

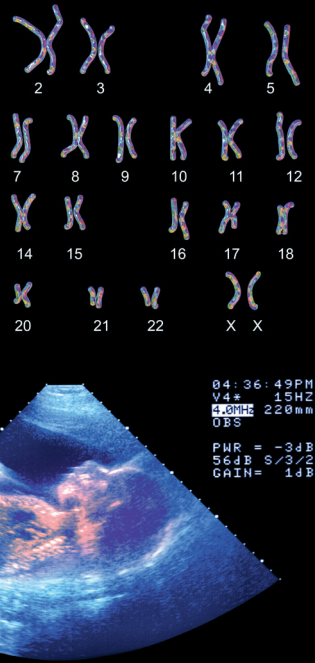


# Cambridge Elements

## High-Risk Pregnancy: Management Options

## Mental Health Disorders in Pregnancy and the Early Postpartum

Zena Schofield and  
Zack Schofield





Cambridge Elements 

Elements in High-Risk Pregnancy: Management Options

edited by

David James

*University of Nottingham*

Philip Steer

*Imperial College London*

Carl Weiner

*Creighton University School of Medicine*

Stephen Robson

*Newcastle University*

MENTAL HEALTH  
DISORDERS IN  
PREGNANCY AND THE  
EARLY POSTPARTUM

Zena Schofield

*Greater Manchester Mental Health NHS*

*Foundation Trust*

Zack Schofield

*Cambridge University*



CAMBRIDGE  
UNIVERSITY PRESS



CAMBRIDGE  
UNIVERSITY PRESS

Shaftesbury Road, Cambridge CB2 8EA, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre,  
New Delhi – 110025, India

103 Penang Road, #05–06/07, Visioncrest Commercial, Singapore 238467

Cambridge University Press is part of Cambridge University Press & Assessment,  
a department of the University of Cambridge.

We share the University's mission to contribute to society through the pursuit of  
education, learning and research at the highest international levels of excellence.

[www.cambridge.org](http://www.cambridge.org)

Information on this title: [www.cambridge.org/9781009518109](http://www.cambridge.org/9781009518109)

DOI: [10.1017/9781009518123](https://doi.org/10.1017/9781009518123)

© Zena Schofield and Zack Schofield 2025

This publication is in copyright. Subject to statutory exception and to the provisions of  
relevant collective licensing agreements, no reproduction of any part may take place  
without the written permission of Cambridge University Press & Assessment.

When citing this work, please include a reference to the DOI [10.1017/9781009518123](https://doi.org/10.1017/9781009518123)

First published 2025

*A catalogue record for this publication is available from the British Library*

ISBN 978-1-009-51810-9 Paperback

ISSN 2976-8330 (online)

ISSN 2976-8322 (print)

Cambridge University Press & Assessment has no responsibility for the persistence or  
accuracy of URLs for external or third-party internet websites referred to in this  
publication and does not guarantee that any content on such websites is, or will  
remain, accurate or appropriate.

Every effort has been made in preparing this Element to provide accurate  
and up-to-date information which is in accord with accepted standards and practice  
at the time of publication. Although case histories are drawn from actual cases, every  
effort has been made to disguise the identities of the individuals involved. Nevertheless,  
the authors, editors and publishers can make no warranties that the information  
contained herein is totally free from error, not least because clinical standards are  
constantly changing through research and regulation. The authors, editors and  
publishers therefore disclaim all liability for direct or consequential damages resulting  
from the use of material contained in this Element. Readers are strongly advised to pay  
careful attention to information provided by the manufacturer of any drugs or equip-  
ment that they plan to use.

# Mental Health Disorders in Pregnancy and the Early Postpartum

Elements in High-Risk Pregnancy: Management Options

DOI: 10.1017/9781009518123  
First published online: January 2025

---

Zena Schofield  
*Greater Manchester Mental Health NHS Foundation Trust*

Zack Schofield  
*Cambridge University*

**Author for correspondence:** Zena Schofield, [zenaschofield@doctors.org.uk](mailto:zenaschofield@doctors.org.uk)

**Abstract:** Mental health disorders are common in pregnancy and after childbirth with over 10% of women manifesting some form of mental illness during this time. Maternity services will encounter women with symptoms that vary in severity from mild self-limiting to potentially life-threatening. These conditions carry risks for both the woman and the fetus/newborn. Detecting women with, or at risk of, a serious mental health disorder and enabling them to access appropriate care in a timely fashion is a shared responsibility. However, given the frequency of contact they have with women through this period, maternity services have a pivotal role. From a mental health perspective, high-risk pregnancies are those primarily associated with serious mental illness (psychotic illnesses, bipolar disorder and severe depressive episodes). Healthcare professionals caring for pregnant women should have the appropriate skills to detect serious mental illness and identify women at risk and how to access specialist mental health care.

**Keywords:** mental health disorders, pregnancy, postpartum, antipsychotics, antidepressants

© Zena Schofield and Zack Schofield 2025

ISBNs: 9781009518109 (PB), 9781009518123 (OC)  
ISSNs: 2976-8330 (online), 2976-8322 (print)

# Contents

Commentary	1
1 Introduction	1
2 Epidemiology	3
3 Risks of Mental Health Disorders in the Perinatal Period	4
4 Management of Mental Health Disorders in the Perinatal Period	5
Further Reading	50
References	52

## Commentary

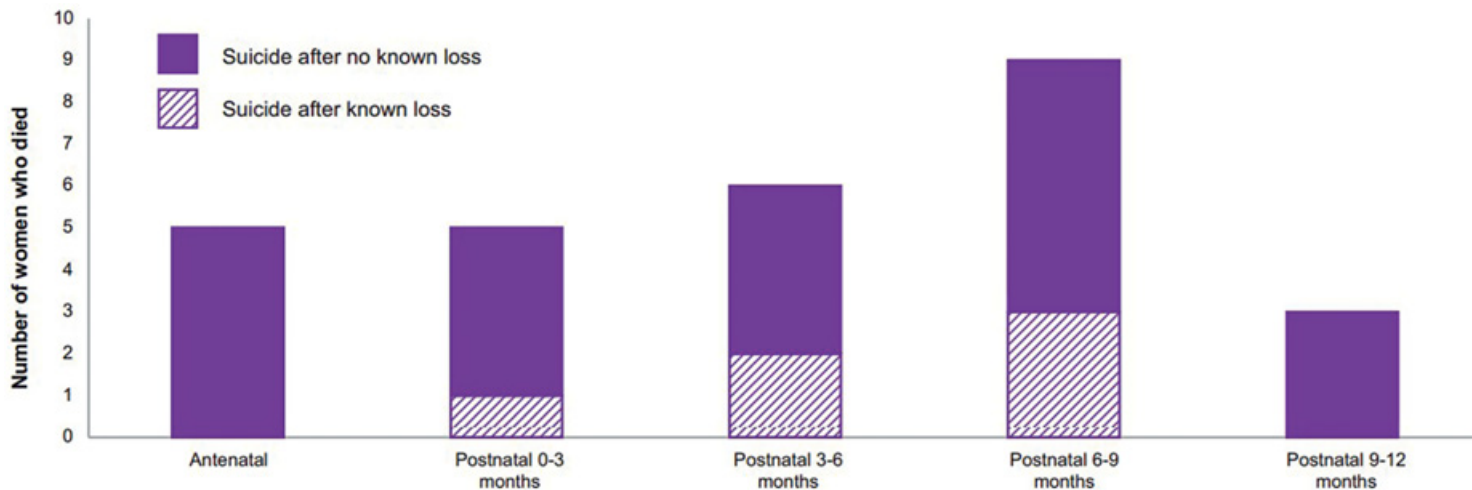
Mental health disorders are common in pregnancy and after childbirth with over 10% of women manifesting some form of mental illness during this time. However, only about 1 in 500 pregnancies will be complicated by serious mental illness. Maternity services will encounter women with symptoms that vary in severity from mild self-limiting to severe. These conditions carry risks for both the woman and the fetus/newborn, with obstetric morbidity increased in those with pre-existing mental health conditions.

Detecting women with, or at risk of, a serious mental health disorder and enabling them to access appropriate care in a timely fashion is a shared responsibility. However, given the frequency of contact they have with women through this period, maternity services have a pivotal role. From a mental health perspective, high-risk pregnancies are those primarily associated with serious mental illness (psychotic illnesses and severe depressive episodes). In addition, given the challenges in interpreting emerging anxiety and mood symptoms, clinicians require a broader understanding of mental health presentations.

Therefore, healthcare professionals caring for pregnant women should have the appropriate skills to detect serious mental illness and identify women at risk. These skills include an understanding of the range of management options, which cover multiprofessional management strategies, non-pharmacological approaches and the implications of prescribing psychotropic medications during pregnancy and breastfeeding. Healthcare professionals should also be aware of how to access specialist mental health care for their patients in their area. For women with serious mental illness or those with a high risk of its occurrence, ideally a multidisciplinary plan for pregnancy (MDPP) should be in place by 32 weeks' gestation. Such women require close monitoring through pregnancy and into the postpartum period. If a mental health admission is required, ideally this should be to a specialist mother and baby unit.

## 1 Introduction

Maternal deaths in the UK are still increasing, with most women dying from medical or mental health-related conditions that are worsened during pregnancy, childbirth or up to one-year postpartum [1]. Of these, 86% die between the end of pregnancy and up to one year postpartum. Suicide is a leading cause of maternal death within a year of the end of pregnancy, with 18% of direct maternal deaths in the UK from 2018 to 2020 being due to suicide (20 of 109 total direct deaths; see [Figure 1](#)). This is a rate of 0.95/100,000 live births [1].



**Figure 1** Timing of death by suicide during pregnancy and the first year after delivery in the UK (MBBRACE, 2022) [1].

**Note:** The cross-hatched areas represent 'Loss events – termination, miscarriage, stillbirth, neonatal loss, or child removal' prior to the suicide.



Other Confidential Enquiries into Maternal Deaths also identify suicide as a leading cause (Netherlands 1.17/100,000 [2]; Italy 2.3/100,000 [3]; Austria 0.89/100,000 [4]; Canada 0.70/100,000 [5]). Reducing maternal morbidity and infant morbidity due to appropriately managing maternal mental health conditions is another important role of mental health services. A 2023 paper estimated that for women with pre-existing mental health conditions who got pregnant there was an increased risk of preterm birth (adjusted odds ratio (aOR) 1.52, 1.35–1.73) [6], increased risk of small for gestational age (SGA; aOR 1.34, 1.30–1.37) [6] and increased risk of neonatal adverse outcomes (aOR 1.21–1.55) [6]. The risks were highest for women who had previously had an admission to a psychiatric hospital at any time or had contact with mental health services within one year of the pregnancy. Serious mental health conditions such as schizophrenia are associated with an increased risk of severe obstetric complications; however, these increased risks are confounded by increased rates of smoking, obesity and substance misuse. Therefore, obstetrician-led care to manage these complex maternity risks is needed. Pregnant women with a diagnosis of schizophrenia have a fourfold increased rate of smoking. A paper in 2019 looking at women with schizophrenia and adverse birth outcomes suggested the elevated risks of preterm birth, SGA and low Apgar scores can be partly explained by factors like smoking that can be modified [7].

## 2 Epidemiology

Mental health disorders are common in pregnancy and after childbirth, with the postnatal period being associated with the greater increased risk (see [Table 1](#)). The epidemiology of perinatal mental health disorders has remained constant for many years.

Most mental health disorders are multifactorial. Genetic factors are significant in some conditions including bipolar disorder and postpartum psychosis. Hypothyroidism can cause depression and hyperthyroidism mimics symptoms of anxiety. Some episodes of psychosis are associated with autoimmune antibodies (e.g. *N*-methyl-D-aspartate receptor antibodies) and symptoms remit with high-dose steroids. There is some evidence that inflammatory markers are raised in postpartum depression and decrease with treatment with a novel agent, zuranolone [12]. Some symptoms can be induced by illicit substances or some prescribed medications. In addition, there can be psychosocial factors such as adverse childhood events, recent adverse life effects, poverty, poor housing, lack of support networks and domestic abuse.

**Table 1** Prevalence of mental health disorders in pregnancy

<b>Diagnosis</b>	<b>Prevalence rate in pregnancy (95% CI)</b>	<b>Prevalence rate in postpartum (95% CI)</b>	<b>Reference *</b>
Anxiety disorders	15% (9.0–21.4%)	15% (13.7–16.4%)	8
Major depression	3.1–4.9%	4.7%	9
Minor depression (mild)	Up to 11%	13%	9
Postpartum psychosis		0.2% Relapse rate postpartum: 31% (22–42%)	10,11
Schizophrenia	0.2%	0.2%	10
Bipolar disorder		Lifetime prevalence 1–2% Relapse rate postpartum: 37% (29–45%)	11
Post-traumatic stress disorder (PTSD) due to childbirth		1–2% in high-income countries	9
PTSD various causes	6–8%	–	9

\* Not all papers reported confidence intervals.

### 3 Risks of Mental Health Disorders in the Perinatal Period

#### Risks for the Woman

These are:

- Suicide – 0.95/100,000 live births in 2018–2020 [1]
- Prolonged maternity morbidity due to lack of treatment
- Death due to misidentification of a physical health condition, such as due to a mental health disorder
- Relationship breakdown
- Loss of social networks
- Loss of functioning
- Poor parenting
- Impact on older children in the family

## Risks for the Fetus/Infant

Prenatal mental health disorders are associated with a moderately increased risk of stillbirth and infant mortality [13]. Untreated depression is associated with increased rates of preterm birth, small for gestational age, stillbirth, low birth weight, increased operative delivery and postpartum depression [14].

Mental health disorders impact on the mother–infant relationship. This can result in emotional and behavioural difficulties in the child and impact on the longer-term mental health of the offspring.

Finally, neurodevelopmental delay is more common in the offspring of women with mental health problems. However, shared genetics of mother and child is a confounder in this adverse outcome. Most research in this area has been on the effects on infant neurodevelopment of an untreated depressive episode or an untreated anxiety disorder.

## 4 Management of Mental Health Disorders in the Perinatal Period

### General Principles

In the UK, National Institute for Health and Care Excellence (NICE) CG192 [15] is the clinical guideline for the management of prenatal and postnatal mental health disorders. Summarised below is a combination of recommendations from NICE CG192 [15], MBRRACE reports [1,16,17] and British Association of Psychopharmacology (BAP) perinatal prescribing guidelines [18] along with relevant data from other articles found in the Further Reading section.

### Prepregnancy

#### General

Physicians and other healthcare professionals in primary care have a role in encouraging women who are considering a pregnancy (or who are of childbearing potential) to improve their physical and mental health to improve pregnancy outcomes. Measures include stopping smoking; managing diabetes, hypertension and other chronic conditions well; for obese women, encouraging weight management; and for those using alcohol or illicit substances, addressing those difficulties. If domestic abuse is identified by any healthcare professional, then appropriate referral to domestic abuse services and, if needed, referral to safeguarding services need to occur. In addition, if a woman is the victim of domestic abuse the fact that rates increase in pregnancy and early postpartum should be sensitively explained and that it would be a reason for a safeguarding

referral in the perinatal period. Obtaining appropriate support prior to pregnancy needs to occur.

All women of childbearing potential who are prescribed a psychotropic medication should also have a detailed discussion about contraception and be encouraged to use contraception. This is particularly important in women taking mood stabilisers and antipsychotics.

Ideally, mental health disorders should be treated prior to conception so a woman has had a period of stability in her mental health prior to conception. For some medications it may be necessary to consider changing these prior to conception, although this is dependent on the woman's history and the evidence of the risk posed by her current medication. Women with serious mental illnesses who want to conceive should be offered referral for preconceptual counselling with a perinatal psychiatrist to discuss management of their mental health in pregnancy and postpartum. This discussion should cover the risk of relapse and medication options.

When a woman has received a diagnosis of bipolar disorder for the first time and is in a period of recovery, it is important her mental health team explain the high risk of relapse postpartum, the importance of contraception, planning pregnancies and of having a preconceptual counselling appointment with a consultant perinatal psychiatrist to discuss the management of her mental health in pregnancy and postpartum before she becomes pregnant. Mental health teams that may give a woman a diagnosis of bipolar disorder include mental health inpatient teams, crisis resolution and home treatment teams, community mental health teams or early intervention in psychosis teams. When a person experiences their first episode of psychosis, the common practice in the UK would be to refer the person to the early intervention in psychosis team to provide mental healthcare in the community for three years. Sometimes early intervention in psychosis teams do not give diagnoses as the working diagnosis can change over time as further episodes of relapse occur and there is more information to inform the diagnosis. This means that sometimes women can be referred to a consultant perinatal psychiatrist having experienced at least two episodes of mood disorder that would fulfil the diagnosis of bipolar disorder, but the community mental health team has not yet given the patient that diagnosis. This means that as part of the preconceptual counselling appointment the perinatal psychiatrist will have completed a diagnostic assessment, then have to explain the diagnosis of bipolar disorder and associated perinatal risks, and then go on to discuss prepregnancy care.

### *Pharmacological*

Perinatal psychiatrists should offer preconceptional counselling appointments to women on psychotropic medications considering conceiving. During these appointments the perinatal psychiatrist, having completed a psychiatric assessment, would explain the current evidence regarding the risks of her condition relapsing during the perinatal period with and without medication, and the risks and benefits of medications for her. There would also be information shared around medication options in breastfeeding so that if a woman would like to consider breastfeeding and medication changes are needed to enable that to occur, these changes can be planned prior to conception. The psychiatrist will collaborate with the woman to develop a care plan for her mental health including medication and services to be involved in the perinatal period. Ideally, this consultation would also identify areas where physical health can be improved prior to conception and identify any substance misuse that needs addressing prior to conception.

Antidepressants are the most prescribed psychotropic medication, usually being managed in primary care. The BAP perinatal guidelines [18] recommend that if an antidepressant is indicated, the medication used should be one that is known to work for that individual. Prior to conception, reviewing how long the person has been in recovery from their most recent depressive episode and how severe that depressive episode was will help inform whether to continue the antidepressant while the woman tries to conceive and into pregnancy, or whether to slowly reduce and stop it prior to conception.

Antipsychotics, which can also be used as mood stabilisers, increase the risk of gestational diabetes. Risperidone increases the risk of fetal anomalies and lithium increases the risk of cardiac abnormalities. In contrast, lamotrigine does not appear to increase risks above baseline rates. In the past, valproate was used as a mood stabiliser, but NICE guidelines [15] are clear: it should not be prescribed to women of childbearing potential for mental health disorders as it carries a 10% risk of causing neural tube defects and up to a 40% risk of causing neurodevelopmental delay, along with a range of other abnormalities such as the ‘valproate syndrome’. The Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK has advised valproate is not prescribed in women of childbearing potential, but if it is prescribed there must be a current Pregnancy Prevention Programme in place [19]. Carbamazepine is rarely used as a mood stabiliser and should not be used in women of childbearing potential due to an increased rate of neural tube defects. For women on antipsychotics or mood stabilisers considering a pregnancy, a preconceptional counselling appointment with a perinatal psychiatrist is vital to enable an individual care plan that

considers the risks and benefits of all options to be considered, including the option of changing medications prior to pregnancy to reduce specific risks to the fetus. For example, for some women on lithium, the increased rates of fetal cardiac defects combined with not being able to breastfeed while taking lithium means a person might choose to change from lithium to a different mood stabiliser prior to trying to conceive.

### *Psychological*

For women who show signs of tokophobia, leading to them avoiding childbirth despite wanting to become a parent, referral for an appropriate psychological intervention prior to pregnancy is important to allow these women the opportunity to overcome their tokophobia and discuss reproductive choices with them. For women with repeated pregnancy losses leading to post-traumatic symptoms or an anxiety disorder, referral for an appropriate psychological intervention rather than waiting for a pregnancy to be established would be helpful. Women considering a pregnancy with current symptoms of mental health difficulties can be encouraged to consider an appropriate psychological intervention to improve their mental health prior to conception. Some women may want to try reducing and stopping psychotropic medication and have a psychological intervention to help them manage their mental health difficulties if they would prefer to avoid psychotropic medication in pregnancy. It will depend on their mental health condition and history of the individual risks of stopping their medication, so this would need to be discussed before changes occur.

### *Prenatal*

#### *General*

Obstetricians, general practitioners (GPs), midwives and other healthcare professionals working with pregnant women should take a history that includes asking about current or previous mental health difficulties and identifying any psychotropic medications that a woman is taking. Screening questions can be used to try to increase the identification of mental health conditions in pregnancy such as PHQ-9 or GAD-7 [20]. In England, the Whooley questions are routinely used by midwives to screen for possible depressive symptoms [15]. The NICE guideline recommends that at a woman's first contact with primary care or her booking visit, and during the early postnatal period, healthcare professionals should consider asking the following depression identification questions as part of a general discussion about a woman's mental health and well-being:

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

It also suggests considering asking about anxiety using the two-item Generalised Anxiety Disorder scale (GAD-2):

- Over the last two weeks, how often have you been bothered by feeling nervous, anxious or on edge?
- Over the last two weeks, how often have you been bothered by not being able to stop or control worrying?

Following positive identification on screening questions, referral to specialist mental health services for a diagnostic assessment is required. Assessments by maternity staff would routinely include questions regarding domestic abuse, because in some mental health conditions there is an increased rate of domestic abuse.

The American College of Obstetricians and Gynecologists recommends that all healthcare professionals providing obstetric care should complete a full assessment of mood and emotional well-being including the use of a validated screening tool during the postpartum visit for all patients. If a screening tool for depression and anxiety was used in pregnancy, this tool should be used again postpartum [21].

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends using routine screening tools for depression and anxiety on four occasions – the first as early as possible in pregnancy, the second later in pregnancy, the third 6–12 weeks postnatal and finally one at 1-year postnatal [22].

Women who have a personal history of a mental health condition managed in primary care and/or a family history of a mental health condition in the perinatal period that required secondary mental health services should be referred to specialist services ('amber flag' in 2018 MBRRACE report [16]). Thus, healthcare workers caring for women with mental health problems should be aware of the specialist perinatal mental health referral pathways for women who currently have or are at risk of a serious mental illness. Referral pathways need to distinguish routine, urgent and emergency cases. Healthcare workers should consider how current mental health difficulties may impact on the woman's engagement with the prenatal care service and what those services can do to facilitate improved engagement in prenatal care.

When women present with sudden onset of new symptoms possibly due to mental health difficulties, physical causes need to be investigated first to prevent misidentifying them as mental health conditions. This applies to both prenatal and postnatal periods.

Where there are known risks, fetal and/or neonatal screening and monitoring should be implemented. Discussion with the neonatologist should occur in advance of delivery.

NHS England recommends trauma-informed compassionate care would be expected from mental health and maternity services [23]. A thorough mental health assessment includes taking a personal history and identifying previous traumatic experiences; considering how these might impact on the care needed in the perinatal period is important. Where indicated, a trauma-informed birth plan can be developed with the woman that identifies psychological strengths and coping strategies the woman has along with identifying how services can provide trauma-informed care personalised to her needs.

Finally, it is essential that all healthcare workers caring for women with mental health problems in pregnancy work collaboratively and communicate well with each other. To that end, a written MDPP for women with or at risk of relapse of a serious mental illness should be agreed by 32 weeks' gestation at the latest. It should be saved in the patient's records in all relevant healthcare settings (for example, GP surgery, mental health services, maternity services and health visiting records) and a copy provided to the woman, so she also has ready access to it when required.

### *Pharmacological*

Women need to be empowered to make informed decisions about the use of psychotropic medications in pregnancy. The information about medication in the pre-pregnancy section is also relevant in pregnancy. Prescribers need to keep their knowledge of medications they commonly prescribe to women of child-bearing potential updated in relation to efficacy and safety of the medication in pregnancy. Prescribers whose patients contact them stating they are pregnant need to prioritise an appointment for the pregnant woman to discuss her psychotropic medication. If a prescriber wants to confirm the current evidence regarding a specific psychotropic medication in pregnancy the prescriber should contact a perinatal psychiatrist to get information about the medication in pregnancy. Then they can have an informed discussion with the woman. If, having received specialist advice, a general practitioner decides to continue to manage the woman's mental health, it is important to maintain effective communication with the midwifery team.



Specialist perinatal mental health staff who are prescribers need to maintain their knowledge about medication in pregnancy and lactation. They should also communicate this information in a comprehensible and accessible way to each woman they see, explaining the risks and benefits, thus obtaining informed consent for the final agreed plan. This plan needs to use the lowest effective dose and monotherapy is preferred [14,15,18].

As stated above, sodium valproate and semi-sodium valproate should not be prescribed to women of childbearing potential without an effective Pregnancy Prevention Programme and a signed consent form that is reviewed annually. If a woman conceives on sodium valproate this will need to be stopped and urgent specialist advice obtained on what to prescribe as an alternative.

Urgent specialist advice from mental health services for women taking antipsychotics and mood stabilisers should be sought rather than stopping them abruptly, as this carries the risk of relapse. The exception is valproate, which should be reduced and stopped in parallel with seeking urgent specialist advice about alternative medication [18].

### *Psychological*

Pregnancy can be a time when women are more motivated to engage in a psychological intervention and they may want to improve their own mental health to impact positively on their parenting. When a woman is seen in pregnancy, along with the use of screening questions, midwives, obstetricians and GPs can also consider discussing a referral for a psychological intervention. The composition of local services and local policies along with the severity of the mental health condition will determine which service would provide that intervention.

## *Labour and Delivery*

### *General*

The prebirth mental health care plan agreed by 32 weeks' gestation should be shared with all professionals involved in the care of the woman and her baby and should include a plan for labour and delivery. This may include a trauma-informed care plan for women who have experienced past trauma that may be triggered by aspects of maternity care in labour, such as vaginal examinations. For women on the autistic spectrum certain sensory stimuli can be overstimulating and cause distress leading to difficulty managing emotions, so a care plan would provide recommendations on minimising those sensory stimuli.

Clear communication is vital for all women in labour and delivery and even more so for women with current symptoms of mental health disorders. Taking time to explain slowly and carefully benefits everyone involved. Risks should be explained clearly, particularly when women are making what appear to be unwise decisions. In such cases it may be necessary to consider a capacity assessment to see if a current mental health disorder is impacting on the woman's specific decision-making capability.

## Postnatal

### *General*

The prebirth care plan agreed in pregnancy should include a postnatal plan for mental health care which should be followed. The plan may have recommendations about whether the woman needs a side room on the postnatal ward. It should also include an indication of whether the baby can sleep with the mother. The plan should also include a clear plan from mental health services of how a woman's mental health will be monitored postnatally, including the frequency of face-to-face contacts and whether the woman needs to be seen by mental health staff prior to discharge from the maternity ward. When relapse prevention work has been undertaken with the woman it is helpful to include 'early warning signs', namely signs suggestive of relapse, in the care plan so that the woman, her 'significant other(s)' (partner or carer) and professionals involved in her care are vigilant for those signs.

Specialist perinatal mental health services use a multidisciplinary approach to providing mental health care with the appropriate clinicians for the individual woman involved in her care. These teams usually include a consultant perinatal psychiatrist, perinatal community psychiatric nurses, perinatal clinical psychologists, occupational therapists and nursery nurses [24]. There may be specialist mental health midwives with additional training in mental health difficulties involved in supporting these women in pregnancy. Specialist perinatal mental health services should work collaboratively with other services involved in the care of the postnatal woman and her baby including the midwife, health visitor and GP. The exact composition of these healthcare professional teams varies between countries. Contact details for accessing mental health services in and out of hours need to be shared with the woman, her partner and all other healthcare professionals involved in her care.

Mental health interventions need to treat both the woman's mental health disorder and focus on the mother–infant relationship. The baby needs to be 'held in mind' by perinatal mental health staff. This includes an assessment of the wisdom of a mother sleeping with her baby.

If an admission to a mental health unit is required before 32 weeks' gestation it would be to a general adult psychiatric unit. From 32 weeks' gestation to term, ideally it would be to a specialist psychiatric mother and baby unit. Postnatally, it would normally be to a specialist psychiatric mother and baby unit unless there is a clinical reason for making a different arrangement, such as the infant having been removed from the woman's care.

Healthcare professionals should know the 'red flags' from the 2015 MBRRACE [17] report that should prompt urgent senior perinatal psychiatric assessment. These are:

- Recent significant change in mental state or emergence of new symptoms.
- New thoughts or actual acts of violent self-harm.
- New and persistent expressions of incompetency as a mother or estrangement from the infant.

It is important to detect sudden changes in mental state, particularly in the early postpartum period when most episodes of postpartum psychosis present. In these circumstances urgent care should be sought from secondary mental health services, which ideally will be the specialist perinatal mental health team. Guidelines for Australia and New Zealand also highlight the need for management of immediate risk for women who are identified as at risk of suicide and recommend an urgent mental health assessment [22].

Women at high risk of relapse should be monitored closely for the first few weeks postpartum. Midwives and health visitors need to know how to raise concerns with the perinatal mental health services if there are changes in the mental health of these women. New onset of acute symptoms that could be due to a mental health cause need to be investigated to exclude organic causes first.

Postnatally, women should be asked about their mental health and their relationship with their baby to identify any concerns and respond appropriately. Women known to have mental health disorders or who are at risk of relapse postnatally of a mental health disorder should have all midwifery appointments in person ('face-to-face').

### *Pharmacological*

The birth plan will include information on whether the woman plans to breast-feed or formula feed her baby and whether she can breastfeed or give breast milk when taking specific psychotropic medications. Information on infant observations needed due to the psychotropic medication being taken by the woman needs to be in the care plan.

A clear discussion about the risks and benefits of pharmacological treatment in breastfeeding should have occurred in pregnancy and a subsequent agreed plan for psychotropic medication to be continued postnatally or a new medication started [12,18].

#### SUMMARY OF MANAGEMENT OPTIONS

### **General Approach to Management of Women with Mental Health Problems in Pregnancy**

#### Prepregnancy

##### *General*

- Optimise the physical and mental health in all women who are planning a pregnancy.
- Advise/encourage weight reduction in obese women and cessation of alcohol and substance abuse.
- In women with mental health problems discuss the implications of these and their management on pregnancy, labour and delivery and after birth.
- Maintain vigilance for domestic abuse and make appropriate referral if recognised including an outline plan for pregnancy and after birth.
- Encourage contraceptive use until the woman's mental health and medication are optimised.
- Develop with the woman a provisional care plan for the perinatal period covering the management for her mental health including medication and services to be involved. When the woman is pregnant this can be amended to form the MDPP.

##### *Pharmacological*

- The risks and benefits of medication(s) during pregnancy and breastfeeding should be discussed.
- Antidepressants: make a decision about the use of these drugs before conception based on the woman's history, their efficacy and their risks in pregnancy and breastfeeding.
- Antipsychotics: drugs with increased fetal/neonatal risks include risperidone, lithium, valproate and carbamazepine. They should not be used in women trying to conceive.

##### *Psychological*

- Offer specific interventions for certain conditions (e.g. pregnancy loss, tokophobia).

(Cont.)

## Prenatal

### *General*

- Obstetricians, GPs, midwives and other healthcare professionals working with pregnant women should take a history that includes asking about current or previous mental health problem and psychotropic medications. The history should include questions about domestic abuse.
- Following identification of mental health problems, advise referral to specialist mental health services. Referral pathways need to distinguish routine, urgent and emergency cases.
- Assess how mental health problems may impact on the woman's engagement with the healthcare services and identify measures to improve engagement in prenatal care.
- Where there are known fetal and/or neonatal risks, screening and monitoring should be implemented, including involvement of the neonatal team.
- Healthcare professionals should identify the triggers with an adverse effect on a woman's mental health and develop a personalised care plan to minimise the effects of these.
- A written MDPP for women with or at risk of relapse of a serious mental illness should be discussed and agreed with the woman by 32 weeks' gestation at the latest. The woman should be asked to carry a copy.
- If an admission to a mental health unit is required before 32 weeks' gestation it would be to a general adult psychiatric unit. From 32 weeks' gestation to term ideally it would be to a specialist psychiatric mother and baby unit.

### *Pharmacological*

- All healthcare professionals who prescribe for pregnant women with mental health disorders need to maintain their knowledge about medication in pregnancy and lactation.
- Ideally, women will have had a discussion about their psychotropic medication before pregnancy, but if they have not, this should be undertaken as soon as possible in the pregnancy.
- Following this discussion, a final plan for medication in the pregnancy should be agreed (using the lowest effective dose and ideally monotherapy) and included in the MDPP (above).
- Certain drugs should not be used in pregnancy because of their risks (see pre-pregnancy section above).

(Cont.)

### *Psychological*

- Where appropriate, healthcare professionals should consider discussing a referral for a psychological intervention.

### Labour and Delivery

#### *General*

- The MDPP should include a plan for labour and delivery and should be shared with all professionals involved in the care of the woman and her baby.

### Postnatal

#### *General*

- The MDPP should include a postnatal plan for mental health care.
- If hospital admission is required postnatally, it would ideally be to a specialist psychiatric mother and baby unit.
- Vigilance is required to detect sudden changes in the mental state, particularly in the early postpartum period and the need for urgent referral to the specialist mental health team.

#### *Pharmacological*

- The MDPP should include information on both whether the woman plans to breastfeed or formula feed her baby and whether she can breastfeed when taking specific psychotropic medications.

## Perinatal Depression

Depression is a common mental health disorder in the perinatal period with a spectrum of severity varying from mild to severe as defined by the International Classification of Diseases 11th edition (ICD-11) [25]. In fact, there are two classification systems for mental health disorders: one is the ICD-11, which is a global standard developed by an international committee of experts and has mental health disorders as one of the chapters. The other classification system is the American Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Both are used in research, but they have differences in their systems that usually result in more people fulfilling the diagnostic criteria in DSM-5 compared to ICD-11. Although DSM-5 has a time frame of within 4 weeks of childbirth for postpartum depression, this is not the case for ICD-11, where there is no separate category for postpartum depressive episodes. Thus,

‘postnatal depression’ is not an ICD-11 ‘condition or diagnosis’ and the same classification system is used as for all other depressive episodes. Perinatal depression clinically is used to refer to depressive episodes that onset in pregnancy or up to one year postpartum. However, depressive episodes typically have two peaks in onset at 2–4 weeks postpartum and 10–12 weeks postpartum.

The symptoms defined in the diagnostic classification from ICD-11 [25] are shown in Table 2. The diagnosis of severe depressive episodes requires at least eight symptoms including all three core symptoms. Functioning is usually impaired in most domains (personal, family, social, educational, occupational or other important domains) and must be present. For moderate depressive episodes there must be at least six symptoms, which must include at least two core symptoms plus functioning impaired in most domains. For mild depressive episodes there must be at least four symptoms including at least one core symptom with impairment in one or more domains. Postnatally, women can also have a severe depressive episode with psychotic symptoms (such as delusions or hallucinations) and rarely catatonic symptoms.

**Table 2** ICD-11 diagnostic classification [25]

<b>Core symptoms</b>	<b>Other symptoms</b>
Sustained low mood (every day, all the time for at least 2 weeks)	Reduced concentration and attention
Anhedonia (loss of interest and pleasure)	Psychomotor retardation
Reduced energy	Disturbed sleep
	Reduced appetite and weight loss
	Hopelessness
	Helplessness
	Excessive guilt
	Suicidal thoughts
	Feelings of incompetence as a mother
	Feelings of being a burden to others
	Negative views of self, the world and the future

The prevalence of depression in pregnancy is up to 10% and postpartum is up to 13% with 3–5% of women after a live birth developing a more severe episode in the first 12 weeks postpartum.

In ICD-11 there is one category for mental or behavioural disorders associated with pregnancy, childbirth or the puerperium without psychotic symptoms and one with psychotic symptoms. However, if the symptoms meet the diagnostic threshold for a specific mental disorder, then that diagnosis should be used. It should be noted that ‘baby blues’ is not the same as depression. The former is a self-limiting condition that occurs in the first week postpartum in most women and resolves within a few days.

### Maternal Risks

These are:

- Suicide
- Impact on mother–infant relationship
- Relationship breakdown and wider impacts on relationships
- Loss of employment

### Fetus/Infant Risks

These are:

- Association with preterm deliveries
- Association with low birth weight
- Association with caesarean section
- Decreased breastfeeding
- Emotional, neurodevelopmental and behavioural difficulties in the child
- Prenatal maternal depression impacts on fetal neurodevelopment (which is also modulated by fetal genetics) [26]

### Management Options

The ‘General approach to management of women with mental health problems in pregnancy’ (above) applies to women with depression. Below are the additional specific management considerations regarding management of perinatal depression.

#### *General*

An MDPP should be developed and implemented for each woman. Of note, a systematic review in 2023 of women’s experiences of care and treatment for perinatal depression identified one theme, namely that women want perinatal-specific care from practitioners with perinatal mental health experience and training [27].



## Prenatal

### *Non-pharmacological*

The NICE guideline CR192 [15] recommends that, for mild depressive episodes in pregnancy, the intervention should be psychosocial and not pharmacological. In the UK this would usually be available through NHS Improving Access to Psychological Therapies (IAPT) services and those services should prioritise people in the perinatal period. Cognitive behavioural therapy (CBT) is an example of a psychosocial intervention used in these women. There are other psychosocial interventions recommended by NICE that are offered for mild depressive episodes. There is conflicting evidence that one modality is superior to another although some modalities are easier to evaluate in research studies. One study identified CBT, interpersonal therapy (IPT), mindfulness-based interventions (MBI) and religious-based interventions [28] as beneficial for depression. IPT was shown to be better than CBT for women with prenatal depression who have experienced childhood trauma [29]. A review of clinical guidelines from 12 different countries found these guidelines supported a psychological intervention such as CBT for mild to moderate depression [30].

The US Preventive Services Task Force recommends counselling interventions for pregnant or postpartum women at increased risk of perinatal depression. The statement concludes that there is moderate certainty that counselling interventions have a moderate net benefit in preventing perinatal depression [31].

Transcranial magnetic stimulation (TMS) might be available in some settings and may be beneficial for treating depression during pregnancy as an alternative to antidepressants or a psychological intervention [32]. Electroconvulsive therapy (ECT) is not usually used in pregnancy due to conflicting evidence on the safety for the fetus unless the situation is immediately life-threatening for mother and the infant [15,33].

### *Pharmacological*

For moderate and severe depressive episodes prescribing medication in addition to a psychological intervention is usually needed, although some women are anxious about taking medication in pregnancy. There is a good evidence base for the effectiveness of antidepressants in severe depression (see below). The BAP perinatal prescribing guidelines [18] recommend continuing the antidepressant that is known to work for the woman unless there are specific risks regarding that antidepressant in pregnancy.

The most prescribed antidepressants are selective serotonin reuptake inhibitors (SSRIs), but tricyclic antidepressants (TCA), serotonin and noradrenaline reuptake inhibitors (SNRIs) and mirtazapine can also be prescribed [15].

A review of clinical guidelines from 12 different countries that included eight perinatal-specific guidelines also supported the use of antidepressants for severe depression, but with a preference for prescribing sertraline and a preference to avoid paroxetine [30]. That paper also highlighted that changing antidepressant for ongoing treatment is discouraged. A detailed discussion should be undertaken with each woman to establish that in general the benefits outweigh the risks when considering prescribing antidepressants in pregnancy [15].

For treatment-resistant depression, combinations of medications may be used, such as an SSRI and low-dose mirtazapine, or an SSRI and low-dose nortriptyline, or an antidepressant and a low-dose antipsychotic, or an antidepressant and a mood stabiliser. Such women should be offered discussions with specialist perinatal psychiatrists to consider these therapeutic options.

### *Current Evidence for Prenatal Use of Antidepressants*

Tricyclic antidepressants have been prescribed since the late 1950s and there have been no concerns over the use of amitriptyline, clomipramine, imipramine or lofepramine in pregnancy. However, prescriptions of TCAs have reduced since the 1990s, whereas SSRIs prescriptions for depression increased after the NICE guidelines recommended using SSRIs as a first-line treatment. This means that more recent meta-analyses have far more data on SSRIs than TCAs.

There have been concerns about SSRIs in pregnancy. Currently the evidence can be summarised as follows:

- It is difficult to separate out the effects of antidepressants from the effects of maternal depression on the fetus.
- There may be a small effect on gestational age [34] and on Apgar scores, with babies being born slightly preterm with lower Apgar scores, but these outcomes may be due to confounding factors.
- There have been concerns about SSRIs being associated with an increased risk of cardiac defects in the fetus. However, more recent large studies that adjusted for depression-associated confounders did not find a significant increase in the risk of cardiac defects [18].
- There is an increased rate of the diagnosis of postpartum haemorrhage when SSRIs are taken in late pregnancy (aRR = 1.84; CI 1.39–2.44) [35], although the clinical significance and severity of this is unclear.

- The absolute risk of persistent pulmonary hypertension of the neonate (PPHN) is low. One study reported an increased risk of PPHN with SSRIs with adjusted odds ratio of 1.28 (CI = 1.01–1.64) [36].
- Poor neonatal adaptation syndrome (PNAS) is a risk with SSRIs and SNRIs that is probably dose-related and appears to be a little worse with SNRIs. Usually, it resolves spontaneously, but at times symptomatic treatment is required [37].
- There is an increased risk of admission to the neonatal intensive care unit (NICU) when antidepressants are used in late pregnancy (aOR = 1.6, CI = 1.5–1.8) [38].
- Autistic spectrum in the offspring is probably not associated with antidepressant use prenatally. Any reported link is probably due to confounding factors [39,40].
- There is no evidence of an increased risk of attention deficit hyperactivity disorder (ADHD) in offspring exposed to antidepressants *in utero* [34,40].
- There is no evidence of an increased risk of behavioural problems at age 7 in children whose mothers took antidepressants prenatally [41].

## Labour and Delivery

### *General*

These are addressed in the ‘General approach to management of women with mental health problems in pregnancy’ section above.

### *Non-pharmacological*

The level of supervision needed immediately after delivery if the woman is severely depressed and at risk of neglecting the baby. After delivery, the baby needs the normal neonatal examination and vigilance for any effects of maternal medications. They may show signs of PNAS but there is no specific guidance on how long the baby needs to remain in hospital. The baby should be feeding well before discharge.

### *Pharmacological*

The MDPP should include a strategy for medication through labour, delivery and the immediate postpartum period, including the decision to start an antidepressant immediately after delivery if the woman does not want to start medication in pregnancy. Neonatologists should be informed of patients delivering on medications that can affect the newborn. This should also be in the care plan.

## Postnatal

### *General*

The MDPP should include the postnatal period. When managing depression in the postnatal period it is important to consider the baby and the whole family unit, as depression can impact on mother's interaction with her infant, which in turn can impact on attachment of the infant to the mother [15].

### *Non-pharmacological*

Psychosocial interventions such as CBT or compassion-focused therapy (CFT) are offered alongside medication. The evidence for these is discussed in the prenatal section for depression above. For a moderate or severe depressive episode care would usually be provided by the specialist perinatal mental health service using a multidisciplinary team (MDT) approach using a biopsychosocial approach to seek to address the multiple factors involved.

For severe depression, if there are imminent risks to mother and/or infant, then admission to a specialist psychiatric mother and baby unit may be necessary. In cases of severe depression ECT may be required [33].

### *Pharmacological*

If a depressive episode occurs postnatally, the treatment will be dependent on its severity and any risks involved (see above for further details on treating depression). For a new onset of depression postnatally where a woman is breastfeeding, sertraline is commonly the preferred treatment due to it having the lowest relative infant dose (RID). The recommendation is if a medication has a RID of less than 10% of maternal plasma levels then it can be used in breastfeeding. British Association of Psychopharmacology perinatal guidelines also recommend for women who have had antidepressants in the past using a medication that is known to be beneficial.

For preterm infants, whose mothers are taking antidepressants postnatally, there needs to be a conversation between neonatologists and perinatal psychiatrists to discuss the use of expressed breast milk. A plan should be agreed on a case-by-case basis.

In the United States, zuranolone has recently been licensed for postpartum depression. It is an oral medication that is a 'positive allosteric modulator of synaptic and extrasynaptic GABA<sub>A</sub> receptors and neuroactive steroid' [42]. This is an exciting novel treatment that has been developed from intravenous

infusion of brexanolone, which was demonstrated to be clinically effective but expensive and difficult to use in day-to-day clinical practice [43]. The research into this novel group of medications has also suggested there are inflammatory pathways involved in postpartum depression and this group of medications leads to a reduction in TNF- $\alpha$  and IL-6 [12].

#### SUMMARY OF MANAGEMENT OPTIONS

### Perinatal depression

See also ‘General approach to management of women with mental health problems in pregnancy’ (above).

#### Prepregnancy

- Review the medication of women being treated for depression and amend if necessary.

#### Prenatal

- Establish and implement an MDPP in collaboration with the woman by 32 weeks.
- Maintain vigilance and identify women at risk or experiencing severe depression, including an initial comprehensive review of history, mental and physical health.
- Optimise the management of co-existent physical disorders, e.g. hypothyroidism.
- Possible interventions:
  - ***Non-pharmacological (especially with mild depression)***
    - Increased social and professional support including counselling.
    - Increased physical activity, improved nutrition, reduce/stop smoking/alcohol/substance misuse.
    - Psychological and psychosocial interventions (e.g. CBT).
    - TMS is available in some settings.
    - ECT is not usually advised. It is reserved for women who are at imminent risk of death.
  - ***Pharmacological (usually used in addition to the non-pharmacological methods with moderate and severe depression)***
    - Antidepressants (SSRIs, TCAs, SNRIs and mirtazapine).
    - Only use after discussion of benefits/risks with the woman.

(Cont.)

## Labour and delivery

- **Non-pharmacological**
  - The MDPP should include who the birth partner will be and specialist involvement.
- **Pharmacological**
  - The MDPP should include a strategy for medication through labour, delivery and the immediate postpartum period, including informing the neonatal team if a woman is taking medication.

## Postnatal

- Implement the MDPP.
- Maintain vigilance for the onset of symptoms
- **Non-pharmacological and pharmacological**
  - *Mild depressive episode*: advice and increased physical activity, psychological and psychosocial interventions (e.g. CBT, CFT).
  - *Moderate and severe depressive episodes*: individualise for woman and her family:
    - psychological interventions
    - antidepressants: ideally those with RID < 10% of maternal plasma levels and a review of whether breastfeeding can continue
    - ECT is reserved for severe depression when the woman is hospitalised with imminent risk of death
    - full assessment of newborn and vigilance for PNAS.

CBT, cognitive behavioral therapy; ECT, electroconvulsive therapy; MDPP, multidisciplinary plan for pregnancy; TMS, transcranial magnetic stimulation; PNAS, poor neonatal adaptation syndrome; SNRIs, serotonin and norepinephrine reuptake inhibitors; SSRIs, serotonin selective reuptake inhibitors; TCAs, tricyclic antidepressants; RID, relative infant dose.

## Bipolar Disorder

*Diagnosis of Bipolar Disorder [25]*

Bipolar disorder is usually subdivided into bipolar disorder type 1 and bipolar disorder type 2.

Bipolar disorder type 1 requires one episode of mania with or without psychotic symptoms plus another mood disorder episode (which could be either hypomania or mixed affective, or depression or psychotic depression).

Bipolar disorder type 2 requires one episode of hypomania or mixed affective episode and one other mood disorder episode that is not mania (usually a depressive episode).

ICD-11 [25] symptoms of mania include:

- Extreme high mood lasting at least one week characterised by euphoria or irritability.
- Increased activity.
- Subjective experience of increased energy.
- Rapid speech or pressure of speech or flight of ideas.
- Racing thoughts.
- Grandiosity.
- Decreased need for sleep (usually sleeping 1–2 hours per 24 hours).
- Distractibility.
- Impulsive and reckless behaviour.
- Labile or irritable affect.
- Severe impairment of functioning, usually requiring admission to psychiatric hospital.

ICD-11 [25] symptoms of hypomania include:

- Persistent mild elated mood or irritability for at least several days.
- Increased activity.
- Rapid speech.
- Racing thoughts.
- Increased self-esteem.
- Increased libido or sociability.
- Decreased need for sleep.
- Distractibility.
- Impulsivity.
- Marked impairment of functioning but not to the extreme of mania and not requiring hospital admission.

A mixed affective episode has a combination of some symptoms of hypomania and some depressive symptoms.

Of all mental health disorders, bipolar disorder has the strongest link to postpartum psychosis, with most episodes of postpartum psychosis being the first presentation of bipolar disorder or a relapse of bipolar disorder. There is a strong heritability of bipolar disorder (approximately 80%), so family history is important in considering the risk of relapse postpartum. Risk of relapse overall postpartum for women with a diagnosis of bipolar disorder is 37% (CI 29%–45%) [11]. This relapse rate is of any episode of bipolar disorder postpartum.

**Table 3** Relapse rates postpartum for bipolar disorder – overall, with and without prophylactic medication [11]

Condition	Relapse rate	95% CI
Overall relapse rate for bipolar disorder	37%	29%–45%
Bipolar disorder with prophylactic medication	22%	14%–37%
Bipolar disorder without prophylactic medication	66%	57%–75%

Prophylactic medication reduces the relapse rate from 66% (CI 57%–75%) without any prophylactic medication to 22% (CI 14%–37%) [11]. This information needs to be discussed with women in the prepregnancy, prenatal and postnatal periods to assist them in making informed decisions about family planning and management of their bipolar disorder in the perinatal period. [Table 3](#) summarises these data.

A study looking at women with a diagnosis of bipolar disorder and the risk of relapse after their second delivery when stratified against their relapse following their first delivery suggests that women are more likely to have a similar relapse after their second delivery to the relapse after their first delivery (see [Table 4](#)). This further highlights the importance of prophylactic medication for women with bipolar disorder who had a severe relapse after their first delivery.

### *Maternal Risks*

Risks can vary depending on whether the woman is in recovery or what type of relapse the woman is experiencing. These risks include:

- Increased risks of adverse outcomes in pregnancy including increased rates of induced labour or planned caesarean section (odds ratio = 2.12, 95% CI = 1.68–2.67). The risk of preterm birth is increased by 50% and there is an increased risk of antepartum haemorrhage [45].
- Disengagement with maternity services.
- Discontinuation of medication leading to relapse or further deterioration.
- Disinhibition and recklessness leading to alcohol use or substance misuse or a vulnerability to exploitation by others or an increased risk of assaulting others.
- Suicide when severely depressed.
- Accidental death when manic.



**Table 4** Risk of relapse of bipolar disorder Type 1 following subsequent pregnancies [44]

First perinatal period (first pregnancy with a live birth)	% Risk of relapse after a future pregnancy	Second perinatal period (second pregnancy with a live birth)	% Risk of relapse after a future pregnancy (95% CI)
Affective psychosis	30.9%	Affective psychosis	42.7% (35.7–50.7)
		Non-psychotic depression	9.2% (2.16–17.17)
		No occurrence	48.1% (41.08–58.09)
Non-psychotic depression	31.3%	Affective psychosis	8.6% (1.6–16.5)
		Non-psychotic depression	49.7% (42.78–57.66)
		No occurrence	41.7% (34.75–59.64)
No occurrence	37.8%	Affective psychosis	9.7% (4.0–16.2)
		Non-psychotic depression	23.9% (20.27–35.66)
		No occurrence	66.4% (60.62–72.86)

- The medications normally used in the management of bipolar disorder including olanzapine and quetiapine have risks including metabolic syndrome, weight gain, gestational diabetes, prenatal and delivery risks associated with obesity and gestational diabetes.
- Impact on wider relationships and relationship breakdown.

### *Fetal/Neonatal Risks*

These are:

- Increased risk of placental abnormalities, lower Apgar scores, 50% increased risk of preterm delivery and increased risk of infants being small for gestational age [45].
- Prenatal maternal relapse leads to increased dosage of medications prenatally.
- Some medications used to treat bipolar are associated with an increased rate of fetal anomalies (see below for further details).
- Risks of neglect if the mother is severely depressed, manic, or hypomanic.

- Risk of infanticide if the mother has psychotic symptoms as part of severe depression or mania, although this is an extremely rare outcome and is far rarer than completed suicide [46].

### *Management Options*

The ‘General approach to management of women with mental health problems in pregnancy’ above applies to women with bipolar disorder. Below are the additional specific management considerations regarding management of bipolar disorder.

## **Prepregnancy**

### *General*

Discuss the risks of recurrence of the condition during and after pregnancy and the risks and benefits of medications.

### *Pharmacological*

If a woman is taking lamotrigine as a mood stabiliser, then her lamotrigine level should be taken and recorded pre-pregnancy to provide a reference baseline level for comparison during pregnancy.

## **Prenatal**

### *General*

An MDPP for the prenatal period, labour and delivery and postnatal period should be developed and implemented for each woman.

### *Possible Legal Consideration in Extreme Cases*

If a woman with bipolar disorder is either severely depressed or manic, with or without psychotic symptoms, to the severity that she lacks capacity to make decisions regarding her maternity care in labour and delivery, then as well as seeking expert opinion from the consultant perinatal psychiatrist the maternity service will need to seek legal advice. If required, there will be a legal process available that will ensure maternity care can proceed legally. In the UK this could involve going to the Court of Protection regarding the delivery and all aspects of care around the delivery.

### *Pharmacological*

Women should have a discussion regarding their medication in pregnancy and the risk of relapse to reach an informed decision to either continue or stop maintenance medication in pregnancy. Maintenance medication usually includes a psychotropic medication with mood-stabilising properties, most commonly an antipsychotic

[15,18]. The medication that is most effective for maintenance treatment is usually continued unless there are specific reasons to stop that medication. Specifically, in the context of bipolar disorder, valproate should not be used in pregnancy because of the fetal risks. Furthermore, it is not a good mood stabiliser and there are better therapeutic options [15,18].

A review of international evidence-based guidelines for the pharmacological management of bipolar disorder in the perinatal period demonstrated moderate levels of agreement regarding the teratogenic effects of lithium, sodium valproate and carbamazepine. The review commented there was less agreement regarding the safety of lamotrigine, antipsychotics and antidepressants in pregnancy [47]. There is less evidence about the safety of antipsychotics than is available for antidepressants.

Antipsychotics do not appear to be associated with significant risk to maternal and infant outcomes once statistical techniques are used to try to reduce the impact confounding factors such as smoking and obesity [7] apart from risperidone, where there may be a small increased risk of fetal malformations following in-utero exposure [48,49]. However, evidence is limited and this needs to be explained to the women [18]. A recent cohort study that followed offspring of mothers who took antipsychotic medication in pregnancy up for 14 years has shown that prenatal exposure is not associated with an increased risk of neurodevelopmental disorders except for aripiprazole [50].

First-generation antipsychotics (e.g. haloperidol, flupentixol, zuclopentixol, fluphenazine, chlorpromazine) are less commonly used in non-pregnant women, and therefore are less commonly used in pregnancy. They are not known to be teratogenic [18], but can cause extrapyramidal side effects (EPSEs) in the woman and EPSEs have been observed in the neonate.

Second-generation antipsychotics, including olanzapine and quetiapine, are used as mood stabilisers. These are associated with an up to twofold increased rate of gestational diabetes [18]. Olanzapine and quetiapine can cause metabolic syndrome, which affects the way lipids and glucose are metabolised and is associated with increased birthweight of the neonate [18].

Lithium can be used in pregnancy as a mood stabiliser, but is associated with increased rates of fetal abnormalities with an absolute risk difference being 7 per 1,000 [51], particularly fetal cardiac malformations. There are differing clinical opinions on the use of lithium in pregnancy. Prepregnancy lithium levels that are therapeutic for the individual woman need to be known so that lithium levels can be monitored regularly in pregnancy and lithium dose titrated appropriately. There are differing protocols on the frequency of monitoring lithium levels in pregnancy; one recommends every month in pregnancy until 36 weeks' gestation and then every week [12,52]. The dose should be adjusted to keep the levels within the therapeutic

range. If lithium is stopped abruptly in pregnancy there is around a 50% risk of recurrence of bipolar disorder in pregnancy, particularly if lithium has been taken for less than 2 years [18].

Polish Psychiatric Association guidelines for pregnant women with bipolar disorder advise to reduce the lithium carbonate dose to 500 mg/day but do not comment on maintaining a therapeutic serum level [53]. In the UK, the lithium dose is usually managed by maintaining a therapeutic serum level of between 0.7 and 1.0 mmol/l, so the dose would not automatically be reduced as this could bring serum levels below the therapeutic level and trigger a relapse. Other than this difference the Polish Psychiatric Association guidelines are similar to the NICE guideline [15]. The period of maximum risk of lithium to the fetus is weeks 2–6 after conception when women may not know they are pregnant [18].

In the past, sodium valproate and semi-sodium valproate have been used as a mood stabiliser, but due to valproate being a major teratogen it should not be used in women of childbearing potential [15]. Any woman who conceives on valproate needs to agree an urgent plan to reduce and stop it and an alternative mood stabiliser would need to be started.

Lamotrigine can be used as a mood stabiliser for bipolar disorder type 2, but is not effective in preventing episodes of mania so should not be used in bipolar disorder type 1. There is no increased risk of major congenital malformations in women who take lamotrigine in pregnancy [45]. Lamotrigine levels can be monitored in pregnancy if there is a prepregnant level for the individual woman that is known because there are differences in pregnant women in their clearance rate of lamotrigine.

Women with known bipolar disorder should not have an antidepressant prescribed alone due to the risk of triggering a hypomanic or manic episode. However, sometimes women with bipolar disorder type 2 have both a mood stabiliser and an antidepressant for maintenance therapy.

A discussion should occur with the woman if she is taking psychotropic medication in pregnancy, informing her of symptoms her newborn baby may manifest which require urgent contact with the healthcare team.

## Labour and Delivery

### *General*

The MDPP should include a section covering labour and delivery.

### *Pharmacological*

Antipsychotics should be continued through labour and delivery. However, lithium is not continued through labour and delivery due to the pharmacodynamic

changes at delivery. Specifically, lithium toxicity can occur at delivery, and it is commonly stopped when labour starts and lithium levels checked 12 hours after the woman's last dose [18]. However, there are differing opinions in this area. Fluid balance needs to be monitored during labour and delivery. Lithium should be stopped 12 hours before an elective caesarean section and lithium plasma levels should be checked after the caesarean section [18].

## Postnatal

### *General*

The MDPP should cover the postnatal period. Vigilance should be maintained because of the high risk of relapse postnatally for women with bipolar disorder, particularly for the first 3 weeks and up to 12 weeks after the birth [15]. Clinicians from the specialist perinatal mental health service should see the women regularly for 12 weeks, with more frequent visits initially. If a woman relapses, that episode needs to be managed appropriately. If the relapse is an episode of mania or mania with psychotic symptoms or severe depression or severe depression with psychotic symptoms then usually admission to hospital is required, this should be to a psychiatric mother and baby unit [15]. If the woman develops an episode that includes psychotic symptoms it should be managed in the same way as for postpartum psychosis except the medication will need to be continued for at least 2 years after full recovery. However, if the relapse comprises a depressive episode or a hypomanic episode, this may be managed in the community.

### *Pharmacological*

Lithium can reduce the likelihood of postpartum psychosis. However, lithium toxicity can occur in the neonate if the woman takes lithium in pregnancy [18]. Breastfeeding is not recommended by NICE CG192 [15] for women taking lithium. However, two articles published in 2021 and 2022 looked at lithium levels in the newborn in groups of either breastfeeding or combination feeding of breast and formula resulted in the Drugs and Lactation Database (LactMed) [54] in December 2022 stating that in a woman taking lithium it is not an absolute contraindication to breastfeeding in healthy full-term infants. There is currently some debate on whether a woman can breastfeed while taking lithium. If a woman insists on breastfeeding while taking lithium, one option is for the infant to have regular blood tests to check their lithium level.

Women can breastfeed while taking olanzapine and quetiapine as the RID is less than 10% [18]. Risperidone has a moderate RID value and amisulpride has a high RID value, so they should not be used in women who choose to breastfeed [18].

Aripiprazole is a partial agonist for D<sub>2</sub> receptors, so may lower prolactin levels and affect milk supply.

First-generation antipsychotics have low RID values so can be used in breastfeeding [18]. Lamotrigine RID averages 30–35% [18], which is high, so women should be advised not to breastfeed while taking lamotrigine.

If a woman with bipolar disorder has a depressive episode, then an antidepressant can be added to the mood stabiliser until she recovers. She can breastfeed on most SSRIs and TCAs. Venlafaxine has RIDs reported between 4% and 15%, making the risks of breastfeeding unclear. The recommendation is to look to use a medication that is known to have been effective for her in the past where possible. A full assessment of the newborn is needed when a woman has taken psychotropic medication in pregnancy.

#### SUMMARY OF MANAGEMENT OPTIONS

### **Bipolar disorder**

See also ‘General approach to management of women with mental health problems in pregnancy’.

#### Prepregnancy

- Counsel women with bipolar disorder about risks of recurrence during pregnancy and postpartum and the benefits and risks of medication in pregnancy.

#### Prenatal

- **General**
  - Develop and implement an MDPP for the prenatal period.
  - Consider legal intervention in extreme cases.
  - Women with confirmed bipolar disorder should have obstetrician-led care.
- **Pharmacological**
  - The decision to continue or stop maintenance treatment depends on the severity and recency of bipolar episodes and the risks of the woman’s current medication.

#### Labour and delivery

- Develop and implement an MDPP for labour and delivery, which should include:
  - A plan for medication.
  - The level of observation needed.

(Cont.)

## Postnatal

### ■ *General*

- Develop and implement an MDPP for the postnatal period; this should include the following:
- Maintain vigilance for recurrence of symptoms after delivery, especially in the first month but continuing for at least 12 weeks.
- Multidisciplinary involvement.
- If admission is required, this should be to a mother and baby unit.
- Full assessment of newborn, especially if the woman has been taking psychotropic medication.

### ■ *Pharmacological*

- Prophylactic medication as agreed in the MDPP.

## Postpartum Psychosis [53,54,55]

Postpartum psychosis usually occurs early in the postnatal period. It is characterised by the rapid onset of psychotic symptoms that almost always have affective (mood) symptoms associated. Initially the woman has a fluctuating mental state that can change rapidly so at times she can seem lucid, but at other times frightened and perplexed. This quickly develops into florid psychotic symptoms usually followed by affective symptoms, although at times the affective symptoms can develop at the beginning of the episode.

### *Epidemiology*

Postpartum psychosis

- Occurs in 1 in 500–1,000 maternities.
- Has a relapse risk after a subsequent delivery with a previous episode of postpartum psychosis of 33% (22–42%) [11].
- Is at greater risk with a personal or family history of bipolar disorder.
- Is more common in first pregnancies and in women having their first baby with a new partner.

### *Symptoms*

These are:

- Hallucinations
- Delusions
- Affective symptoms – either symptoms of mania or depression or mixed affective symptoms
- Disturbed or bizarre behaviour
- Confusion
- Perplexity
- Fearfulness

### *Presentation*

Most women report onset of symptoms within the first few days postpartum and the majority have presented to health services within a month postpartum. In practice, the maternity services are likely to be the services that women or their partners first present to or contact reporting possible psychotic symptoms. Women may present initially with being overtalkative (or the overuse of digital messaging systems), overactive, not sleeping when the infant sleeps, perplexed and having new, rapidly changing emotions ('labile affect') that are not in keeping with the normal emotional changes seen postpartum.

### *Maternal and Fetal Risks*

These are:

- Maternal suicide
- Injury of mother due to disturbed behaviour
- Injury of infant due to disturbed behaviour
- Maternal self-neglect
- Risk to infant due to decrease in mother's level of functioning
- Neglect of infant
- Relationship breakdown

### *Management Options*

The 'General approach to management of women with mental health problems in pregnancy' above applies to women with postpartum psychosis. Below are the additional specific management considerations regarding management of postpartum psychosis.



## Prepregnancy

### *Pharmacological*

If a woman's first episode of mental illness is postpartum psychosis, the recommendation is to continue the treatment regimen of medication for at least 12 months after remission of symptoms occurs. The duration of remission will determine the advice about medication in the current pregnancy. The advice about specific medications is that recorded in the bipolar disorder section above.

## Prenatal

An MDPP should be developed and implemented for each woman covering the prenatal period, labour and delivery and the postnatal period.

### *General*

A woman who has had a previous episode of postpartum psychosis should be referred to a specialist perinatal mental health service for active management of her mental health in the perinatal period, including consideration of prophylactic medication [57].

## *Labour and Delivery*

### **General**

In most cases of postpartum psychosis (92%), the woman is well from a mental health perspective during labour and delivery. In the 8% of cases where psychotic symptoms present before the onset of labour, the plan for delivery should cover:

- The risk to mother and fetus due to the mother's behaviour.
- The risk of challenging or non-cooperative behaviour during delivery due to psychotic symptoms.
- Psychotropic medication that may be needed.
- The woman's capacity to consent to both mental health and obstetric care, noting that as symptoms fluctuate so can a woman's mental capacity.

### **Pharmacological**

If the symptoms first present a few days before delivery and treatment has been commenced, the treatment is usually a combination of antipsychotics (e.g. olanzapine or haloperidol) and benzodiazepines (e.g. lorazepam). These can compromise the newborn. The main concern is respiratory depression necessitating neonatal intensive care.

*Postnatal***General***Admission to Mental Health Mother and Baby Unit*

The NICE guidelines categorise new onset of psychotic symptoms as an emergency that requires an urgent mental health assessment within 4 hours of referral to mental health services [15]. If the presentation is out of hours, general mental health teams would usually conduct the assessment. The team who assesses the woman should consider admitting the woman and her baby together to a specialist psychiatric mother and baby unit as postpartum psychosis is a serious and life-threatening condition with rapidly developing and fluctuating symptoms. If the mother refuses admission, this may necessitate the implementation of the relevant legislation for the country [58,59,60] where the woman is being treated. In England and Wales, the appropriate legislature is the Mental Health Act (1983), which requires one psychiatrist, another doctor who either knows the patient or has training in assessment of mental health disorders and an approved mental health practitioner to assess the woman and decide if compulsory admission to hospital is required. Under the Mental Health Act, the first compulsory admission to hospital is a section 2 and would last up to 28 days. If admission to a mother and baby unit is not arranged, there needs to be clear documentation of the reasoning for that decision. There should be an emergency referral to the specialist perinatal mental health service at the start of the next working day so the woman can be seen urgently by a senior perinatal mental health clinician, if she is not already in a mother and baby unit.

A high level of supervision of the mother is needed. Ideally this should be undertaken with the woman as an inpatient receiving continuous observation to ensure she and her baby are in a safe environment. Clinicians should specifically ask the mother whether her psychotic symptoms relate to the infant, as such symptoms frequently involve hallucinations and delusions about her child. These are associated with increased risk to the child. Once the woman begins to recover, it is important to explain to her what has happened as gaps in memory during episodes of postpartum psychosis are common. Once they have recovered from postpartum psychosis women need to be made aware that they have a 50% risk of relapse following each future childbirth.

The woman, her partner and family members need to be reassured in the management that the short-term prognosis is very good, that women respond rapidly to treatment, symptoms resolve quickly and women recover fully. The partner and family members will need support to understand what has happened. This will probably be their first experience of seeing a psychotic person

and they could be frightened. They should also be made aware of the risk of recurrence after future childbirth.

Mental health, maternity and health visiting services will be required to provide high levels of ongoing physical and psychological support. In future it may become standard practice to perform autoantibody immune screening, as some episodes of psychosis are due to autoantibodies (in non-pregnancy-related first-onset psychosis about 10% are due to autoimmune causes), but currently this is not standard practice.

### Non-pharmacological

Electroconvulsive therapy is an effective treatment for postpartum psychosis [33] that leads to rapid resolution of symptoms, but due to needing a general anaesthetic for each treatment and the side effects of short-term memory loss around the time of the treatments, it is reserved for the most severe cases where the woman is at imminent risk of death. One example would be psychotic depression with catatonic symptoms, where the woman has not been eating or drinking for a few days.

### Pharmacological

The baby should be monitored for respiratory compromise and poor neonatal adaptation following delivery if the woman had psychotropic medications prior to delivery. Treatment is with antipsychotics [15,18,55]. However, there is limited information on which antipsychotic is better [55]. Whether the woman is breastfeeding is an important additional factor in antipsychotic choice.

For rapid tranquilisation benzodiazepines and antipsychotics are used. If a woman was breastfeeding or had expressed her desire to breastfeed, then lorazepam is chosen as it has a short half-life so is less likely to impact on infant respiration. The prescription of an antidepressant in addition to an antipsychotic should be considered if the presentation has a psychotic depression as a component.

Lithium can be an effective treatment if the woman does not want to breastfeed. The issue of a woman breastfeeding while taking lithium was discussed above in the section on bipolar disorder. Lithium can reduce the likelihood of postpartum psychosis so may be used as maintenance therapy if women understand the risks to the next fetus and they do not want to breastfeed [18]. In practice, if lithium is used to treat postpartum psychosis it would be continued for up to 2 years. If the woman became pregnant, she would be advised to continue or restart the treatment and to continue taking for 2 further years to cover the next pregnancy and postpartum period.

## SUMMARY OF MANAGEMENT OPTIONS

**Postpartum psychosis**

The ‘General approach to management of women with mental health problems in pregnancy’ above applies to women with postpartum psychosis.

## Prepregnancy

- Offer prepregnancy counselling with a consultant perinatal psychiatrist. Discussion should cover:
  - Recurrence risk if it has been diagnosed in a previous pregnancy.
  - Medication options and risks in pregnancy and for breastfeeding.

## Prenatal

- **General**
  - Develop and implement an MDPP.
  - Women with a history of a previous episode should be referred to a specialist perinatal mental health team for discussion of management options, especially prophylactic medication.
  - Maintain vigilance, especially during late pregnancy for recurrence.
  - For the 8% that present in late pregnancy before birth, ensure a safe environment; consider admission to a mother and baby unit.

## Labour and delivery

- **General**
  - Implement the section of the MDPP addressing labour and delivery.
  - Specific issues to be addressed are vigilance for recurrence and the management plan for the 8% of women who present with symptoms before delivery.
  - Inform the neonatal team if treatment has been started before delivery (usually a combination of an antipsychotic and a benzodiazepine).

## Postnatal

- **General**
  - If symptoms of postpartum psychosis develop, seek urgent specialist advice from mental health team who should undertake assessment within 4 h of referral.
  - Maintain a safe environment; strongly consider admission to a mother and baby unit.

(Cont.)

- A high level of physical, medical and psychological care is required.
- Offer support to the wider family.
- Following resolution of symptoms, ensure the woman is aware of what occurred and her risk of recurrence (~50%) following future childbirth.
- **Pharmacological**
  - Medication depends on the presentation: antipsychotics are usually the first line of treatment; adding benzodiazepines provides rapid tranquilisation if the woman has marked agitation.
  - Choice of drug may be influenced by whether the woman is breast-feeding and/or mood stabilisers.
- **Non-pharmacological**
  - Electroconvulsive therapy should be considered for the most severe cases where the woman is at imminent risk of death.

## Schizophrenia

Schizophrenia is a severe and enduring mental health disorder that is characterised by relapsing and remitting episodes of psychosis. Symptoms include so-called ‘positive symptoms’, which include hallucinations, delusions and thought disorder, as well as so-called ‘negative symptoms’, which include blunting of affect, apathy, avolition and poor socialisation. Lack of insight is usually present during a relapse, which impacts on willingness to seek and engage with treatment. For some people insight does not return once psychotic symptoms have resolved, which makes engagement with mental health services very difficult indeed.

### Epidemiology

The median prevalence of schizophrenia is 4.6 per 1,000 with no gender difference but a higher prevalence in immigrants [61]. There is limited information on relapse rates of schizophrenia postpartum [62].

### Risks [61]

Maternal risks are:

- Deterioration of the condition.
- Self-neglect.
- Suicide with an increased risk soon after resolution of a psychotic episode and the return of insight.

- Risk of harm to others when psychotic, although the risk of suicide is five times higher than risks of homicide.
- Lack of engagement with maternity care.
- Lack of engagement with mental health services.
- Smoking, obesity, metabolic syndrome (a side effect of some antipsychotics), diabetes, lack of exercise, substance misuse and alcohol use are all higher in people with schizophrenia, which will impact on pregnancy outcomes.
- Later presentation for prenatal care.
- Delayed recognition of labour.
- Increased risk of gestational diabetes, gestational hypertension, pre-eclampsia, domestic abuse and social adversity.

Risks for the fetus/infant are [63]:

- Any maternal risks that impact on the fetus (gestational diabetes, hypertensive disease, maternal drug treatment).
- Fetal growth restriction (some of this risk is due to self-neglect leading to poor diet and failure to seek appropriate medical care in pregnancy).
- Clozapine reduces fetal heart rate variability [18].
- The neonate may be sedated due to sedating antipsychotics, which can impact on neonate feeding sufficiently leading to weight loss.
- The neonate can experience withdrawal symptoms from antipsychotics. The exact symptoms will depend on the antipsychotic and the dose, they may be like neonatal adaptation syndrome seen with some antidepressants.
- The neonate can experience extrapyramidal side effects at birth if they are a side effect of the antipsychotic the mother is taking (commonly typical antipsychotics and risperidone), but these are usually transient and resolve spontaneously.
- Neglect of the infant.
- If delusions involve the infant, then there is an increased risk of harm to infant. Infanticide is very rare, and rates are hard to quantify [46].
- Negative symptoms impact on the mother–infant relationship and child development.
- Evidence of the long-term neurodevelopmental outcomes of infants exposed to antipsychotics *in utero* is limited [18].

### *Management Options*

The ‘General approach to management of women with mental health problems in pregnancy’ above applies to women with schizophrenia. Below are the additional specific management considerations regarding management of schizophrenia.

## Prenatal

An MDPP should be developed and implemented for each woman covering the prenatal period, labour and delivery and the postnatal period.

### *General*

If the woman is disengaging from either maternity and/or mental health services a more proactive and assertive approach is required [15]. Referral to children's social services may be needed depending on social support and other relevant factors.

### *Pharmacological*

When the pregnancy is disclosed to the general mental health service, urgent expert advice should be sought from a consultant perinatal psychiatrist. The woman's antipsychotic medication should be reviewed, ensuring she does not rapidly stop that medication. The conversation will allow the woman to make an informed decision about her medication based on the risks and benefits of that medication in pregnancy. Most women will assume all medications need to be stopped, but for a woman with schizophrenia stopping medication can trigger a relapse and hospital admission. That discussion will be informed by the details of the woman's past psychiatric history [15].

The use of antipsychotics in pregnancy and lactation has been discussed in the management of bipolar disorder above. Antipsychotic levels change during pregnancy due to changes in pharmacokinetics which varies from one medication to another [64]. One article demonstrated quetiapine and aripiprazole levels reduced during pregnancy whereas olanzapine levels were more stable [64]. This may mean doses of antipsychotics need increasing during pregnancy; however, in clinical practice we do not usually measure serum levels of antipsychotics and therefore there will not be a known therapeutic level for the woman, so dose titration will usually be in response to symptoms. If the dose of antipsychotic is increased in pregnancy, it usually needs decreasing postpartum with a return to the effective prepregnancy dose because antipsychotics are commonly sedating and sedation can impact on the woman's ability to care for her infant, particularly for clozapine, olanzapine and quetiapine.

Clozapine is used for treatment-resistant schizophrenia (defined as when a patient's schizophrenia does not respond to two antipsychotic medications at maximum dose) and is usually started as an inpatient. It has the risk of serious side effects including agranulocytosis necessitating ongoing monitoring of white cell counts. The evidence for the safety of clozapine in pregnancy is limited [18]. There is an increased rate of gestational diabetes in pregnant women on clozapine. Thus, it is reasonable to undertake a 75-g oral glucose tolerance test every 2–3 months through

the pregnancy. Women taking clozapine in pregnancy must see a consultant perinatal psychiatrist in pregnancy to discuss their mental health care and these risks.

Antipsychotics can be given as depot injections between weekly and monthly, usually where a patient is non-compliant with respect to oral medication which has led to a relapse. However, the longer half-life of the depot preparations can adversely affect the neonate. This 'conflict' between avoiding a relapse in the woman who is non-concordant with oral medications versus the potential neonatal risks with depot injections requires careful consideration. Unfortunately, there is limited evidence on the use of depot antipsychotics in pregnancy to guide management [65] and therefore the recommendation is to extrapolate based on the findings from studies on oral antipsychotics in pregnancy [65].

## Labour and Delivery

### *General*

The management in labour and delivery will depend on the mental state of the woman at that time and the associated risks. Higher levels of supervision may be required following delivery depending on the woman's mental state.

### *Pharmacological*

Clozapine has the potential to reduce fetal heart rate variability [18].

## Postnatal

### *General*

Sedation is a common effect of antipsychotics so the woman may need her birth partner to stay with her overnight on the maternity ward to check she is waking to attend to the baby.

If a woman with schizophrenia has a relapse, postpartum consideration should be given to an admission with her baby to a mother and baby unit, if there is sufficient time for her to recover and be discharged and assuming there are no safeguarding concerns regarding the mother's ongoing ability to provide for the child's needs.

### *Pharmacological*

First-generation antipsychotics plus olanzapine and quetiapine are in low levels in the breast milk so women can breastfeed while taking them [18]. Risperidone is in moderate levels in breast milk, so caution is needed in breastfeeding [18]. Amisulpride has a high RID so should not be used in breast feeding [18]. Aripiprazole can reduce prolactin levels, which can impact on infant feeding.



Clozapine has the potential to cause risks to the infant including floppy infant syndrome, infant seizures and agranulocytosis [18]. Women taking clozapine should not breastfeed due to risks of seizures and agranulocytosis [18].

Extrapyramidal withdrawal symptoms have been described in neonates of mothers who took antipsychotics in late pregnancy. However, studies that controlled for confounding factors did not confirm a specific association between antipsychotic exposure and poor neonatal adaptation [18].

Women should be advised not to co-sleep with the infants due to the side effect of sedation if they are taking antipsychotics.

#### SUMMARY OF MANAGEMENT OPTIONS

### **Schizophrenia**

#### Prepregnancy

- Discussion of family planning and contraception.
- Optimise physical health.
- Infertility may be commoner and require investigation; first-generation antipsychotic medications can induce hyperprolactinaemia.
- Medication should be reviewed with respect to risks in pregnancy and breastfeeding.

#### Prenatal

- An MDPP developed by the mental health team in liaison with obstetric and neonatal colleagues and the woman (covering management during pregnancy, labour and delivery and postpartum, changes to medication and follow-up arrangements) should be implemented.
- Encourage engagement with maternity and mental health services; special approaches will be necessary with women who disengage with healthcare.
- Review of antipsychotic medication by consultant perinatal psychiatrist and rationalise on the basis of risk (see also bipolar disorder management options).
- Review dosage during pregnancy based on efficacy.
- Clozapine is reserved for treatment-resistant schizophrenia; ideally it should be commenced as inpatient.
- Women taking clozapine should
  - Be screened for gestational diabetes with oral 75-g glucose tolerance test.
  - Have serial monitoring of white cell count.

(Cont.)

- Consider depot injections in women who are non-compliant in taking oral medications.

### Labour and Delivery

- Implement the MDPP.
- The specific approach will depend on the woman's mental state at the time.
- Clozapine reduces fetal heart rate variability.

### Postnatal

- Implement the MDPP including the approach to medication and breastfeeding.
- Partner support should be encouraged.
- Monitor:
  - The woman's mental state postpartum.
  - Medication sedative effects.
- Women should be discouraged from sleeping with their baby.
- Advise antipsychotic medication to reduce symptoms and the risk of recurrence.
- Interventions addressing the mother–infant relationship may be necessary.
- If the woman has a relapse postpartum, admission to a mother and baby unit should be considered.

## Anxiety Disorders

Anxiety is a normal experience that everyone has at different times in their life. Pregnancy and delivery are associated with normal levels of anxiety at some points for most women. Anxiety disorders occur in 10–15% of pregnant women and are diagnosed when their anxiety reaches such a level it impacts on daily functioning, and they meet the diagnostic criteria for an anxiety disorder as defined by ICD-11 [25]. Anxiety disorders include the following:

- Generalised anxiety disorder (GAD) – persistent, free-floating anxiety (anxiety not fixed or focused on one topic) with autonomic symptoms of anxiety.
- Obsessive compulsive disorder (OCD) – a fear that a particular negative event may happen to the person or their loved one (e.g. death or contamination by infection) leading to a particular behaviour that is intended to protect against the underlying fear and relieves the feeling of anxiety.

- Panic disorder – panic attacks that occur repeatedly for at least a month and there is no objective danger triggering the attacks.
- Specific phobias – a fear of a specific object that usually leads to avoidance of that object (e.g. a needle phobia).
- Social anxiety – a fear of scrutiny by other people in social situations that leads to women avoiding social situations.
- Agoraphobia – a fear of crowded places leading to avoiding those places.
- Post-traumatic stress disorder (PTSD) – following a traumatic event, the victim experiences nightmares and flashbacks (in which she sees herself in the event when awake) of the event leading to avoidance of places, people or situations that are connected to the traumatic event with autonomic arousal and hypervigilance.
- Adjustment disorders – adjustment to a significant change in the person's life with associated symptoms of anxiety or low mood. Common after childbirth and resolves spontaneously.

### *Risks for the Woman*

Risks depend on the specific anxiety disorder and what the woman avoids due to her anxiety disorder. For example, if she has a needle phobia, she might decline all blood tests during pregnancy with the associated risks. If she has agoraphobia, she might not leave the house and so might not engage in antenatal care. If she has had a previous traumatic delivery leading to PTSD, she might avoid hospitals, which will impact on maternity care.

### *Risks for the Fetus/Infant*

- Prenatal maternal anxiety and stress is associated with increased risk of the offspring having anxiety disorders, depression, ADHD and conduct disorders. One hypothesis is that the hypothalamic pituitary adrenal axis may, in some way, play a role in how maternal stress impacts on fetal brain development [66]. However, research into this is limited.
- Women with OCD can have obsessional thoughts that they might sexually abuse their own baby, which would be an egodystonic thought that can lead to a woman not cleaning the infant's genital area properly. It can also lead to an unhelpful and unnecessary referral to children's services.
- If a woman with agoraphobia avoids going out, that could impact on her ensuring her infant gets medical care and could impact on the socialisation of the child.
- Comorbidity of anxiety disorders and depression is common so risk factors can be like those of depression.
- Poor neonatal adaptation syndrome can occur in women who are taking SSRIs at delivery, but this is usually self-limiting (see above).

### Management Options [67,68]

The ‘General approach to management of women with mental health problems in pregnancy’ (above) applies to women with anxiety disorders. Below are the additional specific management considerations regarding management of anxiety disorders.

## Prenatal

### General

An MDPP should be developed and implemented for each woman covering the prenatal period, labour and delivery and the postnatal period.

### Non-pharmacological

For mild to moderate anxiety disorders, the NICE guideline CG192 [15] recommends psychosocial and psychological approaches, such as CBT, in managing anxiety disorders. A systematic review and meta-analysis showed CBT and MBI both reduced anxiety symptoms in the perinatal period [69].

### Pharmacological

For severe anxiety disorders a combination of antidepressants (e.g. SSRIs) and psychosocial intervention is recommended [15]. Evidence on the use of antidepressants in pregnancy for anxiety disorders has been discussed above in ‘Perinatal Depression’.

Sometimes propranolol is prescribed to prevent tachycardia due to an anxiety disorder. However, it is not a treatment for an anxiety disorder and is not consistent with NICE guidelines for treating anxiety. In pregnancy, propranolol in the third trimester is associated with a risk of fetal growth restriction and it is advisable to stop its use before then. The 2022 MBRRACE [1] report also recommended stopping propranolol due to risks from an overdose.

Benzodiazepines should only be used short term, for example for up to two weeks, as they cause dependency. However, there may be some women who conceive on regular benzodiazepines. These women will need to slowly reduce and stop their benzodiazepine use in pregnancy and certainly before getting close to being full term to prevent respiratory depression in the infant.

Some women are prescribed pregabalin for anxiety; however, data suggest a small increased risk of major congenital malformations (RR = 1.8, 1.26–2.58) [70]. There are varying opinions on the quality of these data and the conclusions drawn from them. This information needs sharing with women prescribed pregabalin preconceptually and discussed if they become pregnant on pregabalin.

## Labour and Delivery

### *General*

Consideration needs to be given to minimise potential triggers in labour and delivery for women with PTSD. Ironically, labour sometimes appears to function as a useful distraction for women with anxiety disorders in that they are less anxious.

## Postnatal

### *General*

New onset of anxiety symptoms in the early postpartum should be investigated for potential organic causes. The MBRRACE [16] reports have demonstrated cases where women died due to physical causes of symptoms being assumed to be anxiety symptoms. Sepsis can initially present with an impending sense of doom but, in such cases, there should be additional physical signs.

It is important to remember new onset of anxiety symptoms early postpartum can be an indication of a physical health condition. About 15% [10] of women postnatally experience an adjustment reaction to becoming a mother. In the UK this can be monitored by community midwives until 28 days postpartum and the health visitor when they visit to ensure it resolves spontaneously. In other healthcare settings other professionals have this responsibility.

### *Non-pharmacological*

It is important for healthcare staff to be vigilant about whether the anxiety disorder is impacting on the mother–infant relationship and on baby care. Obsessive compulsive disorder is typically exacerbated postnatally due to the responsibility of caring for the newborn baby with, for example, excessive hand washing. Thus, women who are normally able to manage their OCD in primary care but find it difficult with the additional responsibility may need referring to specialist perinatal mental health services for management.

As stated above in the prenatal section of anxiety disorders, CBT and MBI can reduce anxiety symptoms in cases of perinatal anxiety disorders.

### *Pharmacological*

Pharmacological interventions are commonly combined with psychological interventions for the treatment of anxiety disorders. Anxiety disorders are treated with SSRIs. Information regarding these medications is discussed in the ‘Perinatal Depression’ section above. If the symptoms are very severe, the woman may require low-dose antipsychotic as augmentation [15].

## SUMMARY OF MANAGEMENT OPTIONS

**Anxiety Disorders**

The ‘General approach to management of women with mental health problems in pregnancy’ applies to women with anxiety disorders.

## Prepregnancy

- Offer counselling to women with an anxiety disorder about the risks for pregnancy and possible management strategies.

## Prenatal

- Develop and implement an MDPP covering the prenatal period, labour and delivery and the postnatal period.
- Offer reassurance and advice.
- **Non-pharmacological**
  - Psychosocial and psychological interventions are recommended in women with mild to moderate anxiety disorders.
- **Pharmacological**
  - SSRIs can be used for more severe cases.
  - Anxiolytics should be avoided, particularly in the first and third trimesters.
  - In a ‘crisis’ an anxiolytic or low-dose antipsychotic might be used short term for an anxiety disorder in addition to an SSRI.
  - Avoid abrupt cessation of long-term benzodiazepines, gradually reducing and stopping with the onset of pregnancy.
  - Avoid the use of propranolol.

## Labour and Delivery

- Offer reassurance and support.
- Minimise triggers, especially in women with PTSD.

## Postnatal

- **General**
  - Offer reassurance and advice.
  - Consider organic causes with acute presentation of anxiety around delivery.

(Cont.)

- Individualise care according to the specific anxiety disorder, the needs of the woman, her baby and her family.
- Monitor for exaggerated adjustment reactions.
- **Non-pharmacological**
  - Vigilance for adverse impact of anxiety disorder on mother–baby interactions.
  - Cognitive behavioural therapy and/or MBI can be used.
- **Pharmacological**
  - Continue with SSRIs if used in pregnancy.
  - Obsessive compulsive disorder is managed by a combination of SSRIs and psychosocial/psychological interventions (e.g. CBT); antipsychotics may need to be added in the more severe cases.

## Further Reading

- Knight M, Bunch K, Patel R, et al. (eds.) on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care Core Report – Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2018–20*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2022.
- National Institute for health and Care Excellence [NICE] 2014 (last updated February 2020). Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance. Updated edition. NICE clinical guidance 192. London: NICE; 2020. [www.nice.org.uk/guidance/cg192](http://www.nice.org.uk/guidance/cg192).
- Knight M, Bunch K, Tuffnell D, et al. (eds.) on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care – Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014–2016*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2018.
- Knight M, Tuffnell D, Kenyon S, et al. (eds.) on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care – Surveillance of Maternal Deaths in the UK 2011–13 and Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–13*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2015.
- Langham J, Gurol-Urganci I, Muller P, et al. Obstetric and neonatal outcomes in pregnant women with and without a history of specialist mental health care: A national population-based cohort study using linked routinely collected data in England. *Lancet Psychiatry*. 2023; 10: 748–759.
- McAllister-Williams RH, Baldwin DS, Cantwell R, et al. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication in preconception, in pregnancy and postpartum. *J Psychopharmacol*. 2017; 31: 1–34. [www.bap.org.uk/pdfs/BAP\\_Guidelines-Perinatal.pdf](http://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf).
- Deligiannidis KM, Meltzer-Brody S, Maximos B, et al. Zuranolone for the treatment of postpartum depression. *Am J Psychiatry*. 2023 Sep 1; 180(9): 668–675. <https://doi.org/10.1176/appi.ajp.20220785>. Epub 2023 Jul 26. PMID: 37491938.
- Huybrechts KF, Staub L, Karlsson P, et al. Association of in utero antipsychotic medication exposure with risk of congenital malformations in Nordic countries and the US. *JAMA Psychiatry*. 2023 Feb 1; 80(2): 156–166. <https://doi.org/10.1001/jamapsychiatry.2023.0000>



- [.org/10.1001/jamapsychiatry.2022.4109](https://doi.org/10.1001/jamapsychiatry.2022.4109). PMID: 36477338; PMCID: PMC9856848.
- RANZCOG and Women's Health Committee Best Practice Statement: Mental Health Care in the Perinatal Period. <https://ranzocg.edu.au/wp-content/uploads/2022/05/Mental-Health-Care-in-the-Perinatal-Period-C-Obs-48.pdf>.
- ACOG Committee Opinion No. 757: Screening for Perinatal Depression. *Obstet Gynecol*. 2018; 132(5): e208–e212.
- Perinatal Mental Health Services: Recommendations for the provision of services for childbearing women CR232. Royal College of Psychiatrists; September 2021. [www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr232-perinatal-mental-health-services.pdf?Status=Master&sfvrsn=82b10d7e\\_4](http://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr232-perinatal-mental-health-services.pdf?Status=Master&sfvrsn=82b10d7e_4).
- Molenaar NM, Kamperman AM, Boyce P, Bergink V. Guidelines on treatment of perinatal depression with antidepressants: An international review. *Aust N Z J Psychiatry*. 2018 Apr; 52(4): 320–327.
- Graham RK, Tavella G, Parker GB. Is there consensus across international evidence-based guidelines for the psychotropic drug management of bipolar disorder during the perinatal period? *J Affect Disord*. 2018; 228: 216–221.
- Teodorescu A, Dima L, Popa MA, et al. Antipsychotics in postpartum psychosis. *Am J Therapeut*. 2020; 28: e341–e348.
- Lautarescu A, Craig MC, Glover V. Prenatal stress: Effects on fetal and child brain development. *Int Rev Neurobiol*. 2020; 150: 17–40.

## References

1. Knight M, Bunch K, Patel R, et al. (eds.) on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care Core Report – Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2018–20*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2022.
2. Kallianidis AF, Schutte JM, Schuringa LEM, et al. Confidential enquiry into maternal deaths in the Netherlands 2006–2018. *Acta Obstet Gynecol Scand*. 2022; 101: 441–449.
3. Lega I, Maraschini A, D'Aloja P, et al. Regional maternal mortality working group. Maternal suicide in Italy. *Arch Womens Ment Health*. 2020; 23: 199–206. <https://doi.org/10.1007/s00737-019-00977-1>. Epub 2019 May 18. PMID: 31104119.
4. Knasmüller P, Kotal A, König D, et al. Maternal suicide during pregnancy and the first postpartum year in Austria: Findings from 2004 to 2017. *Psychiatry Res*. 2019; 281: 112530. <https://doi.org/10.1016/j.psychres.2019.112530>. Epub 2019 Aug 23. PMID: 31465987.
5. Boutin A, Cherian A, Liauw J, et al. Database autopsy: An efficient and effective confidential enquiry into maternal deaths in Canada. *J Obstet Gynaecol Canada: JOGC*. 2021; 43: 58–66.e4.
6. Langham J, Gurol-Urganci I, Muller P, et al. Obstetric and neonatal outcomes in pregnant women with and without a history of specialist mental health care: A national population-based cohort study using linked routinely collected data in England. *Lancet Psychiatry*. 2023; 10: 748–759.
7. Vigod SN, Fung K, Amartey A, et al. Maternal schizophrenia and adverse birth outcomes: What mediates the risk? *Soc Psychiatry Psychiatr Epidemiol*. 2020 May; 55(5): 561–570. <https://doi.org/10.1007/s00127-019-01814-7>. Epub 2019 Dec 6. PMID: 31811316.
8. Dennis C, Falah-Hassani K, Shiri R. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *Br J Psychiat*. 2017; 210(5): 315–323.
9. Howard LM, Molyneaux E, Dennis CL, et al. Non-psychotic mental disorders in the perinatal period. *Lancet*. 2014; 384: 1775–1788.
10. Oates M. Perinatal psychiatric disorders: A leading cause of maternal morbidity and mortality. *Br Med Bull*. 2003; 67: 219–229.

11. 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(2): 117–127.
12. Therapeutic advances and open questions in postpartum-depression research. *eBioMedicine Lancet*. 2023; 98: 104925.
13. Adane AA, Bailey HD, Morgan VA, et al. The impact of maternal prenatal mental health disorders on stillbirth and infant mortality: A systematic review and meta-analysis. *Arch Womens Mental Health*. 2021; 24: 543–555.
14. Jahan N, Went TR, Sultan W, et al. Untreated depression during pregnancy and its effect on pregnancy outcomes: A systematic review. *Cureus*. 2021; 13(8): e17251.
15. National Institute for Health and Care Excellence (NICE). *Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance*. Updated edition. NICE Clinical Guidance 192. London: NICE; 2020. [www.nice.org.uk/guidance/cg192](http://www.nice.org.uk/guidance/cg192).
16. Knight M, Bunch K, Tuffnell D, et al. on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care – Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014–2016*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; November 2018.
17. Knight M, Tuffnell D, Kenyon S, et al. on behalf of MBRRACE-UK. *Saving Lives, Improving Mothers' Care – Surveillance of Maternal Deaths in the UK 2011–13 and Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–13*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2015.
18. McAllister-Williams RH, Baldwin DS, Cantwell R, et al. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication in preconception, in pregnancy and postpartum 2017. *J Psychopharmacol*. 2017; 31: 1–34. [www.bap.org.uk/pdfs/BAP\\_Guidelines-Perinatal.pdf](http://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf).
19. Valproate: Reminder of current Pregnancy Prevention Programme requirements; information on new safety measures to be introduced in the coming months. GOV.UK. [www.gov.uk/drug-safety-update/valproate-reminder-of-current-pregnancy-prevention-programme-requirements-information-on-new-safety-measures-to-be-introduced-in-the-coming-months](http://www.gov.uk/drug-safety-update/valproate-reminder-of-current-pregnancy-prevention-programme-requirements-information-on-new-safety-measures-to-be-introduced-in-the-coming-months).
20. Dama MH, Van Lieshout RJ. Perinatal depression: A guide to detection and management in primary care. *J Am Board Fam Med*. 2024; 36(6): 1071–1086.

21. ACOG Committee Opinion No. 757: Screening for Perinatal Depression. *Obstet Gynecol.* 2018 Nov; 132(5): e208-e212. [www.rcog.org.uk/ejournals](http://www.rcog.org.uk/ejournals).
22. RANZCOG and Women's Health Committee Best Practice Statement: Mental Health Care in the Perinatal Period. <https://ranzcof.edu.au/wp-content/uploads/2022/05/Mental-Health-Care-in-the-Perinatal-Period-C-Obs-48.pdf>.
23. NHS England. A good practice guide to support implementation of trauma-informed care in the perinatal period. [www.england.nhs.uk/publication/a-good-practice-guide-to-support-implementation-of-trauma-informed-care-in-the-perinatal-period/](http://www.england.nhs.uk/publication/a-good-practice-guide-to-support-implementation-of-trauma-informed-care-in-the-perinatal-period/).
24. Perinatal Mental Health Services: recommendations for the provision of services for childbearing women CR232. Royal College of Psychiatrists; Sept 2021. [www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr232-perinatal-mental-health-services.pdf?Status=Master&sfvrsn=82b10d7e\\_4](http://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/college-reports/college-report-cr232-perinatal-mental-health-services.pdf?Status=Master&sfvrsn=82b10d7e_4).
25. World Health Organization. *ICD-11: International Classification of Diseases* (11th revision). 2019. <https://icd.who.int/>.
26. Qiu A, Shen M, Buss C, et al. Effects of antenatal maternal depressive symptoms and socio-economic status on neonatal brain development are modulated by genetic risk. *Cerebral Cortex.* 2017; 27: 3080–3092.
27. Westgate V, Manchada T, Maxwell M. Women's experiences of care and treatment preferences for perinatal depression: A systematic review. *Arch Womens Ment Health.* 2023 Jun; 26(3): 311–319. <https://doi.org/10.1007/s00737-023-01318-z>. Epub 2023 May 5. PMID: 37147447; PMCID: PMC10191949.
28. Marques A, Ihle A, Souza A, Peralta M, de Matos MG. Religious-based interventions for depression: A systematic review and meta-analysis of experimental studies. *J Affect Disord.* 2022 Jul 15; 309: 289–296. <https://doi.org/10.1016/j.jad.2022.04.126>. Epub 2022 Apr 29. PMID: 35500682.
29. Reuveni I, Lauria M, Monk C, Werner E. The impact of childhood trauma on psychological interventions for depression during pregnancy and postpartum: A systematic review. *Arch Womens Ment Health.* 2021 Jun; 24(3): 367–380. <https://doi.org/10.1007/s00737-020-01066-4>. Epub 2020 Oct 10. PMID: 33040264; PMCID: PMC8176623.
30. Molenaar NM, Kamperman AM, Boyce P, Bergink V. Guidelines on treatment of perinatal depression with antidepressants: An international review. *Aust N Z J Psychiatry.* 2018 Apr; 52(4): 320–327. <https://doi.org/10.1177/0004867418762057>. Epub 2018 Mar 5. PMID: 29506399; PMCID: PMC5871019.

31. US Prevention Services Task Force; Curry S, et al. Interventions to prevent perinatal depression: US preventive services task force recommendation statement. *JAMA*. 2019 Feb 12; 321(6): 580–587.
32. Konstantinou GN, Vigod SN, Mehta S, Daskalakis ZJ, Blumberger DM. A systematic review of non-invasive neurostimulation for the treatment of depression during pregnancy. *J Affect Disord*. 2020 Jul 1; 272: 259–268. <https://doi.org/10.1016/j.jad.2020.03.151>. Epub 2020 May 1. PMID: 32553366.
33. Rose S, Dotters-Katz SK, Kuller JA. Electroconvulsive therapy in pregnancy: Safety, best practices and barriers to care. *Obstet Gynecol Survey*. 2020; 75: 199–203.
34. Sujan AC, Rickert ME, Oberg AS, et al. Associations of maternal antidepressant use during the first trimester of pregnancy with preterm birth, small for gestational age, autism spectrum disorder and attention-deficit/hyperactivity disorder in the offspring. *JAMA*. 2017; 317: 1553–1562.
35. Grzeskowiak LE, Morrison JL, Henriksen TB, et al. Antidepressant use in late gestation and risk of postpartum haemorrhage: A retrospective cohort study. *BJOG*. 2016; 123: 1929–1936.
36. Huybrechts KF, Bateman BT, Hernandez-Diaz S. Antidepressant use late in pregnancy and the risk of persistent pulmonary hypertension of the newborn. *JAMA*. 2015; 313: 2142–2151.
37. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The effect of prenatal antidepressant exposure on neonatal adaptation: A systematic review and meta-analysis. *J Clin Psychiatry*. 2013; 74: e309–320.
38. Norby U, Forsberg L, Wide K, et al. Neonatal morbidity after maternal use of antidepressant drugs during pregnancy. *Pediatrics*. 2016; 138(5): e20160181. <https://doi.org/10.1542/peds.2016-0181>.
39. Vega ML, Newport GC, Bozhdaraj D, et al. Implementation of advanced methods for reproductive pharmacovigilance in autism: A meta-analysis of the effects of prenatal antidepressant exposure. *Am J Psychiatry*. 2020; 177: 506–517.
40. Ames JL, Ladd-Acosta C, Fallin MD, et al. Maternal psychiatric conditions, treatment with selective serotonin reuptake inhibitors, and neurodevelopmental disorders. *Biol Psychiatry*. 2021 Aug 15; 90(4): 253–262. <https://doi.org/10.1016/j.biopsych.2021.04.002>. Epub 2021 Apr 14. PMID: 34116791; PMCID: PMC8504533.
41. Grzeskowiak LE, Morrison JL, Henriksen TB, et al. Prenatal antidepressant exposure and child behavioural outcomes at 7 years of age: A study within the Danish National Birth Cohort. *BJOG*. 2016; 123: 1919–1928. <https://doi.org/10.1111/1471-0528.13611>. Epub 2015 Sep 15.

42. Deligiannidis KM, Meltzer-Brody S, Maximos B, et al. Zuranolone for the treatment of postpartum depression. *Am J Psychiatry*. 2023 Sep 1; 180(9): 668–675. <https://doi.org/10.1176/appi.ajp.20220785>. Epub 2023 Jul 26. PMID: 37491938.
43. Jarman AF, MacLean JV, Barron RJ, Wightman RS, McGregor AJ. Brexanolone for postpartum depression: A novel approach and a call for comprehensive postpartum care. *Clin Ther*. 2020 Jan; 42(1): 231–235. <https://doi.org/10.1016/j.clinthera.2019.11.005>. Epub 2020 Jan 3. PMID: 31910998.
44. Di Florio A, Gordon-Smith K, Forty L, et al. Stratification of the risk of bipolar disorder recurrences in pregnancy and postpartum. *Br J Psychiatry*. 2018; 213: 542–547.
45. Boden 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.
46. Spinelli MG. Maternal infanticide associated with mental illness: Prevention and the promise of saved lives. *Am J Psychiatry*. 2004; 161(9): 1548–1557.
47. Graham RK, Tavella G, Parker GB. Is there consensus across international evidence-based guidelines for the psychotropic drug management of bipolar disorder during the perinatal period? *J Affect Disord*. 2018; 228: 216–221.
48. Huybrechts KF, Staub L, Karlsson P, et al. Association of in utero antipsychotic medication exposure with risk of congenital malformations in Nordic countries and the US. *JAMA Psychiatry*. 2023 Feb 1; 80(2): 156–166. <https://doi.org/10.1001/jamapsychiatry.2022.4109>. PMID: 36477338; PMCID: PMC9856848.
49. Viguera AC, Freeman MP, Kobylski LA, et al. Risk of major malformations following first-trimester exposure to olanzapine: Preliminary data from the Massachusetts General Hospital National Pregnancy Registry for Psychiatric Medications. *J Clin Psychopharmacol*. 2023 Mar–Apr 01; 43(2): 106–112. <https://doi.org/10.1097/JCP.0000000000001665>. PMID: 36825887.
50. Straub L, Hernández-Díaz S, Bateman BT, et al. Association of anti-psychotic drug exposure in pregnancy with risk of neurodevelopmental disorders: A national birth cohort study. *JAMA Intern Med*. 2022 May 1; 182(5): 522–533. <https://doi.org/10.1001/jamainternmed.2022.0375>. PMID: 35343998; PMCID: PMC8961398.
51. Taylor DM, Barnes TRE, Young AH. *The Maudsley Prescribing Guidelines in Psychiatry 14th Edition*, pp. 679–721; 2021. [www.wiley.com](http://www.wiley.com)

- .com/en-gb/The+Maudsley+Prescribing+Guidelines+in+Psychiatry,+14th+Edition-p-9781119772224.
52. Clark CT. Psychotropic drug use in perinatal women with bipolar disorder. *Semin Perinatol*. 2020 Apr; 44(3): 151230. <https://doi.org/10.1016/j.semperi.2020.151230>. Epub 2020 Jan 25. PMID: 32151481.
  53. Rybakowski J, Cubala WJ, Galecki P, et al. Recommendations of the Polish Psychiatric Association regarding the treatment of affective disorders in women of childbearing age. Part II: Bipolar disorder. *Psychiatr Polska*. 2019; 53: 263–276.
  54. Drugs and Lactation Database (LactMed). [www.ncbi.nlm.nih.gov/books/NBK501922/](http://www.ncbi.nlm.nih.gov/books/NBK501922/).
  55. Teodorescu A, Dima L, Popa MA, et al. Antipsychotics in postpartum psychosis. *Am J Therapeut*. 2020; 28: e341–e348.
  56. Osborne LM. Recognizing and managing postpartum psychosis: A clinical guide for obstetric providers. *Obstet Gynecol Clin N Am*. 2018; 45: 455–468.
  57. Meltzer-Brody S, Howard LM, Bergink V, et al. Postpartum psychiatric disorders. *Nat Rev Dis Primers*. 2018; 4: 18022.
  58. Cronin T, Gouda P, McDonald C, Hallahan B. A comparison of mental health legislation in five developed countries: A narrative review. *Ir J Psychol Med*. 2017 Dec; 34(4): 261–269. <https://doi.org/10.1017/ipm.2017.48>. PMID: 30115178.
  59. Fistein EC, Holland AJ, Clare IC, Gunn MJ. A comparison of mental health legislation from diverse Commonwealth jurisdictions. *Int J Law Psychiatry*. 2009 May–Jun; 32(3): 147–155. <https://doi.org/10.1016/j.ijlp.2009.02.006>. Epub 2009 Mar 19. PMID: 19299015; PMCID: PMC2687511.
  60. Dey S, Mellsoy G, Diesfeld K, et al. Comparing legislation for involuntary admission and treatment of mental illness in four South Asian countries. *Int J Ment Health Syst*. 2019 Oct 24; 13: 67. <https://doi.org/10.1186/s13033-019-0322-7>. PMID: 31666805; PMCID: PMC6813093.
  61. Bhugra D. The global prevalence of schizophrenia. *PLoS Med*. 2005 May; 2(5): e151; quiz e175. <https://doi.org/10.1371/journal.pmed.0020151>. Epub 2005 May 31. PMID: 15916460; PMCID: PMC1140960.
  62. Jones I, Chandra PS, Dazzan P, Howard LM. Bipolar disorder, affective psychosis, and schizophrenia in pregnancy and the post-partum period. *Lancet*. 2014 Nov 15; 384(9956): 1789–1799. [https://doi.org/10.1016/S0140-6736\(14\)61278-2](https://doi.org/10.1016/S0140-6736(14)61278-2). Epub 2014 Nov 14. PMID: 25455249.



63. Vigod, SN, Kurdyak, PA, Dennis, CL, et al. Maternal and newborn outcomes among women with schizophrenia: A retrospective population-based cohort study. *BJOG*. 2014; 121: 566–574.
64. Westin AA, Brekke M, Molden E, et al. Treatment with antipsychotics in pregnancy: Changes in drug disposition. *Clin Pharmacol Ther*. 2018 Mar; 103(3): 477–484. <https://doi.org/10.1002/cpt.770>. Epub 2017 Sep 19. PMID: 28643331; PMCID: PMC5836849.
65. O’Sullivan DL, Byatt N, Dossett EC. Long-acting injectable antipsychotic medications in pregnancy: A review. *J Acad Consult Liaison Psychiatry*. 2022; 63: 53–60.
66. Lautarescu A, Craig MC, Glover V. Prenatal stress: Effects on fetal and child brain development. *Int Rev Neurobiol*. 2020; 150: 17–40.
67. Williams KE, Koleva H. Identification and treatment of peripartum anxiety disorders. *Obstet Gynecol Clin N Am*. 2018; 45: 469–481.
68. Thorsness KR, Watson C, LaRusso EM. Perinatal anxiety: Approach to diagnosis and management in the obstetric setting. *Am J Obstet Gynecol*. 2018; 219: 326–345.
69. Clinkscales N, Golds L, Berlouis K, MacBeth A. The effectiveness of psychological interventions for anxiety in the perinatal period: A systematic review and meta-analysis. *Psychol Psychother*. 2023 Jun; 96(2): 296–327. <https://doi.org/10.1111/papt.12441>. Epub 2022 Dec 11. PMID: 36504355.
70. Patorno E, Bateman BT, Huybrechts KF, et al. Pregabalin use early in pregnancy and the risk of major congenital malformations. *Neurology*. 2017 May 23; 88(21): 2020–2025. <https://doi.org/10.1212/WNL.0000000000003959>. Epub 2017 Apr 26. PMID: 28446648; PMCID: PMC5440246.



## High-Risk Pregnancy: Management Options

---

### Professor David James

*Emeritus Professor, University of Nottingham, UK*

David James was Professor of Fetomaternal Medicine at the University of Nottingham from 1992–2009. The post involved clinical service, especially the management of high-risk pregnancies, guideline development, research and teaching and NHS management. From 2009–14 he was Clinical Director of Women's Health at the National Centre for Clinical Excellence for Women's and Children's Health. He was also Clinical Lead for the RCOG/RCM/eLfh eFM E-Learning Project. He is a recognised authority on the management of problem/complicated pregnancies with over 200 peer-reviewed publications. He has published 16 books, the best-known being *High-Risk Pregnancy: Management Options*.

### Professor Philip Steer

*Emeritus Professor, Imperial College, London, UK*

Philip Steer is Emeritus Professor of Obstetrics at Imperial College London, having been appointed Professor in 1989. He was a consultant obstetrician for 35 years. He was Editor-in-Chief of *BJOG – An International Journal of Obstetrics and Gynaecology* – from 2005–2012, and is now Editor Emeritus. He has published more than 150 peer-reviewed research papers, 109 reviews and editorials and 66 book chapters/books, the best known and most successful being *High-Risk Pregnancy: Management Options*. The fifth edition was published in 2018. He has been President of the British Association of Perinatal Medicine and President of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine. He is an honorary fellow of the College of Obstetricians and Gynaecologists of South Africa, and of the American Gynecological & Obstetrical Society.

### Professor Carl Weiner

*Creighton University School of Medicine, Phoenix, AZ, USA*

Carl Weiner is presently Head of Maternal Fetal Medicine for the CommonSpirit Health System, Arizona, Director of Maternal Fetal Medicine, Dignity St Joseph's Hospital, Professor, Obstetrics and Gynecology, Creighton School of Medicine, Phoenix, and Professor, College of Health Solutions, Arizona State University. He is the former Krantz Professor and Chair of Obstetrics and Gynecology, Division Head Maternal Fetal Medicine and Professor Molecular and Integrative Physiology at the University of Kansas School of Medicine, Kansas City, KS and the Crenshaw Professor and Chair of Obstetrics, Gynecology and Reproductive Biology, Division Head Maternal Fetal Medicine, and Professor of Physiology at the University of Maryland School of Medicine, Baltimore. Dr Weiner has published more than 265 peer-reviewed research articles and authored/edited 18 textbooks including *High-Risk Pregnancy: Management Options*. His research was extramurally funded for more than 30 years without interruption.

### Professor Stephen Robson

*Newcastle University, UK*

Stephen C. Robson is Emeritus Professor of Fetal Medicine for the Population and Health Sciences Institute at The Medical School, Newcastle University. He is also a Consultant in Fetal Medicine for Newcastle upon Tyne Hospitals NHS Foundation Trust. He has published over 400 peer-reviewed articles and edited several; books, the highly successful being *High Risk Pregnancy: Management Options*. The fifth edition was published in 2018. He has been President of the British Maternal and Fetal Medicine.

---

## About the Series

Most pregnancies are uncomplicated. However, for some ('high-risk' pregnancies) an adverse outcome for the mother and/or the baby is more likely. Each Element in the series covers a specific high-risk problem/condition in pregnancy. The risks of the condition will be listed followed by an evidence-based review of the management options. Once the series is complete, the Elements will be collated and printed in a sixth edition of *High-Risk Pregnancy: Management Options*.

## High-Risk Pregnancy: Management Options

---

### Elements in the Series

*Fetal Compromise in Labour*

Mark I. Evans, Lawrence D. Devoe and Philip J. Steer

*Spontaneous Preterm Labour and Birth (Including Preterm Pre-labour  
Rupture of Membranes)*

Natasha L. Hezelgrave and Andrew Shennan

*Multiple Pregnancy*

Jack Hamer, Jennifer Tamblyn, James Castleman and R. Katie Morris

*Diabetes in Pregnancy*

Lee Wai Kheong Ryan, Lim Weiyong, Ann Margaret Wright and Lay-Kok Tan

*Caesarean Section Delivery*

Joshua D. Dahlke and Suneet P. Chauhan

*Mental Health Disorders in Pregnancy and the Early Postpartum*  
Zena Schofield and Zack Schofield

A full series listing is available at: [www.cambridge.org/EHRP](http://www.cambridge.org/EHRP)

