression cutoff and below the vitamin D deficiency cutoff (25(OH)D/20 ng/ml), they were more likely to have an adverse perinatal outcome [78].

26.2.5 Polyunsaturated Fatty Acids

A prospective cohort study evaluated the association between serum lipids and depressive symptom scores during pregnancy: HDL-c concentrations were inversely associated with changes in EPDS score [81]. Long-chain polyunsaturated fatty acids (LC-PUFA), particularly DHA and AA, were found to have an important role in fetal and infant development. Observational studies have suggested an association between low DHA status after pregnancy and PD. A study by Otto et al. [82] evaluated mood symptoms with EPDS, reporting a lower DHA availability in the postpartum period in women included in the "possible depressed" group. Since LC-PUFA required by the fetus is supplied by preferential placental transfer of preformed LC-PUFA rather than their precursor, it has been hypothesized that additional LC-PUFA maternal supply, especially DHA, during pregnancy may improve maternal and infant well-being. Chang and colleagues [83] reported in depressed cases significantly lower levels of total n-3, docosahexaenoic acid (DHA), and eicosapentaenoic (EPA) but a higher omega-6 (n-6)/n-3 PUFAs ratio and tumor necrosis factor alpha (TNF-α). PD duration was associated with lower n-3 PUFAs levels, including DHA and EPA. A randomized controlled trial designed to assess whether prenatal EPA- or DHA-rich fish oil supplementation would prevent perinatal depressive symptoms in women at risk found that prenatal supplementation with EPA-rich fish oil significantly reduced levels of several inflammatory cytokines in maternal plasma. Prenatal DHA-rich fish oil, differently, had no significant effect on cytokine concentrations. Both supplementations had no significant effect on umbilical cord blood cytokine concentrations [84]. A recent meta-analysis of RCTs on omega-3 PUFAs for PD reported that omega-3 PUFAs have an overall significant small beneficial effect on PD, with important subgroup differences: the effect was medium to large in postpartum women, whereas during pregnancy a negligible effect was found [85]. Previously no efficacy in supplementation was reported in other studies [86–88].

26.3 Clock Genes

The circadian clock, an internal time-keeping system, regulates various physiological processes, including metabolism, sleep, body temperature, blood pressure, and endocrine, immune, cardiovascular, and renal function, through the generation of approximately 24-h circadian rhythms in gene expression, which are translated into rhythms in metabolism and behavior [89].

Circadian rhythm disruption is common in depressed patients, several researches have demonstrated that major depressed patients present a dysregulation of the CLOCK genes involved in circadian biological activity control including sleep-wake cycle. Some studies have shown that specific "clock" gene polymorphisms are associated with an increased risk of depression. A different expression of "clock" genes would be linked to the circadian rhythm dysregulation, in particular of sleep-wake rhythms, which in turn would contribute to mood

symptoms development [90, 91]. Circadian rhythms seem to be altered in major depressive disorder, as showed by changes in circadian patterns of gene expression [92]. In the study conducted by Buoli and collaborators, depressed pregnant women showed hypermethylation of CLOCK and hypomethylation of CRY1, PER1, and PER2, all involved in circadian rhythms. These alterations are suggestive of a delay in circadian rhythms, with shifts in light melatonin onset [91].

26.4 Epigenetics

Epigenetics study potential heritable molecular modifications in DNA and histone proteins that can modify gene expression without changes in DNA sequence. Epigenetic factors include DNA methylation, a process of cytosine methylation of cytosine-phosphate-guanine (CpG) dinucleotides, which can alter chromatin accessibility and thereby gene transcription [17], and miRNAs, small non-coding RNA molecules acting at cytoplasmic level as regulators of gene expression, either preventing the translation of the target mRNA or making the mRNA filaments unstable [93].

Epigenetic aspects can represent a mechanism through which the stress suffered by an individual can be transmitted to subsequent generations: in offsprings the presence of anomalies in the expression of some genes (e.g., the stress-related gene FKBP5) could be indicative of the well-being of the mother during pregnancy [94]. Women with PD have epigenetic alterations in genes with a role in neuronal differentiation [2], involving several biological functions: HPA axis functioning associated with elevated cortisol and lower levels of serotonin with respect to healthy future mothers. Oxytocin has a role in balancing HPA axis over-activity [95], moreover, facilitates bonding, empathy, and attachment, enabling mothers to be more sensitive to their infants' needs [96–98].

26.5 Conclusions

In the last decades, studies have shown that perinatal mental health disorders involve risks for both mother and offsprings [99]; however the molecular mechanisms mediating long-lasting effects of PD exposure in utero have been only partially explored, involving inflammatory and stress response systems [100]. The identification of mechanisms underlining PD onset may lead to the early identification of novel targets to prevent transmission from mothers to infants; the search for reliable biomarkers in high-risk mothers is a medical priority to prevent PD and its consequences on newborns [101]. Actually, data are too scanty to draw definitive conclusions; future studies with larger samples and methodological similar methods are necessary. In our opinion it is interesting that some biomarkers could be modifiable risk factors (e.g., vitamin D/LC-PUFA maternal supplementation), providing the opportunity for improved and safe treatments in women/newborns' mental health.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013.
2. Lapato DM, Roberson-Nay R, Kirkpatrick RM, et al. DNA methylation associated with postpartum depressive symptoms overlaps findings from a genome-wide association meta-analysis of depression. Clin Epigenetics. 2019;11(1):169.
3. Figueiredo FP, Parada AP, de Araujo LF, et al. The influence of genetic factors on peripartum depression: a systematic review. J Affect Disord. 2015;172:265–73.
4. Woody CA, Ferrari AJ, Siskind DJ, et al. A systematic review and meta-regression of the prevalence and incidence of PD. J Affect Disord. 2017;219:86–92.
5. Meltzer-Brody S, Howard LM, Bergink V, et al. Postpartum psychiatric disorders. Nat Rev Dis Primers. 2018;4:18022.
6. Peñalver Bernabé B, Maki PM, Dowty SM, et al. Precision medicine in PD in light of the human microbiome. Psychopharmacology. 2020;237(4):915–41.
7. Dagher RK, Bruckheim HE, Colpe LJ, et al. PD: Challenges and opportunities. J Womens Health (Larchmt). 2021;30(2):154–9.
8. Galea LAM, Frokjaer VG. PD: Embracing variability toward better treatment and outcomes. Neuron. 2019;102(1):13–6.
9. Serati M, Buoli M, Altamura AC. Factors that affect duration of untreated illness in pregnant women with bipolar disorder. Am J Obstet Gynecol. 2015;213(6):876.
10. Barkin JL, Osborne LM, Buoli M, et al. Training frontline providers in the detection and management of perinatal mood and anxiety disorders. J Womens Health (Larchmt). 2020;29(7):889–90.
11. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. J Clin Psychiatry. 2013;74(4):e321–41.
12. Buoli M, Grassi S, Di Paolo M, et al. Is perinatal major depression affecting obstetrical outcomes? Commentary on "Impact of maternal depression on perinatal outcome in hospitalized women-a prospective study". Arch Womens Ment Health. 2019;23(4):595–6.
13. Serati M, Bertino V, Malerba MR, et al. Obstetric complications and subsequent risk of mood disorders for offspring in adulthood: a comprehensive overview. Nord J Psychiatry. 2020;1–9.
14. Schlotz W, Phillips DI. Fetal origins of mental health: evidence and mechanisms. Brain Behav Immun. 2009;23(7):905–16.
15. Howard LM, Piot P, Stein A. No health without perinatal mental health. Lancet. 2014;384(9956):1723–4.
16. Plant DT, Pariante CM, Sharp D, Pawlby S. Maternal depression during pregnancy and offspring depression in adulthood: role of child maltreatment. Br J Psychiatry. 2015;207(3):213–20.
17. Viuff AC, Sharp GC, Rai D, et al. Maternal depression during pregnancy and cord blood DNA methylation: findings from the Avon Longitudinal Study of Parents and Children. Transl Psychiatry. 2018;8:244.
18. Goodman JH. PD and infant mental health. Arch Psychiatr Nurs. 2019;33(3):217–24.
19. World Health Organization. Maternal mental health and child health and development in low and middle income countries: report of the meeting, Geneva, Switzerland, 30 January–1 February, 2008.
20. Curry SJ, Krist AH, Owens DK, et al. US Preventive Services Task Force Interventions to Prevent PD: US Preventive Services Task Force Recommendation Statement. JAMA. 2019;321(6):580–7.
21. Goldstein Z, Rosen B, Howlett A, et al. Interventions for paternal PD: a systematic review. J Affect Disord. 2020;265:505–10.
22. Bruno A, Celebre L, Mento C, et al. When fathers begin to Falter: a comprehensive review on paternal PD. Int J Environ Res Public Health. 2020;17(4):1139.

23. Serati M, Redaelli M, Buoli M, Altamura AC. Perinatal major depression biomarkers: a systematic review. J Affect Disord. 2016;193:391–404.
24. Konstantinou G, Spyropoulou A, Zervas I. Immune-inflammatory and autoimmune mechanisms in postpartum depression. Psychiatriki. 2020;31(1):47–56. Greek, Modern
25. Strimbu K, Tavel JA. What are biomarkers? Curr Opin HIV AIDS. 2010;5(6):463–6.
26. Aronson JK, Ferner RE. Biomarkers: a general review. Curr Protoc Pharmacol. 2017;76:9.23.1–9.23.17.
27. Gururajan A, Clarke G, Dinan TG, Cryan JF. Molecular biomarkers of depression. Neurosci Biobehav Rev. 2016;64:101–33.
28. Guintivano J, Manuck T, Meltzer-Brody S. Predictors of postpartum depression: a comprehensive review of the last decade of evidence. Clin Obstet Gynecol. 2018;61(3): 591–603.
29. Šebela A, Hanka J, Mohr P. Etiology, risk factors, and methods of postpartum depression prevention. Ceska Gynekol. 2018;83(6):468–73.
30. Šebela A, Hanka J, Mohr P. Diagnostics and modern trends in therapy of postpartum depression. Ceska Gynekol. 2019;84(1):68–72.
31. Bloch M, Daly RC, Rubinow DR. Endocrine factors in the etiology of postpartum depression. Compr Psychiatry. 2003;44(3):234–46.
32. Guintivano J, Arad M, Gould TD, et al. Antenatal prediction of postpartum depression with blood DNA methylation biomarkers. Mol Psychiatry. 2014;19(5):560–7.
33. Pinsonneault JK, Sullivan D, Sadee W, et al. Association study of the estrogen receptor gene ESR1 with postpartum depression—a pilot study. Arch Womens Ment Health. 2013;16(6):499–509.
34. McEvoy K, Payne JL, Osborne LM. Neuroactive steroids and PD: a review of recent literature. Curr Psychiatry Rep. 2018;20(9):78.
35. O'Connor TG, Tang W, Gilchrist MA, et al. Diurnal cortisol patterns and psychiatric symptoms in pregnancy: short-term longitudinal study. Biol Psychol. 2014;96:35–41.
36. Glynn LM, Davis EP, Sandman CA. New insights into the role of perinatal HPA-axis dysregulation in postpartum depression. Neuropeptides. 2013;47(6):363–70.
37. Ferguson EH, Di Florio A, Pearson B, et al. HPA axis reactivity to pharmacologic and psychological stressors in euthymic women with histories of postpartum versus major depression. Arch Womens Ment Health. 2017;20(3):411–20.
38. Zaconeta AM, Amato AA, Motta LD, Casulari LA. Relationship between placental corticotropin-releasing hormone and postpartum depression: can defining what “postpartum depression” means make a difference? Psychosom Med. 2015;77(3):342.
39. Parcells DA. Women's mental health nursing: depression, anxiety and stress during pregnancy. J Psychiatr Ment Health Nurs. 2010;17(9):813–20.
40. Buss C, Davis EP, Shahbaba B, Pruessner JC, Head K, Sandman CA. Maternal cortisol over the course of pregnancy and subsequent child amygdala and hippocampus volumes and affective problems. Proc Natl Acad Sci U S A. 2012;109(20):E1312–9.
41. Buss C, Entringer S, Wadhwa PD. Fetal programming of brain development: intrauterine stress and susceptibility to psychopathology. Sci Signal. 2012a;5(245):pt7.
42. Bergink V, Gibney SM, Drexhage HA. Autoimmunity, inflammation, and psychosis: a search for peripheral markers. Biol Psychiatry. 2014;75(4):324–31.
43. Apter-Levy Y, Zagoory-Sharon O, Feldman R. Chronic depression alters mothers' DHEA and DEHA-to-cortisol ratio: implications for maternal behavior and child outcomes. Front Psychiatry. 2020;11:728.
44. Sundström Poromaa I, Comasco E, Georgakis MK, Skalkidou A. Sex differences in depression during pregnancy and the postpartum period. J Neurosci Res. 2017;95(1–2): 719–30.
45. Osborne S, Biaggi A, Chua TE, et al. Antenatal depression programs cortisol stress reactivity in offspring through increased maternal inflammation and cortisol in pregnancy: The Psychiatry Research and Motherhood-Depression (PRAM-D) Study. Psychoneuroendocrinology. 2018;98:211–21.

46. Figueira P, Malloy-Diniz L, Campos SB, et al. An association study between the Val66Met polymorphism of the BDNF gene and postpartum depression. Arch Womens Ment Health. 2010;13(3):285–9.
47. Comasco E, Sylvén SM, Papadopoulos FC, et al. Postpartum depressive symptoms and the BDNFVal66Met functional polymorphism: effect of season of delivery. Arch Womens Ment Health. 2011;14(6):453–63.
48. Lommatzsch M, Hornych K, Zingler C, et al. Maternal serum concentrations of BDNF and depression in the perinatal period. Psychoneuroendocrinology. 2006;31(3):388–94.
49. Pinheiro RT, Pinheiro KA, daCunha Coelho FM, et al. Brain derived neurotrophic factor levels in women with postpartum affective disorder and suicidality. Neurochem Res. 2010;37(10):2229–34.
50. Fung J, Gelaye B, Zhong QY, et al. Association of decreased serum brain-derived neurotrophic factor (BDNF) concentrations in early pregnancy with antepartum depression. BMC Psychiatry. 2015;15(1):43.
51. Mandolini GM, Lazzaretti M, Delvecchio G, et al. Association between serum BDNF levels and maternal PD: A review: special section on "Translational and Neuroscience Studies in Affective Disorders". J Affect Disord. 2020;261:271–6. (Maria Nobile MD, PhD)
52. Horowitz MA, Zunszain PA. Neuroimmune and neuroendocrine abnormalities in depression: two sides of the same coin. Ann N Y Acad Sci. 2015;1351:68–79.
53. Leff-Gelman P, Mancilla-Herrera I, Flores-Ramos M, et al. The immune system and the role of inflammation in PD. Neurosci Bull. 2016;32(4):398–420.
54. Simpson W, Steiner M, Coote M, Frey BN. Relationship between inflammatory biomarkers and depressive symptoms during late pregnancy and the early postpartum period: a longitudinal study. Braz J Psychiatry. 2016;38(3):190–6.
55. Miller ES, Hoxha D, Pinheiro E, et al. The association of serum C-reactive protein with the occurrence and course of postpartum depression. Arch Womens Ment Health. 2019;22(1):129–32.
56. Cassidy-Bushrow AE, Peters RM, Johnson DA, Templin TN. Association of depressive symptoms with inflammatory biomarkers among pregnant African–American women. J Reprod Immunol. 2012;94(2):202–9.
57. Azar R, Mercer D. Mild depressive symptoms are associated with elevated C-reactive protein and proinflammatory cytokine levels during early to mid- gestation: a prospective pilot study. J Womens Health (Larchmt). 2013;22(4):385–9.
58. Buglione-Corbett R, Deligiannidis KM, Leung K, et al. Expression of inflammatory markers in women with perinatal depressive symptoms. Arch Womens Ment Health. 2018;21(6):671–9.
59. Miller ES, Sakowicz A, Roy A, et al. Plasma and cerebrospinal fluid inflammatory cytokines in PD. Am J Obstet Gynecol. 2019;220(3):271.e1–271.e10.
60. Bränn E, Edvinsson Å, Rostedt Punga A, et al. Inflammatory and anti-inflammatory markers in plasma: from late pregnancy to early postpartum. Sci Rep. 2019;9(1):1863.
61. Bränn E, Papadopoulos F, Fransson E, et al. Inflammatory markers in late pregnancy in association with postpartum depression: a nested case-control study. Psychoneuroendocrinology. 2017;79:146–59.
62. Osborne LM, Gilden J, Kamperman AM, et al. T-cell defects and postpartum depression. Brain Behav Immun. 2020;87:397–403.
63. Cox EQ, Stuebe A, Pearson B, et al. Oxytocin and HPA stress axis reactivity in postpartum women. Psychoneuroendocrinology. 2015;55:164–72.
64. Moura D, Canavarro MC, Figueiredo-Braga M. Oxytocin and depression in the perinatal period-a systematic review. Arch Womens Ment Health. 2016;19(4):561–70.
65. Serati M, Grassi S, Redaelli M, et al. Is there an association between oxytocin levels in plasma and pregnant women's mental health? J Am Psychiatr Nurses Assoc. 2021;27(3):222–30.
66. Skrundz M, Bolten M, Nast I, et al. Plasma oxytocin concentration during pregnancy is associated with development of postpartum depression. Neuropsychopharmacology. 2011;36(9):1886–93.

67. Thul TA, Corwin EJ, Carlson NS, et al. Oxytocin and postpartum depression: a systematic review. Psychoneuroendocrinology. 2020;120:104793.
68. Eyles DW, Smith S, Kinobe R, et al. Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat. 2005;29(1):21–30.
69. Williams ME, Frey BN. Salivary cortisol during memory encoding in pregnancy predicts postpartum depressive symptoms: a longitudinal study. Trends Psychiatry Psychother. 2017;39(4):280–4.
70. Larqué E, Morales E, Leis R, Blanco-Carnero JE. Maternal and foetal health implications of vitamin D status during pregnancy. Ann Nutr Metab. 2018;72(3):179–92.
71. Cui X, Pertile R, Liu P, Eyles DW. Vitamin D regulates tyrosine hydroxylase expression: N-cadherin a possible mediator. Neuroscience. 2015;304:90–100.
72. Murphy PK, Mueller M, Hulsey TC, et al. An exploratory study of postpartum depression and vitamin D. J Am Psychiatr Nurses Assoc. 2010;16(3):170–7.
73. Cassidy-Bushrow AE, Peters RM, Johnson DA. Vitamin D nutritional status and antenatal depressive symptoms in African American women. J Womens Health (Larchmt). 2012;21:1189–95.
74. Brandenbarg J, Vrijkotte T, Goedhart G, VanEijsden M. Maternal early- pregnancy vitamin status is associated with maternal depressive symptoms in the Amsterdam born children and their development Cohort. Psychosom Med. 2012;74:751–7.
75. Gur EB, Gokduman A, Turan GA, et al. Mid pregnancy vitamin D levels and postpartum depression. Eur J Obs Gynecol Reprod Biol. 2014;179:110–6.
76. Robinson M, Whitehouse AJ, Newnham JP, et al. Low maternal serum vitamin during pregnancy and the risk for postpartum depression symptoms. Arch Womens Ment Health. 2014;17(3):213–9.
77. Miyake Y, Tanaka K, Okubo H, et al. Dietary vitamin D intake and prevalence of depressive symptoms during pregnancy in Japan. Nutrition. 2015;31(1):160–5.
78. Accortt EE, Schetter CD, Peters RM, Cassidy-Bushrow AE. Lower prenatal vitamin D status and postpartum depressive symptomatology in African American women: preliminary evidence for moderation by inflammatory cytokines. Arch Womens Ment Health. 2015:1–11.
79. Lamb AR, Lutenbacher M, Wallston KA, et al. Vitamin D deficiency and depressive symptoms in the perinatal period. Arch Womens Ment Health. 2018;21(6):745–55.
80. Sparling TM, Nesbitt RC, Henschke N, Gabrysch S. Nutrients and PD: a systematic review. J Nutr Sci. 2017;6:e61.
81. Teofilo MM, Farias DR, Pinto Tde J, et al. HDL-cholesterol concentrations are inversely associated with Edinburgh Postnatal Depression Scale scores during pregnancy: results from a Brazilian cohort study. J Psychiatr Res. 2014;58:181–8.
82. Otto SJ, de Groot RH, Hornstra G. Increased risk of postpartum depressive symptoms is associated with slower normalization after pregnancy of the functional docosahexaenoic acid status. Prostaglandins Leukot Essent Fatty Acids. 2003;69(4):237–43.
83. Chang JP, Lin CY, Lin PY, et al. Polyunsaturated fatty acids and inflammatory markers in major depressive episodes during pregnancy. Prog Neuro-Psychopharmacol Biol Psychiatry. 2018;80(Pt C):273–8.
84. Mozurkewich EL, Berman DR, Vahratian A, et al. Effect of prenatal EPA and DHA on maternal and umbilical cord blood cytokines. BMC Pregnancy Childbirth. 2018;18(1):261.
85. Mocking RJT, Steijn K, Roos C, et al. Omega-3 fatty acid supplementation for PD: a meta-analysis. J Clin Psychiatry. 2020;81(5):19r13106.
86. Doornbos B, vanGoor SA, Dijck-Brouwer DA, et al. Supplementation of a low dose of DHA or DHAþAA does not prevent peripartum depressive symptoms in a small population based sample. Prog Neuro-Psychopharmacol Biol Psychiatry. 2009;33(1):49–52.
87. Mozurkewich EL, Clinton CM, Chilimigras JL, et al. The mothers, Omega-3, and Mental Health Study: a double-blind, randomized controlled trial. Am J Obs Gynecol. 2013;208(4):313–9.
88. De Giuseppe R, Roggi C, Cena H. N-3LC-PUFA supplementation: effects on infant and maternal outcomes. Eur J Nutr. 2014;53(5):1147–54.

89. Gene Cards. The Human Gene Database, 2020. https://www.genecards.org/.
90. Buoli M, Serati M, Grassi S, et al. The role of clock genes in the etiology of major depressive disorder. J Affect Disord. 2018;234:351–7.
91. Buoli M, Grassi S, Iodice S, et al. The role of clock genes in perinatal depression: the light in the darkness. Acta Psychiatr Scand. 2019;140(4):382–4.
92. Li JZ, Bunney BG, Meng F, et al. Circadian patterns of gene expression in the human brain and disruption in major depressive disorder. Proc Natl Acad Sci U S A. 2013;110:9950–5.
93. Tabano S, Caldiroli A, Terrasi A, et al. A miRNome analysis of drug-free manic psychotic bipolar patients versus healthy controls. Eur Arch Psychiatry Clin Neurosci. 2019;270(7):893–900.
94. Bierer LM, Bader HN, Daskalakis NP, et al. Intergenerational effects of maternal holocaust exposure on FKBP5 methylation. Am J Psychiatry. 2020;177(8):744–53.
95. King L, Robins S, Chen G, et al. Perinatal depression and DNA methylation of oxytocin-related genes: a study of mothers and their children. Horm Behav. 2017;96:84–94.
96. Feldman R, Weller A, Zagoory-Sharon O, Levine A. Evidence for a neuroendocrinological foundation of human affiliation: plasma oxytocin levels across pregnancy and the postpartum period predict mother-infant bonding. Psychol Sci. 2007;18:965–70.
97. Roy B, Yoshino Y, Allen L, et al. Exploiting circulating microRNAs as biomarkers in psychiatric disorders. Mol Diagn Ther. 2020;24(3):279–98.
98. Carnevali GS, Buoli M. The role of epigenetics in PD: are there any candidate biomarkers? J Affect Disord. 2021;280(Pt B):57–67.
99. Stein A, Pearson RM, Goodman SH, et al. Effects of perinatal mental disorders on the fetus and child. Lancet. 2014;384(9956):1800–19.
100. Pariante CM. Depression during pregnancy: molecular regulations of mothers' and children's behaviour. Biochem Soc Trans. 2014;42(2):582–6.
101. Biaggi A, Conroy S, Pawlby S, Pariante CM. Identifying the women at risk of antenatal anxiety and depression: a systematic review. J Affect Disord. 2016;191:62–77.

Maternal Stress and Postpartum Psychosis

27

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27.1 Introduction

Postpartum, or puerperal, psychosis is the most severe psychiatric disorder associated with childbirth [1, 2]. It can result in considerable distress for the woman and may have long-term consequences for their wellbeing and that of their baby and family, as well as having implications for wider society [2]. In rare cases postpartum psychosis can lead to suicide and/or infanticide [3–5] and is consequently considered a psychiatric emergency, typically requiring hospital admission [2, 6, 7].

Whilst there is a lack of consensus around diagnostic classification, the term postpartum psychosis is widely used in clinical practice to describe an affective psychosis or psychosis not otherwise specified with onset in the first 4–6 weeks after childbirth. Symptoms can include both mania and depression, commonly in the form of fluctuating mood, with manic and depressive symptoms often occurring simultaneously or in rapid succession, as in a mixed affective episode [8, 9]. Psychotic symptoms include hallucinations, which can be present in all sensory modalities, and delusions, which are commonly of reference, persecution or grandiosity [5, 10]. Many women with postpartum psychosis will also show signs of confusion and perplexity [2, 4]. Symptoms can begin within days of the delivery and develop rapidly [11, 12].

Postpartum psychosis is relatively rare, occurring in 1–2 per 1000 deliveries in the general population [8]. However, the risk is greatly increased for women with a diagnosis of bipolar disorder, schizoaffective disorder and/or a personal or family history of postpartum psychosis, with up to 50% experiencing an episode after giving birth [13–17].

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Despite the severity of postpartum psychosis, knowing that it has a clearly defined onset following childbirth and that women with certain pre-existing diagnoses are at greatly increased risk, it remains unclear why some women at risk become unwell after giving birth whilst others remain well. One potential theory is that experience of psychosocial stress and dysregulation of the biological stress system play a role in the onset of postpartum psychosis, particularly in women at increased risk. The aim of this chapter is, therefore, to discuss the literature on the role of psychosocial stress and the biological stress system in the onset of postpartum psychosis, including some of our own work in this area.

27.2 Stress and the Perinatal Period

Pregnancy and childbirth are major life events, during which women experience many psychological, social and biological challenges. Like any other life event, the transition to motherhood can be stressful. In addition to general (i.e., not pregnancy specific) stressful life events, pregnant women can experience a variety of pregnancy-specific stressors, including physical health problems, relationship stress and pregnancy-related concerns [18].

Of importance, the occurrence of stressful life events has been shown to be predictive of various mental health problems, including postnatal depression and psychoses unrelated to gestation. Indeed, previous meta-analyses identified stressful life events amongst the strongest predictors for postpartum depression [19, 20], whilst a synthesis of these reviews and the subsequent literature, including evidence from more than 2500 participants, found stressful life events to be a moderate to strong antenatal predictor of postpartum depression, with an effect size (*d*) of 0.61 [21].

Research also suggests a temporal relationship between stressful life events and affective and non-affective psychoses unrelated to gestation, with evidence of an increase in stressful life events occurring in the months preceding psychotic symptoms. A literature review and meta-analysis of 16 studies reported that individuals with psychosis were approximately three times more likely than controls to experience stressful life events in the months prior to the onset of psychotic symptoms [22]. A more recent systematic review of 23 studies also found evidence of an association between recent stressful life events and psychotic *relapse* in individuals with established psychosis [23].

As well as psychosocial challenges, pregnancy and childbirth are also times of dramatic physiological change, including changes to the stress system (i.e., hypothalamic-pituitary-adrenal (HPA) axis) [24]. Indeed, the HPA axis undergoes major changes during pregnancy. As a result of placental corticotropin-releasing hormone (CRH) production, CRH levels increase exponentially from the eighth to tenth week of pregnancy, rising up to a thousand times their non-pregnant levels [25]. Increases in CRH result in a rise in adrenocorticotropic hormone (ACTH) secretion, although levels remain within normal limits [25]. Both CRH and ACTH peak in the third trimester and during labour and delivery [26]. Circulating ACTH is highly correlated with cortisol levels, which rise exponentially from around the eleventh week of pregnancy. The largest increases in cortisol appear to happen between the first and

second trimester, with levels peaking and reaching a plateau in the third trimester, at around two to three times the non-pregnant levels [26]. Such changes are thought to play an important role in maintaining pregnancy, protecting the foetus and determining the length of gestation, as well as being fundamental for foetal development [24, 25, 27]. Following delivery of the placenta, there is a rapid drop in placental CRH, with levels of both CRH and ACTH typically returning to normal within 24 hours of delivery [26]. Whilst levels of cortisol drop rapidly in the immediate postpartum, in contrast to levels of CRH and ACTH, normalisation of plasma cortisol is more prolonged [26], and for many women it can take several weeks for cortisol levels to return to their non-pregnant levels (e.g., [28]). Despite the dramatic increases in circulating levels of cortisol, the typical diurnal pattern (i.e., a sharp increase in the first 30–45 minutes following morning awakening (cortisol awakening response (CAR)), followed by a gradual decline over the course of the day and reaching the lowest levels at night) is maintained during pregnancy [24]. On the other hand, as pregnancy progresses the HPA axis is thought to become less responsive to physiological and psychological stressors, resulting in an attenuated stress response in late gestation [29, 30].

The perinatal period is not only a time of dramatic change to the stress system. The immune system, with which the HPA axis is complexly linked, also undergoes significant alterations during pregnancy and the early postpartum. Indeed, it has been suggested that pregnancy represents a 'unique immune condition', characterised by increased recognition, communication, trafficking and repair [31, 32]. This highly dynamic immune response is essential for establishing and maintaining pregnancy, with the maternal immune system promoting tolerance towards the semi-allogenic foetus whilst also providing protection from pathogens. To achieve this, it has been proposed that pregnancy involves three distinct immune stages, characterised by both pro- and anti-inflammatory states [31, 33]. The first stage is required for successful implantation and placentation. Immune cells, including natural killer (NK) cells, dendritic cells and macrophages, infiltrate the decidua and surround the invading trophoblast cells. However, rather than acting to reject the blastocyst, these immune cells instead play a supportive role, repairing and restructuring uterine tissue [31, 33–36]. Thus, the first and early second trimesters of pregnancy are characterised by a T helper (Th) 1-type proinflammatory response, necessary to repair damaged tissue and remove cell debris [31, 33, 34, 37]. Following successful implantation and placentation, there is a period of rapid foetal growth and development, lasting from weeks 13–27 [31, 33]. In order to maintain pregnancy, and prevent miscarriage or preterm birth during this phase, there is a switch from the Th1 proinflammatory environment to a predominantly Th2-type anti-inflammatory state [31, 33]. As well as promoting immune tolerance towards the foetus, anti-inflammatory responses in this stage also promote uterine growth and foetal development [33, 36, 37]. Thus, the second immunological stage provides a supportive immune environment in which symbiosis is established between maternal and foetal physiology [31, 33, 34, 37]. The final immunological stage occurs in preparation for the delivery. Following the onset of labour, immune cells migrate into the myometrium resulting in a shift back to a proinflammatory state. This proinflammatory

milieu promotes uterine contractions and the subsequent expulsion of the baby and the placenta [31, 33, 34]. It is thought that normal pre-pregnancy immune function does not return for up to several months following the delivery [38].

Whilst essential for pregnancy and foetal development, it is proposed that these dramatic changes in stress and immune physiology during the perinatal period contribute to maternal perinatal psychopathology, particularly in women with an existing vulnerability [39]. Research has indeed shown stress and immune system dysregulation in women with perinatal depression. Our research group recently showed both cortisol dysregulation (a blunted CAR and increased daily and evening cortisol levels) and elevated immune markers (IL-6, IL-10, TNF-α and VEGF) in pregnant women with a diagnosis of major depressive disorder, compared with pregnant controls [40]. Furthermore, there is evidence of an association between cortisol reactivity to stress during pregnancy and antenatal depression [41], as well as research showing that both cortisol reactivity to stress and increased CRH during pregnancy are associated with depression in the postnatal period [42, 43]. There is also some evidence of a heightened proinflammatory response, including increased IL-6, IL-1β and TNF-α, in women with postnatal depressive symptoms [44, 45].

There is also substantial research showing that both HPA axis and immune system dysregulation play a role in the onset and course of psychopathology unrelated to gestation. Indeed, there is evidence of a specific pattern of cortisol dysregulation in individuals with bipolar disorder and psychosis unrelated to childbirth, characterised by increased cortisol levels during the day and a blunted CAR [46, 47]. Furthermore, these alterations in HPA axis activation have also been reported in individuals at risk for psychosis [48–50], and are greatest in those who become unwell [51], suggesting a marker of biological vulnerability to psychosis, present prior to illness onset. Immune system dysregulation has also been implicated in the pathophysiology of both bipolar disorder and psychosis unrelated to gestation. Indeed, research has consistently shown elevations in various cytokines (e.g. IL-1β, sIL-2, IL-6 and TNF-α) in individuals with psychosis [52, 53] and those with bipolar disorder [54]. Furthermore, there is emerging evidence that elevated immune markers could be predictive of later mental illness [53, 55].

Given that pregnancy and childbirth are stressful life events, as well as a time when the body's main stress and immune systems undergo dramatic physiological change [24, 31, 33], and the fact that stressful life events, and HPA axis and immune dysregulation have been linked to other psychopathology, both related and unrelated to gestation (e.g., [21, 22, 40, 47]), it is indeed highly plausible that these psychosocial and biological factors play a role in the onset of postpartum psychosis.

27.3 Stressful Life Events in Postpartum Psychosis

Despite the extensive research into the relationship between both early (childhood) adversity and more recent stressful life events and psychopathology both related and unrelated to gestation, relatively few studies have examined the role of these factors in relation to postpartum psychosis.

Of the few studies conducted to date, the majority examining the impact of early life stress have found no association between experience of various childhood adversities and postpartum psychosis [56–58]. Indeed, Perry and colleagues found that women with bipolar disorder who had experienced an episode of postpartum psychosis were no more likely to have experienced an adverse childhood life event (including sexual, physical or emotional abuse, loss of a parent, sibling or close friend or parental separation) than women with bipolar disorder who had no lifetime history of affective or psychotic episodes in the perinatal period [58]. Similar findings have also been reported in general population samples. Data by Dowlatshahi and Paykel and, more recently, Meltzer-Brody and colleagues found no association between experience of adverse childhood experiences (including parental or sibling loss or separation, familial disruption, parental somatic illness, psychopathology or substance use disorder and parental criminality) and postpartum psychosis [56, 57].

Similarly, our own work has not found an association between parental loss or separation and postpartum relapse in women at increased risk of postpartum psychosis, although women at risk who relapsed in the first 4 weeks' postpartum were significantly more likely than women at risk who remained well to have experienced *severe* childhood maltreatment [59]. It is possible that discrepancies in findings result from methodological differences across studies. For example, Perry and colleagues did not specifically ask about experience of childhood abuse, which we did; instead they required women to voluntarily disclose any experience of abuse, which the authors suggest could have resulted in underreporting [58]. Alternatively, these differences could be due to differences in the definition of relapse and particularly whether any affective relapse, or only a psychotic relapse, was considered.

The role of more recent stressful life events (i.e., those occurring in the months prior to illness onset) has also been examined in relation to postpartum psychosis. A growing body of research suggests that women at risk of postpartum psychosis are *no* more likely to have experienced stressful life events prior to postpartum illness onset than those at risk who remain well in the postpartum period [60–63], suggesting experience of recent stressful life events may not represent a risk factor for postpartum relapse in women already at increased risk. Furthermore, studies in general population samples have found no association between maternal stressful life events during pregnancy and a psychotic episode in the postpartum period (e.g., [56, 63, 64]).

Interestingly, we have recently found that women with postpartum psychosis had significantly higher *perceived* stress compared to healthy postpartum women [60]. Furthermore, whilst women with postpartum psychosis did not differ significantly from those at risk who were well in the postpartum period, women at risk who remained well had perceived stress scores that were intermediate between those of women with postpartum psychosis and the healthy postpartum women [60]. Taken together these findings suggest that whilst stressful life events themselves may not represent a risk factor for postpartum psychosis, a woman's perception of stressful life events might play a role in the onset of postpartum symptoms in this disorder.

27.4 Presence of Biological Markers of Stress in Postpartum Psychosis

There is emerging evidence for the role of biological stress in the onset of postpartum psychosis. For example, our own work in this area has recently shown that women at risk of postpartum psychosis who relapsed following delivery had increased daily cortisol compared with women at risk who remained well in the early postpartum period [59]. This finding confirms and extends our earlier published data, in which we showed elevated daily cortisol levels at approximately 15 weeks postpartum in women with postpartum psychosis compared with healthy *postpartum* controls [60]. These findings suggest that daily cortisol dysregulation is an important underlying pathophysiological mechanism in the onset of psychosis after childbirth. Interestingly, we did not find any differences in CAR between the women at risk of postpartum psychosis who relapsed and those at risk who remained well [59], which also fits with our earlier findings measuring cortisol levels in postpartum women with postpartum psychosis [60]. This lack of a difference between the groups might, therefore, suggest that this particular element of the cortisol profile (i.e. the CAR) is a stable feature in women with postpartum psychosis.

It has also been proposed that dysregulation of the immune system might play an important role in the pathophysiology of postpartum psychosis, and we have recently suggested this may occur through immune system-mediated myelination processes, namely, disturbance in the regulatory T cell-CCN3 protein-(re)myelination axis [65]. Consistent with this hypothesis, there is accumulating evidence of immune system dysfunction in postpartum psychosis. Research has shown that compared with healthy postpartum women, women with postpartum psychosis show decreased levels of T cells and cytotoxic NK cells whilst showing an increase in regulatory NK cells, suggesting a possible defect in normal postpartum immune restoration [66, 67]. Furthermore, there is evidence of an upregulation of immune system-related monocyte genes and elevated monocyte and cytokine levels in women with postpartum psychosis, compared with healthy postpartum women [66, 68]. More recently, our own research group showed women with postpartum psychosis were more likely to have elevated C-reactive protein (CRP), an overall marker of systemic inflammation, compared with healthy postpartum controls [60]. Finally, higher rates of both autoimmune thyroiditis and pre-eclampsia (considered a disease of immunological maternal-foetal incompatibility) have been found in women with postpartum psychosis [69, 70], providing further evidence for the role of immune system dysregulation in this disorder.

27.5 Conclusion

Given the potentially devastating nature of postpartum psychosis, establishing risk factors for the illness is fundamental in helping us understand which women at increased risk are likely to relapse in the early postpartum period and ultimately develop preventative interventions aimed at reducing the risks. Furthermore, as a

time of increased contact with professionals, including midwives and general practitioners, the perinatal period provides a unique opportunity for intervention.

There is now a well-established link between stress and the onset of various mental disorders, both related and unrelated to gestation. Furthermore, pregnancy and childbirth are themselves potential stressors and times of major physiological change to the body's main stress and immune systems. As such, it is possible that stress also plays a role in the onset of postpartum psychosis.

The current literature to date provides little evidence of a link between childhood adversity and postpartum psychosis, although we have recently found preliminary evidence to suggest that *severe* childhood maltreatment may be associated with postpartum relapse in women at increased risk. If replicated, this finding would highlight the importance of screening women at risk of postpartum psychosis for the experience of severe childhood maltreatment to establish which of these women are likely to relapse in the postpartum and could, therefore, benefit from increased support throughout pregnancy. Furthermore, whilst experience of stressful life events has not been found to be associated with postpartum psychosis, a woman's perception of stressful life events might play a role and could, therefore, be a target for appropriate stress-coping interventions. Finally, there is emerging evidence to support the role of HPA axis and immune system dysregulation in postpartum psychosis. If confirmed, these findings point to alterations in maternal stress-related biology as a marker that could be used to identify which women at risk of postpartum psychosis are most likely to experience a psychiatric relapse, as well as providing a possible basis for prophylactic pharmacological and psychological interventions to prevent women most at risk from becoming unwell.

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References

1. Meltzer-Brody S, Howard LM, Bergink V, Vigod S, Jones I, Munk-Olsen T, et al. Postpartum psychiatric disorders. Nat Rev Dis Prim. 2018;4:1–18.
2. Jones I, Chandra PS, Dazzan P, Howard LM. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. Lancet. 2014;384:1789–99.
3. Knight M, Bunch K, Tuffnell D, Jayakody H, Shakespeare J, Kotnis R, et al. MBRRACE—UK Report: saving lives, improving mothers' care, 2014-16. Oxford: National Perinatal Epidemiology Unit; 2018.
4. Rai S, Pathak A, Sharma I. Postpartum psychiatric disorders: early diagnosis and management. Indian J Psychiatry. 2015;57(6):216–21.
5. Spinelli MG. Postpartum psychosis: detection of risk and management. Am J Psychiatry. 2009;166(4):405–8.
6. Di Florio A, Smith S, Jones I. Postpartum psychosis. Obstet Gynaecol. 2013;15(1):45–50.
7. Sharma V, Sommerdyk C. Postpartum psychosis: what is in a name? Aust N Z J Psychiatry. 2014;48(12):1081–2.
8. Jones I. Perinatal psychiatry. Medicine (Baltimore). 2012;40(12):654–7.

9. Oates MR. Perinatal psychiatric syndromes: clinical features. Psychiatry. 2009;8(1):1–6.
10. Paschetta E, Berrisford G, Coccia F, Whitmore J, Wood AG, Pretlove S, et al. Perinatal psychiatric disorders: an overview. Am J Obstet Gynecol. 2014;210(6):501–9.
11. Heron J, Robertson Blackmore E, McGuinness M, Craddock N, Jones I. No "latent period" in the onset of bipolar affective puerperal psychosis. Arch Womens Ment Health. 2007;10(2):79–81.
12. Heron J, McGuinness M, Blackmore ER, Craddock N, Jones I. Early postpartum symptoms in puerperal psychosis. BJOG Int J Obstet Gynaecol. 2008;115(3):348–53.
13. Dean C, Williams RJ, Brockington IF. Is puerperal psychosis the same as bipolar manic-depressive disorder? A family study. Psychol Med. 1989;19(3):637–47.
14. Di Florio A, Forty L, Gordon-Smith K, Heron J, Jones L, Craddock N, et al. Perinatal episodes across the mood disorder spectrum. JAMA Psychiatry. 2013;70(2):168–75.
15. Doyle K, Heron J, Berrisford G, Whitmore J, Jones L, Wainscott G, et al. The management of bipolar disorder in the perinatal period and risk factors for postpartum relapse. Eur Psychiatry. 2012;27(8):563–9.
16. Jones I, Craddock N. Familiality of the puerperal trigger in bipolar disorder: results of a family study. Am J Psychiatry. 2001;158(6):913–7.
17. Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJM, Kushner SA, Bergink V. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatry. 2016;173(2):117–27.
18. Lobel M, Cannella DL, Graham JE, DeVincent C, Schneider J, Meyer BA. Pregnancy-specific stress, prenatal health behaviors, and birth outcomes. Health Psychol. 2008;27(5):604–15.
19. Beck CT. Predictors of postpartum depression: an update. Nurs Res. 2001;50(5):275–85.
20. O'Hara MW, Swain AM. Rates and risk of postpartum depression: a meta-analysis. Int Rev Psychiatry. 1996;8(1):37–54.
21. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry. 2004;26(4):289–95.
22. Beards S, Gayer-Anderson C, Borges S, Dewey ME, Fisher HL, Morgan C. Life events and psychosis: a review and meta-analysis. Schizophr Bull. 2013;39(4):740–7.
23. Martland N, Martland R, Cullen AE, Bhattacharyya S. Are adult stressful life events associated with psychotic relapse? A systematic review of 23 studies. Psychol Med. 2020;50(14):2302–16.
24. Duthie L, Reynolds RM. Changes in the maternal hypothalamic-pituitary-adrenal axis in pregnancy and postpartum: Influences on maternal and fetal outcomes. Neuroendocrinology. 2013;98(2):106–15.
25. Mastorakos G, Ilias I. Maternal and fetal hypothalamic-pituitary-adrenal axes during pregnancy and postpartum. Ann N Y Acad Sci. 2003;997(1):136–49.
26. Lindsay JR, Nieman LK. The hypothalamic-pituitary-adrenal axis in pregnancy: challenges in disease detection and treatment. Endocr Rev. 2005;26(6):775–99.
27. Makrigiannakis A, Zoumakis E, Kalantaridou S, Coutifaris C, Margioris AN, Coukos G, et al. Corticotropin-releasing hormone promotes blastocyst implantation and early maternal tolerance. Nat Immunol. 2001;2(11):1018–24.
28. Owens PC, Smith R, Brinsmead MW, Hall C, Rowley M, Hurt D, et al. Postnatal disappearance of the pregnancy-associated reduced sensitivity of plasma cortisol to feedback inhibition. Life Sci. 1987;41(14):1745–50.
29. Giesbrecht GF, Campbell T, Letourneau N, Kooistra L, Kaplan B. Psychological distress and salivary cortisol covary within persons during pregnancy. Psychoneuroendocrinology. 2012;37(2):270–9.
30. Glover V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. Best Pract Res Clin Obstet Gynaecol. 2014;28(1):25–35.
31. Mor G, Cardenas I, Abrahams V, Guller S. Inflammation and pregnancy: the role of the immune system at the implantation site. Ann N Y Acad Sci. 2011;1221(1):80–7.
32. Racicot K, Kwon JY, Aldo P, Silasi M, Mor G. Understanding the complexity of the immune system during pregnancy. Am J Reprod Immunol. 2014;72(2):107–16.
33. Mor G, Aldo P, Alvero AB. The unique immunological and microbial aspects of pregnancy. Nat Rev Immunol. 2017;17:469–82.

34. Maguire J, McCormack C, Mitchell A, Monk C. Neurobiology of maternal mental illness. In: EAP S, Cipolla MJ, Mille EC, editors. Handbook of clinical neurology. Elsevier; 2020. p. 97–116.
35. Leff-Gelman P, Mancilla-Herrera I, Flores-Ramos M, Cruz-Fuentes C, Reyes-Grajeda JP, del Pilar García-Cuétara P, et al. The immune system and the role of inflammation in perinatal depression. Neurosci Bull. 2016;32(4):398–420.
36. Sherer ML, Posillico CK, Schwarz JM. The psychoneuroimmunology of pregnancy. Front Neuroendocrinol. 2018;51:25–35.
37. Dutta S, Sengupta P. Defining pregnancy phases with cytokine shift. J Pregnancy Reprod. 2017;1(4) https://doi.org/10.15761/jpr.1000124.
38. Groer ME, Jevitt C, Ji M. Immune changes and dysphoric moods across the postpartum. Am J Reprod Immunol. 2015;73(3):193–8.
39. Yim IS, Tanner Stapleton LR, Guardino CM, Hahn-Holbrook J, Dunkel Schetter C. Biological and psychosocial predictors of postpartum depression: systematic review and call for integration. Annu Rev Clin Psychol. 2015;11(1):99–137.
40. Osborne S, Biaggi A, Chua TE, Du Preez A, Hazelgrove K, Nikkheslat N, et al. Antenatal depression programs cortisol stress reactivity in offspring through increased maternal inflammation and cortisol in pregnancy: The Psychiatry Research and Motherhood – Depression (PRAM-D) Study. Psychoneuroendocrinology. 2018;98:211–21.
41. Murphy SE, Braithwaite EC, Hubbard I, Williams KV, Tindall E, Holmes EA, et al. Salivary cortisol response to infant distress in pregnant women with depressive symptoms. Arch Womens Ment Health. 2015;18(2):247–53.
42. Yim IS, Glynn LM, Schetter CD, Hobel CJ, Chicz-DeMet A, Sandman CA. Risk of postpartum depressive symptoms with elevated corticotropin- releasing hormone in human pregnancy. Arch Gen Psychiatry. 2009;66(2):162–9.
43. Nierop A, Bratsikas A, Zimmermann R, Ehlert U. Are stress-induced cortisol changes during pregnancy associated with postpartum depressive symptoms? Psychosom Med. 2006;68(6):931–7.
44. Maes M, Lin AH, Ombelet W, Stevens K, Kenis G, De Jongh R, et al. Immune activation in the early puerperium is related to postpartum anxiety and depressive symptoms. Psychoneuroendocrinology. 2000;25(2):121–37.
45. Boufidou F, Lambrinoudaki I, Argeitis J, Zervas IM, Pliatsika P, Leonardou AA, et al. CSF and plasma cytokines at delivery and postpartum mood disturbances. J Affect Disord. 2009;115(1–2):287–92.
46. Belvederi Murri M, Prestia D, Mondelli V, Pariante C, Patti S, Olivieri B, et al. The HPA axis in bipolar disorder: systematic review and meta-analysis. Psychoneuroendocrinology. 2016;63:327–42.
47. Mondelli V, Dazzan P, Hepgul N, Di Forti M, Aas M, D'Albenzio A, et al. Abnormal cortisol levels during the day and cortisol awakening response in first-episode psychosis: the role of stress and of antipsychotic treatment. Schizophr Res. 2010;116(2–3):234–42.
48. Collip D, Nicolson NA, Lardinois M, Lataster T, Van Os J, Myin-Germeys I. Daily cortisol, stress reactivity and psychotic experiences in individuals at above average genetic risk for psychosis. Psychol Med. 2011;41(11):2305–15.
49. Day FL, Valmaggia LR, Mondelli V, Papadopoulos A, Papadopoulos I, Pariante CM, et al. Blunted cortisol awakening response in people at ultra high risk of developing psychosis. Schizophr Res. 2014;158(1–3):25–31.
50. Walker EF, Trotman HD, Pearce BD, Addington J, Cadenhead KS, Cornblatt BA, et al. Cortisol levels and risk for psychosis: initial findings from the North American Prodrome Longitudinal Study. Biol Psychiatry. 2013;74(6):410–7.
51. Labad J, Stojanovic-Pérez A, Montalvo I, Solé M, Cabezas Á, Ortega L, et al. Stress biomarkers as predictors of transition to psychosis in at-risk mental states: roles for cortisol, prolactin and albumin. J Psychiatr Res. 2015;60:163–9.
52. Zajkowska Z, Mondelli V. First-episode psychosis: an inflammatory state? Neuroimmunomodulation. 2014;21(2–3):102–8.

53. Miller BJ, Goldsmith DR. Inflammatory biomarkers in schizophrenia: implications for heterogeneity and neurobiology. Biomark Neuropsychiatry. 2019;1:100006. https://doi.org/10.1016/j.bionps.2019.100006.
54. Pereira AC, Oliveira J, Silva S, Madeira N, Pereira CMF, Cruz MT. Inflammation in Bipolar Disorder (BD): identification of new therapeutic targets. Pharmacol Res. 2021;163:105235. https://doi.org/10.1016/j.phrs.2020.105325.
55. Khandaker GM, Pearson RM, Zammit S, Lewis G, Jones PB. Association of serum interleukin 6 and C-reactive protein in childhood with depression and psychosis in young adult life a population-based longitudinal study. JAMA Psychiatry. 2014;71(10):1121–8.
56. Dowlatshahi D, Paykel ES. Life events and social stress in puerperal psychoses: absence of effect. Psychol Med. 1990;20(3):655–62.
57. Meltzer-Brody S, Larsen JT, Petersen L, Guintivano J, Florio AD, Miller WC, et al. Adverse life events increase risk for postpartum psychiatric episodes: a population-based epidemiologic study. Depress Anxiety. 2018;35(2):160–7.
58. Perry A, Gordon-Smith K, Di Florio A, Forty L, Craddock N, Jones L, et al. Adverse childhood life events and postpartum psychosis in bipolar disorder. J Affect Disord. 2016;205:69–72.
59. Hazelgrove K, Biaggi A, Waites F, Fuste M, Osborne S, Conroy S, Howard LM, Mehta MA, Miele M, Nikkheslat N, Seneviratne G, Zunszain PA, Pawlby S, Pariante CM, Dazzan P. Risk factors for postpartum relapse in women at risk of postpartum psychosis: The role of psychosocial stress and the biological stress system. Psychoneuroendocrinology. 2021;128. https://doi.org/10.1016/j.psyneuen.2021.105218.
60. Aas M, Vecchio C, Pauls A, Mehta M, Williams S, Hazelgrove K, et al. Biological stress response in women at risk of postpartum psychosis: the role of life events and inflammation. Psychoneuroendocrinology. 2020;113:104558. https://doi.org/10.1016/j.psyneuen.2019.104558.
61. Marks MN, Wieck A, Checkley SA, Kumar R. Life stress and post-partum psychosis: a preliminary report. Br J Psychiatry. 1991;158(Suppl 10):45–9.
62. McNeil TF. A prospective study of postpartum psychoses in a high-risk group: 4. Relationship to life situation and experience of pregnancy. Acta Psychiatr Scand. 1988;77(6):645–53.
63. Warselius P, Cnattingius S, Li J, Wei D, Valdimarsdottir UA, Kosidou K, et al. Maternal bereavement shortly before or during pregnancy and risk of postpartum psychotic illness: a population-based study from Denmark and Sweden. Clin Epidemiol. 2019;11:285–98.
64. Brockington IF, Martin C, Brown GW, Goldberg D, Margison F. Stress and puerperal psychosis. Br J Psychiatry. 1990;157:331–4.
65. Dazzan P, Fusté M, Davies W. Do defective immune system-mediated myelination processes increase postpartum psychosis risk? Trends Mol Med. 2018;24(11):942–9.
66. Bergink V, Burgerhout KM, Weigelt K, Pop VJ, De Wit H, Drexhage RC, et al. Immune system dysregulation in first-onset postpartum psychosis. Biol Psychiatry. 2013;73(10):1000–7.
67. Kumar MM, Venkataswamy MM, Sathyanarayanan G, Thippeswamy H, Chandra PS, Mani RS. Immune system aberrations in postpartum psychosis: an immunophenotyping study from a tertiary care neuropsychiatric hospital in India. J Neuroimmunol. 2017;310:8–13.
68. Sathyanarayanan G, Thippeswamy H, Mani R, Venkataswamy M, Kumar M, Philip M, et al. Cytokine alterations in first-onset postpartum psychosis-clues for underlying immune dysregulation. Asian J Psychiatr. 2019;42:74–8.
69. Bergink V, Kushner SA, Pop V, Kuijpens H, Lambregtse-van Den Berg MP, Drexhage RC, et al. Prevalence of autoimmune thyroid dysfunction in postpartum psychosis. Br J Psychiatry. 2011;198(4):264–8.
70. Bergink V, Laursen TM, Johannsen BMW, Kushner SA, Meltzer-Brody S, Munk-Olsen T. Pre-eclampsia and first-onset postpartum psychiatric episodes: a Danish population-based cohort study. Psychological Medicine 2015;45(16):3481–9. https://doi.org/10.1017/S0033291715001385

Domestic Violence and Perinatal Mental Health

28

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28.1 Domestic Violence

Violence against women is recognised by the World Health Organization (WHO) as a major public health problem, the majority of which comprises intimate partner violence (IPV) [1]. IPV is behaviour by an intimate partner or ex-partner causing physical, sexual or psychological harm. The broader definition of domestic violence and abuse (DVA) adopted in the United Kingdom (UK) includes such behaviour perpetrated by other family members aged 16 years or older, as well as by partners and ex-partners [2]. However, most research on the perinatal period focuses on IPV. Examples of DVA include physical aggression, sexual coercion, psychological, emotional, financial abuse and controlling behaviours. The growth of digital technology means that DVA may continue online, when survivors and perpetrators are not physically co-located.

IPV is common, worldwide. Global prevalence estimates suggest that around 30% of ever-partnered women have experienced IPV [3]. The WHO multi-country study, which surveyed 24,000 women across 10 low-, middle-, and high-income countries, found high rates of physical IPV (13–61%), sexual IPV (6–59%) and psychological IPV (20–75%) [4]. In England and Wales, 29% of women and 14% of men have experienced DV [5]. In the United States (US), a national survey found that 36% of women and 33% of men experienced IPV in their lifetime [6].

IPV appears to be even commoner among people experiencing mental health problems. England's Adult Psychiatric Morbidity Survey of over 7400 people identified elevated odds of lifetime IPV among women with common mental disorders (adjusted odds ratio (aOR) = 4.4) [7]. A UK survey also found higher odds of IPV

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among female mental health service users than the general population (aOR = 2.7) [8]. A review of the literature found that lifetime prevalence of severe DV among people admitted to psychiatric inpatient wards ranged from 30% to 60%, although rates were lower for men, when disaggregated by gender. Routine detection of DV in clinical mental health settings was uncommon [9]. It is important that mental health professionals are aware of and consider DV as part of patient-centred bio-psycho-social assessment and management plans.

28.2 Domestic Violence in Pregnancy

IPV during pregnancy is associated with a range of adverse health outcomes for the woman and foetus [10]. Fatal outcomes are homicide and suicide, whilst non-fatal outcomes include physical and mental ill-health and injuries, reproductive and sexual health problems and deleterious health behaviours (see Fig. 28.1).

The WHO multi-country study of women's health applied standardised instruments and research methods to survey populations across ten countries. It found that

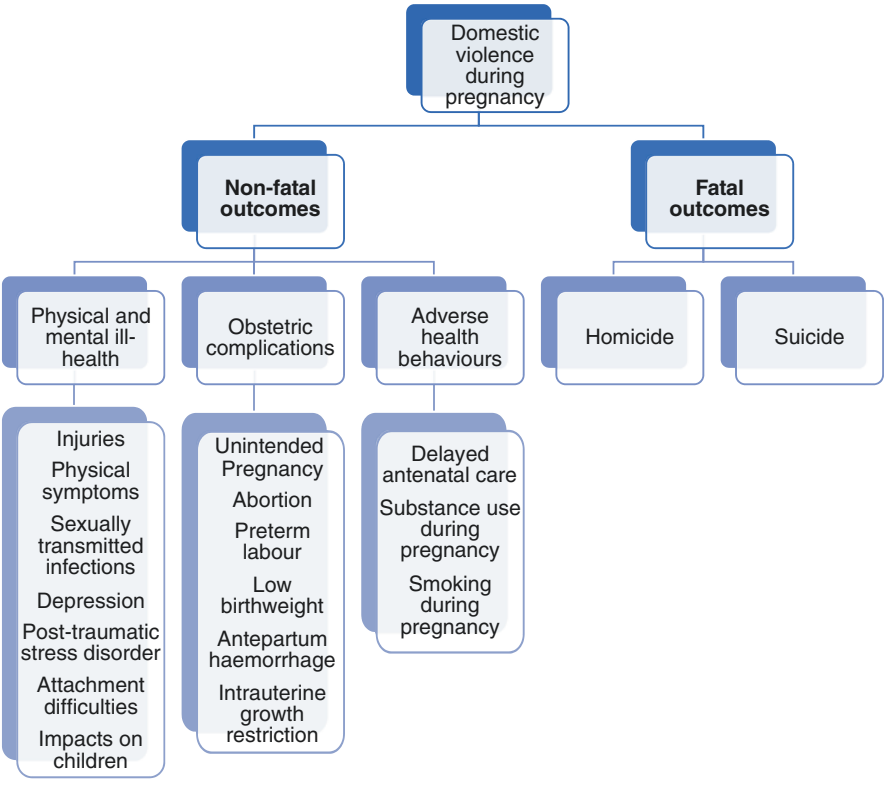

Fig. 28.1 Health impacts of DV during pregnancy [10]

the prevalence of physical IPV during pregnancy ranged from 1% in urban Japan to 28% in provincial Peru, ranging from 4% to 12% in most sites [11]. A meta-analysis of 92 studies of DV during pregnancy found an average reported prevalence of 28% for emotional abuse, 14% for physical abuse and 8% for sexual abuse [12]. In the 55 studies reporting risk factors, pre-pregnancy abuse and lower education were strong predictors of IPV during pregnancy; lower socio-economic status, being unmarried and 'unintended' abuse were moderate predictors.

A meta-analysis of African studies found high heterogeneity of reported IPV prevalence (e.g. between 2% and 49% in Nigerian studies) during pregnancy but an overall prevalence of 15% across 13 studies [13]. Five studies showed a significant association between HIV-positive status and experiencing IPV during pregnancy (OR = 1.48–3.10) after adjusting for confounders, although two studies found no association. Alcohol use by the partner (OR = 2.52–4.10) or the woman (OR = 4.59–11.60) was significantly associated with IPV during pregnancy in the five Nigerian, South African and Rwandan studies examining this relationship. Seven studies reported associations between prior abuse and IPV during pregnancy. It is therefore important that all health professionals are aware of the potential for DV during their contacts with pregnant and postpartum women.

28.3 Impacts on Physical Health

Homicide and suicide are fatal outcomes associated with IPV. A study of female victims of reproductive age using the US National Violent Death Reporting System between 2003 and 2007 found pregnancy-associated suicide and femicide rates of 2.0 and 2.9 per 100,000 live births, respectively [14]. Fifty-four percent of pregnancy-associated suicides featured contributory intimate partner conflict, and 45% of pregnancy-associated femicides were associated with IPV. IPV during pregnancy is a risk factor for intimate partner femicide [15], making it particularly important that health professionals in contact with pregnant and post-partum women always consider the possibility of IPV. Risks, including femicide, can escalate when the woman tries (or is suspected of planning) to leave and after separation [16], making safety planning a central part of supporting women experiencing IPV (see Box 28.1).

IPV can cause a range of direct and indirect non-fatal injuries. The WHO multi-country study identified significant associations between lifetime IPV and self-reported poor health (OR = 1.6), emotional distress, suicidal thoughts (OR = 2.9) and suicide attempts [17]. Lifetime IPV was also associated with past month pain (OR = 1.6), dizziness (OR = 1.7), memory loss (OR = 1.8), vaginal discharge (OR = 1.8), difficulty walking (OR = 1.6) and difficulty with daily activities (OR = 1.6).

Large studies [18] and meta-analyses [19] show that the risk of smoking during pregnancy is greater for women experiencing IPV. Smaller studies support a similar relationship for alcohol [20] and other substance use [21]. A review of research into

adverse health consequences of prenatal IPV proposed a range of intersecting pathways between maternal stress, mental ill-health, attachment, substance use, nutritional intake, antenatal care use and infection and long-term child development [22]. The authors highlighted the need for more research in low- and middle-income countries (LMICs), studies designed to overcome confounding and research into interventions addressing these pathways.

Box 28.1 Inquiring About DV in Perinatal Settings

WHO recommends the LIVES framework for providing women with first-line support for IPV in any clinical context [23]. Healthcare professionals should:

- **Listen** closely, with empathy, without judging.
- **Inquire** about the woman's emotional, physical, social and practical needs and concerns.
- **Validate her**: Show that you understand, respect and believe the woman, assuring her that she is not to blame.
- **Enhance her safety**: Does she feel safe to go home today? What would she do if DV recurred?
- **Support** her to make her own decisions. Help her to access information, services and social support. She may prefer you to refer her for support or to refer herself when she feels ready. DV agencies can advocate for women, help them to access accommodation and support them with safety planning to mitigate risks associated with continuing the relationship or leaving.

Antenatal care is a particularly important opportunity to provide women with first-line support, because the regularity of appointments and potential for continuity of care can build trusting relationships that enable women to disclose DV.

28.4 Impacts on Pregnancy

Studies in low- [24] and high-income countries [25] indicate that IPV is associated with late presentation to antenatal care (ANC). A review of demographic and health surveys in 10 LMICs found that in the Dominican Republic and Zambia, women experiencing IPV were less likely to seek antenatal care within the first 3 months of pregnancy, after multivariate adjustment [26]. In Rwanda, women experiencing IPV were less likely to deliver at a health facility, after multivariate adjustment.

Analysis of WHO multi-country study data for over 17,500 women across 10 countries found elevated odds of unintended pregnancy (aOR = 1.69) and abortion (aOR = 2.68) among women experiencing physical and/or sexual IPV after adjusting for confounders [27]. Assaults during pregnancy are associated with immediate

(e.g. uterine rupture) and long-term (e.g. premature delivery) harm to the woman and foetus [28].

Meta-analyses support an association between DV and low birthweight (aOR = 1.53) and preterm birth (aOR = 1.46) [29]. A cohort study of 4750 pregnant women in Canada found an increased risk of antepartum haemorrhage (aOR = 3.79), intrauterine growth restriction (aOR = 3.06) and perinatal death (aOR = 8.06) in women experiencing physical IPV [30]. Mechanisms which may explain the relationship between IPV and adverse maternal and foetal outcomes include physical trauma, negative maternal coping, poor maternal nutrition, inadequate ANC and elevated stress levels [31].

28.5 Impacts on Mental Health

An analysis of WHO multi-country study data for almost 21,000 women across 13 rural and urban sites showed that after adjusting for common mental disorders, the most consistent risk factors for suicide attempts were IPV, non-partner physical violence, relationship separation, childhood sexual abuse and maternal history of IPV [32]. Twenty-five to 50% of women with suicidal thoughts in the past 4 weeks had seen a health worker during that time, underscoring the role clinicians can play in supporting women experiencing DV.

IPV and mental health have a bidirectional relationship: IPV increases the risk of mental health problems, and mental health problems increase vulnerability to IPV. For example, systematic reviews show associations between IPV and subsequent depression and alcohol use disorders and that depressive symptoms and alcohol use disorders predict later IPV [33, 34]. A meta-analysis found associations between the severity of IPV and the severity of depression and post-traumatic stress disorder (PTSD) and that rates of depression decrease with time since cessation of IPV [35]. A systematic review suggested that IPV frequency is associated with risk of depression and PTSD and that IPV severity was associated with anxiety symptoms [36].

Qualitative interviews with mental health service users and staff in South London identified a range of barriers to disclosing DV [37]. Survivor barriers to disclosure included fears of social services involvement and subsequent child protection proceedings, not being believed, disclosure leading to further violence and feelings of shame. Staff barriers to inquiry included concerns about their role and its boundaries, their confidence and competence. Both groups considered the biomedical model of care to be a barrier to disclosure and inquiry but reported that a supportive and trusting relationship between service users and professionals is facilitative. A qualitative meta-synthesis of 12 studies found that mental health services often fail to inquire and facilitate disclosure of DV or to respond in ways that prioritise safety [38]. Insufficient consideration was given to the impact of DV in triggering or worsening mental ill-health, and the stigma associated with DV obstructed effective responses. These findings demonstrate the need for strong leadership to prioritise DV in mental health settings, for high-quality training, clear referral pathways and supervision structures for staff.

28.6 Impacts on Perinatal Mental Health

A meta-analysis of 67 studies found that the odds of postpartum depressive symptoms (OR = 3.1) were elevated in women who experienced IPV during pregnancy and that women with high perinatal depressive, anxiety and post-traumatic stress disorder symptoms had increased odds of having experienced DV [39]. A large UK birth cohort study of over 13,500 child-mother dyads found that after adjusting for potential confounders, antenatal DV was associated with antenatal (OR = 4.02) and postnatal (OR = 1.29) depressive symptoms [40]. Antenatal DV predicted future behavioural problems in children at 42 months of age (OR = 1.87), but the association was not significant after adjustment for maternal antenatal or postnatal depressive symptoms or postpartum DV.

A Swedish longitudinal cohort study of almost 1,700 pregnant women found that a history of childhood or adulthood abuse (including DV) was associated with depressive symptoms, lower stress management scores, unemployment, being single, living apart from a partner and financial hardship [41]. Women with a history of abuse were more likely to have premature labour and to require caesarean section (OR = 1.33). Women with a history of emotional abuse were more likely to have a planned or emergency caesarean (OR = 1.5).

A prospective cohort study of over 1,500 nulliparous women in Australia found that postpartum depressive symptoms were associated with emotional abuse alone (aOR = 2.72), physical abuse (aOR = 3.94), antenatal depression (aOR = 2.89) and unemployment in early pregnancy (aOR = 1.6) [42].

Smaller studies have found associations between DV during pregnancy and maternal attachment [43] and maternal assessments of infant temperament [44]. A systematic review which included 16 papers found that in half or more of the studies reporting relevant data, IPV was associated with shorter breastfeeding duration and early cessation of exclusive breastfeeding [45]. Evidence for an association between IPV and reduced initiation of breastfeeding was mixed. One study of 1,200 Chinese women in Hong Kong found that women who did not experience IPV during pregnancy were more likely to initiate breastfeeding (aOR = 1.84) than those who did, after adjusting for potential demographic, socioeconomic and obstetric confounders [46].

Box 28.2 Additional Considerations when Working Remotely

Increased help-seeking for DV and higher numbers of domestic homicides were reported in the UK [47] and internationally [48] during the coronavirus (COVID-19) pandemic [49]. Many in-person clinical services stopped, with much routine healthcare (including some ANC) being delivered remotely. Telemedicine has a range of potential benefits but limits women's opportunities to disclose DV to clinicians outside their home. During any national

emergency, women and families may have less contact with schools, community centres, voluntary sector agencies and other settings where DV might usually be detected. Guidance on safeguarding [50] and responding to DV [51] during COVID-19 remains relevant to any remotely delivered perinatal care:

- Consider social, emotional and financial stressors women are experiencing. Ask them about their life and relationships as well as their health.
- Remember that DV can happen to anyone. Do not assume that a pregnant woman cannot be experiencing DV because she does not look or act distressed.
- Do not forget that DV is perpetrated by family members as well as intimate partners. During national emergencies, family members may be living in more confined proximity for longer periods of time than is usual, increasing the risk of abuse.
- In cases of social distancing and lockdown, remember that women and children experiencing DV may be trapped at home with an abuser, isolated from support.
- For all telephone and video consultations, check who else is in the room or at home and if it is safe to talk.
- For remote contact via email, text messaging or apps, discuss with the woman whether an abusive partner has access to her phone or computer.
- Consider using closed 'yes'- or 'no'-answered questions, so that the content of discussion cannot be understood by someone else in the room.
- Agree a 'safe phrase' which the woman will use if interrupted by an abusive partner during the contact, such as 'thanks but I am not interested'. Agree how you will contact her to follow up, if the call is terminated in this way.
- Do not use friends, family members or carers to provide language interpretation. Plan a separate call involving a professional interpreter at a time when the conversation will not be overheard.
- Offer telephone follow-up at another time.
- Encourage women to use telephone or online means to connect with friends, family and professionals.
- Share contact details of relevant support organisations, and inform women that DV is a justification for breaking lockdown rules.
- Consider whether a face-to-face assessment is required where you have concerns about a woman's safety. Call the police in an emergency.
- In maternity settings, accompaniment by partners to routine appointments is sometimes restricted. Whilst this increases opportunities to enquire about DV, abusive partners may try to control women's hospital attendance. Ensure that all unattended appointments are followed up.

28.7 Perinatal Mental Health Interventions for Women Experiencing DV

Given the risks to the health and wellbeing of the woman and foetus during pregnancy, ANC is an important opportunity to support women experiencing DV. In low-resource contexts, ANC may be a woman's only healthcare contact. Furthermore, regular appointments, potential for continuity of care provider and postpartum follow-up make ANC well-suited to building the trust and rapport required to discuss sensitive subjects [10].

A systematic review identified 17 interventions for pregnant women experiencing IPV, of which two targeted mental health and three addressed both mental health and violence [52]. The first mental health-focused study was a randomised feasibility study of five sessions of interpersonal psychotherapy between pregnancy and 2 weeks postpartum, for women with low incomes experiencing IPV in Rhode Island [53]. The intervention was associated with lower PTSD symptoms at 3 months postpartum but not fewer perinatal depressive episodes. The second mental health-focused study was an uncontrolled pilot study of weekly perinatal child-parent psychotherapy from the third trimester until 6 months postpartum, for women experiencing IPV in San Francisco [54]. The intervention was associated with improvements in depressive and post-traumatic stress symptoms, but drop-out rates were high (44%).

One integrated intervention for mental health and IPV was evaluated by a cluster-randomised trial of 12 months of weekly at-home befriending, advocacy, parenting support and referrals, from trained, supervised English- and Vietnamese-speaking local mothers in Melbourne [55]. The authors found significant reductions in IPV scores for the intervention group compared with the control group, but only non-significant differences in depression and mental wellbeing.

A Hong Kong randomised controlled trial (RCT) of a one-off ANC empowerment intervention for women experiencing IPV found improved physical functioning and role limitation due to physical and emotional problems in the intervention group [56]. Women in the intervention group reported less psychological and minor physical abuse, but the same levels of sexual and severe physical abuse as women in the control group, post-participation. Women who received the intervention had lower postnatal depression scores but reported more body pain than control participants.

Four studies identified by the systematic review [52] evaluated the (Washington) DC Healthy Outcomes of Pregnancy Expectations (DC-HOPE) integrated education and counselling intervention. Aimed at African American women experiencing at least one of smoking, environmental tobacco smoke exposure, depression and IPV, DC-HOPE was delivered in four to eight sessions. The RCT found no difference between the intervention and control groups in depressive symptom improvement at follow-up [57], but frequency of minor IPV during pregnancy and severe IPV postpartum was reduced in the intervention group [58]. Obstetric findings were

lower rates of very preterm birth in the intervention group [59] but no difference in a range of other adverse pregnancy and neonatal outcomes [60].

A systematic review of interventions for pregnant women reporting DV in LMICs identified only six eligible studies [61]. Of these, only one reported impacts on depression. This quasi-experimental study evaluated an empowerment-based three-session psychosocial intervention focused on explaining gender-based violence, safety assessment and signposting to support in Kisumu, Kenya. Women in the intervention group had lower mean depressive symptom scores post-participation than women in the control arm [62].

Reviews of the evidence show that most DV-focused and mental health-DV integrated interventions have only limited impacts on perinatal mental health. Our recent meta-analysis found that five generic psychological interventions (n = 728) for common mental disorders in LMICs showed greater improvements in anxiety symptoms among women reporting IPV than women not reporting IPV [63]. There was no significant difference in women's treatment response for depression (12 interventions, n = 2940), PTSD (8 interventions, n = 1436) or psychological distress (4 interventions, n = 1591), by IPV status. Only three included studies were conducted with pregnant women, and several listed pregnancy as an exclusion criterion. These findings suggest that psychological interventions delivered by appropriately trained and supervised health-care staff in LMICs are effective for women experiencing IPV, even when not tailored for this population or targeting violence directly. More research is required to determine whether tailoring perinatal mental health interventions for the needs of women experiencing IPV improves their feasibility, acceptability and efficacy.

28.8 Conclusion

DV is common worldwide, both during and outside the perinatal period. DV has a range of consequences for the health, wellbeing and safety of pregnant women, the foetus and other children. Women with pre-existing mental health disorders are at increased risk of experiencing DV, and people who have experienced DV are at risk of developing mental health problems. A relatively small number of studies have evaluated integrating DV and mental health support for pregnant women, with mixed results. In LMICs, brief psychological interventions for common mental disorders are at least as effective for women experiencing IPV as for women not experiencing IPV, but more research is needed that explores tailoring perinatal mental health treatments for survivors. The 'LIVES' framework of listening, inquiry, validating, enhancing the woman's safety and connecting her with sources of support should be used by all clinicians to provide first-line support to women experiencing DV. Holistic perinatal mental healthcare requires clinicians to identify and respond to all bio-psycho-social factors precipitating and perpetuating symptoms, to promote women and families' health, wellbeing and safety.

References

1. WHO. violence against women 2017. Available from https://www.who.int/en/news-room/fact-sheets/detail/violence-against-women.
2. Home_Office. Information for local areas on the change to the definition of domestic violence and abuse 2013. Available from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/142701/guide-on-definition-of-dv.pdf.
3. WHO. Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence: World Health Organization; 2013.
4. Garcia-Moreno C, Jansen HA, Ellsberg M, Heise L, Watts CH. Prevalence of intimate partner violence: findings from the WHO multi-country study on women's health and domestic violence. Lancet. 2006;368(9543):1260–9.
5. Office_for_National_Statistics. Domestic abuse prevalence and trends, England and Wales: year ending March 2019; 2019. Available from https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/domesticabuseprevalenceandtrendsenglandandwales/yearendingmarch2019.
6. Smith SG, Zhang X, Basile KC, Merrick MT, Wang J, Kresnow M-J, et al. National intimate partner and sexual violence survey: 2015 data brief; 2018.
7. Jonas S, Khalifeh H, Bebbington PE, McManus S, Brugha T, Meltzer H, et al. Gender differences in intimate partner violence and psychiatric disorders in England: results from the 2007 adult psychiatric morbidity survey. Epidemiol Psychiatric Sci. 2014;23(2):189–99.
8. Khalifeh H, Moran P, Borschmann R, Dean K, Hart C, Hogg J, et al. Domestic and sexual violence against patients with severe mental illness. Psychol Med. 2015;45(4):875–86.
9. Howard L, Trevillion K, Khalifeh H, Woodall A, Agnew-Davies R. Domestic violence and severe psychiatric disorders: prevalence and interventions. Psychol Med. 2010;40(6):881–93.
10. WHO. Intimate partner violence during pregnancy 2011. Available from https://apps.who.int/iris/bitstream/handle/10665/70764/WHO_RHR_11.35_eng.pdf?sequence=1.
11. WHO. WHO multi-country study on women's health and domestic violence against women: initial results on prevalence, health outcomes and women's responses: World Health Organization; 2005.
12. James L, Brody D, Hamilton ZJV. Victims. Risk factors for domestic violence during pregnancy: a meta-analytic review. Violence Victims. 2013;28(3):359–80.
13. Shamu S, Abrahams N, Temmerman M, Musekiwa A, Zarowsky C. A systematic review of African studies on intimate partner violence against pregnant women: prevalence and risk factors. PLoS One. 2011;6(3):e17591.
14. Palladino CL, Singh V, Campbell J, Flynn H, Gold K. Homicide and suicide during the perinatal period: findings from the National Violent Death Reporting System. Obstetr Gynecol. 2011;118(5):1056.
15. Campbell JC, Webster D, Koziol-McLain J, Block C, Campbell D, Curry MA, et al. Risk factors for femicide in abusive relationships: results from a multisite case control study. Am J Public Health. 2003;93(7):1089–97.
16. BMA_Board_of_Science. Domestic abuse 2014. Available from https://www.bma.org.uk/collective-voice/policy-and-research/equality/healthcare-for-vulnerable-group/domestic-abuse-report.
17. Ellsberg M, Jansen HA, Heise L, Watts CH, Garcia-Moreno C. Intimate partner violence and women's physical and mental health in the WHO multi-country study on women's health and domestic violence: an observational study. Lancet. 2008;371(9619):1165–72.
18. Cheng D, Salimi S, Terplan M, Chisolm MS. Intimate partner violence and maternal cigarette smoking before and during pregnancy. Obstetr Gynecol. 2015;125(2):356.
19. Crane CA, Hawes SW, Weinberger AH. Intimate partner violence victimization and cigarette smoking: a meta-analytic review. Trauma Violence Abuse. 2013;14(4):305–15.

20. Flynn HA, Walton MA, Chermack ST, Cunningham RM, Marcus S. Brief detection and co-occurrence of violence, depression and alcohol risk in prenatal care settings. Arch Women's Mental Health. 2007;10(4):155–61.
21. Udo IE, Lewis L, Jessica B, Tobin JN, Ickovics JR. Intimate partner victimization and health risk behaviors among pregnant adolescents. Am J Public Health. 2016;106(8):1457–9.
22. Murray AL, Kaiser D, Valdebenito S, Hughes C, Baban A, Fernando AD, et al. The intergenerational effects of intimate partner violence in pregnancy: mediating pathways and implications for prevention. Trauma Violence Abuse. 2020;21(5):964–76.
23. WHO. Responding to intimate partner violence and sexual violence against women: WHO clinical and policy guidelines 2013. Available from https://apps.who.int/iris/bitstream/handle/10665/85240/9789241548595_eng.pdf;jsessionid=E19DCC3CDAB9BE390EE6F8360C6F1D7E?sequence=1.
24. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and use of reproductive health services among married women: evidence from a national Bangladeshi sample. BMC Public Health. 2012;12(1):913.
25. Goodwin MM, Gazmararian JA, Johnson CH, Gilbert BC, Saltzman LE, Group PW. Pregnancy intendedness and physical abuse around the time of pregnancy: findings from the pregnancy risk assessment monitoring system, 1996–1997. Matern Child Health J. 2000;4(2):85–92.
26. Hindin MJ, Kishor S, Ansara DL. Intimate partner violence among couples in 10 DHS countries: Predictors and health outcomes. Calverton, MD: Macro International Inc.; 2008.
27. Pallitto CC, García-Moreno C, Jansen HA, Heise L, Ellsberg M, Watts C. Intimate partner violence, abortion, and unintended pregnancy: results from the WHO Multi-country Study on Women's Health and Domestic Violence. Int J Gynecol Obstetr. 2013;120(1):3–9.
28. El Kady D, Gilbert WM, Xing G, Smith LH. Maternal and neonatal outcomes of assaults during pregnancy. Obstetr Gynecol. 2005;105(2):357–63.
29. Shah PS, Shah J. Maternal exposure to domestic violence and pregnancy and birth outcomes: a systematic review and meta-analyses. J Women's Health. 2010;19(11):2017–31.
30. Janssen PA, Holt VL, Sugg NK, Emanuel I, Critchlow CM, Henderson AD. Intimate partner violence and adverse pregnancy outcomes: a population-based study. Am J Obstetr Gynecol. 2003;188(5):1341–7.
31. Alhusen JL, Ray E, Sharps P, Bullock L. Intimate partner violence during pregnancy: maternal and neonatal outcomes. J Women's Health. 2015;24(1):100–6.
32. Devries K, Watts C, Yoshihama M, Kiss L, Schraiber LB, Deyessa N, et al. Violence against women is strongly associated with suicide attempts: evidence from the WHO multi-country study on women's health and domestic violence against women. Soc Sci Med. 2011;73(1):79–86.
33. Devries K, Child JC, Bacchus LJ, Mak J, Falder G, Graham K, et al. Intimate partner violence victimization and alcohol consumption in women: a systematic review and meta-analysis. Addiction. 2014;109(3):379–91.
34. Devries KM, Mak JY, Bacchus LJ, Child JC, Falder G, Petzold M, et al. Intimate partner violence and incident depressive symptoms and suicide attempts: a systematic review of longitudinal studies. PLoS Med. 2013;10(5):e1001439.
35. Golding JM. Intimate partner violence as a risk factor for mental disorders: a meta-analysis. J Fam Violence. 1999;14(2):99–132.
36. Lagdon S, Armour C, Stringer M. Adult experience of mental health outcomes as a result of intimate partner violence victimisation: a systematic review. Eur J Psychotraumatol. 2014;5(1):24,794.
37. Rose D, Trevillion K, Woodall A, Morgan C, Feder G, Howard L. Barriers and facilitators of disclosures of domestic violence by mental health service users: qualitative study. Br J Psychiatry. 2011;198(3):189–94.
38. Trevillion K, Hughes B, Feder G, Borschmann R, Oram S, Howard LM. Disclosure of domestic violence in mental health settings: a qualitative meta-synthesis. Int Rev Psychiatry. 2014;26(4):430–44.

39. Howard LM, Oram S, Galley H, Trevillion K, Feder G. Domestic violence and perinatal mental disorders: a systematic review and meta-analysis. PLoS Medicine. 2013;10(5):e1001452.
40. Flach C, Leese M, Heron J, Evans J, Feder G, Sharp D, et al. Antenatal domestic violence, maternal mental health and subsequent child behaviour: a cohort study. Br J Obstetr Gynaecol. 2011;118(11):1383–91.
41. Finnbogadóttir H, Baird K. Thies-Lagergren LJBp, childbirth. Birth outcomes in a Swedish population of women reporting a history of violence including domestic violence during pregnancy: a longitudinal cohort study. BMC Pregnancy Childbirth. 2020;20(1):1–10.
42. Woolhouse H, Gartland D, Hegarty K, Donath S, Brown S. Depressive symptoms and intimate partner violence in the 12 months after childbirth: a prospective pregnancy cohort study. Br J Obstetr Gynaecol. 2012;119(3):315–23.
43. Pires de Almeida C, Sá E, Cunha F, Pires EP. Violence during pregnancy and its effects on mother–baby relationship during pregnancy. J Reprod Infant Psychol. 2013;31(4):370–80.
44. Quinlivan JA, Evans S. Impact of domestic violence and drug abuse in pregnancy on maternal attachment and infant temperament in teenage mothers in the setting of best clinical practice. Arch Women's Mental Health. 2005;8(3):191–9.
45. Normann AK, Bakiewicz A, Madsen FK, Khan KS, Rasch V, Linde DS. Intimate partner violence and breastfeeding: a systematic review. BMJ Open. 2020;10(10):e034153.
46. Lau Y, Chan KS. Influence of intimate partner violence during pregnancy and early postpartum depressive symptoms on breastfeeding among Chinese women in Hong Kong. J Midwifery Women's Health. 2007;52(2):e15–20.
47. Kelly J, Morgan T. Coronavirus: domestic abuse calls up 25% since lockdown, charity says. BBC News; 2020. Available from https://www.bbc.co.uk/news/uk-52157620.
48. Graham-Harrison E, Giuffrida A, Smith H, Ford L. Lockdowns around the world bring rise in domestic violence. The Guardian; 2020. Available from https://www.theguardian.com/society/2020/mar/28/lockdowns-world-rise-domestic-violence.
49. Roesch E, Amin A, Gupta J, García-Moreno C. Violence against women during covid-19 pandemic restrictions. Br Med J. 2020;369.
50. Royal_College_of_General_Practitioners. COVID-19 and safeguarding; 2020. Available from https://elearning.rcgp.org.uk/pluginfile.php/149180/mod_resource/content/2/COVID-19%20and%20Safeguarding%20%286%29.pdf.
51. IRISi. Guidance for general practice teams responding to domestic abuse during telephone and video consultations; 2020. Available from https://irisi.org/wp-content/uploads/2020/04/Guidance-for-General-Practice-Covid-19-FINAL.pdf.
52. Howell KH, Miller-Graff LE, Hasselle AJ, Scrafford KE. The unique needs of pregnant, violence-exposed women: a systematic review of current interventions and directions for translational research. Aggression Violent Behav. 2017;34:128–38.
53. Zlotnick C, Capezza NM, Parker D. An interpersonally based intervention for low-income pregnant women with intimate partner violence: a pilot study. Arch Women's Mental Health. 2011;14(1):55–65.
54. Lavi I, Gard AM, Hagan M, Van Horn P, Lieberman AF. Child-parent psychotherapy examined in a perinatal sample: depression, posttraumatic stress symptoms and child-rearing attitudes. J Soc Clin Psychol. 2015;34(1):64–82.
55. Taft AJ, Small R, Hegarty KL, Watson LF, Gold L, Lumley JA. Mothers' AdvocateS In the Community (MOSAIC)-non-professional mentor support to reduce intimate partner violence and depression in mothers: a cluster randomised trial in primary care. BMC Public Health. 2011;11(1):178.
56. Tiwari A, Leung W-C, Leung T, Humphreys J, Parker B, Ho P. A randomised controlled trial of empowerment training for Chinese abused pregnant women in Hong Kong. Br J Obstetr Gynaecol. 2005;112(9):1249–56.
57. El-Mohandes AA, Kiely M, Joseph JG, Subramanian S, Johnson AA, Blake SM, et al. An integrated intervention in pregnant African Americans reduces postpartum risk: a randomized trial. Obstetr Gynecol. 2008;112(3):611.

58. Kiely M, El-Mohandes AA, El-Khorazaty MN, Gantz MG. An integrated intervention to reduce intimate partner violence in pregnancy: a randomized trial. Obstetr Gynecol. 2010;115(2 Pt 1):273.
59. El-Mohandes AA, Kiely M, Gantz MG, El-Khorazaty MN. Very preterm birth is reduced in women receiving an integrated behavioral intervention: a randomized controlled trial. Matern Child Health J. 2011;15(1):19–28.
60. Subramanian S, Katz KS, Rodan M, Gantz MG, El-Khorazaty NM, Johnson A, et al. An integrated randomized intervention to reduce behavioral and psychosocial risks: pregnancy and neonatal outcomes. Matern Child Health J. 2012;16(3):545–54.
61. Daley D, McCauley M, van den Broek N. Interventions for women who report domestic violence during and after pregnancy in low-and middle-income countries: a systematic literature review. BMC Pregnancy Childbirth. 2020;20(1):1–9.
62. Mutisya RK, Ngure K, Mwachari C. A psychosocial intervention to reduce gender-based violence and antepartum depressive symptoms in pregnant women in Kisumu County, Kenya: a quasi-experimental study. Pan African Med J. 2018;29(1):1–9.
63. Keynejad RC, Hanlon C, Howard LM. Psychological interventions for common mental disorders in women experiencing intimate partner violence in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Psychiatry. 2020;7(2):173–90.

Motherhood in Adolescence: Risk Factors, Parent-Infant Relationship, and Intervention Programs

29

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29.1 Introduction

Motherhood in adolescence (under 18) and at a young age (up to 21) in Italy accounts for around 1.2% of all births each year [1]. In other countries such as the USA and UK, although it is decreasing compared to the 1970s [2, 3], it continues to be a significant phenomenon, accounting for between 11 and 14% of total births. In some countries, for example, the USA, it mainly concerns specific sectors of the population, Hispanic and black adolescent [4].

Early motherhood is often accompanied by aspects of risk in pregnancy and in the perinatal period to the health of the mother and infant, including complications during pregnancy, premature birth, low birth weight, neonatal death, and stillbirth [5, 6]. Young mothers also often stop breastfeeding their infant or do not begin at all [7].

Young motherhood is frequently correlated with various social, family, and individual risk factors which can have a negative effect on the wellbeing of the mother and on her relationship with her infant, with consequent negative short- and long-term outcomes. Therefore, intervention programs aimed at promoting and supporting the relationship of the mother and of the father with the infant from the very first stages, are very important.

29.2 Adolescent and Young Mother Risk Profile

Adolescent motherhood is a complex developmental challenge since adolescent and young adult mothers, faced with the birth of their infant, have to deal with a dual transition process: on the one hand, that of moving from adolescence to young

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adulthood with individuation from the parental figure [8] and, on the other, that of becoming a parent, which involves emotional and imaginative investment in the future newborn. In dealing with these two developmental tasks, the young mother can easily feel torn between her desire to satisfy her growing need for independence and identity consolidation [9] and that of taking care of the needs of her child [10, 11]. The newborn's strong need for physical and emotional care competes with the adolescent mother's needs, exacerbating her feelings of vulnerability and low self-esteem [12].

It is also important in this regard to consider that cognitive and neurophysiological development in adolescent and young adult mothers still has to be completed [13, 14]. Such immaturity may be an obstacle for the young mother when she is making choices as to which methods of parenting to adopt with her infant. Studies show that mothers under 20 are also less cognitively competent with regard to taking on their parental role (cognitive readiness to parent) and to knowledge of the stages of development of their infants [15].

From a psychodynamic perspective, adolescent pregnancy may be considered, in many cases, to be an attempt to gain independence from the family of origin and to construct one's own adult identity which is otherwise difficult to achieve through more usual means (study, work, etc.) given the scarce financial and educational resources available to young mothers.

Early pregnancy in this regard may also be considered an opportunity for young mothers, a catalyst for change, above all if she is adequately supported by friendly and non-stigmatizing primary care [16, 17] and by dedicated intervention programs. The young mother can experience the birth of her infant as a turning point with respect to defining her identity, increasing her investment in herself, and reducing possible risky behavior adopted prior to the birth, e.g., substance abuse, promiscuity, etc.

It is, however, important to consider that adolescent pregnancy is often correlated with numerous, frequently interrelated socio-economic, psychological, individual, and family risk factors [18]. The main ones are socio-economic disadvantage [19], low levels of education, school difficulties and interruption of studies [20], lack of social support, unstable relationships with partners, and consequently a greater likelihood of being a single parent, multiproblematic family of origin with absent father [21], and a history of young parenthood, above all on the part of the mother [22]. Lastly the pregnancy is often unwanted or unplanned [23]. However, a number of studies have shown that, even when the effect of some of these variables such as weekly hours of maternal employment, maternal verbal intelligence, and family socio-economic status is controlled, adolescence is still, per se, a high-risk factor for a mother's parenting skills [2, 24].

The frequency of adverse childhood experiences of physical, sexual, and emotional abuse in adolescent mothers is also very high. Studies show that such mothers have experienced abuse more often than adult mothers [25, 26] and non-mother adolescents [27]. This may lead to an increase in maltreatment of and hostile behavior towards the infant [28], with intergenerational transmission of traumatic experiences from mother to child [29].

Multiproblematic family contexts and many episodes of maltreatment mean that adolescent mothers are at high risk of developing insecure and unresolved/disorganized attachment models [11, 30]. In the perinatal period, adolescent mothers also often tend to live with their parents, in multiproblematic families, having unstable relations with the father of the infant [23], also being exposed to intimate partner violence (IPV) [31].

It is interesting in this regard to note that some of the above risk factors are considered to be characteristics of adolescents or of their family environment which are predictive of adolescent motherhood. Of these some authors highlight conduct disorders [32], aggressive and delinquent behavior, bullying in pre-adolescence [33, 34], and depression prior to pregnancy [34]. A history of childhood abuse and maltreatment [35–38] and having a mother who gave birth during adolescence are also predictive of early parenthood [22].

Adolescent mothers often have mental health issues during both pregnancy and the perinatal period. They are 50% more likely to display high levels of depression than adult mothers [39–41], such depression often being correlated with anxious states [23]. A higher level of post-traumatic stress disorder (PTSD) due to frequent adverse experiences and a higher probability of substance abuse were also found [42–44].

In the perinatal period, moreover, having to care for their child, often with little support from family and partner, they feel more parenting stress and emotional distress [13], with consequent low levels of self-esteem and self-efficacy. Many of them feel socially isolated from their peers with respect to whom they cannot share the same school and social experiences, the absence of which they feel acutely [45]. In this regard it has been highlighted how the support of friends can considerably reduce perceived stress of the young mothers, as does involvement of the father of the infant in its care [45, 46].

There are many fewer studies on teen and young fathers [17]. Some have shown that young fathers are more socially and economically disadvantaged than older fathers [47]. Others have highlighted that there are few programs which also involve teenage fathers, who are often stigmatized, more than the mothers, with regard to their early parenting, also by primary care [17]. Like the mothers the young fathers suffer more depression than older fathers and can be aggressive in the perinatal period [48].

29.3 Mother-Infant Relationship and Maternal Mind-Mindedness and Reflective Functioning

The psychological condition of potential conflict between different developmental tasks and the frequent presence of risk factors relative to young motherhood has a strong impact on the young mother's relationship with the child from the very first months, influencing her parenting methods and responsiveness.

In general, adolescent mothers have difficulty understanding the needs of their infants and have little knowledge of their stages of development [15]. They often adopt intrusive and neglecting styles [10, 49, 50] and are also more likely to adopt harsh parenting, accompanied by both physical and verbal abuse [51]. They also use

more instrumental behavior in caring for their children [52]. Compared to adult mothers, adolescent mothers are also less verbally stimulating [53] and less vocally responsive [54] and interact with their infants with a peer-like interaction [55].

Adolescent mothers attune themselves to a lesser degree with the emotions of their children compared to adult mothers, displaying poor emotional availability [55] and less structuring of their infant's activity [56]. Dyadic emotional regulation is also less adequate than it is between adult mothers and infants, with more negative emotion states related to the difficulty of the mothers in regulating the negative emotions of their infants [10]. Dyadic regulation is even more problematic if the mothers have had a large number of adverse experiences. In this case they display greater difficulty in regulating negative emotions, and there are more negative matches in the mother-infant dyad [26].

Young mothers have also been shown to have a low capacity for mentalization at the level of both adult reflective functioning [10] and parental reflective functioning [57] and for mind-mindedness [56, 58]. In one of our studies, adolescent mothers used fewer attuned mind-related comments and more non-attuned mind-related comments than adult mothers [56]. This is of particular interest since it has been shown that the capacity for mentalization is correlated with both good maternal sensitivity and secure infant attachment [59].

29.4 Early Motherhood and Developmental Trajectories of Mothers and Infants

The described numerous risk aspects relating to early motherhood lead to problematic outcomes for both infants and mothers. The children of adolescent mothers are at risk for insecure and disorganized attachment [60, 61], for suffering maltreatment by mothers [37], and for having delays in language [62] and cognitive development [63]. In the short term, they also display less ability in affective communication [64] and delays in their psychomotor development [62]. They also suffer more psychofunctional symptoms such as sleep and eating problems [65].

In adolescence and adulthood, they show a range of adverse outcomes, such as poor academic achievement, early parenthood, underemployment, violent offending, externalizing problems, and substance abuse [22, 35, 51, 66].

Early motherhood, at the same time, limits the subsequent life opportunities of the young women [35], leading to low levels of education and underemployment and giving rise to a higher probability of being involved in less stable relationships and of suffering depression and social isolation [16, 67].

29.5 Intervention Programs

Since the 1990s there have been various programs aimed at improving the relationship between adolescent mothers and their infants [68]. Diverse approaches have been taken including school-based programs aimed at preventing mothers giving up

their studies [69]; clinical-based programs, focusing on monitoring the health of the infant and the wellbeing of its parents, providing medical assistance and social support [70]; and psychotherapeutic approaches for mothers who have particular problems linked to their difficult or traumatic infant experiences [71].

Some of these programs are specifically attachment-based, i.e., aimed at increasing the responsiveness of mothers and thus improving the quality of infant attachment. These include the pioneering program of Carter [72] "Speaking for the Baby," which uses video feedback and aims to give a voice to infant communication, which is often either not understood or misunderstood by young mothers. Of particular interest is the MTB (Minding the Baby) [73], a mentalization-based intervention which combines the home visiting approach with the use of video feedback. The program begins with pregnancy and lasts until the infant is two. Its main aims are to increase the sensitivity and reflective functioning of young mothers at risk and to promote secure attachment in the infant. The efficacy of the program has been demonstrated both by an increase in the reflective functioning of mothers and by the promotion of infant secure attachment.

Shorter programs were, however, less effective. For example, the recent randomized study of Firk [74] shows how a program of home visiting based on the STEP protocol [75] aimed at young mothers at risk and limited to the second 6 months of the infant's life was not effective in increasing maternal sensitivity.

29.5.1 Promoting Responsiveness, Emotion Regulation, and Attachment in Young Mothers and Infants –PRERAYMI

We shall now briefly illustrate a longitudinal intervention program which we carry out at an Italian hospital and which was aimed at adolescent and under 21 young adult mothers [11, 50, 76]. The intervention was developed out of an interdisciplinary collaboration between the Infant Neuropsychiatric Unit of ASST Santi Paolo and Carlo Hospital of Milano and the Department of Psychology of University of Milano-Bicocca and conducted by a team of psychologists, infant neuropsychiatrists, and psychomotricists. The two main objectives of the intervention are to increase sensitivity and reflectivity of the young mothers so as to foster secure attachment of the infant to the mother and other attachment figures. It is well known that secure infant attachment is predictive of adequate socio-emotional development and, at the same time, serves a protective function with respect to psychopathological risk in the subsequent stages of development [77].

The intervention takes place in a specially dedicated outpatient unit of the hospital and starts in pregnancy or post-partum. In pregnancy there are periodic meetings with the young women during which the relaxation technique is used [78] aimed at increasing their capacity to listen to the movements of the fetus and to the changes in their body. Counselling sessions also take place to support the construction of the mother's attachment to the future baby and to increase the capacity of the young women to feel and express their emotions.

In post-partum the intervention proceeds for the young women who have already been followed in pregnancy. For the young women who have not been followed in pregnancy, the intervention begins when the infant is 2 months old and concludes at 12 months, and it consists of monthly video feedback meetings and monthly developmental guidance meetings.

Video feedback, carried out by a psychologist and a psychomotricist, has two aims: to support the mother's sensitivity, with particular emphasis on her capacity for positive involvement and regulation of the negative emotions of the infant, and to promote the mother's reflective capacity and mind-mindedness, helping her to explore her feelings and thoughts with respect to her infant and attribute feelings to her infant, giving meaning to his activity and communication [79]. Self-observation of their interaction with the infant by means of the video is a particularly strong stimulus for adolescent mothers, allowing them in a short space of time to render otherwise unexpressed emotions and representations explicit and to thus activate specific resources [80].

A second level of intervention provides mothers with developmental guidance [81], illustrating, through sessions carried out by a psychomotricist, the stages of development of the infant and its rhythms of regulation. In this context the motor and cognitive development of the child is monitored by observing with parents the new developmental skills of the child. Infants' fathers are included in the developmental guidance meetings.

The third level of the intervention program offers mothers counselling sessions with the aim of supporting the process of integrating their experience of motherhood and their relationship with the infant with their transition toward adulthood. The counselling intervention begins with the Adult Attachment Interview which allows the young mother's history of attachment—often marked by traumatic experiences—to be explored and shared with her.

The mother's elaboration of trauma is an important feature of the counselling we offer. In those most at risk cases, an adolescent mother may distance herself from her experience of maternity, perceiving it as extraneous to her existential and developmental condition, delegating care of the infant to others both physically and emotionally, with the infant being abandoned in the most problematic cases. This may be due to the fact that many adolescent mothers (around 40% of the mothers who used our intervention) have had adverse or traumatic experiences with their parents and caregivers which are reactivated by having to deal with their infants and the intense emotions the infants suscitate in them. In such cases the mother is helped to reflect in depth upon her past and her adverse relationships with her own parents and upon how these now reflect her relationship with her infant [82].

The PRERAYMI intervention demonstrated its effectiveness with regard to maternal and infant styles of interaction, helping to increase the sensitivity and cooperativeness, respectively, of mother and infant [11, 76]. A significant increase in dyadic affective coordination was also observed in the young mother-infant dyads who attended the intervention (vs mother-infant dyads who did not) with more time spent by the dyads in positive affective matches, less time spent in affective

mismatches, and a greater ability to repair mismatches. The increase in affective coordination in the intervention dyads must be considered a key piece of data with respect to the effectiveness of intervention in that it is held by various researchers to be a particularly significant indicator with regard to the adequacy of the mother-infant relationship [83].

At the same time, the intervention helped to increase the quality of maternal mind-mindedness, improving mothers' capacity for attunement, through verbal mind-related comments, with the activity and communication of their infant, respecting his level of development [50]. Moreover, the intervention contributed to improving the quality of maternal sensitivity and mind-mindedness and the dyadic affective coordination also when there were risk conditions other than the mother's young age, such as insecure attachment and traumatic experiences. The results, therefore, indicate that the intervention can be applied in the first year with adolescent and young mothers who have a number of conditions of risk such as insecurity and adverse experiences, since it was shown to have an influence on the mothers who participated at a double level with regard to their sensitivity and their capacity to "keep in mind" the infant. Achieving this double objective is very important for an attachment-based intervention given that it is now clear [84] that maternal capacity for mind-mindedness measured in the first year is a predictor of the quality of infant attachment on a par with maternal sensitivity, since it is shown to have a direct effect on future infant attachment in ways in part independent of the quality of maternal sensitivity.

29.6 Conclusions

Adolescent maternity is a turning point in the life of the young mother, entailing potentially positive reorganization of her developmental trajectories. Very often, however, it is weighed down by cumulative risk factors which make her relationship with the infant difficult, with short- and long-term effects on the development of the infant and on the wellbeing and mental health of the mother. It is, therefore, very important to offer the young mother intervention which can support her in the transition to parenthood and in the first contact with the infant, also involving if possible the father of the infant.

So far various intervention programs have been conducted which are aimed at making this relationship easier, weakening the action of the various risk factors. Of these the most effective has been the long-term attachment-based interventions, beginning in pregnancy and lasting until the end of the first year of the infant's life and implemented with a multidisciplinary and multifocal approach. The longitudinal approach in this regard allows for creation of a secure and trusting relationship between the young parents and the operators [85] which can be used by the young parents as the basis for their relationship with their infant.

Particularly important in this regard is focusing the intervention both on increasing the mother's sensitivity and capacity for mentalization and on facilitating the

support of the partner, the family of origin, and peers. A likewise important focus is that of past and present traumatic experiences which are a significant obstacle in the mother-infant relationship. It is also important to monitor the mental health of the mother, in particular with respect to depression and parenting stress. Lastly, the young mothers and fathers can gain an essential benefit from primary care (obstetricians, pediatricians etc.) which is non-stigmatizing and friendly with respect to their young parenthood [17, 18].

References

1. ISTAT. Rilevazione degli iscritti in anagrafe per nascita; 2019. [Survey of those registered in the birth registry]. Available from http://www.demo.istat.it/altridati/IscrittiNascita/index.php.
2. Bornstein MH, Putnick DL, Suwalsky JTD, Gini M. Maternal chronological age, prenatal and perinatal history, social support, and parenting of infants. Child Dev. 2006;77(4):875–92. https://doi.org/10.1111/j.1467-8624.2006.00908.x.
3. Centers for Disease Control and Prevention. Health, United States, 2018 – Data Finder; 2018. Available from https://www.cdc.gov/nchs/hus/contents2018.htm?search=Births.
4. Martin CG, Kim HK, Freyd JJ. In the spirit of full disclosure: maternal distress, emotion validation, and adolescent disclosure of distressing experiences. Emotion. 2018;18(*3*):*400*–11. https://doi.org/10.1037/emo0000363.
5. Hadian T, Mousavi S, Meedya S, Mohammad-Alizadeh-Charandabi S, Mohammadi E, Mirghafourvand M. Adolescent pregnant women's health practices and their impact on maternal, fetal and neonatal outcomes: a mixed method study protocol. Reprod Health. 2019;16(1):45. https://doi.org/10.1186/s12978-019-0719-4.
6. Kingston D, Heaman M, Fell D, Chalmers B. Comparison of adolescent, young adult, and adult women's maternity experiences and practices. Pediatrics. 2012;129:e1228–37. https://doi.org/10.1542/peds.2011-1447.
7. Cota-Robles S, Pedersen L, LeCroy C. Challenges to breastfeeding initiation and duration for teen mothers. MCN Am J Matern Child Nurs. 2017;42(3):173–8. https://doi.org/10.1097/NMC.0000000000000327.
8. Aiello R, Lancaster S. Influence of adolescent maternal characteristics on infant development. Infant Ment Health J. 2007;28(5):496–516. https://doi.org/10.1002/imhj.20150.
9. Arnett JJ. Oxford library of psychology.The Oxford handbook of emerging adulthood. Oxford: University Press; 2016.
10. Riva Crugnola C, Ierardi E, Gazzotti S, Albizzati A. Motherhood in adolescent mothers, maternal attachment, mother-infant styles of interaction and emotion regulation at three months. Infant Behav Dev. 2014;37(1):44–56. https://doi.org/10.1016/j.infbeh.2013.12.011.
11. Riva Crugnola C, Ierardi E, Albizzati A, Downing G. Effectiveness of an attachment based intervention program in promoting emotion regulation and attachment in adolescent mothers and their infants: a pilot study. Front Psychol. 2016;7:195. https://doi.org/10.3389/fpsyg.2016.00195.
12. Reid V, Meadows-Oliver M. Postpartum depression in adolescent mothers: an integrative review of the literature. J Pediatr Health Care. 2007;21(5):289–98. https://doi.org/10.1016/j.pedhc.2006.05.010.
13. Giedd JN. Structural magnetic resonance imaging of the adolescent brain. Ann N Y Acad Sci. 2005;1021:77–85. https://doi.org/10.1196/annals.1308.009.
14. Steinberg L. Cognitive and affective development in adolescence. Trends Cogn Sci. 2005;9(29):69–74. https://doi.org/10.1016/j.tics.2004.12.005.

15. Tamis-LeMonda CS, Shannon J, Spellman M. Low-income adolescent mothers' knowledge about domains of child development. Infant Ment Health J. 2002;23(1–2):88–103. https://doi.org/10.1002/imhj.10006.
16. SmithBattle L, Loman DG, Cibulka NJ. Family centered primary care for teen parents and their children. J Pediatr Health Care. 2019;34(3):204–11. https://doi.org/10.1016/j.pedhc.2019.09.010.
17. SmithBattle L, Punsuwun S, Phengnum W. An umbrella review of qualitative research on teen mothering. West J Nurs Res. 2020; https://doi.org/10.1177/0193945920943213.
18. SmithBattle L. Helping teen mothers succeed. J Sch Nurs. 2006;22(3):130–5. https://doi.org/10.1177/10598405060220030201.
19. Osofsky JD, Hann DM, Peebles C. Adolescent parenthood: risks and opportunities for mothers and infants. In: Zeanah CH, editor. Handbook of infant mental health. New York: Guildford Press; 1993. p. 106–99.
20. Ruedinger E, Cox JE. Adolescent childbearing: consequences and interventions. Curr Opin Pediatr. 2012;24(4):446–52. https://doi.org/10.1097/MOP.0b013e3283557b89.
21. Manlove J, Ikramullah E, Mincieli L, Holcombe E, Danish S. Trends in sexual experience: contraceptive use, and teenage childbearing, 1992–2002. J Adolesc Health. 2009;44(5):413–23. https://doi.org/10.1016/j.jadohealth.2008.09.006.
22. Meade C, Kershaw TS, Ickovics JR. The intergenerational cycle of teenage motherhood: an ecological approach. Health Psychol. 2008;27(4):419–29. https://doi.org/10.1037/0278-6133.27.4.419.
23. Albizzati A, Ierardi E, Moioli M, Riva CC. Profilo psicopatologico e di rischio psicosociale in madri adolescenti e di giovane età nel postpartum [Psychopathological and psychosocial risk profile of adolescents and young mothers in the post-partum period]. Medico e Bambino. 2020;39(7):445–51.
24. Rafferty Y, Griffin KW, Lodise M. Adolescent motherhood and developmental outcomes of children in early head start: the influence of maternal parenting behaviors, well-being, and risk factors within the family setting. Am J Orthopsychiatry. 2011;81(2):228–45. https://doi.org/10.1111/j.1939-0025.2011.01092.x.
25. Madigan S, Vaillancourt K, Mckibbon A. The reporting of maltreatment experiences during the Adult Attachment Interview in a sample of pregnant adolescents. Attach Hum Dev. 2012;14(2):119–43. https://doi.org/10.1080/14616734.2012.661230.
26. Riva Crugnola C, Ierardi E, Bottini M, Verganti C, Albizzati A. Childhood experiences of maltreatment, reflective functioning and attachment in adolescent and young adult mothers: effects on mother-infant interaction and emotion regulation. Child Abuse Negl. 2019;93:277–90. https://doi.org/10.1016/j.chiabu.2019.03.024.
27. Boden J, Fergusson D, Horwood J. Early motherhood and subsequent life outcomes. J Child Psychol Psychiatry. 2008;49(2):151–60. https://doi.org/10.1111/j.1469-7610.2007.01830.x.
28. Vaillancourt K, Pawlby S, Fearon RMP. History of childhood abuse and mother-infant interaction: a systematic review of observational studies. Infant Ment Health J. 2017;38(2):226–48. https://doi.org/10.1002/imhj.21634.
29. Stevens-Simon C, Nelligan D, Kelly L. Adolescents at risk for mistreating their children. Part I, prenatal identification. Child Abuse Negl. 2001;25(6):737–51. https://doi.org/10.1016/s0145-2134(01)00237-x.
30. Madigan S, Moran G, Pederson DR. Unresolved states of mind, disorganized attachment relationships, and disrupted interactions of adolescent mothers and their infants. Dev Psychol. 2006;42(2):293–304. https://doi.org/10.1037/0012-1649.42.2.293.
31. Bekaert S, SmithBattle L. Teen mothers' experience of intimate partner violence: a metasynthesis. ANS Adv Nurs Sci. 2016;39(3):272–90. https://doi.org/10.1097/ANS.0000000000000129.
32. Bardone AM, Moffitt TE, Caspi A, Dickson N, Stanton WR, Silva PA. Adult physical health outcomes of adolescent girls with conduct disorder, depression, and anxiety. J Am Acad Child Adolesc Psychiatry. 1998;37(6):594–601. https://doi.org/10.1097/00004583-199806000-00009.

33. Gaudie J, Mitrou F, Lawrence D, Stanley FJ, Silburn SR, Zubrick SR. Antecedents of teenage pregnancy from a 14-year follow-up study using data linkage. BMC Public Health. 2010;10:63. https://doi.org/10.1186/1471-2458-10-63.
34. Lehti V, Niemelä S, Heinze M, Sillanmäki L, Helenius H, Piha J, Kumpulainen K, Tamminen T, Almqvist F, Sourander A. Childhood predictors of becoming a teenage mother among Finnish girls. Acta Obstet Gynecol Scand. 2012;91(11):1319–25. https://doi.org/10.1111/j.1600-0412.2012.01517.x.
35. Jaffee S, Caspi A, Moffitt TE, Belsky J, Silva P. Why are children born to teen mothers at risk for adverse outcomes in young adulthood? Results from a 20-year longitudinal study. Dev Psychopathol. 2001;13(2):377–97. https://doi.org/10.1017/s0954579401002103.
36. Madigan S, Vaillancourt K, McKibbon A, Benoit D. The reporting of maltreatment experiences during the Adult Attachment Interview in a sample of pregnant adolescents. Attach Hum Dev. 2012;14(2):119–43. https://doi.org/10.1080/14616734.2012.661230.
37. Valentino K, Nuttall AK, Comas M, Borkowski JG, Akai CE. Intergenerational continuity of child abuse among adolescent mothers: authoritarian parenting, community violence, and race. Child Maltreat. 2012;17(2):172–81. https://doi.org/10.1177/1077559511434945.
38. Felitti VJ, Anda RF. The relationship of adverse childhood experiences to adult health, well-being, social function, and health care. In: Lanius R, Vermetten E, Pain C, editors. The effects of early life trauma on health and disease: the hidden epidemic. Cambridge: Cambridge University Press; 2010; Chapter 8.
39. Brown JD, Harris SK, Woods ER, Buman MP, Cox JE. Longitudinal study of depressive symptoms and social support in adolescent mothers. Matern Child Health J. 2012;16(4):894–901. https://doi.org/10.1007/s10995-011-0814-9.
40. Easterbrooks MA, Kotake C, Raskin M, Bumgarner E. Patterns of depression among adolescent mothers: resilience related to father support and home visiting program. Am J Orthopsychiatry. 2016;86(1):61–8. https://doi.org/10.1037/ort0000093.
41. Hymas R, Girard LC. Predicting postpartum depression among adolescent mothers: a systematic review of risk. J Affect Disord. 2019;246:873–85. https://doi.org/10.1016/j.jad.2018.12.041.
42. Hodgkinson S, Beers L, Southammakosane C, Lewin A. Addressing the mental health needs of pregnant and parenting adolescents. Pediatrics. 2014;133(1):114–22. https://doi.org/10.1542/peds.2013-0927.
43. Chapman SWC, Wu L. Substance use among adolescent mothers: a review. Child Youth Serv Rev. 2013;35(5):806–15. https://doi.org/10.1016/j.childyouth.2013.02.004.
44. Moffitt TE. Teen-aged mothers in contemporary Britain. J Child Psychol Psychiatry. 2002;43(6):727–42. https://doi.org/10.1111/1469-7610.00082.
45. Erfina E, Widyawati W, McKenna L, Reisenhofer S, Ismail D. Adolescent mothers' experiences of the transition to motherhood: an integrative review. Int J Nurs Sci. 2019;6(2):221–8. https://doi.org/10.1016/j.ijnss.2019.03.013.
46. Huang CY, Roberts YH, Costeines J, Kaufman JS. Longitudinal trajectories of parenting stress among ethnic minority adolescent mothers. J Child Fam Stud. 2019;28(5):1368–78. https://doi.org/10.1007/s10826-019-01356-1.
47. Mollborn S. Teenage mothers today: what we know and how it matters. Child Dev Perspect. 2017;11(1):63–9. https://doi.org/10.1111/cdep.12205.
48. Lee Y, Fagan J, Chen WY. Do late adolescent fathers have more depressive symptoms than older fathers? J Youth Adolesc. 2012;41(10):1366–81. https://doi.org/10.1007/s10964-011-9717-8.
49. Berlin LJ, Brady-Smith C, Brooks-Gunn J. Links between childbearing age and observed maternal behaviors with 14-month-olds in the early Head Start research and evaluation project. Infant Mental Health J. 2002;23(1–2):104–29. https://doi.org/10.1002/imhj.10007.
50. Riva Crugnola C, Ierardi E, Peruta V, Moioli M, Albizzati A. Video-feedback attachment based intervention aimed at adolescent and young mothers: Effectiveness on infant-mother interaction and maternal mind-mindedness. Early Child Dev Care. 2021;191(3):475–89. https://doi.org/10.1080/03004430.2019.1652172.

51. Lee Y, Guterman NB. Young mother-father dyads and maternal harsh parenting behavior. Child Abuse Negl. 2010;34(11):874–85. https://doi.org/10.1016/j.chiabu.2010.06.001.
52. Krpan KM, Coombs R, Zinga D, Steiner M, Fleming AS. Experiential and hormonal correlates of maternal behavior in teen and adult mothers. Horm Behav. 2005;47(1):112–22. https://doi.org/10.1016/j.yhbeh.2004.08.006.
53. Lacroix V, Pomerleau A, Malcuit G. Properties of adult and adolescent mothers' speech, children's verbal performance and cognitive development in different socioeconomic groups: a longitudinal study. First Language. 2002;22(2):173–96. https://doi.org/10.1177/014272370202206503.
54. Pomerleau A, Scuccimarri C, Malcuit G. Mother-infant behavioral interactions in teenage and adult mothers during the first six months postpartum: relations with infant development. Infant Mental Health J. 2003;24(5):495–509. https://doi.org/10.1002/imhj.10073.
55. Easterbrooks MA, Chaudhuri JH, Gestsdottir S. Patterns of emotional availability among young mothers and their infants: a dyadic, contextual analysis. Infant Ment Health J. 2005;26(4):309–26. https://doi.org/10.1002/imhj.20057.
56. Riva Crugnola C, Ierardi E, Canevini MP. Reflective functioning, maternal attachment, mind-mindedness, and emotional availability in adolescent and adult mothers at infant 3 months. Attach Hum Dev. 2018;20(1):84–106. https://doi.org/10.1080/14616734.2017.1379546.
57. Sadler LS, Novick G, Meadows-Oliver M. "Having a Baby Changes Everything" reflective functioning in pregnant adolescents. J Pediatr Nurs. 2016;31(3):e219–31. https://doi.org/10.1016/j.pedn.2015.11.011.
58. Demers I, Bernier A, Tarabulsy GM, Provost MA. Mind-mindedness in adult and adolescent mothers: relations to maternal sensitivity and infant attachment. Int J Behav Dev. 2010;34(6):529–37. https://doi.org/10.1177/0165025410365802.
59. Slade A, Grienenberger J, Bernbach E, Levy D, Locker A. Maternal reflective functioning, attachment, and the transmission gap: a preliminary study. Attach Hum Dev. 2005;7(3):283–98. https://doi.org/10.1080/14616730500245880.
60. van Ijzendoorn MH, Schuengel C, Bakermans-Kranenburg MJ. Disorganized attachment in early childhood: meta-analysis of precursors, concomitants, and sequelae. Dev Psychopathol. 1999;11(2):225–49. https://doi.org/10.1017/s0954579499002035.
61. Lounds JT, Borkowski J, Whitman T. The potential for child neglect: the case of adolescent mothers and their children. Child Maltreat. 2006;11(3):281–94. https://doi.org/10.1177/1077559506289864.
62. Jahromi LB, Umaña-Taylor AJ, Updegraff KA, Lara EE. Birth characteristics and developmental outcomes of infants of Mexican-origin adolescent mothers: risk and promotive factors. Int J Behav Dev. 2012;36(2):146–56. https://doi.org/10.1177/0165025411430777.
63. Whitman TL, Borkowski JG, Keogh DA, Weed K. Interwoven lives: adolescent mothers and their children. Mahwah, NJ: Erlbaum; 2001.
64. Osofsky JD, Eberhart-Wright A, Ware LM, Hann DM. Children of adolescent mothers: a group at risk for psychopathology. Infant Ment Health J. 1992;13(2):119–31. https://doi.org/10.1002/1097-0355(199223)13:2<119::AID-IMHJ2280130203>3.0.CO;2-X.
65. Maia GN, Frizzo GB, Levandowski DC. Psychofunctional symptoms in infants of young mothers: association with maternal mental health and parental bonding. Early Hum Dev. 2020;141:104,938. https://doi.org/10.1016/j.earlhumdev.2019.104938.
66. Hoffman SD, Maynard RA. Kids having kids: economic costs & social consequences of teen pregnancy. Washington, DC: The Urban Institute Press; 2008.
67. Herrman JW, Palen LA, Kan M, Feinberg M, Hill J, Magee E, Haigh KM. Young mothers' and fathers' perceptions of relationship violence: a focus group study. Violence Against Women. 2019;25(3):274–96. https://doi.org/10.1177/1077801218780356.
68. Savio Beers LA, Hollo RE. Approaching the adolescent-headed family: a review of teen parenting. Curr Probl Pediatr Adolesc Health Care. 2009;39(9):216–33. https://doi.org/10.1016/j.cppeds.2009.09.001.
69. Strunk JA. The effect of school-based health clinics on teenage pregnancy and parenting outcomes: an integrated literature review. J Sch Nurs. 2008;24(1):13–20. https://doi.org/10.1177/10598405080240010301.

70. Cox JE, Buman MP, Woods ER, Famakinwa O, Harris SK. Evaluation of raising adolescent families together program: a medical home for adolescent mothers and their children. Am J Public Health. 2012;102(10):1879–85. https://doi.org/10.2105/AJPH.2012.300766.
71. Mayers H, Siegler AL. Finding each other using a psychoanalytic-developmental perspective to build understanding and strengthen attachment between teenaged mothers and their babies. J Infant Child Adolesc Psychother. 2004;3(4):444–65. https://doi.org/10.1080/15289160309348480.
72. Carter SL, Osofsky JD, Hann DM. Speaking for the baby: a therapeutic intervention with adolescent mothers and their infants. Infant Ment Health J. 1991;12(4):291–301. https://doi.org/10.1002/1097-0355(199124)12:4<291::AID-IMHJ2280120403>3.0.CO;2-3.
73. Slade A, Holland ML, Ordway MR, Carlson EA, Jeon S, Close N, Mayes LC, Sadler LS. *Minding the Baby*®: enhancing parental reflective functioning and infant attachment in an attachment-based, interdisciplinary home visiting program. Dev Psychopathol. 2020;32(1):123–37. https://doi.org/10.1017/S0954579418001463.
74. Firk C, Dahmen B, Dempfle A, Niessen A, Baumann C, Schwarte R, Koslowski J, Kelberlau K, Konrad K, Herpertz-Dahlmann B. A mother-child intervention program for adolescent mothers: results from a randomized controlled trial (the TeeMo study). Dev Psychopathol. 2020;10:1–14. https://doi.org/10.1017/S0954579420000280.
75. Erickson MF, Egeland B, Simon J, Rose T. STEEP™ facilitator's guide. Minneapolis, MN: Irving B. Harris Training Center, University of Minnesota; 2002.
76. Riva Crugnola C, Ierardi E, Albizzati A, Downing G. Promoting responsiveness, emotion regulation, and attachment in young mothers and infants: an implementation of video intervention therapy and psychological support. In: Steele H, Steele M, editors. Handbook of attachment intervention. New York: Guildford Press; 2017. Chapter 20.
77. Sroufe LA. Attachment and development: a prospective, longitudinal study from birth to adulthood. Attach Hum Dev. 2005;7(4):349–67. https://doi.org/10.1080/14616730500365928.
78. Bergès-Bounes M, Bonnet C, Ginoux G, Pecarelo AM, Sironneau-Bernardeau C. La relaxation thérapeutique chez l'enfant: corps, langage, sujet. Méthode Jean Bergès [Relaxation therapy in children: Body, language, subject. The Jean Bergès method]. Paris: Dunod; 2008.
79. Downing G, Wortmann-Fleischer S, von Einsiedel R, Jordan W, Reck C. Video intervention therapy with parents with a psychiatric disturbance. In: Brandt K, Perry B, Seligman S, Tronick E, editors. Infant and early childhood mental health: core concepts and clinical practice. Washington, DC: American Psychiatric Association; 2013. p. 261–80.
80. Steele M, Steele H, Bate J, Knafo H, Kinsey M, Bonuck K, Meisner P, Murphy A. Looking from the outside in: the use of video in attachment-based interventions. Attach Hum Dev. 2014;16(4):402–15. https://doi.org/10.1080/14616734.2014.912491.
81. Papousek M, Schieche M, Wurmser H. Regulatory disorders in infancy: early risks and intervention within the developing system of parent-infant relationships. Washington, DC: Zero-to-Three Press; 2008.
82. Lieberman A, Diaz MA, Castro G, Bucio GO. Make room for baby: perinatal child-parent psychotherapy to repair trauma and promote attachment. New York: Guilford Press; 2004.
83. Tronick E. The neurobehavioral and social-emotional development of infants and children. New York: WW Norton & Company; 2007.
84. Zeegers MAJ, Potharst ES, Veringa-Skiba IK, Aktar E, Goris M, Bögels SM, Colonnesi C. Evaluating mindful with your baby/toddler: observational changes in maternal sensitivity, acceptance, mind-mindedness, and dyadic synchrony. Front Psychol. 2019;24(10):753. https://doi.org/10.3389/fpsyg.2019.00753.
85. Emde RN, Everhart KD, Wise BK. Therapeutic relationships in infant mental health and the concept of leverage. In: Sameroff AJ, McDonough SC, Rosenblum KL, editors. Treating parent-infant relationship problems: strategies for intervention. New York: Guilford Press; 2004. p. 267–92.

Maternal Embodied Sensitivity: Could Interoception Support the Mother's Ability to Understand Her Infant's Signals?

30

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30.1 Introduction

The importance of sensitive maternal behaviors for the child's well-being is widely recognized [1]. Maternal sensitivity is defined as a mother's skill to respond to her infant in ways that are contingent to their needs [2]. This competence is typically described along the emotional-cognitive dimension which includes skills such as (a) perceiving, experiencing, and empathizing with infant's emotions and (b) mentalizing infant's needs [3]. Neuroimaging studies on parenting indicate that, while activation of insula-cingulate regions is related to parental skill to intuitively resonate with their infant's emotions, a mentalizing network (including the medial prefrontal cortex, the superior temporal sulcus, and the temporo-parietal junction) underlies parents' ability to infer mental states from their infant's behavior [4]. These brain circuits match with the neural networks known to be involved in empathy [5, 6], and the anterior insula is specifically related to maternal sensitivity [7]. The insular cortex is not only a core region of affective and socio-cognitive information processing involving the self and others [8], but it also plays a key role in interoception (i.e., perception of one's own bodily signals [9]). Importantly, an increasing number of studies show that interoception is associated with empathy [10, 11], suggesting that perception of one's own bodily signals is crucially involved in the ability to understand emotion in others. As a consequence, interoception could play a prominent

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role in sensitive maternal behaviors, and one might wonder whether, and to which extent, the mother's ability to perceive her own internal signals might support responsivity to her infant's cues. This view is in line with an embodied cognition theoretical framework which suggests that emotional and cognitive processes are situated in bodily systems, highlighting a putative role of interoception in perception of self and others [12–14].

In light of the above-mentioned evidence, in this chapter we would like to provide an initial perspective for a conceptual shift in our understanding of maternal caregiving which goes beyond the traditional view of maternal sensitivity [15]. Considering the perspective of body experiences, we will discuss the potential role of maternal subjective experience in early interaction with her infant, which we refer to as *maternal embodied sensitivity*. First, we will argue that mothers may use their interoceptive sensitivity (i.e., ability to perceive internal input about one's own body state) to support their moment-by-moment adaptation to interactive demands and to infant's needs. Second, we will propose potential mechanisms related to maternal interoceptive sensitivity which could extend the mother's ability to perceive her infant's bodily signals. Third, we will discuss possible links with post-partum maternal depression, which might be associated with interoceptive dysregulation. Finally, we will also suggest that interventions aimed to improve body sensation awareness may be a potential approach to support parenting competences and increase parental social engagement and emotional responsiveness [16].

30.2 Understanding the Role of Interoception in Socio-emotional Processes

From a general point of view, interoception is defined as the ability to perceive the physiological condition of one's body as well as the extent to which one is able to represent one's internal states, and it is associated with homeostatic regulation of internal states [9, 17, 18]. While interoception is functionally separate from exteroception (e.g., visual perception) and proprioception (i.e., position of muscles/joints), it is interwoven with these systems by multimodal sensory integration [19]. It includes a wide range of different sensations such as pain [20], temperature [21], touch [22, 23], and heart rate [24] that, taken together, provide an integrated sense of one's physiological condition [9]. Although these internal signals might be not perceived as subjective feelings and occur below the level of conscious awareness, interoception is implicated in the development and function of perception and higher-order cognitive and social affective processes [25], including intuitive decision-making, self-regulation [26], and, even more importantly, emotional experience [27–30]. On the other hand, it should be noted that conscious awareness about sensory signals exists, in particular trying to reach homeostasis in demanding situations (e.g., increased heart rate during fear, chills during awe [31]).

As mentioned above, interoception is fundamental to emotional processes [32]. One study reported an association between increased interoception and a lower-intensity threshold of emotional facial expression in response to which participants reported feeling an emotion [32]. Interoception may modulate the relationship between bodily responses and affective variables [33], connecting subjective feelings experienced in the first person and objective external experiences lived in the third person [34]. Additionally, interception is related to activation of insular cortex, a core region of the emotional empathy network [9, 35]. Neuroimaging evidence suggests that interoceptive awareness significantly enhances neural activity during empathy in bilateral anterior insula [11, 29]. Overall, these results suggest an association between the ability to understand the emotional state of another individual and interoceptive awareness, which is reflected in brain activity and connectivity. Unfortunately, while research has mainly focused on the link between empathy and interoception in non-caregiver adults, this link remains understudied in the context of early parenting. Nevertheless, the focus on parental bodily states might provide a new perspective of maternal sensitivity suggesting that interoception may contribute to supporting the caregiver's ability to understand (and respond to) their infant's signals and emotional states—an ability which could be defined as *maternal embodied sensitivity*.

30.3 Parental Interoceptive Functioning: Rethinking Maternal Sensitivity

Over the past decades, maternal sensitivity has been conceptualized as a crucial aspect of the mother-infant relationship [1]. Although maternal sensitivity implies both emotional and cognitive dimensions (i.e., to perceive, experience, and empathize with infant's emotions and mentalize their needs), recent evidence suggests that appropriate caregiving requires coordination of multiple systems, which relies on different components that are useful to read infant signals and respond sensitively [36, 37]. For example, one study has investigated the association between maternal sensitivity and refinement of maternal visuo-perceptual processes in perceiving infant's body [38]. The authors found that a more refined maternal perception of her infant's body cues was associated with higher maternal sensitivity. Furthermore, maternal sensitivity has been related to the parent's ability to understand infant's kinesthetic signals as expression of mental states and adjust their own kinesthetic pattern accordingly – the so-called parental embodied mentalization [39]. Although these aspects represent innovative views of parental caregiving behaviors, both perspectives remain focused on the infant body. In our view, interoception may provide parents with a broader repertoire of possible sensations and experiences, allowing them to better understand their child's experience [24]. In other words, to interpret and understand infant's bodily signals and link them with specific emotional meanings and with appropriate responses, the mother should be aware (even if implicitly) of their own body experiences. Even

if interoceptive sensitivity does not imply full consciousness, the ability to represent one's own internal body state seems to be associated with social attitudes [40]. Interestingly, functional imaging studies found a significant neural activation in the insula associated with thinking about oneself, which suggests a unique role of this cortical area in self-reflection [41]. Furthermore, one *f*MRI study of neural correlates of maternal attachment reported that a mother's view of her child versus a familiar child (i.e., a friend's child) evoked stronger responses in areas associated with emotional responses, including the insular cortex [42]. In sum, interoceptive sensitivity (and insula-related functioning) is not only crucial for personal emotional experience processing and self-perception [43], but most importantly it is related to the ability to understand emotion in others [10]. Taken together, this evidence supports the notion that the insula and interoception might play a crucial implicit role in *maternal embodied sensitivity*. On the one hand, the insula and interoception are connected with internal body signal processing that might be implied in self-processing contributing to mother's sense of self. One the other hand, the insula and interoception seem to support maternal social sensitivity toward her infant.

But how could maternal interoception work? Awareness of inner body sensations and a better ability to feel bodily reactions could underlie an abundance of emotional experiences, which in turn might support greater understanding of others' emotions and empathy [44]. Accordingly, a recent study has reported that activation of the parent's anterior insula (i.e., the cerebral hub supporting interoceptive sensitivity) in response to a video showing parent-infant interaction predicted lower somatic problems in the child 6 years later, and this link was mediated by the parent's sensitive behavior at age four [45]. Furthermore, maternal interoception might generate subjective feelings and body sensations which support interaction. For example, intuitive maternal stroking velocity in infants aged 4–54 weeks was significantly correlated to maternal interoception, as measured by heart rate, suggesting that maternal affectionate touch behavior might be moderated by some aspects of maternal interoception [46]. Finally, the mothers' ability to identify signals from her own body might support her emotional experience which, in turn, can modulate the relationship with her child. For example, mothers' interoceptive knowledge about their own emotions has been found to be associated with social affective skills (i.e., emotion regulation, social initiative, cooperation, self-control) in middle childhood [24]. In sum, if maternal sensitivity was, at least partially, associated with the accuracy with which mothers perceive their own bodily signals, then maternal interoceptive sensitivity might facilitate caregiver's inferences about infant's physiological and emotional states and infant's ability to form accurate perceptions of bodily sensations. Mothers could be able to teach infants interoceptive cues, which could help them to differentiate bodily states (i.e., distress, hunger, tiredness, etc.). In addition, as suggested by studies documenting a link between interoception and empathy [10], interoceptive sensitivity might support a mothers' ability to attune to her infant's bodily states, using her own bodily cues for modeling her emotion regulation and social skills while interacting with her infant.

30.4 Interoception and Maternal Depression: Possible Links and Potential for Interventions

Focusing on parental interoceptive functioning during early interaction could shed a different light on parental sensitivity even in mothers with mental health problems. As interoception refers to the process by which the nervous system senses, interprets, and integrates signals originating from within the body and contributing to cognitive and emotional experiences, dysfunction of interoception could be implicated in different mental health conditions, including anxiety disorders, mood disorders, eating disorders, addictive disorders, and somatic symptom disorders [47, 48]. Specifically, depression is associated with decreased insular cortex activity during interoception and abnormal functional connectivity in the insula [49]. Furthermore, one study found that the insula, along with other cerebral regions, was reduced in volume in individuals with depressive disorder compared to controls, suggesting that this cortical area represents a key neural correlate of core symptoms [50]. Overall, this evidence highlights that individuals at risk for depression show an altered insular cortex activation which could be associated with interoceptive dysregulation [51].

Depressive symptoms are also associated with reduced levels of parental affective empathy toward their own child [52], and maternal depressive symptoms have been found to be related to lower sensitivity toward infants [53]. Remarkably, mothers with post-partum depression demonstrated decreased connectivity between amygdala and insular cortex as compared to mothers without post-partum depression [54]. One could hypothesize that reduced connectivity between the amygdala and the insular cortex, which is important for representing physiological states useful for the evaluations of one's own bodily sensations and guide one's own subjective emotional experience, might be an indirect mark of interoceptive dysregulation. Therefore, dysfunctional interoception could provide a unique approach to better understand how post-partum depression may pose a particular threat to sensitive parenting. In other words, although low levels of maternal sensitivity associated with depression can be related to several factors, including both behavioral and physiological components, interoceptive dysregulation might alter a mother's ability to use her own bodily feelings to support reading and to respond sensitively to her infant's cues.

If interoceptive dysregulation is implicated in altered emotional experience of mothers with post-partum depression, enhancing maternal body sensation awareness might diminish levels of depression, which in turn could improve their quality of interaction with their infants. While in many cases post-partum depressive symptomatology reduction and interventions aimed at improving post-partum bonding require psychological and psychiatric treatments [55], interventions such as video feedback, in which parents view themselves engaging in naturally occurring interactions with their infants under the guidance of a therapist, might be integrated with techniques aiming to improve interoceptive accuracy with an impact on parent-infant bonding. Indeed, while video feedback intervention in mothers with depressive symptomatology and relationship difficulties has proven to be effective in promoting a significant

increase in maternal sensitivity [56], taking a maternal body experience perspective in a video feedback intervention could provide an opportunity to mothers to process and reflect on their own body sensation awareness and understand their body expressions while interacting with their infants. A recent qualitative study suggests that supporting mother's attention to her own emotions and body sensation modulates infant care and how mothers regulate emotions in the post-natal period [16]. Although the study was not focused on mothers with post-partum depression, findings suggest that supporting mothers to "tune in" to their own internal states and encouraging them to use this awareness in their exchanges with their infants might be key factors to improve both their mental well-being as well as their ability to detect and respond to the infant's signals. Awareness of body sensations becomes a significant and effective resource of emotional regulation and symptom reduction. Of course, further research is needed to identify specific processes associated with poor or disrupted interoception and how and to which extent it is possible to use maternal interoception in order to promote mothers' emotional competence.

30.5 Conclusions and Future Perspectives

The links between maternal sensitivity and embodied experiences of mothers have been so far a neglected issue both in research and clinical practice. This is surprising since, as suggested by Ciaunica [57], an infant "meets" the mother's body before meeting her mind. To some extent the opposite is equally true, namely, the mother "meets" her infant's body before meeting her infant's mind. Additionally, a mother "meets" her own body before meeting her infant's body. In this perspective, *maternal embodied sensitivity* could improve a mother's ability to perceive her infant's body, which in turn would affect the mother's social engagement and emotional responsiveness. We should emphasize that the *maternal embodied sensitivity* concept is of a rather tentative nature. There is no doubt that future research is necessary to examine the implications of these hypotheses. For example, it could be important to examine the role of maternal interoceptive sensitivity in adjusting her own bodily sensations to understand and promptly respond to her infant's cues, supporting her infant's regulatory ability. Furthermore, disrupted interoception has not been thoroughly investigated in association to mental health conditions in the post-partum period, and to the best of our knowledge, no study has been designed to test this hypothesis directly. Thus, studying mother's body and maternal activity levels during early mother-infant exchanges takes on a crucial importance. Future studies are needed in order to better identify specific mechanisms associated with maternal interoceptive sensitivity and disrupted interoception that could be targeted in parental support interventions placing the mother's body "at the center" of the intervention. In this sense, planning interventions for new mothers and focusing and supporting their perception of their own body are essential. For example, novel methods can be devised to facilitate interoceptive learning and offer crucial insights to mothers and clinicians. In conclusion, the concept of *maternal embodied sensitivity* provides a theoretical framework and a future research perspective to investigate how maternal

awareness of internal body changes could be related to understanding of infant's emotional signals during early interaction, both in typical and atypical parenthood.

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References

1. Norholt H. Revisiting the roots of attachment: a review of the biological and psychological effects of maternal skin-to-skin contact and carrying of full-term infants. Infant Behav Dev. 2020;60. [Internet]. Available from https://www.embase.com/search/results?subaction=viewrecord&id=L2006864037&from=export.
2. Ainsworth MDS, Blehar MC, Waters E, Wall S. Patterns of attachment: a psychological study of the strange situation. Patterns of attachment: a psychological study of the strange situation. Oxford, England: Lawrence Erlbaum; 1978. p. xviii, 391–xviii, 391.
3. Deans CL. Maternal sensitivity, its relationship with child outcomes, and interventions that address it: a systematic literature review. In: Deans CL, editor. Early child development and care, vol. 190. Taylor & Francis; 2020. p. 252–75.
4. Musser ED, Kaiser-Laurent H, Ablow JC. The neural correlates of maternal sensitivity: an fMRI study. Dev Cogn Neurosci. 2012;2(4):428–36.
5. Reniers RLEP, Völlm BA, Elliott R, Corcoran R. Empathy, ToM, and self-other differentiation: an fMRI study of internal states. Soc Neurosci. 2014;9(1):50–62.
6. Shamay-Tsoory SG. Dynamic functional integration of distinct neural empathy systems. In: Social cognitive and affective neuroscience, vol. 9; 2014. p. 1–2.
7. Mielke EL, Neukel C, Bertsch K, Reck C, Möhler E, Herpertz SC. Maternal sensitivity and the empathic brain: influences of early life maltreatment. J Psychiatr Res. 2016;77:59–66.
8. Namkung H, Kim S-H, Sawa A. The insula: an underestimated brain area in clinical neuroscience, psychiatry, and neurology. Trends Neurosci. 2017;40(4):200–7.
9. Craig AD. How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci. 2002;3(8):655–66.
10. Fukushima H, Terasawa Y, Umeda S. Association between interoception and empathy: evidence from heartbeat-evoked brain potential. Int J Psychophysiol Off J Int Organ Psychophysiol. 2011;79(2):259–65.
11. Stoica T, Depue B. Shared characteristics of intrinsic connectivity networks underlying interoceptive awareness and empathy. Front Hum Neurosci [Internet]. 2020;14:524. Available from: https://www.frontiersin.org/article/10.3389/fnhum.2020.571070.
12. Gallese V. Before and below "theory of mind": embodied simulation and the neural correlates of social cognition. Philos Trans R Soc London Ser B, Biol Sci. 2007;362(1480):659–69.
13. Tsakiris M. The multisensory basis of the self: From body to identity to others. Q J Exp Psychol [Internet]. 2017;70(4):597–609. https://doi.org/10.1080/17470218.2016.1181768.
14. Fotopoulou A, Tsakiris M. Mentalizing homeostasis: the social origins of interoceptive inference. Neuropsychoanalysis [Internet]. 2017;19(1):3–28. https://doi.org/10.1080/15294145.2017.1294031.
15. Montirosso R, McGlone F. The body comes first. Embodied reparation and the co-creation of infant bodily-self. Neurosci Biobehav Rev [Internet]. 2020;113:77–87. https://doi.org/10.1016/j.neubiorev.2020.03.003.

16. Shuper Engelhard E, Ayana Zaides J, Federman D. The mother's perspective of body knowledge and expressions as a language in mother-infant relationships. Arts Psychother [Internet]. 2021;72:101746. Available from: https://www.sciencedirect.com/science/article/pii/S0197455620301192.
17. Craig AD. Emotional moments across time: a possible neural basis for time perception in the anterior insula. Philos Trans R Soc Lond B Biol Sci. 2009;364(1525):1933–42.
18. Craig AD. Interoception and emotion: a neuroanatomical perspective. Handbook of emotions. 3rd ed. New York, NY: The Guilford Press; 2008. p. 272–92.
19. Craig AD. How do you feel? An interoceptive moment with your neurobiological self. Princeton University Press; 2015.
20. LaMotte RH, Thalhammer JG, Torebjörk HE, Robinson CJ. Peripheral neural mechanisms of cutaneous hyperalgesia following mild injury by heat. J Neurosci. 1982;2(6):765–81.
21. Craig AD, Bushnell MC. The thermal grill illusion: unmasking the burn of cold pain. Science. 1994;265(5169):252–5.
22. Vallbo AB, Olausson H, Wessberg J, Kakuda N. Receptive field characteristics of tactile units with myelinated afferents in hairy skin of human subjects. J Physiol. 1995;483(Pt 3):783–95.
23. Olausson H, Lamarre Y, Backlund H, Morin C, Wallin BG, Starck G, et al. Unmyelinated tactile afferents signal touch and project to insular cortex. Nat Neurosci. 2002;5(9):900–4.
24. MacCormack JK, Castro VL, Halberstadt AG, Rogers ML. Mothers' interoceptive knowledge predicts children's emotion regulation and social skills in middle childhood. Soc Dev [Internet]. 2020;29(2):578–99. Available from https://onlinelibrary.wiley.com/doi/abs/10.1111/sode.12418.
25. Allen M, Tsakiris M. The body as first prior: Interoceptive predictive processing and the primacy of self-models. In: The interoceptive mind [Internet]. Oxford: Oxford University Press; 2018. Available from https://oxford.universitypressscholarship.com/10.1093/oso/9780198811930.001.0001/oso-9780198811930-chapter-2.
26. Herbert BM, Ulbrich P, Schandry R. Interoceptive sensitivity and physical effort: implications for the self-control of physical load in everyday life. Psychophysiology. 2007;44(2):194–202.
27. Critchley HD, Garfinkel SN. Interoception and emotion. Curr Opin Psychol [Internet]. 2017;17:7–14. Available from: https://www.sciencedirect.com/science/article/pii/S2352250X17300106.
28. Dunn BD, Galton HC, Morgan R, Evans D, Oliver C, Meyer M, et al. Listening to your heart. How interoception shapes emotion experience and intuitive decision making. Psychol Sci. 2010;21(12):1835–44.
29. Ernst J, Northoff G, Böker H, Seifritz E, Grimm S. Interoceptive awareness enhances neural activity during empathy. Hum Brain Mapp. 2013;34(7):1615–24.
30. Füstös J, Gramann K, Herbert BM, Pollatos O. On the embodiment of emotion regulation: interoceptive awareness facilitates reappraisal. Soc Cogn Affect Neurosci. 2013;8(8):911–7.
31. Schoeller F, Haar AJH, Jain A, Maes P. Enhancing human emotions with interoceptive technologies. Phys Life Rev. 2019;31:310–9.
32. Nummenmaa L, Hari R, Hietanen JK, Glerean E. Maps of subjective feelings. Proc Natl Acad Sci U S A. 2018;115(37):9198–203. https://doi.org/10.1073/pnas.1807390115. Epub 2018 Aug 28. PMID: 30154159; PMCID: PMC6140475.
32. Terasawa Y, Moriguchi Y, Tochizawa S, Umeda S. Interoceptive sensitivity predicts sensitivity to the emotions of others. In: Terasawa Y, editor. Cognition and emotion, vol. 28. Taylor & Francis; 2014. p. 1435–48.
33. Grynberg D, Pollatos O. Perceiving one's body shapes empathy. Physiol Behav. 2015;140:54–60.
34. Seth AK, Critchley HD. Extending predictive processing to the body: emotion as interoceptive inference. Behav Brain Sci. 2013;36(3):227–8.
35. Singer T, Lamm C. The social neuroscience of empathy. Ann N Y Acad Sci. 2009;1156:81–96.
36. Barrett J, Fleming AS. Annual Research Review: all mothers are not created equal: neural and psychobiological perspectives on mothering and the importance of individual differences. J Child Psychol Psychiatry. 2011;52(4):368–97.

37. Welch MG. Calming cycle theory: the role of visceral/autonomic learning in early mother and infant/child behaviour and development. Acta Paediatr. 2016;105(11):1266–74.
38. Montirosso R, Casini E, Borgatti R, Urgesi C. Relationship between maternal sensitivity during early interaction and maternal ability in perceiving infants' body and face. Infancy [Internet]. 2016;21(5):582–602. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/infa.12129.
39. Shai D, Belsky J. Parental embodied mentalizing: how the nonverbal dance between parents and infants predicts children's socio-emotional functioning. Attach Hum Dev. 2017;19(2):191–219.
40. Ferri F, Ardizzi M, Ambrosecchia M, Gallese V. Closing the gap between the inside and the outside: interoceptive sensitivity and social distances. PLoS One. 2013;8(10):e75758.
41. Modinos G, Ormel J, Aleman A. Activation of anterior insula during self-reflection. PLoS One. 2009;4(2):e4618.
42. Leibenluft E, Gobbini MI, Harrison T, Haxby JV. Mothers' neural activation in response to pictures of their children and other children. Biol Psychiatry. 2004;56(4):225–32.
43. Herbert BM, Pollatos O. The body in the mind: on the relationship between interoception and embodiment. Top Cogn Sci. 2012;4(4):692–704.
44. Arnold AJ, Winkielman P, Dobkins K. Interoception and social connection. Front Psychol [Internet]. 2019;10:2589. Available from: https://www.frontiersin.org/article/10.3389/fpsyg.2019.02589.
45. Abraham E, Hendler T, Zagoory-Sharon O, Feldman R. Interoception sensitivity in the parental brain during the first months of parenting modulates children's somatic symptoms six years later: the role of oxytocin. Int J Psychophysiol Off J Int Organ Psychophysiol. 2019;136:39–48.
46. Bytomski A, Ritschel G, Bierling A, Bendas J, Weidner K, Croy I. Maternal stroking is a fine-tuned mechanism relating to C-tactile afferent activation: an exploratory study. In: Croy I, editor. Psychology & neuroscience, vol. 13. Educational Publishing Foundation; 2020. p. 149–57.
47. Khalsa SS, Adolphs R, Cameron OG, Critchley HD, Davenport PW, Feinstein JS, et al. Interoception and mental health: a roadmap. Biol psychiatry Cogn Neurosci neuroimaging. 2018;3(6):501–13.
48. Quadt L, Critchley HD, Garfinkel SN. The neurobiology of interoception in health and disease. Ann N Y Acad Sci. 2018;1428(1):112–28.
49. Avery JA, Drevets WC, Moseman SE, Bodurka J, Barcalow JC, Simmons WK. Major depressive disorder is associated with abnormal interoceptive activity and functional connectivity in the insula. Biol Psychiatry. 2014;76(3):258–66.
50. Sprengelmeyer R, Steele JD, Mwangi B, Kumar P, Christmas D, Milders M, et al. The insular cortex and the neuroanatomy of major depression. J Affect Disord. 2011;133(1–2):120–7.
51. Paulus MP, Stein MB. Interoception in anxiety and depression. Brain Struct Funct. 2010;214(5–6):451–63.
52. Salo VC, Schunck SJ, Humphreys KL. Depressive symptoms in parents are associated with reduced empathy toward their young children. PLoS One. 2020;15(3):e0230636.
53. Bernard K, Nissim G, Vaccaro S, Harris JL, Lindhiem O. Association between maternal depression and maternal sensitivity from birth to 12 months: a meta-analysis. Attach Hum Dev. 2018;20(6):578–99.
54. Wonch KE, de Medeiros CB, Barrett JA, Dudin A, Cunningham WA, Hall GB, et al. Postpartum depression and brain response to infants: differential amygdala response and connectivity. Soc Neurosci. 2016;11(6):600–17.
55. Mascheroni E, Ionio C. The efficacy of interventions aimed at improving post-partum bonding: a review of interventions addressing parent-infant bonding in healthy and at risk populations. J Neonatal Nurs [Internet]. 2019;25(2):61–8. Available from: https://www.sciencedirect.com/science/article/pii/S1355184118301157.
56. Olhaberry M, León MJ, Seguel M, Mena C. Video-feedback intervention in mother-baby dyads with depressive symptomatology and relationship difficulties. Res Psychother Psychopathol Process Outcome. 2015;18(2):82–92.
57. Ciaunica A. The 'Meeting of Bodies': empathy and basic forms of shared experiences. Topoi [Internet]. 2019;38(1):185–95. https://doi.org/10.1007/s11245-017-9500-x.

Cancer and Pregnancy: Becoming Parents After an Oncological Diagnosis in Women

31

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31.1 Introduction

There is no clinical context that is not influenced by the results of the research which, in addition to providing new intervention tools and allowing to assess their effectiveness, improves the quality of care.

This is particularly true in psycho-oncology, a professional discipline that focuses on the psychosocial and behavioral dimensions of neoplastic diseases, as part of a comprehensive and global approach to the patient and his family.

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In the last 20 years, the research activity in psycho-oncology has grown considerably, offering important contributions on the most significant aspects of the disease experience and providing timely and personalized responses to the needs not only of patients but also of the family members and of the nursing staff. Psychological research on the complex issue of women diagnosed with cancer at childbearing age is still in its infancy.

In Italy, about half of women with an oncological diagnosis express the motherhood desire, but due to the age, the diagnosis, and the type of treatment, only few of them succeed in this project. An adequate counseling about oncofertility could sustain the motherhood desire in women with cancer history. Since this topic will become more and more frequent, emerge the need and the importance to create multidisciplinary support interventions, in order to allow the young women to face not only the hard path related to cancer but also the challenge related to motherhood.

Pregnancy complicated by a medical diagnosis makes woman face a *double risk*: motherhood's desire is counterbalanced by the difficult and painful experience of illness that deeply undermines her safety and future planning.

In particular, when oncological and onco-hematological diagnoses are made during the childbearing period, they profoundly affect the woman's well-being and her future motherhood's project. A cancer diagnosis alters psychological protective factors that are fundamental to effectively cope with both pregnancy and postpartum period; specifically, an oncological diagnosis represents a challenge for the construction of prenatal and postnatal attachment.

With *cancer and pregnancy*, we refer both to a cancer diagnosed during pregnancy or within 12 months from childbirth (gestational cancer) and also to a pregnancy occurring after diagnosis and treatment (pregnancy after cancer).

During perinatal period it's not rare that cancer diagnosis is delayed due to the misinterpretation (of pregnant women but also of the medical staff) of physical symptoms. For example, hormonal changes caused by gestation, *puerperium*, and breastfeeding may alter the normal appearance of breasts, thus retarding diagnosis [1, 2]. Moreover, many of the first symptoms of malignancies may be confused by common pregnancy signs, such as tiredness, nausea, abdominal pain, vaginal discharge, and pigmented lesions of the skin [2].

When an oncological diagnosis occurs during pregnancy, chemotherapy can be safely administered after the first trimester, without harming the fetus [2–4]. Moreover, antitumoral treatments given during gestation do not impact negatively on the future child's health, including cognitive and cardiac development [3]. Nonetheless, there is an increased risk of a preterm birth, intrauterine growth restriction, hematopoietic suppression, and stillbirth [2].

Women diagnosed with cancer in childbearing age have noteworthy doubts about fertility and recurrence, especially those who may wish to have a child [5]. On one side, although it is true that tumor and its treatments can reduce fertility, oncofertility innovations allow to delay pregnancy at the end of the oncological iter. Therefore, healthcare provider (oncologist, gynecologist, and psychologist) should be ready to

discuss with patients in childbearing age all the relevant information about future fertility, pregnancy, and breastfeeding, in other words to offer an oncofertility counseling. It is important to note that pregnancy after most cancers is not linked to an increased risk of recurrence. Actually, at least for breast cancer, there are data that pregnancy is a protective factor for recurrence and mortality [6] even if the *healthy mother effect* (i.e., self-selection of patients at better prognosis who get pregnant) should not be underestimated [5].

Given the rising trend of women delaying first gestation in their 30s and early 40s, when cancer diagnoses are increasing [2], the issue of oncological pregnancy will be increasingly topical. In 2019, about 21,000 Italian women have been diagnosed with malignancies during the childbearing period [7], and 500–600 women have been diagnosed during pregnancy.

Oncological and oncofertility progresses have allowed women who are diagnosed during pregnancy to carry on gestation [8–10] and women with a past oncological history to satisfy their desire for maternity [3, 11, 12].

Despite these advances, there is still little information about the adjustments of women who face an oncological diagnosis during pregnancy and the transition to motherhood and about how the cancer event affects the mother-child relationship.

To expand the literature about this issue and to make population aware with target programs, in 2016 a research has been started with the aim of verifying how the cancer event affects the mother-child relationship.

31.2 Research Project

In 2016, we started a project called "Becoming parents after an oncological diagnosis in women: evaluation of an Italian sample of oncological patients" (Ethics Committee 196/2016). The project, conducted in collaboration with many different clinical and research centers in Italy, aimed to answer some questions about cancer and pregnancy, to better understand peculiarities and challenges of women who experience pregnancy after or during cancer. In order to reach our goal, we designed a short-longitudinal research in pregnant women with cancer, structured in two phases, the first one in the last trimester of pregnancy and the second 1–3 months after delivery. We compared a clinical group of pregnant women with cancer experience before or during gestation (and their partners) with a control sample consisting of non-oncological pregnant women and their partners. Subjects with a medical or psychiatric diagnosis of cognitive or psychiatric disorders, which could interfere with the assessment, were excluded from the study.

The research project consisted in the administration of questionnaires (Table 31.1) which, in addition to detecting important variables about the history of pregnancy, assessed the psychological status of the future mother and father. We evaluated prenatal attachment, negative experiences, the meaning that pregnancy assumes in their life, quality of life, and resilience.

Table 31.1 Questionnaires and stage of administration

Stages	Tools
Pregnancy The last trimester of pregnancy	• Detection of cortisol levels using blood and urine (24-h) samples • Demography and clinical history • Prenatal Attachment Inventory (PAI) (only for mothers) [13, 14] • Maternal Antenatal Attachment Scale (MAAS) (only for mothers) [15, 16] • Multidimensional Scale of Perceived Social Support (MSPSS) [17, 18] • Profile of Mood States (POMS) [19, 20] • Impact of Event Scale-Revised (IES-R) [21, 22] • Centrality of Event Scale (CES) [23, 24] • The Interview of Maternal Representations during Pregnancy (IRMAG) [25] • Baby Care Questionnaire (BCQ) [26] • World Health Organization Quality of Life-26 items (WHOQOL-BREF) [27, 28] • Resilience Scale for adults (RSA) [29, 30] • Edinburgh Postnatal Depression Scale (EPDS) [31, 32]
Postpartum 3 months after childbirth	• Clinical history • Parenting Stress Index–Short Form (PSI-SF) [33, 34] • Multidimensional Scale of Perceived Social Support (MSPSS) [17, 18] • Profile of Mood States (POMS) [19, 20] • Baby Care Questionnaire (BCQ) [26] • World Health Organization Quality of Life-26 items (WHOQOL-BREF) [27, 28] • Edinburgh Postnatal Depression Scale (EPDS) [31, 32]

31.3 Results

The research team focused on the following thematic areas.

31.3.1 Impact of Cancer in the Construction of Prenatal Attachment

Women with cancer history have a higher risk of developing psychological difficulties; they frequently report emotional difficulties following diagnosis and treatment [35] and higher levels of anxiety compared with healthy controls [36]. Moreover, younger cancer survivors experience higher levels of depression, more psychological distress, and more difficulties related to their psychosocial roles than older women during the illness trajectory [37, 38]. The higher number of psychosocial needs reported by young cancer survivors may influence negatively prenatal attachment and, subsequently, the building process of a close and positive mother-infant relationship.

A total of 123 pregnant women, of which 36 were cancer survivors and 87 women without a history of cancer, were recruited during their last trimester at different hospitals in Northern Italy [39]. Firstly, we explored mother's mood states and post-traumatic symptomatology comparing the two samples. Secondly, we detected if cancer survivors perceived their pregnancy more as a central event for their life history and for their identity than women without a cancer diagnosis. Additionally, we investigated perceived quality of life and prenatal attachment in both samples, to understand if there were differences. Finally, we explored whether the centrality of the cancer diagnosis, investigated in the clinical sample, correlated with the building process of prenatal attachment, with higher levels of negative mood states, and with PTSD symptoms.

Our results showed that women with past cancer diagnosis had significantly higher levels of PTSD symptoms, confirming the results reported in literature [40–42]. Moreover, those women perceived pregnancy as more central to their identity and life history. This result may provide insight in the meaning of maternity for women that experience cancer and subsequent pregnancy. Becoming a mother after cancer may be considered as a chance of redemption from the illness. It is interesting to notice that the extent to which the cancer diagnosis is considered central for these women's life story and identity is not associated with psychological aspects, such as the building process of prenatal attachment, mood states, and PTSD symptoms.

Results also showed that women of the clinical sample reported lower levels of quality of life, specifically in the domain related to their life environment, which measures aspects related to safety and security, health and social care availability, as well as information and activity accessibility. Generally, women who have experienced cancer before pregnancy have to deal with a state of uncertainty regarding the effects of the oncological treatment and the fear of recurrence, and this can accentuate their fears and worries about their own safety and survival.

Moreover, women with past cancer diagnosis, compared with control sample, had lower intensity of prenatal attachment, in terms of behaviors that indicate interaction and affiliation with their fetus. These aspects of prenatal interaction are fundamental for the construction of the maternal representation and for the future mother-child relationship in the postpartum period [43, 44]. These women might be unable to create a mental space for the progressive relationship with their child, as some space is used to elaborate their experience of the illness. These preliminary results suggest that a past cancer diagnosis can influence the mother's psychological functioning and the development of the relationship with their child.

31.3.2 Resilience: A Protective Factor

Although few studies have explored the psychological aspects of cancer during pregnancy [45], it is plausible that a diagnosis of cancer might interfere with factors that are necessary to deal positively with an ongoing or future gestation. For this purpose, we investigated if resilience could be considered a protective factor in the

construction of the mother-fetus relationship. Resilience can be defined as the ability to positively deal with adverse conditions to overcome stress and difficulties while maintaining relatively good psychological and physical health [46]. It is a protective factor for prenatal attachment and for negative moods during pregnancy.

For this study [47], 26 pregnant women (25 with breast cancer and 1 with hepatic pecoma) were enrolled during the last trimester of pregnancy. Of these women, 20 have a pregnancy after cancer diagnosis, while 6 had a cancer occurring during pregnancy. Analyses showed positive correlations between resilience factors and prenatal attachment and negative correlations between resilience factors and negative mood states. In particular, there was a significant correlation between social resources and the quality of prenatal mother-fetus relationship and intensity of attachment. Moreover, there were a correlation between planned future and anxiety and fatigue and a correlation between family cohesion and anxiety, depression, and anger. Finally, there was a correlation between social resources and anxiety. These data indicate that it is important to assess resilience and family support in pregnant women with current or past experience of oncological diagnosis.

31.3.3 Psychological Dynamics and Maternal Representations

In order to have a deeper understanding of the psychological dynamics that, starting from the first stages of pregnancy, help women with cancer diagnosis to develop the maternal identity and maternal representations, we conducted a qualitative study on the transition to motherhood [48].

In this qualitative study, we investigated maternal representations in pregnant women with diagnosis of breast cancer and those with any oncological history. For this study, only patients with breast cancer were recruited, in order to reduce confounding variables, as cancer management and treatment are different depending on tumor type. We choose to include in the clinical sample both women who become pregnant after an oncologic disease and those who received a diagnosis during pregnancy. A total of 38 women were recruited, 19 women who had received a breast cancer diagnosis and 19 who had not. The Interview of Maternal Representations [25] administered in the last trimester of pregnancy asks the mothers-to-be to narrate the experience of their pregnancy and of becoming mothers. It allows to explore pregnant woman's mental representations, focusing on the woman's past experiences, impressions, and emotions related to pregnancy and maternity and on how she builds an image of the fetus and of the future child. Analysis of interviews allows to identify four main themes related to the fear and concerns about pregnancy, meaning of motherhood, mother-fetus relationship, and fears and concerns to postpartum and breastfeeding.

31.3.3.1 Fear and Concerns About Pregnancy

Women with breast cancer diagnosed during pregnancy expressed fears connected to their health and expressed concerns regarding the child's health as

possibly affected by their treatments. These women described the decision process related to treatment as colored with negative feelings: the benefits and harms for both women and their child have to be weighted, and the choice is often difficult to do.

31.3.3.2 Meaning of Motherhood

Despite the concerns about their and their baby's health, the notice of pregnancy is positively received by women of clinical group. Women with cancer diagnosed during pregnancy and those with past oncologic pathology were charmed by the news of being a mother much more than healthy women. Creating a family for women of clinical group means reconstructing a positive dimension with their partner and taking their chance for redemption from the illness [49]. In particular, primiparous women with past breast cancer considered the gestation as an unexpected gift. This positive reaction was less manifested in healthy women, as the pregnancy was seeing as a regular event in their lives, occurred without significant obstacles.

31.3.3.3 Partner Role

Women of clinical group stress the role of the cancer diagnosis on the couple's relationship. Both women with past and actual cancer attributed to their partners a protective role and perceived heightened support from them. In particular, women with previous breast cancer recognized support and acceptance from their partners in desiring children and evaluating fertility options by sharing their doubts before the final decision. The significant role of partner during pregnancy expressed by women of clinical group [48] is in line with results of other studies conducted on oncological women [50]. The women perception of a good level of support from the partner during pregnancy, in fact, seems to constitute an important protective factor both for the psychological well-being and for the relationship built with the child-to-be. Expecting women who perceived their partner as more supportive, in fact, perceive the couple relationship as less difficult but also feel more at ease in exercising their parental role [50].

31.3.3.4 Mother–Fetus Relationship

According to previous literature, in our study women evidenced how the first ultrasound screening was seen as a crucial moment of developing a relationship with their unborn child and a start for feeling a bonding with their inside growing fetus. This development of bonding was conducted on different levels among the sample. Cancer survivors based this relationship on sensations that their body and medical screenings gave them, while the other women on concrete actions referred to the baby. Anyway, the perception of fetus activated the reflection on their maternal identity. Often, the women with cancer diagnosed during pregnancy believed that "they might not be good enough mothers, as treatments might force them to spend time away from their new-born and that they might feel tired or lack energy to take adequate care of their child" [48].

31.3.4 After the Birth: Fears and Concerns About Breastfeeding

Women with breast cancer diagnosed during pregnancy expressed fears associated with breastfeeding. From one hand breastfeeding is perceived as relevant to strengthen the mother-child relationship; on the other side, the possibility of not breastfeeding is experienced as challenging. Women with actual cancer who can choose to do or not, in fact, had to evaluate whether delaying even further the beginning of treatment because of breastfeeding might be deleterious for their health. Otherwise, expecting women with a previous history of cancer, who were unable to breastfeed, were concerned about the negative consequences for the bonding with their infant. The impossibility to breastfeed for pregnant women with past breast cancer and the fear of not being able to breastfeed in those with actual breast cancer make them feel inadequate in their role as mothers so that their worries will obstacle the construction of a positive relationship with their child [1, 51]. The topic of breastfeeding in women with cancer history is actual because it is registered the lack of guidelines in this clinical population [52] conflicting with ongoing promotion of breastfeeding in the general population. Specifically, the recommendations of the World Health Organization encourage women to breastfeed emphasizing positive effects of breastfeeding for both mother and child [53]. Together to the positive impact on health, breastfeeding promotion is often accompanied by the message that it is a matter of "moral choice" associated to "optimal parenting" as opposed to potential risk in choosing formula [54]. As result, women with cancer experience who do not breastfeed may be exposed to unjustified stress, frustration, and guilt which increase fatigue during the postpartum period. Analogue emotions of guilt and dissatisfaction have been found in normative sample of women who cannot breastfeed due to not fulfill the criteria of "optimal parenting" [55].

Moving from these considerations, we conducted another study aimed to explore the breastfeeding choice in women with a past oncological diagnosis. The questions that guided the study were:

Do women with previous oncologic history choose to breastfeed and for how long? How is the feeding method related to mother's mood states in women with cancer history?

To answer these questions, we selected a sample of women with previous oncological history and a control group of women without oncological diagnosis, and we prospectively followed them from the third trimester of pregnancy to 3 months after childbirth.

We found that mothers with a cancer history choose to breastfeed significantly less than control sample at 3 months of age of the newborn, preferring more bottle-feed or using mixed feeding methods [56]. Moreover, among women with an oncological history, those who did not breastfeed reported higher levels of psychological distress and confusion compared to those who bottle-feed or use mixed feeding methods. Confusion related to feeding methods in women with past breast cancer may be due to the lack of target information, in line with the results of a previous study [52]. Moreover, these emotions expressed by women with cancer are in line

with the sense of guilt and the dissatisfaction that it has been found in the normative sample, in women who cannot breastfeed [55].

31.3.5 Cortisol: An Objective Indicator

It is well known that self-report questionnaires are subject to risk that respondents may not answer truthfully, because of social desirability and defense mechanisms. For this reason, we decided to combine self-report tools with measurement of cortisol concentration, that is, a biological marker, free of risk of manipulation. Cortisol is a glucocorticoid hormone conventionally considered as a biomarker of stress that rises steadily during the 40 weeks of gestation. Dysregulations in the rhythm of cortisol can lead to serious health and mental problems that can negatively affect the mother-infant relationship [57].

Recent studies have focused on different factors that could represent a risk for the construction of the mother-child bonding both during pregnancy and in the early months postpartum [58, 59].

When pregnancy has to face the burden of cancer, women are at greater risk of experiencing high levels of distress [60] and negative emotional states (such as anxiety and depression), which contribute to modifications in the hormonal and biochemical status of pregnant women [61].

A sample of plasma cortisol and one of urinary cortisol (24 h) have been collected for each participant over the last trimester of pregnancy. Plasma cortisol test was performed using a blood sample (normal values for plasma cortisol samples in non-pregnant women are between 5 and 25 μg/dL). Urine samples collected over 24 h provide an integrated measure of total free cortisol secretion.

Data were explored to examine the relationship between clinical variables (cortisol levels) and psychological variables, investigated by the questionnaires.

Sample were collected from 50 pregnant women, 8 belonging to the clinical group and 42 belonging to the control group. Both groups revealed a tendency of significance in the positive correlation between level of depression and concentration of urinary cortisol. Specifically, in the clinical group, a negative correlation has been found between both family cohesion (RSA) and structured lifestyle (RSA) and level of urinary cortisol, while in the control group, it has been found a significant positive correlation between level of depression and plasma cortisol. Results have also shown a significant negative correlation, in the control group, between social resources (RSA) and urinary cortisol. Similarly, a negative correlation has been found between planned future (RSA) and plasma cortisol.

In conclusion, when pregnancy is marked by the experience of cancer, an increase in levels of depression occurs that appears to be associated with higher level of cortisol. On the other hand, resilience resources seem to have a protective role against chronic distress experienced by pregnant women with a history of cancer.

From a practical point of view, level of cortisol can be used as a biomarker to identify women that are at greater risk of depression in the postpartum period, especially in those with a history of cancer.

Box BRCA

Hereditary breast-ovarian cancer (HBOC) is one of the most common hereditary cancer syndromes, and it is associated with alteration in the BRCA1 and BRCA2 genes. This alteration confers a 72% risk of developing breast cancer and 17% of developing ovarian cancer.

There is a genetic test for the screening of the genetic mutation of BRCA 1/2 genes. However, the choice to undergo this test on one hand represents a better control of cancer, but, on the other hand, it has a deep emotional impact on women. The positive result may be associated with a sense of uncertainty and feelings of anger, anxiety, depression, or guilt [62]. Indeed, BRCA1/2 tests may carry negative psychosocial consequences for women carriers and their families.

Since BRCA1/2 is usually transmitted as multiple generations, children of BRCA1/2 variant carriers have a 50% risk of receiving the genes and developing cancer in their life. For oncological women with BRCA 1 /2 mutation, transition to motherhood could represent a challenge.

We have done a study to explore differences in prenatal attachment in a sample of 23 women with a history of cancer before pregnancy: 5 of them were BRCA1/2 variant carriers, while 18 were not.

Results showed a statistically significant difference between the two groups among the prenatal attachment dimension (PAI): BRCA1/2 variant carriers had lower levels of prenatal attachment. In other words, these women seem to have a lower disposal to anticipate emotionally and cognitively the child during the last trimester of pregnancy. This difficulty could be associated with the sense of guilt for the high possibility of transmission of the genetic mutation to the child but also with the fear of leaving him prematurely orphaned [63].

It can be, therefore, concluded that clinicians should give pregnant BRCA1/2 variant women a particular attention and provide them psychological support.

31.4 Conclusion

Our results clearly show that young women diagnosed by cancer have a deep and rarely expressed desire to become mothers, which seems not to be weakened by cancer diagnosis. Thus, healthcare providers should inform patients about the possibility of motherhood despite cancer.

It is very important to give women with oncological history the adequate support during puerperium, with a particular focus on breastfeeding. It appears evident the need of a multidisciplinary team, able to consider and take care of the fragility of these women over different areas. The team should include oncologists, midwives,

gynecologists, psychologists, radiologists, and pediatricians. Consequently, an adequate training is essential to help these healthcare professionals to manage and better support motherhood after cancer.

Furthermore, the substantial contribution of patients' associations should not be underestimated. In our project has been valuable the collaboration with "*Salute Donna onlus*" (salutedonnaonlus.it), an association spread throughout the Italian territory, founded by Anna Mancuso. From its foundation, Salute Donna onlus actively promotes cancer patients' rights and needs. This partnership has allowed the extension of our project all over Italy with the ambitious goal of establishing guidelines for the strengthening of health policies in support of oncofertility.

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References

1. Alder J, Bitzer J. Psychooncologic care in young women facing cancer and pregnancy. In: Surbone A, Peccatori F, Pavlidis N, editors. Cancer and Pregnancy. Berlino: Springer Verlag; 2008.
2. Van Calsteren K, Amant F. Cancer during pregnancy. Acta Obstet Gynecol Scand. 2014;93(5):443–6.
3. Amant F, Vandenbroucke T, Verheecke M, Fumagalli M, Halaska MJ, Boere I, et al. Pediatric outcome after maternal cancer diagnosed during pregnancy. N Engl J Med. 2015;373(19):1824–34.
4. Peccatori FA, Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(6):160–70.
5. Gorman JR, Roesch SC, Parker BA, Madlensky L, Saquib N, Newman VA, et al. Physical and mental health correlates of pregnancy following breast cancer. Psycho-Oncol. 2010;19(5):517–24.
6. Sankila R, Heinävaara S, Hakulinen T. Survival of breast cancer patients after subsequent term pregnancy: "healthy mother effect". Obstet Gynecol. 1994;170(3):818–23.
7. AIOM. I Numeri del Cancro 2019. Istituto Superiore di Sanitàl; 2019. https://www.epicentro.iss.it/tumori/pdf/NC2019-operatori-web.pdf.
8. Harrison P. Psychosocial impact of a cancer diagnosis during pregnancy. Nurs Womens Health. 2013;17(5):437–42.
9. Henry M, Huang LN, Sproule BJ, Cardonick EH. The psychological impact of a cancer diagnosed during pregnancy: determinants of long-term distress. Psycho-Oncol. 2012;21(4):444–50.
10. Ives A, Musiello T, Saunders C. The experience of pregnancy and early motherhood in women diagnosed with gestational breast cancer. Psycho-Oncol. 2012;21:754–61.
11. Azim HA Jr, Santoro L, Pavlidis N, Gelber S, Kroman N, Azim H, et al. Safety of pregnancy following breast cancer diagnosis: a meta-analysis of 14 studies. Eur J Cancer. 2011;47(1):74–83.
12. Schmidt R, Richter D, Sender A, Geue K. Motivations for having children after cancer–a systematic review of the literature. Eur J Cancer Care. 2016;25(1):6–17.
13. Müller ME. Development of the prenatal attachment inventory. West J Nurs Res. 1993;15(2):199–215.
14. Della Vedova AM, Dabrassi F, Imbasciati A. Assessing prenatal attachment in a sample of Italian women. J Reprod Infant Psychol. 2008;26(2):86–98.

15. Condon JT. The assessment of antenatal emotional attachment: development of a questionnaire instrument. Br J Med Psychol. 1993;66(2):167–83.
16. Busonera A, Cataudella S, Lampis J, Tommasi M, Zavattini GC. Investigating validity and reliability evidence for the maternal antenatal attachment scale in a sample of Italian women. Arch Womens Ment Health. 2016;19:329–36.
17. Zimet GD, Dahlem NW, Zimet SG, Farley GK. The multidimensional scale of perceived social support. J Pers Assess. 1988;52(1):30–41.
18. Di Fabio A, Busoni L. Misurare il supporto sociale percepito: proprietà psicometriche della Multidimensional Scale of Perceived Social Support (MSPSS) in un campione di studenti universitari. Risorsa Uomo. 2008.
19. McNair D, Lorr M, Droppleman LF. POMS: profile of mood states: manuale. Giunti O. S.; 1991.
20. Farnè M, Sebellico A, Gnugnoli D, Corallo A. POMS. Profile of mood states. Italian version. Firenze: Giunti O. S.; 1991.
21. Weiss DS, Marmer CR. The impact of event scale–revised. Assessing psychological trauma and PTSD. New York: Guilford; 1997.
22. Giannantonio M. Psicotraumatologia e psicologia dell'emergenza. Ecomind: Salerno; 2003.
23. Berntsen D, Rubin DC. The Centrality of Event Scale: A measure of integrating a trauma into one's identity and its relation to post-traumatic stress disorder symptoms. Behav Res Ther. 2006;44(2):219–31.
24. Ionio C, Smorti M, Mascheroni E, Ongaro G, Cattaneo E, Gemignani A, et al. What is the role played by pregnancy in the construction of a woman's identity and her association with her child-to-be? J Reprod Infant Psychol. 2019; https://doi.org/10.1080/02646838.2019.1695042.
25. Ammaniti M, Candelori P, Pola M, Tambelli R. Maternità e gravidanza: studio delle rappresentazioni materne. Raffaello Cortina Editore: Milano; 1995.
26. Winstanley A, Gattis M. The Baby Care Questionnaire: A measure of parenting principles and practices during infancy. Infant Behav Dev. 2013;36:762–75.
27. The WHOQOL Group. The development of the World Health Organization quality of life assessment instrument (the WHOQOL). In: Orley J, Kuyken W, editors. Quality of life assessment: international perspective. Heidelberg: Springer Verlag; 1994. p. 41–57.
28. De Girolamo G, Rucci P, Scocco P, Becchi A, Coppa F, D'Addario A, et al. La valutazione della qualità della vita: validazione del WHOQOL-Breve. Epidemiologia e Psichiatria Sociale. 2000;9(1):45–55.
29. Friborg O, Hjemdal O, Rosenvinge JH, Martinussen M. A new rating scale for adult resilience: what are the central protective resources behind healthy adjustment? Int J Methods Psychiatr. 2003;12(2):65–76.
30. Capanna C, Stratta P, Hjemdal O, Collazzoni A, Rossi A. The Italian validation study of the Resilience Scale for Adults (RSA). BPA—Appl Psychol. 2015;63(272):16–24.
31. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150(6):782–6.
32. Benvenuti P, Ferrara M, Niccolai C, Valoriani V, Cox JL. The Edinburgh postnatal depression scale: validation for an Italian sample. J Affect Disord. 1999;53(2):137–41.
33. Abidin RR. Parenting stress index: professional manual (PSI). PAR; 1995.
34. Guarino A, Di Blasio P, D'Alessio M, Camisasca E, Serantoni M. Parenting stress index short form: Adattamento italiano. Firenze: Giunti, O. S.; 2008.
35. Burgess C, Cornelius V, Love S, Graham J, Richards M, Ramirez A. Depression and anxiety in women with early breast cancer: five-year observational cohort study. BMJ. 2005;330:702.
36. Mitchell AJ, Ferguson DW, Gill J, Paul J, Symonds P. Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. Lancet Oncol. 2013;14:721–32.
37. Thewes B, Butow P, Girgis A, Pendlebury S. The psychosocial needs of breast cancer survivors; a qualitative study of the shared and unique needs of younger versus older survivors. Psycho-Oncol. 2004;13:177–89.

38. Northouse LL. Breast cancer in younger women: effects on interpersonal and family relations. J Natl Cancer Inst Monographs. 1994;16:183–90.
39. Mascheroni E, Bonassi L, Ionio C, Nastasi G, Peccatori FA, Faccio F, et al. Representations and narratives during pregnancy in women with oncological diagnosis. Tumori J. 2018;104(4S):201.
40. Cordova MJ, Riba MB, Spiegel D. Post-traumatic stress disorder and cancer. Lancet Psychiatry. 2017;4:330–8.
41. Arnaboldi P, Riva S, Crico C, Pravettoni G. A systematic literature review exploring the prevalence of post-traumatic stress disorder and the role played by stress and traumatic stress in breast cancer diagnosis and trajectory. Breast Cancer Targets Ther. 2017;9:473–85.
42. Abbey G, Thompson SBN, Hickish T, Heathcote D. A metanalysis of prevalence rates and moderating factors for cancer related post-traumatic stress disorder. Psycho-Oncol. 2015;24:371–81.
43. Cannella BL. Maternal-fetal attachment: an integrative review. J Adv Nurs. 2005;50:60–8.
44. Yarcheski A, Mahon NE, Yarcheski TJ, Hanks MM, Cannella BL. A meta-analytic study of predictors of maternal-fetal attachment. Int J Nurs Stud. 2009;46:708–15.
45. Vanderbroucke T, Han SN, Van Calsteren K, Wilderjans TF, Van den Bergh BRH, Claes L, et al. Psychological distress and cognitive coping in pregnant women diagnosed with cancer and their partners. Psycho-Oncol. 2017;26(8):1215–21.
46. Rutter M. Psychosocial resilience and protective mechanisms. Am J Orthopsychiatry. 1987;57(3):316–31.
47. Bonassi L, Peccatori FA, Ionio C, Nastasi G, Mascheroni E, Liuzzo A, et al. Becoming mothers after cancer: resilience as a protective factor for prenatal attachment and for negative moods during pregnancy. J Clin Oncol. 2018;36(15):22,156.
48. Faccio F, Peccatori FA, Ionio C, Mascheroni E, Bonassi L, Liuzzo A, et al. A qualitative analysis of the experience of becoming mothers during or after a breast cancer diagnosis. Psycho-Oncol. 2018;27(S3):136.
49. Crawshaw MA, Sloper P. Swimming against the tide'–the influence of fertility matters on the transition to adulthood or survivorship following adolescent cancer. Eur J Cancer Care. 2010;19(5):610–20.
50. Ferrari F, Faccio F, Peccatori F, Pravettoni G. Psychological issues and construction of the mother-child relationship in women with cancer during pregnancy: a perspective on current and future directions. BMC Psychol. 2018;6(1):10.
51. DiPietro JA, Costigan KA, Gurewitsch ED. Maternal psychophysiological change during the second half of gestation. Biol Psychol. 2005;69(1):23–38.
52. Gorman JR, Usita PM, Madlensky L, Pierce JP. A qualitative investigation of breast cancer survivors' experiences with breastfeeding. J Cancer Surviv. 2009;3(3):181–91.
53. World Health Organization. Protecting, promoting and supporting breast-feeding: the special role of maternity services: a joint WHO/UNICEF statement. Geneva: WHO; 1989. http://apps.who.int/iris/bitstream/10665/39679/1/9241561300.pdf.
54. Knaak SJ. Contextualizing risk, constructing choice: Breastfeeding and good mothering in risk society. Health Risk Soc. 2010;12:345–55.
55. Fallon V, Komninou S, Bennett KM, Halford JC, Harrold JA. The emotional and practical experiences of formula-feeding mothers. Matern Child Nutr. 2017;13(4):12,392.
56. Smorti M, Testa I, Gallese M, Dotti A, Ionio CA, Andreol A, et al. Protect, promote and support: a warm chain of breastfeeding for oncological women. Results from a survey of Italian young cancer mothers. ecancer. 2020;14:1151.
57. Graignic-Philippe R, Dayan J, Chokron S, Jacquet AY, Tordjman S. Effects of prenatal stress on fetal and child development: a critical literature review. Neurosci Biobehav Rev. 2014;43:137–62.
58. Beauquier-Maccotta B, Chalouhi GE, Picquet AL, Carrier A, Bussières L, Golse B, et al. Impact of monochorionicity and twin to twin transfusion syndrome on prenatal attachment, post-traumatic stress disorder, anxiety and depressive symptoms. PloS One. 2016;11(1):0145649.

59. Goecke TW, Voigt F, Faschingbauer F, Spangler G, Beckmann MW, Beetz A. The association of prenatal attachment and perinatal factors with pre-and postpartum depression in first-time mothers. Arch Gynecol Obstet. 2012;286(2):309–16.
60. Surbone A, Peccatori F, Pavlidis N. Why is the topic of cancer and pregnancy so important? Why and How to read this book. In: Surbone A, Peccatori F, Pavlidis N, editors. Cancer and pregnancy. Berlino: Springer Verlag; 2008.
61. Obel C, Hedegaard M, Henriksen TB, Secher NJ, Olsen J, Levine S. Stress and salivary cortisol during pregnancy. Psychoneuroendocrinology. 2005;30(7):647–56.
62. Battistuzzi L, Ciliberti R, Forzano F, De Stefano F. Regulating the communication of genetic risk information: The Italian legal approach to questions of confidentiality and disclosure. Clin Genet. 2012;82(3):205–9.
63. Quinn GP, Vadaparampil ST, Tollin S, Miree CA, Murphy D, Bower B, et al. BRCA carriers' thoughts on risk management in relation to preimplantation genetic diagnosis and childbearing: when too many choices are just as difficult as none. Fertil Steril. 2010;94(6):2473–5.

Psychopathology and COVID-19 Pandemic in the Perinatal Period

32

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32.1 Introduction

On March 11, 2020, the World Health Organization (WHO) declared the novel coronavirus disease 2019 (COVID-19) outbreak a global pandemic, with social distancing and confinement measures being implemented worldwide in order to

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contain the spread of the virus [1]. One year later and more than 130 million confirmed cases globally, including more than 2.8 million deaths [2], the COVID-19 pandemic has become the greatest global health crisis of the twenty-first century with a significant impact on people's life at the individual, familial, professional, and community levels. Thus, COVID-19 emerged nowadays as a major negative life event and, therefore, very likely to affect perinatal mental health.

Perinatal mental disorders are the most frequent health problems during the child-bearing period and are associated with considerable negative maternal and fetal/infant outcomes [3]. According to the literature, about 10% of pregnant women and 13% of those who have given birth experience some type of mental disorder, most commonly depression or anxiety [4]. Despite the natural vulnerability of women in the perinatal period, previous evidence showed that exposure to disasters or stressful life events is a major predictor of mental health disorders among pregnant and postpartum women [5]. Therefore, we may expect exacerbation of adverse emotional outcomes as a result of COVID-19 pandemic.

The present chapter aims to summarize the evidence available so far regarding major changes in individual and system-based features as a result of the COVID-19 pandemic which are associated with increased perinatal psychopathology. The chapter will end with major practical implications for perinatal mental health during the COVID-19 pandemic.

32.2 Changes in Perinatal Practices During the COVID-19 Pandemic

The rapid human-to-human transmission and preventive measures (e.g., lockdowns, physical distancing) imposed to contain the spread of the virus resulted in the creation of safety protocols with a direct impact on standard perinatal care practices. The most common changes in routine prenatal/postnatal care due to the COVID-19 outbreak included cancellation or postponement of medical appointments, change from in-person to remote consultations with health professionals, and restrictions on the partner's presence during childbirth or postnatal visitation in maternity wards [6, 7]. Similarly, access to other perinatal professionals or services (e.g., doulas, childbirth education classes) was limited or modified, and, in some cases, separation of the mother and newborn was considered in cases of confirmed COVID-19 infection [6]. These changes might result in lower quality of care, higher risks for mothers' and infants' health, and increased psychological distress, especially in low- and middle-income countries [8].

In this regard, several studies, conducted in different countries, have already investigated which specific changes in perinatal practices were experienced by pregnant and postpartum women during the COVID-19 pandemic. For example, a study carried out in Wuhan (epicenter of the pandemic in China) showed that only 16.3% of the pregnant women maintained their prenatal care visits as planned, whereas hospitalized delivery proceeded as planned in 25% of the cases [9]. Additional changes in delivery mode, choice of infant feeding, and the place for

resting after delivery were also reported by the authors. In another study in Canada with 1987 pregnant women, surveyed in April 2020, 89% of the participants reported suffering changes in their prenatal care routines, namely, cancellation of appointments (36%), restrictions on the accompaniment by a support person (90%), and changes in their birth plan (35%) [10]. In a study conducted in the United Kingdom with 614 postnatal mothers, 38% of the respondents reported being less satisfied with changes in their healthcare, whereas a negative change in social support was perceived in 56% of the cases, due to the introduction of social distancing measures [11]. Also, among UK postpartum women who delivered during the first national lockdown, 39% reported modifications to their birth plans as a result of the pandemic (e.g., delivery in hospital setting rather than in a low-risk/midwife-led unit; their birth partner's presence was allowed only during active labor), and 45% of the mothers felt they had received insufficient feeding support [12]. Nevertheless, other perinatal practices seemed unaffected despite difficulties caused by the pandemic, so that 89% of women were able to practice skin-to-skin contact with their babies short after delivery and 82% of those intended to breastfeed could initiate breastfeeding within the first hour after delivery [12]. Finally, a study conducted with 21,763 pregnant women in Nepal, during a period comprising 12.5 weeks before and 9.5 weeks during the national lockdown, also found several changes in intrapartum care [13]. More specifically, companionship to women during labor, intrapartum fetal heart rate monitoring, and breastfeeding within 1 h after delivery decreased during lockdown, while improvements were seen regarding hand hygiene practices by health workers during childbirth and the rate of babies placed in skin-to-skin contact with their mothers. The authors highlighted that, despite the overall decrease in use of health facilities that was accentuated during the lockdown period, the lower attendance was registered in women from more disadvantaged ethnic groups [13].

It seems that COVID-19 pandemic has clearly affected women's expectations and childbirth experience. A period of life that was typically described using positive words (e.g., joy) is now experienced with more fear and sadness, mostly due to restrictions, loneliness, anxiety, and worries during COVID-19 pandemic [14]. Thus, it is possible that some women may feel grief from missing or not sharing important experiences of the perinatal period the way they planned and with their family and friends, which may, in turn, contribute to elevated psychological distress during this time [15].

32.3 Perinatal Depression During COVID-19 Pandemic

Depression is the third cause of disease-related disability among women [16] and the most common psychiatric condition during the perinatal period [17]. Perinatal depression shares the same diagnostic criteria for major depressive disorders, with an onset specifier in the peripartum period [18]. It is estimated to affect 12% of women during the perinatal period [19], with depressive symptoms often beginning during pregnancy with 1/3 of cases occurring in the first trimester [20].

Although hormonal and clinical factors must be considered [21], as well as specific risk factors increasing women's susceptibility to perinatal depression (e.g., economic status, social support) [22], the exposure to stressful events may also predispose emotional distress during this period [23]. In this regard, the COVID-19 pandemic represents a "life-threatening event" for elevated psychological distress, including in pregnant and postpartum women. As far as we know, four published systematic reviews and meta-analyses have investigated the impact of COVID-19 pandemic on perinatal mental health [24–27]. The overall prevalence of prenatal depression was 25% [24], 30% [26], and 31% [27], whereas rate of postpartum depression was 22% [27], as measured through different assessment tools. However, Hessami et al. [25] reviewed studies assessing perinatal depression using the Edinburgh Postnatal Depression Scale (EPDS) [28] and found that, despite the higher EPDS scores among study participants during the COVID-19 pandemic, the difference was not statistically significant when compared to data from the pre-pandemic period. The comorbidity with anxiety symptomatology was also common, with 1/5 of pregnant and delivery women suffering simultaneously from anxiety and depression during the COVID-19 pandemic [26].

The aforementioned systematic reviews and meta-analyses have also reported substantial heterogeneity across the included studies, and, for that reason, caution is needed in the interpretation of the findings. More specifically, perinatal depression was measured using different assessment tools, and distinct cut-off scores were sometimes adopted in studies with the same questionnaire [24, 26, 27], and one review suggested a potential bias in publishing [26]. Another limitation is that most of the included studies were cross-sectional and used online surveys [24, 27], highlighting the need for longitudinal studies assessing the long-term impact of the COVID-19 pandemic on perinatal mental health. Despite the limitations, the results have demonstrated the negative psychological impact caused by the COVID-19 pandemic and consequent quarantine measures and disruptions in healthcare practices, in such a vulnerable population as pregnant and postpartum women. Given the potential deleterious effect of untreated depression [29], efforts should be devoted to the development of preventive and treatment psychological interventions, especially during the ongoing pandemic.

32.4 Perinatal Anxiety During the COVID-19 Pandemic

A recent meta-analysis estimated that one in five women (20.7%) meet diagnostic criteria for at least one anxiety disorder across pregnancy and the postpartum period, also becoming a prevalent mental disorder during this period [30]. Likewise depression, anxiety symptomatology constitutes one of the most studied mental health indicators during the COVID-19 pandemic, in the general population [31] and in pregnant and postpartum women [27].

Several systematic reviews and meta-analyses investigating the impact of COVID-19 pandemic on perinatal mental health reported an overall prevalence of

anxiety symptomatology ranging from 34% to 42% in pregnant women [24, 26, 27], representing almost a double of prevalence rate compared to pre-pandemic cohorts [30]. In fact, a systematic review of studies using the State-Trait Anxiety Inventory (STAI) [32] to assess women in the perinatal period found significantly higher anxiety scores during the pandemic when compared to previous non-pandemic data [25]. Also, a significant between-study heterogeneity was reported by the different systematic reviews and meta-analyses [24, 26, 27], which can be explained by the fact that studies may have applied different assessment tools and cut-off scores to measure anxiety, as well as the current level of severity and restriction measures of the COVID-19 pandemic in the countries where studies were conducted. For example, in a cross-sectional study conducted with pregnant women in China during the early phase of the COVID-19 outbreak, significantly higher rates of anxiety and depressive symptoms were registered in pregnant women assessed after the public announcement of human-to-human transmission and worsening of the epidemiological situation [33]. Similarly, in a sample of UK mothers in the early postnatal period, participants perceived a negative change in their psychological state (i.e., feelings of depression, anxiety, motherhood-related anxiety) as a direct consequence of the introduction of social distancing measures [11].

Increased anxiety is a common emotional response triggered by unpredicted and stressful events that may require periods of social isolation, as shown in past epidemics with similar characteristics to the ongoing COVID-19 outbreak [34]. Especially for women in the perinatal period, the pandemic context brings an additional risk factor likely to increase their levels of stress and anxiety, since they are doubly concerned with their own's and their unborn/newborn baby's health. Besides, social distancing measures and lockdowns may have also limited or disrupted their access to potential sources of professional help (e.g., doulas, childbirth preparation classes) [6], therefore exacerbating women's feelings of anxiety and worries.

32.5 Post-Traumatic Stress Disorder During the COVID-19 Pandemic

Post-traumatic stress disorder (PTSD) is a mental health condition that occurs after exposure to particularly stressful and life-threatening situations, such as natural disasters and health crises [18]. When occurring during the perinatal period, severe traumatic events make pregnant and postpartum women extremely vulnerable to develop mental health distress [5, 35]. Childbirth in itself can sometimes be experienced as a traumatic event due to subjective (need of support, fear) or objective (obstetric complications) components [36]. Thus, it is possible that the unprecedented COVID-19 crisis, and related concerns about the possibility of vertical transmission and negative obstetric outcomes, may become too demanding for maternal mental health by posing additional stressors to the childbirth experience.

A large body of evidence shows that developing PTSD symptoms was a common psychological response observed in past infectious disease outbreaks (e.g., SARS,

MERS) and after exposure to quarantine and social isolation periods, similar to those experienced during the ongoing COVID-19 pandemic [1, 34, 37]. PTSD symptoms associated with direct or vicarious exposure to COVID-19 may include nightmares, intrusive thoughts, or memories related to COVID-19. Although less studied, a few studies have already addressed PTSD symptoms in pregnant and postpartum women during the pandemic. For example, a study conducted from May to August, 2020, with US women who were on their second trimester of pregnancy or were up to 6 months postpartum, found that 10.3% participants presented clinically significant levels of PTSD from the past month [15]. In addition, having a pre-existing diagnosis of generalized anxiety or PTSD was significantly associated with PTSD symptoms at the clinical level [15]. Another Canadian study assessing two cohorts of pregnant women, one of them recruited before the COVID-19 pandemic and the other one during the pandemic, observed that pregnant women from the COVID-19 cohort reported higher symptoms of post-traumatic stress disorder than the pre-pandemic group [38].

Two other studies in Italy, with pregnant [39] and postpartum women [40] during the national lockdown, found that around 10% and 29% of the participants, respectively, experienced clinically significant PTSD symptoms, especially among those with a history of mood disorders [39]. Interestingly, perceived support by healthcare staff during birth and quietness on the ward during hospitalization (due to hospital visitor restrictions) were protective factors against PTSD symptoms [40]. Finally, in another US study with a sub-sample of participants recruited within a randomized control trial on perinatal mental health, 19% of the women screened positive for PTSD symptoms [41]. Moreover, increased psychological distress during the pandemic, including PTSD, was associated with perceived changes in access to mental healthcare [41].

32.6 Pregnancy Loss During the COVID-19 Pandemic

Pandemic-related disruptions to obstetric and gynecologic care delivery, which included remote consultation methods and postponing of nonurgent surgical procedures [6], may have had a particularly detrimental effect on women and families facing pregnancy loss. Pregnancy loss and death of a baby can be an extremely painful and traumatic experience that affects the women, their partners, but also other members of the family.

Evidence of perinatal loss during the COVID-19 is limited. A few studies conducted in the United Kingdom [42], Italy [43], and India [44] reported a significant increase in stillbirth rates during the pandemic, when compared to a previous non-pandemic period. However, none of the studies found a direct causal relation of the stillbirth cases with COVID-19 infection [42–44]. For example, none of the stillbirth cases was among pregnant women with symptoms suggestive of COVID-19 infection nor did the postmortem/placental examinations confirm the presence of the virus [42]. Studies were mostly based on small sample sizes, single-center

settings, a short time window studied, and information on causes of stillbirth was missing or insufficient; therefore further investigation of this topic is needed. In addition, the authors suggest that increase in stillbirth could be a consequence of changes in obstetric services induced by the pandemic/lockdowns, such as reduced antenatal visits, postponing or cancellation of medical exams (e.g., ultrasound scans), staff shortages, and reluctance in going to the hospital when needed due to fear of getting infected [42, 43].

Although pregnant women are considered at high risk due to increased vulnerability during pregnancy, the relationship between COVID-19 infection and risk of miscarriage remains unclear with mixed findings. In a cohort study in Denmark, pregnant women with COVID-19 infection in the first trimester were not at significantly increased risk of pregnancy loss [45]. Similarly, another study examining data from 116 pregnant women with COVID-19 found no higher risk of spontaneous abortion and preterm birth, as well as no evidence of maternal-fetal transmission when the infection occurs during the last trimester of pregnancy [46]. However, a case study of women with COVID-19 who had a miscarriage at 20 weeks confirmed placental infection with COVID-19 supported by virological results [47].

When couples and women experience pregnancy loss, their mental health needs to be addressed alongside their grief. Loss and grieve can act as stressors and trigger mental health disorders [48], so that women exposed to pregnancy loss during this period are deemed vulnerable and uniquely affected by COVID-19 outbreak. Due to changes in obstetric and perinatal care services during the pandemic, some women may have had to deal with perinatal loss without adequate psychosocial and emotional support, provided by specialized mental health professionals, and have faced potential health complications as a result of postponed medical screenings or delayed diagnosis of gynecological emergencies.

32.7 Risk Factors for Perinatal Psychopathology During the COVID-19 Pandemic

Several social, psychological, and biological factors have been identified in the literature as interacting with the emergence of psychopathology in the perinatal period. More specifically, previous experience of mental health problems, biological causes, lack of support, difficult childhood experiences, experience of abuse, low self-esteem stressful living conditions, and major life events are well-known risk factors that increase women's susceptibility to psychological problems during this period [49]. Some studies addressing the impact of COVID-19 pandemic—and the associated restrictive measures imposed throughout the world to contain the spread of the virus—on perinatal mental health have reported some psychosocial factors that seem critical in this regard during the current outbreak.

A cross-sectional study undertaken in Italy with women who gave birth between March and June 2020 reported higher prevalence of postnatal depression and posttraumatic stress symptoms when compared to pre-pandemic cohorts. Additionally,

the authors also found that level of pain experienced during childbirth, perceived support from healthcare staff, and attachment style were associated with psychological distress during the postpartum period [40]. On the other hand, factors specifically related to the COVID-19 pandemic seemed to play an indirect role in increasing psychological distress [40]. Importantly in this study is the fact that individual factors (e.g., attachment style) significantly contributed to the level of symptomatology, highlighting the need of targeted preventive and/or tailored therapeutic psychological interventions. Another study carried out during the first lockdown in Italy also demonstrated that pregnant women were very concerned about COVID-19 infection, namely, with regard to the health of their baby and of their elderly relatives, displaying higher levels of anxiety and post-traumatic stress disorder symptoms [39]. Increased concern and psychological distress were significantly associated with a previous diagnosis of anxiety and/or depression [39]. This study also emphasizes the importance of considering previous clinical history of these women, in order to prevent or early intervene to attenuate the negative impact of the current pandemic.

Also, studies conducted with pregnant women showed that those who were younger seemed more prone to display anxiety and depression [10, 33] and those from low socio-economic background also experienced higher depressive symptoms [33] and stress levels [50] during the COVID-19 pandemic. Importantly, women receiving more social support and engaged in more physical work were less likely to report psychological problems [10, 51], which highlights the relevance of taking appropriate measures, which may serve as protective factors, to alleviate the adverse mental impact of the COVID-19 pandemic on pregnant women.

Besides the known risk factors previously mentioned, other specific COVID-19-related risk factors were also examined. The COVID-19 pandemic seems to affect pregnant women's expectations of childbirth and obstetric decisions as well [10] and increase their feelings of worries about others rather than about themselves, especially the elderly relatives' health [39]. In particular, disruptions to prenatal/postnatal care and birth plans contribute to women's psychological distress [52]. In a Canadian study, worries about not getting adequate prenatal care due to the COVID-19 pandemic were associated with higher depression and anxiety symptoms in pregnant women [10]. Additionally, perceived risk of exposure to COVID-19 infection and alterations to prenatal appointments were associated with greater levels of pandemic-related stress among US pregnant women [53].

Taken together, studies conducted during the ongoing pandemic have identified risk factors previously associated with perinatal psychopathology and pointed out specific COVID-19 pandemic-related stressors in explaining elevated psychological distress. Although further studies are required to examine the contribution of both well-known risk factors and specific pandemic-related stressors to perinatal mental health, the evidence available so far corroborate the negative psychological impact caused by the COVID-19 pandemic and claim for the need of mental health promotion strategies targeting this particularly vulnerable population.

32.8 Changes in Mental Health Treatment During the COVID-19 Pandemic

The COVID-19 pandemic brought about many changes in daily life and a negative impact on women's mental health during the perinatal period. Services provisions have also changed due to social distancing, quarantines, lockdowns, and employment layoffs [54]. These changes have had an especially significant impact on the provision of continuous mental health services [55]. As a result, mental healthcare providers had to quickly change their standard of care provision and adapt to the new reality [54] in order to provide continuous and effective mental health treatment with minimal disruptions [56]. The most prominent response in most countries has been to move to tele-mental health, which includes usage of various technologies with different media and degrees of human support, such as telephone, videoconferencing, and Internet-based self-help interventions [57]. Also, insurance companies expanded coverage of telehealth services for the provision of mental health services [58].

Tele-mental health treatment has been available for many years, and several studies conducted on the matter have shown promising results for treating emotional distress, in general, and perinatal distress, in particular [59]. Yet, several barriers have hindered the implementation of such interventions in routine care up until the COVID-19 pandemic [60]. One major barrier has been the low acceptance of these types of interventions by mental health professionals [61]. However, since the massive shift toward tele-mental health due to COVID-19, therapists' attitudes toward this mode of treatment have become more favorable [62]. Still, for some mental health professionals, the challenges of transferring to tele-mental health provision have reinforced their view of the limitations of such services [54].

Although no research was found on consumers' views of tele-mental health treatment specifically during the COVID-19 pandemic, mental health service users have noted their satisfaction with this form of mental healthcare delivery over the years [63] and specifically in the perinatal period [59], since it offers flexibility and easy access from anywhere a person is [58]. Nonetheless, it is important to adapt specific types of tele-mental health interventions to various populations. For instance, online tools have been reported to be less accessible for people from lower socio-economic status with limited Internet access, while hotlines are more accessible for such populations [64].

32.9 Practical Implications for Perinatal Mental Health During the COVID-19 Pandemic

One year after the onset of the pandemic, we may more clearly measure its psychological impact on women in the perinatal period and draw important lessons for the future, namely, what procedures were found to have a positive effect or should be improved and next steps to help mitigate the devastating effect of the pandemic on perinatal mental health.

Changes in perinatal care practices and reduced access to mental health services may have contributed to increased prevalence of psychological distress, or worsening of existing psychopathology, during the pandemic. However, some studies showed that specific practices aimed to promote immediate newborn care were maintained or even increased (e.g., skin-to-skin contact with the mother) [12, 13], which may attenuate mothers' emotional distress and preserve early mother-newborn bonding. Thus, it is important that safety protocols during the pandemic follow evidence-based recommendations in order to keep women, their partners, the baby, and healthcare workers protected, while ensuring that women still have access to all available resources to meet their physical, emotional, and psychological needs. In those cases in which the partner's presence was not allowed during childbirth and postnatal visitation was prohibited, positive activities after home return may strengthen family connection and parent-infant affective bonding.

Empirical evidence corroborates the high costs of the COVID-19 pandemic to mental health and suggests that a wide range of psychological symptoms (depression, anxiety, PTSD, among others) may be experienced by pregnant and postpartum women during this crisis, with potential significant effects on their long-term mental health and offspring's development. Thus, it is important that these various psychological manifestations be included in screening initiatives and targeted in treatment programs. Several psychological practices may alleviate the negative impact of COVID-19 and promote adjustment in pregnant and postpartum women, namely, encourage to maintain regular social contact with family and friends through alternative means (e.g., telephone, social media, video calls), facilitate sources of self-help and encourage to adopt positive coping strategies, reinforce the care and support from other family members, offer tele-mental health resources and telepsychotherapy, and promote positive mother-infant practices from birth (e.g., skin-to-skin, breastfeeding) [65]. Special attention should be devoted to pregnant and postpartum women with pre-existing mental health conditions since, as expected, evidence shows that history of mood disorders is a risk factor to elevated psychological distress during the COVID-19 pandemic [15, 39].

Thus, interventions for perinatal mental health should be a priority in order to prevent long-term impacts on the mothers and offsprings [66]. Future research avenues should focus on examining risk factors for high vulnerability to mental distress during the pandemic but also identify potential protective factors and sources of resilience (e.g., self-care behaviors, partner emotional support, physical activity) [52]. Additionally, timely and tailored psychological interventions should be designed and implemented, taking into account the specificities of perinatal mental health during the COVID-19 pandemic, and their effectiveness should be evaluated when delivered in a tele-health format [66, 67].

32.10 Conclusions

The COVID-19 pandemic and associated social distancing measures have caused a significant impact on pregnant and postpartum women's mental health, with elevated depression, anxiety, and post-traumatic stress disorder symptoms among the

most prevalent psychological reactions during this global crisis. Specific groups of perinatal women may be at higher risk, e.g., those with pre-existing mental health conditions, those who have experienced perinatal loss during the pandemic, and women from socially disadvantaged backgrounds. Thus, health and mental health professionals and researchers should work together to define the best practices and intervention programs in perinatal mental health to adequately manage the short- and long-term psychological consequences of the COVID-19 crisis in women, families, and offsprings.

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References

1. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet. 2020;395(10,227):912–20. https://doi.org/10.1016/S0140-6736(20)30460-8.
2. World Health Organization. COVID-19 weekly epidemiological update [Internet]. Geneva; 2021 [updated 2021 Apr 6; cited 2021 Apr 7]. Available from https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19%2D%2D-6-april-2021
3. Stein A, Pearson RM, Goodman SH, Rapa E, Rahman A, McCallum M, et al. Effects of perinatal mental disorders on the fetus and child. Lancet. 2014;384(9956):1800–19. https://doi.org/10.1016/S0140-6736(14)61277-0.
4. O'Hara MW, Swain AM. Rates and risks of postpartum depression - a meta-analysis. Int Rev Psychiatry. 1996;8(1):37–54. https://doi.org/10.3109/09540269609037816.
5. Harville E, Xiong X, Buekens P. Disasters and perinatal health: a systematic review. Obstet Gynecol Surv. 2010;65(11):713–28. https://doi.org/10.1097/OGX.0b013e31820eddbe.
6. Onwuzurike C, Meadows AR, Nour NM. Examining inequities associated with changes in obstetric and gynecologic care delivery during the coronavirus disease 2019 (COVID-19) pandemic. Obstet Gynecol. 2020;136(1):37–41. https://doi.org/10.1097/AOG.0000000000003933.
7. Thapa SB, Mainali A, Schwank SE, Acharya G. Maternal mental health in the time of the COVID-19 pandemic. Acta Obstet Gynecol Scand. 2020;99(7):817–8. https://doi.org/10.1111/aogs.13894.
8. Graham WJ, Afolabi B, Benova L, Campbell OM, Filippi V, Nakimuli A, et al. Protecting hard-won gains for mothers and newborns in low-income and middle-income countries in the face of COVID-19: call for a service safety net. BMJ Glob Health. 2020;5(6):e002754. https://doi.org/10.1136/bmjgh-2020-002754.
9. Liu X, Chen M, Wang Y, Sun L, Zhang J, Shi Y, et al. Prenatal anxiety and obstetric decisions among pregnant women in Wuhan and Chongqing during the COVID-19 outbreak: a cross-sectional study. BJOG. 2020;127(10):1229–40. https://doi.org/10.1111/1471-0528.16381.
10. Lebel C, MacKinnon A, Bagshawe M, Tomfohr-Madsen L, Giesbrecht G. Elevated depression and anxiety symptoms among pregnant individuals during the COVID-19 pandemic. J Affect Disord. 2020;277:5–13. https://doi.org/10.1016/j.jad.2020.07.126.
11. Fallon V, Davies SM, Silverio SA, Jackson L, De Pascalis L, Harrold JA. Psychosocial experiences of postnatal women during the COVID-19 pandemic. A UK-wide study of prevalence rates and risk factors for clinically relevant depression and anxiety. J Psychiatr Res. 2021;136:157–66. https://doi.org/10.1016/j.jpsychires.2021.01.048.
12. Vazquez-Vazquez A, Dib S, Rougeaux E, Wells JC, Fewtrell MS. The impact of the Covid-19 lockdown on the experiences and feeding practices of new mothers in the UK: preliminary data

from the COVID-19 new mum study. Appetite. 2021;156:104,985. https://doi.org/10.1016/j.appet.2020.104985.
13. Ashish KC, Gurung R, Kinney MV, Sunny AK, Moinuddin M, Basnet O, et al. Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study. Lancet Glob Health. 2020;8(10):e1273–81. https://doi.org/10.1016/S2214-109X(20)30345-4.
14. Ravaldi C, Wilson A, Ricca V, Homer C, Vannacci A. Pregnant women voice their concerns and birth expectations during the COVID-19 pandemic in Italy. Women Birth. Available online 13 July 2020. doi: https://doi.org/10.1016/j.wombi.2020.07.002
15. Liu CH, Erdei C, Mittal L. Risk factors for depression, anxiety, and PTSD symptoms in perinatal women during the COVID-19 pandemic. Psychiatry Res. 2021;295:113,552. https://doi.org/10.1016/j.psychres.2020.113552.
16. World Health Organization. Depression and other common mental disorders global health estimates [Internet]. Geneva; 2007 [cited 2021 Feb 8]. Available from: https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf;jsessionid=ED9EAAD84FF10E86369ACDF40348804B?sequence=1
17. Rasmussen M-LH, Strøm M, Wohlfahrt J, Videbech P, Melbye M. Risk, treatment duration, and recurrence risk of postpartum affective disorder in women with no prior psychiatric history: a population-based cohort study. PLoS Med. 2017;14(9):e1002392. https://doi.org/10.1371/journal.pmed.1002392.
18. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). Washington: American Psychiatric Publishing; 2013.
19. Woody CA, Ferrari AJ, Siskind DJ, Whiteford HA, Harris MG. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. J Affect Disord. 2017;219:86–92. https://doi.org/10.1016/j.jad.2017.05.003.
20. Wilcox M, McGee BA, Ionescu DF, Leonte M, LaCross L, Reps J, et al. Perinatal depressive symptoms often start in the prenatal rather than postpartum period: results from a longitudinal study. Arch Womens Ment Health. 2021;24:119–31. https://doi.org/10.1007/s00737-020-01017-z.
21. Silverman ME, Reichenberg A, Savitz DA, Cnattingius S, Lichtenstein P, Hultman CM, et al. The risk factors for postpartum depression: a population-based study. Depress Anxiety. 2017 Feb;34(2):178–87. https://doi.org/10.1002/da.22597.
22. Gelaye B, Rondon MB, Araya R, Williams MA. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. Lancet Psychiatry. 2016;3(10):973–82. https://doi.org/10.1016/S2215-0366(16)30284-X.
23. Giarratano GP, Barcelona V, Savage J, Harville E. Mental health and worries of pregnant women living through disaster recovery. Health Care Women Int. 2019;40(3):259–77. https://doi.org/10.1080/07399332.2018.1535600.
24. Fan S, Guan J, Cao L, Wang M, Zhao H, Chen L, et al. Psychological effects caused by COVID-19 pandemic on pregnant women: a systematic review with meta-analysis. Asian J Psychiatr. 2021;56:102,533. https://doi.org/10.1016/j.ajp.2020.102533.
25. Hessami K, Romanelli C, Chiurazzi M, Cozzolino M. COVID-19 pandemic and maternal mental health: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2020:1–8. Published online 01 Nov. https://doi.org/10.1080/14767058.2020.1843155.
26. Sun F, Zhu J, Tao H, Ma Y, Jin W. A systematic review involving 11,187 participants evaluating the impact of COVID-19 on anxiety and depression in pregnant women. J Psychosom Obstet Gynaecol. 2020:1–9. Published online 17 Dec. https://doi.org/10.1080/0167482X.2020.1857360.
27. Yan H, Ding Y, Guo W. Mental health of pregnant and postpartum women during the coronavirus disease 2019 pandemic: a systematic review and meta-analysis. Front Psychol. 2020;11:617,001. https://doi.org/10.3389/fpsyg.2020.617001.
28. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150(6):782–6. https://doi.org/10.1192/bjp.150.6.782.

29. Gentile S. Untreated depression during pregnancy: short-and long-term effects in offspring. A systematic review. Neuroscience. 2017;342:154–66. https://doi.org/10.1016/j.neuroscience.2015.09.001.
30. Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The prevalence of anxiety disorders during pregnancy and the postpartum period: A multivariate Bayesian meta-analysis. J Clin Psychiatry. 2019;80(4):18r12527. https://doi.org/10.4088/JCP.18r12527.
31. Santabárbara J, Lasheras I, Lipnicki DM, Bueno-Notivol J, Pérez-Moreno M, López-Antón R, et al. Prevalence of anxiety in the COVID-19 pandemic: an updated meta-analysis of community-based studies. Prog Neuro-Psychopharmacol Biol Psychiatry. 2021;109:110,207. https://doi.org/10.1016/j.pnpbp.2020.110207.
32. Knight RG, Waal-Manning HJ, Spears GF. Some norms and reliability data for the state-trait anxiety inventory and the Zung self-rating depression scale. Br J Clin Psychol. 1983;22(4):245–9. https://doi.org/10.1111/j.2044-8260.1983.tb00610.x.
33. Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. Am J Obstet Gynecol. 2020;223(2):240.e1–9. https://doi.org/10.1016/j.ajog.2020.05.009.
34. Esterwood E, Saeed SA. Past epidemics, natural disasters, COVID19, and mental health: learning from history as we deal with the present and prepare for the future. Psychiatry Q. 2020;91:1121–33. https://doi.org/10.1007/s11126-020-09808-4.
35. Xiong X, Harville EW, Mattison DR, Elkind-Hirsch K, Pridjian G, Buekens P. Hurricane Katrina experience and the risk of post-traumatic stress disorder and depression among pregnant women. Am J Disaster Med. 2010;5(3):181–7. https://doi.org/10.5055/ajdm.2010.0020.
36. Patterson J, Hollins Martin C, Karatzias T. PTSD post-childbirth: a systematic review of women's and midwives' subjective experiences of care provider interaction. J Reprod Infant Psychol. 2019;37(1):56–83. https://doi.org/10.1080/02646838.2018.1504285.
37. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiatry. 2020;7(7):611–27. https://doi.org/10.1016/S2215-0366(20)30203-0.
38. Berthelot N, Lemieux R, Garon-Bissonnette J, Drouin-Maziade C, Martel É, Maziade M. Uptrend in distress and psychiatric symptomatology in pregnant women during the coronavirus disease 2019 pandemic. Acta Obstet Gynecol Scand. 2020;99(7):848–55. https://doi.org/10.1111/aogs.13925.
39. Ravaldi C, Ricca V, Wilson A, Homer C, Vannacci A. Previous psychopathology predicted severe COVID-19 concern, anxiety, and PTSD symptoms in pregnant women during "lockdown" in Italy. Arch Womens Ment Health. 2020;23(6):783–6. https://doi.org/10.1007/s00737-020-01086-0.
40. Ostacoli L, Cosma S, Bevilacqua F, Berchialla P, Bovetti M, Carosso AR, et al. Psychosocial factors associated with postpartum psychological distress during the Covid-19 pandemic: a cross-sectional study. BMC Pregnancy Childbirth. 2020;20:703. https://doi.org/10.1186/s12884-020-03399-5.
41. Masters GA, Asipenko E, Bergman AL, Person SD, Brenckle L, Simas TM, et al. Impact of the COVID-19 pandemic on mental health, access to care, and health disparities in the perinatal period. J Psychiatr Res. 2021;137:126–30. https://doi.org/10.1016/j.jpsychires.2021.02.056.
42. Khalil A, Von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. JAMA. 2020;324(7):705–6. https://doi.org/10.1001/jama.2020.12746.
43. De Curtis M, Villani L, Polo A. Increase of stillbirth and decrease of late preterm infants during the COVID-19 pandemic lockdown. Arch Dis Child Fetal Neonatal Ed. 2020:F1. https://doi.org/10.1136/fetalneonatal-2020-320682.
44. Anand P, Yadav A, Debata P, Bachani S, Gupta N, Gera R. Clinical profile, viral load, management and outcome of neonates born to COVID 19 positive mothers: a tertiary care Centre experience from India. Eur J Pediatr. 2021;180:547–59. https://doi.org/10.1007/s00431-020-03800-7.

45. la Cour FN, Egerup P, Hviid KV, Severinsen ER, Kolte AM, Westergaard D, et al. SARS-CoV-2 in first trimester pregnancy: a cohort study. Hum Reprod. 2021;36(1):40–7. https://doi.org/10.1093/humrep/deaa311.
46. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. Am J Obstet Gynecol. 2020;223(1):111.e1–111.e14. https://doi.org/10.1016/j.ajog.2020.04.014.
47. Baud D, Greub G, Favre G, Gengler C, Jaton K, Dubruc E, et al. Second-trimester miscarriage in a pregnant woman with SARS-CoV-2 infection. JAMA. 2020;323(21):2198–200. https://doi.org/10.1001/jama.2020.7233.
48. De Montigny F, Verdon C, Meunier S, Dubeau D. Women's persistent depressive and perinatal grief symptoms following a miscarriage: the role of childlessness and satisfaction with healthcare services. Arch Womens Ment Health. 2017;20:655–62. https://doi.org/10.1007/s00737-017-0742-9.
49. Biaggi A, Conroy S, Pawlby S, Pariante CM. Identifying the women at risk of antenatal anxiety and depression: a systematic review. J Affect Disord. 2016;191:62–77. https://doi.org/10.1016/j.jad.2015.11.014.
50. Effati-Daryani F, Zarei S, Mohammadi A, Hemmati E, Ghasemi Yngyknd S, Mirghafourvand M. Depression, stress, anxiety and their predictors in Iranian pregnant women during the outbreak of COVID-19. BMC Psychol. 2020;8:99. https://doi.org/10.1186/s40359-020-00464-8.
51. Yue C, Liu C, Wang J, Zhang M, Wu H, Li C, et al. Association between social support and anxiety among pregnant women in the third trimester during the coronavirus disease 2019 (COVID-19) epidemic in Qingdao, China: the mediating effect of risk perception. Int J Soc Psychiatry. 2020:1–8. Published online 2020 Jul 9. https://doi.org/10.1177/0020764020941567.
52. Farewell CV, Jewell J, Walls J, Leiferman JA. A mixed-methods pilot study of perinatal risk and resilience during COVID-19. J Prim Care Community Health. 2020;11:2150132720944074. https://doi.org/10.1177/2150132720944074.
53. Preis H, Mahaffey B, Heiselman C, Lobel M. Vulnerability and resilience to pandemic-related stress among US women pregnant at the start of the COVID-19 pandemic. Soc Sci Med. 2020;266:113,348. https://doi.org/10.1016/j.socscimed.2020.113348.
54. Jurcik T, Jarvis GE, Zeleskov Doric J, Krasavtseva Y, Yaltonskaya A, Ogiwara K, et al. Adapting mental health services to the COVID-19 pandemic: reflections from professionals in four countries. Couns Psychol Q. 2020. Published Online 16 Jul 2020.; https://doi.org/10.1080/09515070.2020.1785846.
55. Fernández-Álvarez J, Fernández-Álvarez H. Videoconferencing psychotherapy during the pandemic: exceptional times with enduring effects? Front Psychol. 2021;12:589,536. https://doi.org/10.3389/fpsyg.2021.589536.
56. Khan AN, Bilek E, Tomlinson RC, Becker-Haimes EM. Treating social anxiety in an era of social distancing: adapting exposure therapy for youth during COVID-19. Cogn Behav Pract. Available online 5 February 2021. https://doi.org/10.1016/j.cbpra.2020.12.002.
57. Costa M, Reis G, Pavlo A, Bellamy C, Ponte K, Davidson L. Tele-mental health utilization among people with mental illness to access care during the COVID-19 pandemic. Community Ment Health J. 2021;57:720–6. https://doi.org/10.1007/s10597-021-00789-7.
58. Werner EA, Aloisio CE, Butler AD, D'Antonio KM, Kenny JM, Mitchell A, et al. Addressing mental health in patients and providers during the COVID-19 pandemic. Semin Perinatol. 2020;44(7):151,279. https://doi.org/10.1016/j.semperi.2020.151279.
59. Ashford MT, Olander EK, Ayers S. Computer- or web-based interventions for perinatal mental health: a systematic review. J Affect Disord. 2016;197:134–46. https://doi.org/10.1016/j.jad.2016.02.057.
60. Tuerk PW, Keller SM, Acierno R. Treatment for anxiety and depression via clinical videoconferencing: evidence base and barriers to expanded access in practice. Focus. 2018;16(4):363–9. https://doi.org/10.1176/appi.focus.20180027.
61. Wind TR, Rijkeboer M, Andersson G, Riper H. The COVID-19 pandemic: the 'black swan' for mental health care and a turning point for e-health. Internet Interv. 2020;20:100,317. https://doi.org/10.1016/j.invent.2020.100317.

62. Békés V, Aafjes-van DK. (2020). Psychotherapists' attitudes toward online therapy during the COVID-19 pandemic. J Psychother Integr. 2020;30(2):238–47. https://doi.org/10.1037/int0000214.
63. Thomas N, McDonald C, de Boer K, Brand RM, Nedeljkovic M, Seabrook L. Review of the current empirical literature on using videoconferencing to deliver individual psychotherapies to adults with mental health problems. Psychol Psychother. 2021; https://doi.org/10.1111/papt.12332.
64. Yao H, Chen JH, Xu YF. Rethinking online mental health services in China during the COVID-19 epidemic. Asian J Psychiatr. 2020;50:102,015. https://doi.org/10.1016/j.ajp.2020.102015.
65. Motrico E, Mateus V, Bina R, Felice E, Bramante A, Kalcev G, et al. Good practices in perinatal mental health during the COVID-19 pandemic: a report from task-force RISEUP-PPD COVID-19. Clin Salud. 2020;31(3):155–60. https://doi.org/10.5093/clysa2020a26.
66. Holmes EA, O'Connor RC, Perry VH, Tracey I, Wessely S, Arseneault L, et al. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. Lancet Psychiatry. 2020;7(6):547–60. https://doi.org/10.1016/S2215-0366(20)30168-1.
67. Fischer R, Bortolini T, Karl JA, Zilberberg M, Robinson K, Rabelo A, et al. Rapid review and meta-meta-analysis of self-guided interventions to address anxiety, depression, and stress during COVID-19 social distancing. Front Psychol. 2020;11:563,876. https://doi.org/10.3389/fpsyg.2020.563876.