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Women with severe mental illness

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INTRODUCTION: WHY IS MENTAL ILLNESS IMPORTANT?

The link between childbirth and severe mental illness has been described for hundreds if not thousands of years[1], but postpartum episodes are not merely of historical interest. Mental disorders in the perinatal period are of great public health importance in the 21st century – as illustrated by a number of cases in which women suffering from severe illness have killed themselves or harmed their infants[2], and by the findings of the Confidential Enquiries in the UK which find suicide to be a leading cause of maternal death[3–6]. Despite its undoubted clinical importance, perinatal mental illness has not received the attention, both in terms of clinical practice and research, that it clearly deserves.

The decision to start a family is fraught with difficulties for women with a history of severe mental illness as well as their partners. Such couples face a number of important questions and often encounter difficulties accessing the information they need. This chapter reviews what is known about severe mental illness in relation to pregnancy and childbirth. A number of issues are discussed, including the risk of childbirth impacting their illness, difficult decisions regarding medication in pregnancy, and questions that women and their partners may have about the risk of passing the illness on to their children.

WHAT EPISODES OF PSYCHIATRIC ILLNESS OCCUR RELATED TO PREGNANCY AND CHILDBIRTH?

Despite the widespread focus on postpartum depression, a wide variety of psychiatric disorders occur in relation to parturition – both in pregnancy and following childbirth. These include anxiety disorders, chronic psychoses such as schizophrenia, eating disorders and substance misuse. Pregnancy impacts on each of these conditions, and each, in turn, can have a significant effect on antenatal and postnatal care. Episodes may be the first presentation of a disorder or represent a recurrence of a pre-existing condition. Although many potential conditions may occur, attention is often focused on mood disorders and the trio of baby blues, postpartum depression and postpartum psychosis (Table 1).

The blues – over 50% of women experience a brief episode of minor mood change in the first postpartum week[8]. Such episodes are self-limiting, last no more than a few days, do not require treatment and should not be considered a 'disorder'.

Postpartum depression – significant depressive symptoms occur following more than 10% of deliveries and may last for months or even years[9]. Episodes of major depression at this time may cause significant emotional impairment and lead to severe long-term consequences. The symptoms of postpartum depression are no different to those of depression occurring at other times[10].

Table 1 The clinical features of postpartum psychosis, postnatal depression and the baby blues

	'Baby blues'	*Postnatal depression*	*Postpartum psychosis*
Incidence per delivery	~50%	~5–15%	~0.1%
Typical onset after delivery	Around days 2–5	Within 6 months	First 2 weeks
Duration	Few days	Weeks to months	Weeks to months
Symptoms	Depressed mood, irritability, lability of mood, crying	Depressed mood, lack of pleasure, poor sleep, poor appetite, suicidal thoughts, self blame, guilt	Elated, irritable or depressed mood, lability of mood, confusion/perplexity, psychotic symptoms including delusions and hallucinations, rapidly changing clinical picture
Treatment	Requires no intervention	Self help strategies (e.g. exercise, computerized cognitive behavioral therapy (CBT) and guided self-help), non-directive counseling, psychological therapies (e.g. CBT or interpersonal psychotherapy), antidepressant medication. Most often may be treated at home but severe cases may need admission	Antipsychotic medication, antidepressant medication, mood stabilizers (e.g. lithium), support and counseling. Often requires admission

Adapted from reference 7

Postpartum psychosis – the most severe forms of postpartum mood disorder have traditionally been labeled as postpartum (or puerperal) psychoses[11]. Although the boundaries of this condition are difficult to define, the core concept is the acute onset of a manic or affective psychosis in the immediate postpartum period; the incidence is approximately 1 in 1000 deliveries. Symptoms are those of severe affective psychosis accompanied by delusions and hallucinations. Mixed episodes, in which manic and depressive symptoms occur simultaneously, are common, and the clinical picture often shows a constantly changing, 'kaleidoscopic', picture. The term 'postpartum psychosis' is usually used to refer to the new onset, although not necessarily the first episode, of a severe affective psychosis in the immediate puerperium. Accordingly, the continuation of a chronic psychosis such as schizophrenia would not be appropriately labeled as a postpartum psychosis.

The classification of episodes of psychiatric disorder in relationship to childbirth is an area that leads to much confusion, both clinically and in research. The classification systems of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD) do not contain categories for the postpartum conditions described above. They do, however, follow the generally accepted position that postpartum psychosis and depression are not separate nosological entities, but merely represent episodes of mood disorder triggered by childbirth. Consistent with this approach, in

DSM IV a postpartum onset specifier can be employed for mood episodes with onset within 4 weeks of delivery. Despite the postpartum labels not having a place in the classification system, they remain in common use, by both professionals and the lay public. One potential problem, unfortunately, is the ubiquitous use of the term 'postpartum depression' to refer to all forms of psychological distress following pregnancy – from mild and transient mood changes to some of the most severe psychotic conditions seen in psychiatry. This inappropriate usage not only trivializes severe episodes of illness with an underestimation of risk in future pregnancies, but also supports the inappropriate labeling as a psychiatric disorder of a normal mood variation.

WHAT DO WE MEAN BY 'SEVERE MENTAL ILLNESS'?

This chapter focuses on the care of women with pre-existing severe mental illness remembering, of course, that many women experience their first episode of illness in relation to childbirth. Although severe mental illness can be defined in various manners, here it includes women with a history of a psychotic illness such as schizophrenia or those with a severe mood disorder (bipolar disorder or severe recurrent unipolar depression).

WHAT ARE THE ISSUES FOR WOMEN WITH SEVERE MENTAL ILLNESS CONTEMPLATING PREGNANCY?

For women with severe mental illness, pregnancy can present some very complicated issues and necessitate some of the most difficult decisions faced in psychiatry. The questions that women and their partners face include:

- What are the implications of pregnancy and childbirth on the psychiatric illness?
- What is the risk to children of developing psychiatric illness?
- What are the risks and benefits of taking medication in pregnancy?
- How can the risks of becoming unwell be reduced?

Each will be considered in turn.

What are the implications of pregnancy and childbirth on the psychiatric illness?

Although the link between severe psychiatric disorder and childbirth is well established, the increased risk of depressive illness in the postpartum period has come into question following the publication of a number of controlled studies suggesting that depression is no more common in the postpartum period than at any other time in a woman's reproductive life[12–14]. These surprising findings have been attributed to methodological problems in terms of appropriate comparison groups. In particular, the work of Munk-Olsen and colleagues with the Danish psychiatric admission and birth registries demonstrated a 'selection into parenthood' bias, in that women who become mothers are a group at lower risk for psychiatric disorders[15] and studies taking this into account do show an increased risk of depression in the postpartum period, for example an over three-fold increased risk of admission with unipolar depression on postpartum days 31–60 (RR 3.53, 95% CI 2.37–5.05) in the Danish study[15]. In addition, Eberhard-Gran and colleagues[16] found that although rates of depression appeared to be lower in the postpartum period, when other risk factors for depression were controlled for, the risk was actually two-fold higher than at other times.

In contrast, clear evidence supports a specific relationship to childbirth for episodes of severe affective psychosis and for bipolar disorder, in particular[2]. In a large study of the Danish

admission and birth registries that examined over 600,000 pregnancies and their postpartum consequences, women were over 23 times more likely to be admitted with an episode of bipolar disorder in the first postpartum month (RR 23.33, 95% CI 11.52–47.24)[15]. A previous history of admission with bipolar disorder was associated with an even larger increased risk of admission following pregnancy (RR 37.22, 95% CI 13.58–102.4)[17]. Women with bipolar disorder have at least a 1 in 4 risk of suffering a severe recurrence following delivery[18]. Those with a previous history of a severe postpartum episode (postpartum/puerperal psychosis) and those with a family history of postpartum psychosis are at particularly high risk, with greater than 1 in 2 deliveries being affected[18,19] (Figure 1). Postpartum episodes on the bipolar spectrum present a characteristic and close temporal relationship to childbirth. In a study of 111 episodes of postpartum psychosis, 97% of women retrospectively reported the onset of symptoms within the first 2 weeks postpartum, with the majority being on days 1–3[20]. Familial factors have been implicated in the vulnerability to postpartum triggering of bipolar episodes[18]; evidence from linkage studies indicates the possible location of susceptibility genes[21,22].

The risk of admission in the postpartum period also appears to be higher in women with a history of schizophrenia, with Scandinavian register studies documenting increased postpartum admission rates[15,23]. Indeed, one study from the Swedish register found 15% of women with a previous diagnosis of schizophrenia were admitted in the postpartum months[23]. However, the association with childbirth is not as dramatic as it is for bipolar disorder nor does it have such a close temporal relationship to delivery (Figure 2). For bipolar disorder, the risk is for the new onset of an episode of severe affective psychosis. In contrast, women with schizophrenia may be admitted for different reasons, due to difficulties in parenting for example, or owing to the influence of more longstanding psychotic symptoms.

In summary, although the postpartum may be a period of risk for women with a wide variety of psychiatric disorders, it is women with a history of bipolar disorder who are at a particularly high risk of a severe recurrence.

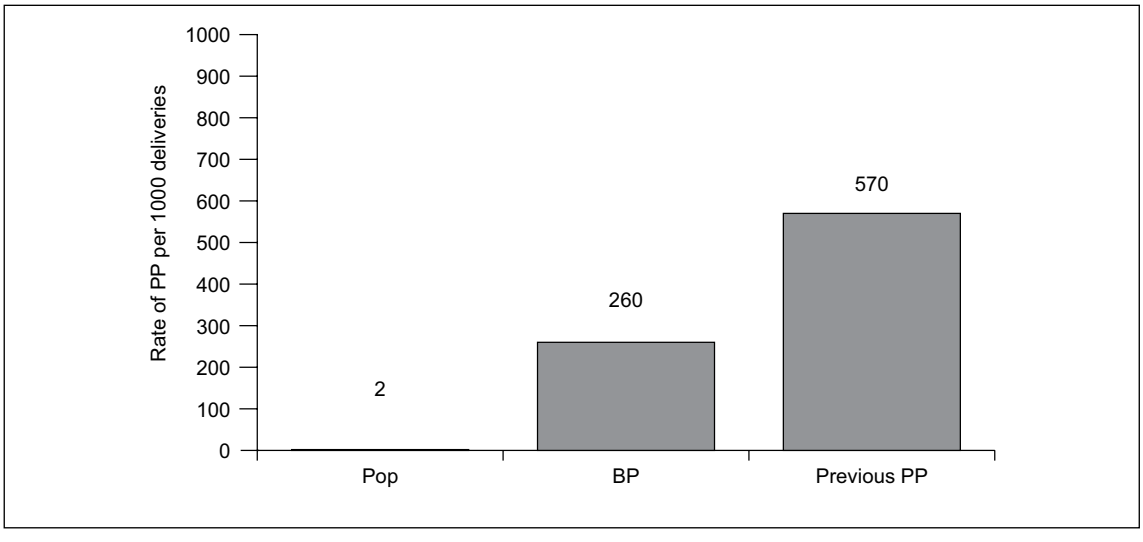

Figure 1 Rates of postpartum psychosis (PP) per 1000 deliveries for women in the general population (Pop), bipolar women (BP) and women who have suffered a previous episode of bipolar affective puerperal psychosis (previous PP). Data from references 18 and 19

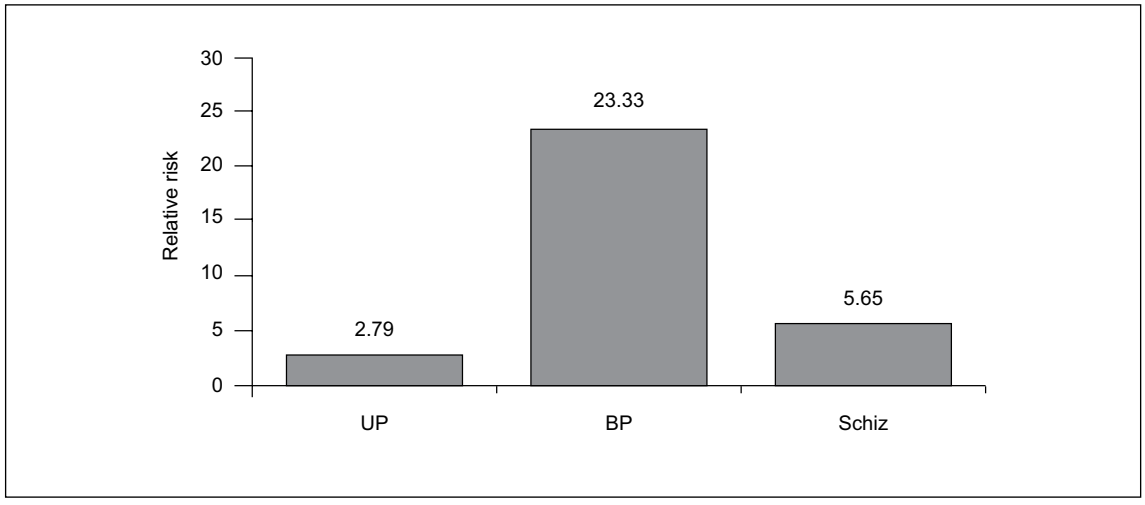

Figure 2 Increased risk of admission following delivery compared to at other times in a woman's life for women with a history of unipolar depression (UP), bipolar disorder (BP) and schizophrenia (Schiz). Data from reference 15

What is the risk to children of developing psychiatric illness?

In addition to considering the effects of pregnancy and childbirth on a woman's illness, families with a history of severe mental illness have another issue to consider when starting a family. It has long been obvious that psychiatric disorders run in families, and family, twin and adoption studies have confirmed a high levels of hereditability for many severe mental illnesses[24]. Prospective parents may have experienced illness themselves or witnessed first hand the suffering of a family member and be concerned about passing on this risk to their children; on occasion, the risk to offspring may be the main concern of women seeking advice. It is usual, however, for prospective parents to overestimate the risk to their children, and it is generally possible to reassure women and their partners.

As is typical for a complex genetic disorder, the risk falls off quickly with the distance from the affected relative. Couples who are concerned, therefore, about a history in their families but who have remained well themselves can be reassured that for them the risk is low. For women or their partners who have suffered episodes of illness themselves, on the other hand, it is still likely that the true risk is lower than they imagine. Table 2 gives the approximate lifetime risk of mood disorder for children of a parent with bipolar I disorder. There are few data to give meaningful estimates for more distant family members, but available evidence suggests rates that are between those for first degree relatives and the general population. These figures can be used as very approximate 'order of magnitude' guides and, with appropriate caveats, can be used to provide information to women and their partners.

What are the risks and benefits of taking medication in pregnancy?

For women with a history of severe mental illness, the biggest issues faced when starting a family often relate to medication. Decisions are made all the more problematic by the lack of data on the reproductive safety of many of

Table 2 The lifetime risks of mood disorder for the offspring of parents who suffer with bipolar I disorder. There are few data to give meaningful estimates for more distant family members but the available evidence suggests rates that are between those for first degree relatives and the general population

Relationship to child	*Lifetime risk of bipolar I disorder*	*Lifetime risk of major depression*
General population	0.5–1.5%	5–10%
Bipolar disorder in mother, father or sibling	4–9%	8–20%

Modified from reference 24

the medications commonly used to treat psychiatric illness. It is disappointing that even for a medication such as lithium that has been in use for over half a century, the sum total of the world literature is not even 200 prospective cases of exposure in pregnancy. In contrast, the situation is certainly better for medications used in psychiatry and additionally used in the treatment of epilepsy, but there are potentially important differences in how medications are prescribed in other disorders, for example in dose and in the particular combinations with other medications.

It is clearly not appropriate in a book such as this to make definitive statements about what are the safest and the most problematic medications to use in pregnancy, as the evidence base is constantly changing, and pronouncements such as these can become dangerously out of date very quickly. Rather, it is more appropriate to deal in general principles that should guide care.

Principles of drug management

There is no right or wrong answer to the question of whether an individual woman should continue a particular medication throughout her pregnancy. Although some medications clearly carry a higher risk than others, sodium valproate being a prime example, each decision should involve consideration of a complex balance of risks and benefits.

The risks involved in continuing specific medications include teratogenicity, toxicity or withdrawal symptoms in the newborn as well as the less certain risks of long-term developmental and cognitive problems in children exposed to the medication *in utero*. Weighed against these risks, however, are the risks of untreated psychiatric disorders, including the risk of a severe recurrence of illness. A range of studies implicate psychiatric disorder as having important consequences on pregnancy, birth weight and gestational age at delivery[25]; in addition, both animal and human literature document the detrimental effect of stress during pregnancy on the fetus[26]. Furthermore, concerns exist that having a severe episode of psychiatric illness at this time may impact on mother–infant attachment with possible longer-term effects on the child[27].

Compelling evidence also suggests that women with unipolar and/or bipolar disorder who discontinue medication in order to conceive risk a severe recurrence of illness. In a naturalistic study of 89 women with bipolar disorder throughout pregnancy, recurrence risk was two-fold greater among women who discontinued versus those who continued mood stabilizer treatment, median time to first recurrence was more than four-fold shorter, and the proportion of weeks ill during pregnancy was five times greater[28]. A similar difference in recurrence risk has been described in women with unipolar depression. Of 201 euthymic women with a history of major mental disorder (MDD), 68% of those who discontinued

their antidepressant experienced a recurrence in pregnancy compared to 26% of those who remained on their medication[29]. In the latter study, however, it is important to note that the women studied had a severe form of unipolar depression (mean duration of 15.4 years with 44% having had five or more episodes), and the same recurrence risks may not apply to the many women with a less severe mood disorder who become pregnant on antidepressant medication.

As a general principle, some women will clearly be looking for guidance, and professionals should not shirk their responsibility to advise on appropriate options. Fully documenting the nature and extent of any discussion is clearly important.

When it comes to the decision about which medication to use, it is important to consider drugs with the best evidence of reproductive safety. However, an individual woman's history of response to various medications is clearly of vital importance. Polypharmacy should be avoided if possible, and the lowest dose of any medication should be used for the shortest period. However, if the fetus is to be exposed to a medication in pregnancy, it would not be sensible to use it in a dose too small to be effective or to stop medication too soon, thus leading to a high risk of relapse.

Inadvertent conception on medication

In an ideal world, all women with a history of severe mental illness would seek advice on a prospective pregnancy at the preconception stage, ideally a number of months or even years before pregnancy is desired, thus giving plenty of time to explore alternative medication options prior to conception. This situation, however, remains unusual. In addition, the regularly estimated 50% of pregnancies that are unplanned may even be higher in women with severe mental illness. Clearly, many women with mental illness will be faced with making difficult decisions in early pregnancy about continuing medication treatments when exposure of the fetus has already occurred.

Decisions regarding the final choice of possible options may be agonizing for the patient and difficult for the health care professional. Possibilities include stopping a medication altogether, although an abrupt discontinuation may lead to withdrawal phenomena or withdrawal precipitation of an episode; switching to a drug with greater evidence of reproductive safety, although this often involves exposure to two medications and the second drug may not have the efficacy of the original; and, finally, continuing the current medication with close monitoring of the fetus and the neonate. Clearly, there are no easy answers, and again a full and individualized risk–benefit analysis is important and should be meticulously documented in the patient record which should also state that the analysis had been accepted and understood by the patient.

How can the risks of becoming unwell be reduced?

As discussed above, women with bipolar disorder are at particularly high risk for severe postpartum episodes[2]. For women with a bipolar history, additional factors that increase risk include having experienced a previous episode of severe illness in relationship to childbirth[19] and having a first degree relative who has experienced an episode of postpartum psychosis[18]. Unfortunately, women at high risk according to these criteria may be well, not in contact with mental health services and may fail to recognize the seriousness of their situation. It is clear, therefore, that all antenatal women should be asked about the above risk factors and protocols should be put in place to ensure that women at potential risk receive a formal risk assessment and management plan[2,30]. How screening and risk management is delivered

may differ considerably according to local circumstances, but all women with a history of bipolar or severe postpartum episodes should be identified by antenatal services.

The risks of illness following childbirth should be discussed with all women with a history of severe mental illness in the childbearing years, and the need for contraception and the importance of seeking help if contemplating pregnancy (or if unexpectedly becoming pregnant) emphasized. As a large proportion of pregnancies are unplanned, all women with childbearing potential merit thorough consideration of potential pregnancy when making decisions about initiating a given medication. This fact lies behind the widespread recognition that, due to its particular teratogenic and developmental effects, sodium valproate should not be used in women in their reproductive years if it can be avoided[30].

Decisions about continuing or stopping medications prior to or during pregnancy are difficult and should be the result of a detailed and individualized cost–benefit analysis. As noted above, stopping medication is not without its own risks[28]. No universal recommendations can be made, and the decision ultimately must rest with the woman and her family. Stopping medication should always be a carefully considered decision and never a reflex response; on the other hand, the decision to start medication for women who become symptomatic in pregnancy or when breastfeeding must be the result of weighing the potential risks from taking medication and the risks posed by the illness itself.

For women with a history of mental illness, attention should also be given to the wide range of additional factors that can influence the health of the pregnancy and the newborn. It is easy to focus exclusively on medication and neglect other issues such as drug and alcohol usage, smoking, diet, obesity and routine antenatal care, including folic acid supplementation prior to the onset of pregnancy and the need for monitoring throughout the gestation. For women taking anticonvulsants that deplete folic acid, a high dose (4–5 mg/day) is a sensible option to consider as opposed to the usual dose of 400 μg. In either situation, the patient must be carefully advised that the neural tube closes by the 28th day of gestation and that initiation of supplementation after that date is without effect. Therefore, patients with a history of mental illness who *might* become pregnant are well advised to supplement as a routine health care measure.

For women at risk, perhaps the most important aspect of management is to maintain close contact with their health care professionals and remain under review during the perinatal period. It is also important to address other avoidable factors that may increase risk such as decreasing general levels of stress, for example, and paying attention to sleep patterns in late pregnancy and the early postpartum weeks. Finally, for women who have discontinued medication during or prior to pregnancy, it is appropriate to consider the introduction of prophylactic medication in the immediate postpartum period. Some evidence exists for the use of lithium in this context[31], but the few studies conducted have been open and retrospective, and there are practical problems with obtaining therapeutic levels quickly to cover the period of risk. These issues have led some psychiatrists to use typical or atypical neuroleptics as prophylaxis and, despite some anecdotal reports of success with this strategy, there are few data in the literature.

EXPLAINING RISK – HOW DO WE EXPLAIN THE COMPLEXITIES OF THESE RISKS AND BENEFITS?

First, it is important to consider the strength of the available evidence. Is there a real risk of teratogenicity? For example, how consistent is the evidence of risk across a range of studies employing differing methodologies? Moreover, although seemingly exact figures

are often given for the risk of particular medications causing malformations, it is important to consider the accuracy of these estimates. With lithium, for example, although a 7% malformation rate is often quoted, the confidence intervals around this estimate are very wide and it is important to convey this uncertainty.

Another major consideration is how to determine what level of information women want or are able to assimilate. Health care professionals need to be sensitive to differences between individual women and, wherever possible, individualize the information as well as the manner in which it is delivered. Finally, what language should be used in our explanations – how do we frame risk? The same data, delivered in a variety of manners, can confer very different messages. Health care professionals must be aware of their own biases and of the temptation to frame the information provided in a way that results in the decision they believe is correct.

Undoubtedly, this whole area is difficult and one in which more research is needed. Regardless, some general guidelines are appropriate. Information should be provided in a user-friendly manner. Changes in risk should be given in absolute rather than relative terms with a uniform denominator[30]. For example, patients are better informed when they are told that risk is increased from 1 in 100 to 3 in 100 rather than risk is increased three fold. Using visual aids, providing written (preferably individualized) information and even audiotaping advice have all been recommended[29].

Because any decision(s) is complex and based on a difficult balance of risks and benefits, a woman may require time to process the information and discuss her thoughts and feelings with her partner, friends and family. These are not discussions that can be fit into a few minutes at the end of a consultation; where a specialist opinion is available (specialists in perinatal/reproductive psychiatry are increasingly found in many countries), women should be referred as early as possible to discuss their options.

SUMMARY AND CONCLUSIONS

For women with a history of severe mental illness, pregnancy raises a number of difficult issues. Severe recurrences are common in relationship to childbirth, and for women with bipolar disorder the risk is very high. Many medications used to keep women well are of known or potential teratogenicity, but stopping medication may be associated with a very high risk of disorder recurrence. At least 50% of pregnancies are unplanned which means that these are issues that must be discussed with all women with reproductive potential. Clearly, the earlier potential pregnancy is considered the better; many months or even years may be required to explore alternative treatment options prior to pregnancy. Finally, although there is a case to be made for perinatal psychiatry specialists and services, mental health is an important consideration for all professionals who come into contact with women in the preconception, antenatal and postpartum periods.

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