Healthcare Improvement Scotland

SIGN
Scottish Intercollegiate Guidelines Network

SIGN 127 • Management of perinatal mood disorders

A national clinical guideline

March 2012

Evidence

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

☑	Recommended best practice based on the clinical experience of the guideline development group

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Contents

1 Introduction

1.1 BACKGROUND

1.1.1 MOOD DISORDERS

There is a particular relationship between mood disorders and pregnancy and the postnatal period. As well as the longstanding recognition of the specific risk faced by some women in the early postpartum, there is an increasing understanding of the effects of antenatal and postnatal mood disorders on pregnancy and the developing child.

Although not distinctive in their presentation at this time, depressive and anxiety disorders are linked to adverse developmental outcomes for infants. How this occurs, however, and the interventions necessary to modify outcomes, is not clear.

Psychosis occurring in the antenatal period may pose particular challenges in terms of management, but the distinct risk, and clinical features, associated with postpartum psychosis place an onus on clinicians to ensure effective and timely risk assessment, detection and management.

1.1.2 DEPRESSION

Depression is a common condition, affecting a large proportion of women of childbearing age. Studies are evenly divided in reporting postnatal depression as either more or less severe than depression at other times[1-4] and there is little evidence that the nature of symptoms differs between antenatal, postnatal and non-postnatal depression.[5,6] In diagnosing depression in the antenatal or postnatal period, there is a risk that normal emotional changes may be mistaken for depression or may mask depressive symptoms.[7]

Perinatal depression is particularly important because it occurs at such a critical time in the lives of the mother, her baby and her family. Failure to treat promptly may result in a prolonged, deleterious effect on the relationship between the mother and baby and on the child's psychological, social and educational development.[8] The relationship between the mother and her partner may also be adversely affected.

A large number of studies have assessed the prevalence of postnatal depression. In those where robust methodology was used, prevalence (whether point or period) ranges from 4.5% to 28% of women in the postnatal period.[4,9-22] The majority cluster around 10% to 15% with one meta-analysis giving a prevalence of 13%.[23] There is some evidence that, while the overall prevalence of postnatal depression is not significantly different from that of depression at other times, there is an increased risk of depression occurring in the early postnatal period (threefold in the first five postnatal weeks).[22,24]

A smaller body of literature has examined the prevalence of antenatal depression, but the findings also suggest little difference in prevalence from depression at other times.[25]

Although research exists on the prevalence of perinatal depression in other cultures, little work has been published on ethnic minority groups within Scotland. It is important to remember that there are widely varying cultural traditions and rituals surrounding pregnancy and childbirth and a lack of cross-cultural equivalence in concepts of depression. Effective detection and management requires an understanding of these differences.

The morbidity of clinical depression is often prolonged by a delay in diagnosis or an inadequate course of treatment. The stigma and shame felt by sufferers who may be reluctant to 'confess' their feelings are frequently important factors in delayed diagnosis. Such reticence is particularly common in perinatal depression, when feelings of guilt and failure may be intense. A mother may fear that she will be thought unfit to care for her child.

Mental illness is also a significant factor in maternal mortality. The UK Confidential Enquiry into Maternal Deaths (CEMD) reports that suicide, although rare, remains one of the leading causes of maternal death in the UK.[26] Serious mood disorder was present in the majority of women who died by suicide.

Antenatal depression is a risk factor for postnatal depression, and many cases of depression detected in the postnatal period may have begun antenatally.[27] Studies using self report questionnaires suggest an association between antenatal depression and adolescent depression in offspring.[28] There is also developing evidence of an association between antenatal depression and poor behavioural outcomes in offspring.[29,30]

Untreated postnatal depression is associated with detrimental effects on infant development. The cognitive, emotional, social and behavioural development of the infant may be affected both in the short and long term.[8,31,32] Depressed mothers give more negative and fewer positive responses in their interactions with their infants. Longer term negative influences of mothers' postnatal depression in the first year of life on infants' language skills, social and emotional development and intelligence quotients (particularly in boys) have been demonstrated.[33-36] More recent evidence appears to confirm the link between postnatal depression and continuing impaired cognitive outcomes into adolescence.[37,38] Cognitive development in the children of postnatally depressed women is not universally impaired. The effect appears limited to those children whose mothers find it difficult to maintain sensitive and active engagement with the infant.[39]

Fathers are significantly more likely to suffer from depression and general health problems if their partners are diagnosed with postnatal depression.[9] This is important in the context of the detrimental effects which depressed partners may have on each other and the consequences for the infant being cared for by depressed parents.

1.1.3 ANTENATAL ANXIETY

Antenatal stress and anxiety have been the focus of much recent research. One study found a prevalence of 14.6% at 18 weeks gestation in a UK community sample,[40] and perinatal anxiety disorders may be more common than depression at this time.[41]

The evidence around the effects of maternal antenatal anxiety on infant outcomes is conflicting[42] and although antenatal anxiety has been linked to alterations in stress response in infants and poorer developmental outcomes,[43,44] there is little evidence on the identification and management of anxiety specifically in the perinatal period. Relaxation exercises have been reported to lower subjective anxiety levels.[45]

This is an important area of research but the current evidence does not yet allow translation of understanding of the links between anxiety and adverse infant outcomes into recommendations on effective interventions.

1.1.4 POSTPARTUM PSYCHOSIS

Postpartum psychosis is a much less common condition, affecting one to two per thousand women.[46-49] This rate represents a significantly increased risk for psychotic illness when compared with other times in a woman's life. Postpartum psychosis is largely affective in nature, although several studies comment on atypical features in the presentation such as mixed affective state, confusion and disturbed behaviour.[50] It typically presents in the early postnatal period, usually within the first month. There is a close link with bipolar affective disorder; the risk of developing postpartum psychosis being substantially increased in women with bipolar disorder, particularly where there is also family history of postnatal bipolar episodes.[51]

1.1.5 MULTIDISCIPLINARY TREATMENT

Delay in delivering adequate treatment for perinatal depression or postpartum psychosis is particularly unfortunate since the response to treatment is good.[52] Effective detection and adequate management of these disorders requires coordination of a wide variety of primary and secondary care services, including midwives, health visitors, clinical psychologists, community mental health services, general practitioners, pharmacists, obstetricians and psychiatrists, with other community agencies, such as voluntary organisations and social services, providing further support.

1.2 REMIT OF THE GUIDELINE

1.2.1 UPDATING THE EVIDENCE

This guideline updates SIGN guideline 60 Postnatal depression and puerperal psychosis, to reflect the most recent evidence. The remit was expanded to include mood and anxiety disorders in the antenatal period. The key questions used to develop the guideline can be found in Annex 1.

Where no new evidence was identified to support an update, text and recommendations are reproduced from SIGN 60. The original supporting evidence was not re-appraised by the current guideline development group.

This guideline provides recommendations based on current evidence for best practice in the management of antenatal and postnatal mood and anxiety disorders. The guideline covers prediction, detection and prevention as well as management in both primary and secondary care. It also outlines the evidence in relation to the use of psychotropic medications in pregnancy and during breastfeeding. This guideline will assist in the development of local evidence based integrated care pathways and networks.

The guideline does not cover the management of other disorders which pose particular risks for women, their pregnancies and infants such as schizophrenia, emotionally unstable personality disorder, eating disorders and substance misuse disorders.

1.2.2 TARGET USERS OF THE GUIDELINE

The guideline will be of interest to midwives, health visitors, general practitioners, pharmacists, psychiatric nurses, psychiatrists, obstetricians, neonatologists, paediatricians, clinical psychologists, social workers, public health physicians, users of services, and all other professionals caring for women and their families. It will also be of value to those commissioning services.

1.3 DEFINITIONS

1.3.1 ANTENATAL POSTNATAL AND PERINATAL PERIODS

This guideline, defines the antenatal period as that from conception to childbirth, the postnatal period as that from childbirth to the end of the first postnatal year, and the perinatal period as an overarching term encompassing both. Although for disorders arising later in the first postnatal year, childbirth is less likely to act as a direct precipitant, our understanding of the importance to both mother and child of early detection and intervention justifies the broad time period.

1.3.2 BABY BLUES

'Baby blues' describes the emotionally labile state experienced by the majority of women following childbirth. Commonly presenting on the second or third postnatal day, it normally resolves by the fifth day with regular professional support and reassurance.

1.3.3 POSTNATAL DEPRESSION

Postnatal depression is regarded as any non-psychotic depressive illness occurring during the first postnatal year. For a significant proportion of women, the illness may have its onset in the antenatal period.[27] The term postnatal depression should not be used as a generic term for all mental illness following birth.

1.3.4 POSTPARTUM PSYCHOSIS

Postpartum psychosis, in the majority of cases, is a severe affective psychosis of acute onset, temporally linked to the postnatal period, and typically presenting in the early postnatal period, usually within the first month.[53] It often presents as a mixed-affective, schizoaffective or manic state, with prominent confusion and fluctuating symptoms, but depressive and schizophrenia-like presentations may also occur. There is increasing evidence of a close link with bipolar affective disorder.[51] This guideline has chosen to adopt the term 'postpartum' rather than 'puerperal'.

1.3.5 NEONATAL ADAPTATION SYNDROME

Neonatal adaptation syndrome refers to a cluster of symptoms in the neonate including irritability, sleep disturbance, persistent crying, tachypnoea, hypoglycaemia, poor thermal regulation, and occasionally seizures, which has been related to the use of psychotropic medication in pregnancy.[54,55] The condition is varyingly referred to as poor neonatal adaptation, neonatal withdrawal or neonatal abstinence syndrome. There is uncertainty whether it is, in all cases, caused by withdrawal, or whether it may be related to excess of the relevant drug in the neonate. For this reason, the guideline has chosen a term which does not ascribe causality.

1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.4.1 PATIENT VERSION

A patient version of this guideline is available from the SIGN website, **www.sign.ac.uk**

1.4.2 PRESCRIBING OF LICENSED MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (product licence). This is known as 'off label' use. It is not unusual for medicines to be prescribed outwith their product licence and this can be necessary for a variety of reasons.

Generally the unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.[56]

Medicines may be prescribed outwith their product licence in the following circumstances:

- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose.

"Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines."[56] Any practitioner following a SIGN recommendation and prescribing a licensed medicine outwith the product licence needs to be aware that they are responsible for this decision, and in the event of adverse outcomes, may be required to justify the actions that they have taken.

Prior to prescribing, the licensing status of a medication should be checked in the most recent version of the British National Formulary (BNF).[56] The summary of product characteristics (SPC) should also be consulted in the electronic medicines compendium (www.medicines.org.uk).

1.4.3 ADDITIONAL ADVICE TO NHSSCOTLAND FROM HEALTHCARE IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

Healthcare Improvement Scotland processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products. No relevant SMC advice or NICE MTAs were identified.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation. The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.

2.1 PREDICTING AND REDUCING RISK

D **All pregnant women should be asked about personal history of postpartum psychosis, other psychotic disorders** (especially bipolar affective disorder and schizophrenia)**, and severe depressive disorder.**

D **All pregnant women should be asked about family history of bipolar disorder or postpartum psychosis.**

D **Women at high risk of postnatal major mental illness should have a detailed plan for their late pregnancy and early postnatal psychiatric management, agreed with the woman and shared with maternity services, the community midwifery team, GP, health visitor, mental health services and the woman herself. With the woman's agreement, a copy of the plan should be kept in her hand held records. The plan should identify what support should be in place and who to contact if problems arise, together with their contact details** (including out of hours)**, and address decisions on medication management in late pregnancy, the immediate postnatal period and with regard to breastfeeding.**

2.2 PREVENTION AND DETECTION

D **Enquiry about depressive symptoms should be made, at minimum, on booking in and postnatally at four to six weeks and three to four months.**

2.3 MANAGEMENT

B **Cognitive behavioural therapies should be considered for treatment of mild to moderate depression in the postnatal period.**

2.4 PRESCRIBING ISSUES

D **All women of childbearing potential who take psychotropic medication should be made aware of the potential effects of medications in pregnancy. The use of reliable contraceptive methods should be discussed.**

C **In view of the risk of early teratogenicity and longer term neurobehavioural toxicity, valproate** (when used as a mood stabiliser) **should not be prescribed to women of childbearing potential.**

✓ If there is no alternative to valproate treatment for a woman of childbearing potential, long-acting contraceptive measures should be put in place. Check the Medicines and Healthcare products Regulatory Agency (MHRA) website for current advice.

3 Predicting and reducing risk

3.1 PREDICTING RISK

3.1.1 RISK FACTORS FOR ANTENATAL DEPRESSION

In a systematic review of risk factors associated with antenatal depression, bivariate analysis identified the following factors: [57]

- maternal anxiety
- life stress
- prior depression
- lack of social support
- domestic violence
- unintended pregnancy
- relationship factors.

2+

Life stress, lack of social support, and domestic violence continued to be associated with antenatal depressive symptoms in multivariate analyses.

3.1.2 RISK FACTORS FOR POSTNATAL DEPRESSION

The evidence suggests that risk factors for postnatal depression are, in the main, no different to the risk factors for non-postnatal depression. Three systematic reviews identified the following risk factors as having moderate to strong associations with postnatal depression:[23,58,59]

- past history of psychopathology and psychological disturbance during pregnancy
- lack of social support
- poor partner relationship
- recent life events
- baby blues.

2+

Weak associations were found with obstetric complications, a history of abuse, low family income and lower occupational status.[23,58-60]

2+
3

In addition to the above factors, cohort and case control studies identified the following as risk factors:[4,61-68]

- parents' perceptions of their own upbringing
- unplanned pregnancy
- unemployment
- not breast feeding
- antenatal parental stress
- antenatal thyroid dysfunction
- coping style
- longer time to conception
- depression in fathers
- having two or more children.

2+

There is evidence from one cohort study of narrowly defined early postnatal unipolar depression, that this type of depression is more likely to occur where there is a family history of such illness, suggesting that there may be a subtype of postnatal depression with specific familial risk.[69]

2+

There is no conclusive evidence on hormonal changes as a risk factor for postnatal depression. In a small experimental study, artificial medical simulation of hormonal conditions, as they would be after a birth, led to a significant change in mood in five of eight women with a previous history of postnatal depression compared with none of eight comparison women, suggesting differential sensitivity to hormone change.[70]

1-

Mothers' mental health may also be affected by the health of the baby. In cohort studies depression has been associated with neonatal risk,[71] stillbirth, neonatal death or Sudden Infant Death Syndrome (SIDS),[72] and very low birth weight (less than 1,500 g).[73,74] **2+**

3.1.3 RISK FACTORS FOR POSTPARTUM PSYCHOSIS

Previous psychiatric history

In a large Swedish registry study the incidence of psychiatric hospitalisation for a postpartum psychotic episode or bipolar episode was significantly increased for women with previous psychiatric hospitalisation, especially if that admission was during pregnancy. Incidence of postpartum psychotic or bipolar episodes among women with no previous history was 0.04% and 0.01%, but among women with previous history, the incidence was 9.24% (psychotic) and 4.48% (bipolar). In this study, 44% of woman hospitalised for a psychotic episode and 41% of those hospitalised for a bipolar episode during the antenatal period were hospitalised again in the postnatal period. Around 90% of hospitalisations in the postnatal period occurred within the first four weeks.[75] A critique of this study suggests that it underestimates the incidence of postpartum psychosis in women with a history of bipolar disorder.[76] **3**

A Danish study found that women with bipolar disorder are at very high risk of readmission in the postnatal period (relative risk (RR) [37,22], 95% confidence interval (CI) 13.58 to102.04 between 10 and 19 days postpartum). A total of 26.9% of women with bipolar disorder were readmitted in the first postpartum year. Women with schizophrenia were also at increased risk of relapse in the first postnatal year, when compared with a range of other psychiatric diagnoses.[77] **3**

Family history

In a UK study examining the influence of family history, women with bipolar disorder who had a family history of postpartum psychosis were at more than a sixfold greater risk of suffering an episode of postpartum psychosis (odds ratio (OR) 6.54, 95% CI 2.55 to 16.76) than parous women with bipolar disorder who had no such family history.[51] **2+**

In a Danish cohort study of first time mothers with no previous history of mental disorders, family psychopathology was a risk factor for onset of postpartum mental disorders (PPMD). The relative risk of PPMD (at up to 30 days) was increased for women with a first degree relative with bipolar affective disorders, (RR 24.03, 95% CI 15.69 to 36.82) schizophrenia-like disorder (RR 8.34, 95% CI 5.34 to 13.04) and unipolar depressive disorder (RR 8.55, CI 6.27 to 11.67). The risk was also raised for women whose partner reported psychopathology (RR 6.86, 95% CI 3.95 to 11.90), although this was based on only 11 cases.[78] **3**

Discontinuation of mood stabiliser

A study from the USA examining discontinuation of mood stabiliser in pregnant and non-pregnant women reported that women who discontinued their mood stabiliser prophylaxis were at increased risk of relapse if they had recently given birth (70% (n=14/20) compared to 24%, (n=6/25) for non-pregnant woman in the same time frame.[79] **3**

Obstetric risk factors in women with previous history of psychiatric disorder

A retrospective single cohort using within-subject comparisons (n=129) explored obstetric risk factors for development of postpartum psychosis in women with bipolar affective disorder or schizoaffective disorder (bipolar type). Primiparity (OR 3.76, 95% CI 1.94 to 7.27), and delivery complications eg breech, fetal distress or cord accidents (OR 2.68, 95% CI 1.15 to 6.25), were independently associated with an episode of postpartum psychosis.[80] **2+**

Summary

The following risk factors are associated with postpartum psychosis:

- pre-existing psychotic illness (especially bipolar disorder)[75,77]
- personal history of postpartum psychosis[75]
- antenatal admission for psychosis or bipolar disorder[75]
- family history of affective psychosis[51,78]
- discontinuation of mood stabiliser prophylaxis[79]
- primiparity[80]
- delivery complications.[80]

3.2 REDUCING RISK

Where risk factors for perinatal mood disorders are present, it may be possible to identify women at high risk of developing mood disorder during pregnancy or the early post partum.

In a survey of NHS Boards in Scotland, although all had policies for the prevention of postnatal depression, few had policies specifically around prevention of postpartum psychosis.[81] **3**

The World Health Organisation (WHO) consider that effective screening programmes should have:[82] **4**

- adequate understanding of the condition
- a simple, safe, validated screening test with appropriate cut-off levels
- effective treatment for those screened as positive
- adequate resources to ensure any programme is implemented in an acceptable, expert manner.

Screening for postnatal depression has been assessed by the UK National Screening Committee (NSC). It concluded that "the Edinburgh Postnatal Depression Scale (EPDS) should not be used as a screening tool. It may, however, serve as a checklist as part of a mood assessment for postnatal mothers, when it should only be used alongside professional judgement and a clinical interview. The professional administering it should have training in its appropriate use, and should not use it as a pass/fail screening tool."[83] A consultation document from the NSC published in 2010, which reviewed and updated the evidence, continued to recommend that there was insufficient evidence to support the implementation of a population screening programme for postnatal depression.[84] **4**

While evidence may not yet be available to recommend population screening programmes, if risk reduction strategies are instigated they should conform to the best available research evidence on effectiveness, be adequately resourced, and include ongoing evaluation as an integral part of the programme.

3.2.1 ANTENATAL RISK REDUCTION – POSTNATAL DEPRESSION

A systematic review identified three studies validating the EPDS in the antenatal period. The positive predictive value (PPV) for antenatal major depression ranged from 60-88%.[85] **2++**

A Cochrane systematic review of two randomised controlled trials (RCTs) concluded that, although the use of antenatal psychosocial assessment tools, EPDS and Antenatal Psychosocial Health Assessment (ALPHA), may increase clinician awareness of psychosocial risk, there is insufficient evidence that routine assessment itself leads to improved perinatal mental health outcomes.[86] **1++**

B **Psychosocial assessment in the antenatal period for the purposes of identifying risk of postnatal depression should not be routinely offered.**

3.2.2 ANTENATAL RISK REDUCTION – POSTPARTUM PSYCHOSIS

While no specific screening tools have been devised to identify women at high risk of postpartum psychosis, there is a convincing body of evidence that certain risk factors can be easily identified in pregnancy and are highly predictive *(see section 3.1.3)*. These include:

- personal history of postpartum psychosis
- personal history of bipolar affective disorder.

Risk is further increased if there is a family history of postpartum psychosis or bipolar affective disorder. Based on this evidence, enquiry about such risk factors has been recommended in expert reports.[87,88] **4**

D **All pregnant women should be asked about personal history of postpartum psychosis, other psychotic disorders** (especially bipolar affective disorder and schizophrenia)**, and severe depressive disorder.**

D **All pregnant women should be asked about family history of bipolar disorder or postpartum psychosis.**

The Confidential Enquiries into Maternal Deaths and the Royal College of Obstetricians and Gynaecologists (RCOG) also recommend that all pregnant women who are identified as being at high risk of postpartum psychosis should be assessed by mental health services (even if currently well) and should have a written plan for their management in late pregnancy and the early postnatal period, which is shared with the woman and all professionals involved.[26,87] **4**

D **The following groups should be considered as high risk for post partum psychosis:**

- **women with a personal history of postpartum psychosis**
- **women with a personal history of bipolar affective disorder**

Risk is further increased if there is additional family history of postpartum psychosis or bipolar affective disorder.

D **Women at high risk of postnatal major mental illness should have a detailed plan for their late pregnancy and early postnatal psychiatric management, agreed with the woman and shared with maternity services, the community midwifery team, GP, health visitor, mental health services and the woman herself. With the woman's agreement, a copy of the plan should be kept in her hand held records. The plan should identify what support should be in place and who to contact if problems arise, together with their contact details** (including out of hours)**, and address decisions on medication management in late pregnancy, the immediate postnatal period and with regard to breast feeding.**

D

- **Referral for specialist psychiatric assessment should be considered for women with current mood disorder of mild or moderate severity who have a first degree relative with a history of bipolar disorder or postpartum psychosis.**
- **In the absence of current illness, such a family history indicates a raised, but low, absolute risk of early postpartum serious mental illness. Where family history only is identified, information should be shared between primary care and maternity services, and any evidence of mood disturbance during pregnancy or in the postnatal period should lead to referral to mental health services.**

A sample care plan is provided in the RCOG Good Practice Statement on management of women with mental health issues during pregnancy and the postnatal period and this is reproduced in Annex 2.[87]

4 Prevention and detection

4.1 PREVENTION OF ANTENATAL DEPRESSION

No evidence was identified on prevention of antenatal depression.

4.2 PREVENTION OF POSTNATAL DEPRESSION

An effective intervention to prevent postnatal depression would benefit women in reducing depression and its impact on their child and close relationships. Much of the existing research in this area uses populations scoring highly on measures of depressed mood (most commonly the EPDS). It may be argued that these women have current illness and any interventions are therefore targeted at treatment rather than prevention. For the purposes of this review, studies were included where interventions occurred in pregnancy and postnatal outcomes were measured, or where the study intention was clearly stated as prevention rather than treatment.

4.2.1 PSYCHOLOGICAL AND PSYCHOSOCIAL INTERVENTIONS

The NICE Antenatal and Postnatal Mental Health (APMH) guideline reviewed studies on non-pharmacological treatments for the prevention of depression in groups where risk factors were present. Most of the studies were focused on the postnatal period.[89] The review concluded that there is some benefit in providing interventions in this group of women in the postnatal period, particularly for those with subthreshold symptoms. Interventions which were recommended included social support and short term structured psychological treatments such as interpersonal therapy (IPT). In study populations without risk factors or without specific identification of risk factors, treatments showed no effect.[89] **2+**

A meta-analysis of 15 trials covering a range of psychosocial and psychological interventions for preventing postnatal depression found that the only intervention to have a clear preventive effect was intensive postnatal support provided by a health professional, although this effect was not maintained up to 16 postnatal weeks. Although caution was advised due to heterogeneity in the studies, interventions with greater effect were those which were individual rather than group based, postnatal rather than antenatal and postnatal, and those focusing on at-risk populations. Overall the authors concluded that there was insufficient evidence to support psychosocial or psychological interventions to prevent postnatal depression.[90] **2++**

Since this meta-analysis, two further studies have demonstrated effectiveness for brief interpersonal psychotherapy for women who have depressive symptoms in pregnancy, in reducing progression to depression in the postnatal period.[91,92] **1+**

One study found evidence for the effectiveness of individualised telephone-based peer support (by trained mothers with experience of postnatal depression) administered in the first two weeks postpartum to high-risk women.[93] **1+**

In a further study, no effect was found for intensive health visitor follow up, beginning at 35 weeks gestation, for women at high risk of postnatal depression.[94] **1+**

There is insufficient consistent evidence on which to base a recommendation for psychological or psychosocial interventions for the prevention of postnatal depression.

4.2.2 PHARMACOLOGICAL THERAPIES

A Cochrane review identified two studies on the use of antidepressants to prevent postnatal depression in women who had previously suffered from postnatal depression; one on nortriptyline and one on sertraline.[95] Only the sertraline intervention demonstrated an effect in reducing progression to depression. It was concluded that the evidence base was not strong enough to recommend the use of antidepressants for the prophylaxis of postnatal depression in women at high risk. **1++**

A Cochrane review on the use of oestrogens and progestins for the treatment and prevention of postnatal depression identified one study comparing synthetic progestogen (norethisterone enanthate) with placebo, administered within 48 hours of birth for the prevention of postnatal depression.[96] Norethisterone enanthate treatment was associated with a significantly higher risk of recurrence of postnatal depression. **1++**

There is insufficient evidence to make any recommendations for or against the use of antidepressants or oestrogen hormonal therapies in the prevention of postnatal depression. There is some evidence that progestins may worsen outcome.

4.3 PREVENTION OF POSTPARTUM PSYCHOSIS

Two cohort studies examined the use of prophylactic lithium given either in late pregnancy or immediately after delivery for prevention of postpartum psychosis in women at high risk. The first (n=21) found that only two of the treated patients developed illness (<10%), substantially lower than their estimate of 20%.[97] The second study examined 27 women with bipolar mood disorder. Only one of 14 who received mood stabilisers developed postpartum psychosis compared with eight of 13 untreated women.[98] Both of these studies were limited by their open design, but their findings are reinforced by a further study showing a high risk of postnatal relapse in bipolar women who discontinue lithium during pregnancy.[79] **2-**

One study compared the use of olanzapine, either alone or in combination with other drug treatments with use of previously effective medication or no medication, in 25 postnatal women with a history of bipolar disorder. Two women (18.2%) in the olanzapine group relapsed compared to eight (57.1%) in the non-olanzapine group.[99] This difference failed to reach significance. The study was limited by small numbers and open design. One further study, again with an open design, failed to find a benefit for sodium valproate in preventing postnatal relapse in women with bipolar disorder.[100] **1-**

The evidence suggests that lithium and possibly olanzapine are effective treatments when used to prevent postpartum psychosis in high risk groups but it is not of sufficient quality to support a recommendation.

✓ Women who have been treated with effective prophylaxis for psychotic disorder should have prophylactic treatment reinstated after birth.

4.4 DETECTION OF ANTENATAL AND POSTNATAL DEPRESSION

✓ When assessing women in the perinatal period it is important to remember that normal emotional changes may mask depressive symptoms or be misinterpreted as depression.

✓ Tools to detect depression will not aid in the detection of other mental illnesses, such as anxiety, obsessive compulsive disorder, eating disorders or psychotic disorders.

The NICE APMH guideline describes studies indicating that the use of brief focused questions (Whooley questions) addressing mood and interest and requiring simply a 'yes' or 'no' response may be effective in detecting depression when compared with a standardised psychiatric interview. ("During the last month, have you often been bothered by feeling down, depressed or hopeless?" and "During the last month have you often been bothered by having little interest or pleasure in doing things?"). With the addition of a third question, "Is this something with which you would like help?", this interview was found to have a positive predictive value (PPV) for depression of 32% and a negative predictive value (NPV) of 99%.[89] **2+**

A comprehensive health technology assessment (HTA) examining the evidence around methods to identify postnatal depression in primary care concluded that the evidence surrounding clinical effectiveness and cost effectiveness of methods to identify postnatal depression is lacking and there is insufficient evidence to support the use of the Whooley questions.[101] **2++**

The most commonly used tool in the postnatal period is the EPDS. The sensitivity, specificity and predictive value of this self report tool are dependent on the cut-off scores chosen. A systematic review of validation studies for the tool identified 34 studies conducted in a postnatal population. There was heterogeneity between the studies and large variation in estimates of sensitivity and specificity. At cut-off value of 9 or 10 for detecting postnatal depression, the scale had a PPV ranging from 9-64% for major depression. At cut-off value 12 or 13, the PPV for major depression ranged from 17-100%. The review also examined use of the tool in languages other than English and concluded that the EPDS performs best at higher cut-off point and is best for English speaking populations.[85] **2++**

Concerns have been expressed that the EPDS may perform less well in patients who have psychomotor symptoms (often suggestive of severe depression). There is no clear evidence on the timing and number of administrations, and limited evidence on appropriate cut-offs to use.[89] **2++**

Whilst there is expert consensus on the benefits of detecting depression,[26,89] there is insufficient evidence to recommend the use of the EPDS or Whooley Questions as tools with sufficient accuracy in either the antenatal or postnatal period. However, their use is likely to have benefit in facilitating discussion of emotional issues and aiding ongoing clinical monitoring.[84] **4**

The NICE APMH guideline provides guidance on when enquiry around depressive symptoms should be made.[89] **4**

D **Enquiry about depressive symptoms should be made, at minimum, on booking in and postnatally at four to six weeks and three to four months.**

D **For women regarded to be at high risk** (those with previous or current depressive disorder)**, enquiry about depressive symptoms should be made at each contact.**

✓ The EPDS or the Whooley Questions may be used in the antenatal and postnatal period as an aid to clinical monitoring and to facilitate discussion of emotional issues.

✓ Where there are concerns about the presence of depression, women should be re-evaluated after two weeks. If symptoms persist, or if at initial evaluation there is evidence of severe illness or suicidality, women should be referred to their general practitioner or mental health service for further evaluation.

4.5 DETECTION OF POSTPARTUM PSYCHOSIS

The presentation of postpartum psychosis is described in section 1.1.4.[10,53,77] The Confidential Enquiries into Maternal Deaths also highlight the rapid progression from mild symptoms of anxiety and emotional lability to profound psychosis, sometimes within a matter of hours. In the most recent Enquiry initial symptoms led to incorrect diagnosis in 27.5% of reported cases.[26]

✓ Any significant and unexpected change in mental state in late pregnancy or the early postnatal period should be closely monitored and should prompt referral to mental health services for further assessment.

5 Management

5.1 INTRODUCTION

Antenatal depression is the best predictor of postnatal depression. Timely intervention may help prevent consequent adverse effects on the child and family. Postpartum psychosis is typified by early onset and rapid progression. Prompt recognition and management may help prevent the most severe consequences for the woman and her family.[26]

Untreated postnatal depression may be prolonged and may have a deleterious effect on the relationship between mother and baby and on the child's cognitive and emotional development.[8,102] However, the response to both pharmacological and psychosocial interventions is good.[52] **2+** **1+**

The choice of treatment for postnatal depression should be governed by efficacy, previous response to treatment, incidence of side effects, likely compliance, patient preference and, in the case of pharmacological therapies, safety of use when pregnant or breast feeding *(see section 6)*.

While maternal mental illness, in itself, does not place children at risk, or imply that they will not receive good parenting, there are instances where the mother and infant may be at risk because of the mother's mental illness. Although rare, suicide and infanticide do occur. Multidisciplinary risk assessment and risk management protocols and, where necessary, local child protection procedures should always be followed when there is the potential for serious harm to the mother and/or baby.[103] These should provide a protective framework by ensuring good communication between the family and professionals. Further guidance on child protection issues is available in the Children (Scotland) Act 1995 and associated guidance,[104] and in local child protection guidelines. Health professionals should always work closely with social services and other agencies where risk is identified, and share information according to local protocols, always recognising that the safety of the child takes precedence over issues of confidentiality.

5.2 PSYCHOSOCIAL MANAGEMENT

5.2.1 PSYCHOLOGICAL THERAPIES

✓ Practitioners delivering psychological therapies should be trained to accepted levels of competency, participate in continuing professional development and receive ongoing supervision.

✓ Given the importance of early intervention in a maternity context, services delivering psychological therapies should prioritise early response to pregnant and postnatal women.

A Cochrane meta-analysis examining effectiveness of psychological interventions compared with usual care (measured at final study assessment within the first year) in patients with postnatal depression found benefit when all interventions from nine trials were combined. In examining variation by intervention type there was benefit for cognitive behavioural therapy (CBT) (five studies) (RR 0.72, 95% CI 0.57 to 0.90) and for IPT (one study) (RR 0.80, 95% CI 0.66 to 0.98). There was no effect for psychodynamic therapy. This is consistent with an earlier meta-analysis which incorporated medicines and psychological therapies.[105] A third meta-analysis found no evidence favouring one intervention over another when it compared psychosocial and psychological approaches. This conclusion was, however, based on a small number of comparisons.[106] **1++**

A subsequent systematic review examined home based interventions to prevent and treat postnatal depression. It found evidence in favour of CBT, non-directive counselling and psychodynamic therapies, but acknowledged that the patient numbers were small and conclusions of limited usefulness.[107] **1+**

One high quality cluster RCT addressing the effectiveness of training health visitors from 101 practices to provide psychologically informed sessions to women with an EPDS score ≥12 at six weeks postnatally, found reduced depression scores in the intervention groups at six and 12 months. There were no differences between cognitive behavioural approaches and person centred approaches.[108] **1+**

Overall, there is good evidence that psychological interventions are more effective than treatment as usual. The greatest evidence is for the effectiveness of CBT, cognitive behavioural approaches, and IPT in treating non-psychotic depressive symptoms in the postnatal period. The evidence is less strong, for non-directive counselling, psychodynamic therapy and group therapy. Cognitive behavioural approaches emerge with the best, though limited, evidence base.

B **Cognitive behavioural therapies should be considered for treatment of mild to moderate depression in the postnatal period.**

No evidence was identified for the effectiveness of self directed or computer based interventions in this patient group.

No evidence was identified for the effectiveness of psychological interventions for postpartum psychosis.

5.2.2 SUPPORTIVE THERAPIES

The evidence base for supportive and family-focused interventions for perinatal depression is based on a very wide range of interventions and settings with great diversity in the composition of patient groups and the range of outcome measures examined. Studies tend to be small and, although many report benefits, it is not possible to provide evidence based recommendations for specific interventions.

A systematic review identified no evidence to support universal provision of postnatal support to improve maternal mental health but some evidence to suggest that high risk populations may benefit from interventions postnatally, such as home visits and peer support.[109] **1+**

A systematic review identified a small pilot study (n=42) suggesting that mothers who had telephone-based peer support had a decrease in depressive symptoms compared with mothers having usual care.[110] **1++**

5.2.3 COUPLE INTERVENTIONS

Women diagnosed with antenatal depression (n=47) had reduced depression and anxiety symptoms following a couple-based massage intervention where partners were taught to provide massage twice each week for 12 weeks. The comparison was with a more general support group. Scores on a relationship quality questionnaire were improved and partners reported a reduction in depressed mood, anxiety and anger across the course of the massage therapy period.[111] **1+**

One small study (n=29) suggests that couples involved in an individual or group intervention focused on parenting, and their reactions, to it experience a reduction in their depressive symptoms and a benefit to their general health as measured by the general health questionnaire.[112] **1+**

5.2.4 MOTHER INFANT INTERVENTIONS

There is evidence that interventions to address postnatal depression may not alter developmental outcomes for infants.[37] For this reason, specific interventions that addressed the mother-infant relationship were examined. No evidence was found in relation to antenatal depression, anxiety disorders or postpartum psychosis.

An RCT found that a toddler-parent psychotherapy intervention significantly improved the proportion of secure attachments in mother-infant pairs where the mothers had major depression since the birth of the child.[113] **1+**

An RCT examined the effect of mother-baby interventions on the quality of mother-child interaction, infant-mother attachment security, and infant socioemotional functioning in a group of depressed mothers with infants aged 1-12 months. The intervention group received home visits and the control group received support by telephone. The intervention had a positive effect on mother-infant interaction. Infants in the experimental group had higher scores for attachment security and for competence (one aspect of socioemotional functioning).[114] **1-**

In a pilot study mothers attending an infant massage group showed a clinical reduction in EPDS scores over four weeks and had improved outcomes in comparison with mothers attending support groups. There was no evidence of harm from the intervention.[115] **1-**

A small randomised controlled study demonstrated that attending infant massage classes had a significant and positive effect on both mother-infant interaction and depressive symptoms in the mother.[116,117] 1-

C **Where there is evidence of impairment in the mother-infant relationship, additional interventions, specifically directed at that relationship, should be offered.**

5.2.5 PHYSICAL ACTIVITY

The SIGN guideline on non-pharmaceutical management of depression recommended that structured exercise may be considered as a treatment option for patients with depression.[118] Structured exercise was defined as exercise undertaken three or more times each week at an intensity sufficient to provide an energy expenditure of 70-80% of heart rate reserve. The guideline recommendation was based largely on a Cochrane systematic review and meta-analysis which found exercise to be clinically effective.[119] 4

A well conducted meta-analysis of five randomised and quasi-randomised trials reported that, when compared with no exercise, exercise reduced the symptoms of postnatal depression (weighted mean difference in EPDS score -4.00 points (95% CI -7.64 to -0.35). There was significant heterogeneity and statistical significance was lost when a study using exercise as part of a combined intervention was excluded.[120] 1++

An RCT concluded that women with postnatal depression who adhered to an exercise intervention which consisted of an individually prescribed programme as well as ongoing support and guidance had significant reductions in the Hamilton Depression Rating Scale (HAM-D) and EPDS when compared with women receiving care as usual.[121] 1+

Reducing fatigue through exercise may help alleviate other symptoms of depression. A 12 week home based exercise programme was effective in decreasing physical fatigue in new mothers who have depression.[122] 1+

B **Support for structured exercise may be offered as a treatment option for patients with postnatal depression.**

5.3 PHARMACOLOGICAL MANAGEMENT

5.3.1 ANTENATAL DEPRESSION

It is reasonable to assume that depression in the antenatal period will respond to the same interventions demonstrated to be effective for treating depression at other times. When considering interventions in pregnancy there should be an emphasis on timely non-pharmacological treatments, unless there is clear benefit to be gained from drug therapies.

5.3.2 POSTNATAL DEPRESSION

Antidepressants

A meta-analysis of effectiveness of treatments for depression in pregnancy and postpartum found large effect sizes for antidepressant medication alone.[105] 1+

An RCT comparing paroxetine with placebo for eight weeks in women diagnosed with major depression within three months post-delivery showed that paroxetine treatment resulted in a higher remission rate compared to placebo (OR 3.5, 95% CI 1.1 to 11.5). The rate of adverse effects did not differ significantly between the two study groups.[123] 1+

A double blind RCT of eight weeks treatment of sertraline versus nortriptyline in women diagnosed with major postnatal depression showed that the proportion of women who responded and remitted with sertraline treatment (56%) was not significantly different from those who were treated with nortripyline (69%).[124] 1+

See section 6 for recommendations on the use of pharmacological therapies in women who are breast feeding.

B **Selective serotonin reuptake inhibitors and tricyclic antidepressants may be offered for the treatment of moderate to severe postnatal depression, but with additional considerations regarding the use of antidepressants when breast feeding.**

Hormonal therapies

A Cochrane review of RCTs on the use of oestrogens and progestins for the treatment of postnatal depression identified one study comparing transdermal oestrogen therapy with placebo for the treatment of postnatal depression diagnosed within 12 weeks postnatally. Oestrogen therapy in women with severe depression was associated with a greater improvement in depression scores compared to placebo. Concerns about the possible adverse effects of oestrogens, such as endometrial hyperplasia and thrombosis, limit its use, with harms likely to outweigh benefits.[96] **1++**

B **The use of oestrogen therapy in the routine management of patients with postnatal depression is not recommended.**

St John's Wort

No evidence was identified relating specifically to the treatment of postnatal depression with St John's Wort *(Hypericum perforatum)* or other alternative medicines. The potential for interactions with other prescription medicines including antidepressants and oral contraceptives, and the lack of standardisation and robust pharmacoregulation of these products means their use cannot be recommended in pregnancy and lactation.[118]

✓ St John's Wort and other alternative medicines should not be used during pregnancy and lactation.

5.3.3 POSTPARTUM PSYCHOSIS

As the nature of postpartum psychosis is usually affective, treatments used for affective and schizoaffective psychoses in general are also appropriate for postpartum psychosis. Such treatments would typically involve one or more drugs from the antidepressant, mood stabilising or neuroleptic groups and/or ECT.

The NICE APMH guideline recommends the use of medication which would normally be used in the management of bipolar disorder, schizoaffective disorder or schizophrenia, prioritising treatments which have less evidence of adverse effects in breast feeding *(see section 6)*.[89] **4**

D **Postpartum psychosis should be managed in the same way as psychotic disorders at any other time, but with the additional considerations regarding medication use during breast feeding.**

5.4 ELECTROCONVULSIVE THERAPY

No good quality evidence was identified relating to the use of electroconvulsive therapy (ECT) in pregnancy. Based on case reports, a review concluded that ECT administered during pregnancy is effective and that the risks to the woman and child are low.[171] **3**

5.5 SERVICE DESIGN

A service evaluation study highlighted variation in practice around service design and delivery in the area of perinatal mental health services with practice based on local clinical interest.[125] Whilst this study was in England it, in part, reflects care in Scotland. **3**

The NICE APMH Guideline, and the Confidential Enquiries into Maternal Deaths, recommend the development of specialised perinatal mental health services. NICE recommends the development of clinical networks which would provide local specialist multidisciplinary perinatal mental health services, including community and maternity liaison teams (or specialised functions within general teams in smaller areas) and access to regional inpatient specialist services for all women requiring admission in the first postnatal year.[26,89] These are supported by further guidance from the Royal College of Psychiatrists and the Royal College of Obstetricians and Gynaecologists.[76,77] The guideline development group has applied these recommendations to a Scottish setting, recognising the particular needs and strengths of service organisation in this context. **4**

D **A national managed clinical network for perinatal mental health should be centrally established in Scotland. The network should be managed by a coordinating board of health professionals, health and social care managers, and service users and carers. The network should:**

- **establish standards for the provision of regional inpatient specialised mother and baby units, community specialised perinatal teams** (or specialised perinatal functions of general adult mental health teams in smaller, or more remote, areas)**, and maternity liaison services**
- **establish pathways for referral and management of women with, or at risk of, mental illness in pregnancy and the postnatal period**
- **establish standards** (in liaison with specialist mental health pharmacists) **for the provision of advice and guidance to maternity and primary care services on the use of psychotropic medication in pregnancy and breast feeding**
- **establish competencies and training resources for health professionals caring for pregnant or postnatal women with, or at risk of, mental illness, at levels appropriate to their need**
- **ensure that all pregnant and postnatal women with, or at risk of, mental illness have equitable access to advice and care appropriate to their level of need.**

A systematic review examined the effectiveness of mother and baby units for mothers with schizophrenia or psychoses, and their children, who required admission during the first postnatal year, in comparison to standard care on a ward without a mother and baby unit. The review found no evidence to support or refute the effectiveness of mother and baby units.[126] **1++**

Admission of mothers with their babies to general psychiatric wards is unlikely to ensure the safety and security of the baby. Guidelines published by the Royal College of Psychiatrists discourage such ad hoc arrangements and recommend the provision of mother and baby units.[88] In Scotland, the Mental Health (Care and Treatment) (Scotland) Act 2003 and associated national guidance states that infants should not be admitted to general psychiatric wards.[127,128] **4**

D **Mothers and babies should not routinely be admitted to general psychiatric wards.**

6 Prescribing issues

6.1 GENERAL PRINCIPLES

Clinicians are understandably cautious about prescribing drugs during pregnancy or when a mother is breast feeding due to the possible risks to the fetus and infant. In early pregnancy the risk of teratogenesis is the main concern. The risks associated with psychotropic drugs in later pregnancy include neonatal toxicity or poor neonatal adaptation following delivery and the possibility of a long term impact on the infant's neurodevelopment.[129] Individual drugs may have other specific risks. During breast feeding many drugs taken by the mother are excreted in milk and ingested by the infant, with consequent concerns about their impact on the infant with regard to both short term toxicity and longer term neurodevelopment.[130] The level of concern about prescribing during pregnancy and lactation is reflected in the Terms of Marketing Authorisation with most psychotropic drugs not being licensed for use in pregnancy and lactation *(see section 1.4.2)*. This underlines the need to give very careful consideration to the risks and benefits of prescribing psychotropic medication at this time. Expert guidance provides a number of general principles for prescribing in pregnancy.[89,131]

✓ When prescribing psychotropic medication during pregnancy or breast feeding the following principles should be applied:

- involve the woman, and her family where appropriate, in all decisions about treatment, including an individualised assessment of benefit versus risk
- be aware that not treating mental illness in pregnancy or the postpartum period may in itself be associated with adverse outcomes for the woman, her pregnancy, and her infant
- establish a clear indication for drug treatment (ie the presence of significant illness in the absence of acceptable or effective alternatives)
- choose treatments with the lowest known risk
- in choosing medication in pregnancy consider the implications for breast feeding and the benefits of avoiding the need to switch drugs (including the minimisation of withdrawal effects)
- use treatments in the lowest effective dose for the shortest period necessary
- be aware of potential drug interactions, particularly with non-psychotropics, and aim for monotherapy
- where there is no clear evidence base that one drug is safer than another, the safest option is not to switch. The only drug with a clear indication for switching on safety grounds is valproate *(see section 6.3.4)*
- be aware of the potential effects of pregnancy and childbirth on drug pharmacokinetics and pharmacodynamics (eg the need for dose adjustments as pregnancy progresses and specific risks during labour and following birth)
- be aware that although knowledge of teratogenic effects of psychotropic drugs is increasing, understanding of the long term neurodevelopmental effects of such medications in pregnancy and breast feeding is extremely limited
- be aware of the need for close monitoring for change in mental state where a woman decides to cease her usual medication. Stopping medication may lead to relapse of illness
- where there is known risk, ensure that women are offered appropriate fetal screening and monitoring of the neonate for adverse effects. This may include involvement of neonatal and or paediatric services
- be aware that premature or ill babies are more at risk of harmful drug effects
- monitor the infant for specific drug side effects as well as feeding patterns, growth and development
- caution women against sleeping in bed with the infant, particularly if taking sedative drugs.

6.2 PSYCHOTROPIC MEDICATION USE IN THE PRE-PREGNANCY PERIOD

As many pregnancies are unplanned, some are exposed inadvertently to psychotropic medication.

While no evidence was identified on the effectiveness of preconception counselling for patients taking psychotropic medications, the Maudsley Prescribing Guidelines suggest that the possibility of pregnancy should always be discussed and where there are known teratogenic effects women should be made aware of them even if not planning a pregnancy.[131] **4**

D **All women of childbearing potential who take psychotropic medication should be made aware of the potential effects of medications in pregnancy. The use of reliable contraceptive methods should be discussed.**

✓ If a woman taking psychotropic drugs is planning a pregnancy, consideration should be given to discontinuing treatment if the woman is well and at low risk of relapse.

6.3 PSYCHOTROPIC MEDICATIONS IN PREGNANCY

6.3.1 INTRODUCTION

For newly diagnosed mental illness in pregnancy, clinicians should establish whether there is a clear indication for drug treatment. If non-drug treatments are not effective or appropriate, use an established drug at the lowest effective dose.[131] For a woman with serious mental illness, at high risk of relapse, abrupt discontinuation of treatment on discovering the pregnancy is unwise: relapse may ultimately be more harmful to the mother and child than continued effective drug therapy. Unless there is a clear indication, clinicians should consider continuing with the current (effective) medication rather than switching to an alternative.[131] **4**

Therapeutic drug monitoring is advised for women taking mood stabilisers (such as lithium, carbamazepine, and lamotrigine) due to pregnancy-related changes in absorption, distribution, metabolism and elimination, which may lead to treatment failures.[132,133] **4**

6.3.2 ANTIDEPRESSANTS

Spontaneous abortion

Two systematic reviews investigated the association of spontaneous miscarriage with exposure to the most commonly used selective serotonin reuptake inhibitors (SSRIs), which include citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline, within the first 20 weeks of pregnancy. The poor quality of studies and the risk of confounding due to depression itself and the inclusion of elective abortions in some studies prevent robust conclusions being drawn about the association between SSRI use and spontaneous abortion.[134,135] **2++** **2+**

Exposure to trycyclic antidepressants (TCAs), which included amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline and trimipramine, within the first 20 weeks of pregnancy was associated with a non-statistically significant trend towards increased risk of spontaneous abortion but robust conclusions are limited by poor study quality and lack of controlling for women's reproductive history. The authors of the systematic review point out that confounding by the underlying depressive illness is likely.[134] **2++**

Congenital malformation

A systematic review identified four meta-analyses, three of which found no association of antidepressant exposure in the first trimester (SSRI or other antidepressant) with increased risk of major or of cardiac malformations. One meta-analysis found that first trimester paroxetine exposure was associated with increased risk of major and of cardiac malformations. The review also examined 26 cohort studies and five case control studies. Of the fifteen prospective cohort studies, the design likely to provide the most robust evidence, only two studies reported a significant association between antidepressant exposure and congenital malformation. The first examined fluoxetine exposure and found a significant association with at least three minor congenital malformations. The second study examined both fluoxetine and paroxetine exposure and found fluoxetine but not paroxetine to be associated with cardiac malformation.[136] **2++** **2+**

Two studies were examined separately, the design of which addressed potential confounding factors related to the depression itself by having as a control group women with depression who were not using medication. Both the studies found no association with malformation but both were underpowered.[136]

A retrospective cohort study noted low absolute risks of malformations but confirmed a statistically significant increase in risk of ventricular septal defects with fluoxetine, risk of right ventricular outflow tract defect with paroxetine and neural tube defect with citalopram.[137] **2++** **2+**

The UK Teratology Information Service has since expanded the evidence review to include additional retrospective and prospective cohort studies and note that the available data on antenatal paroxetine exposure and those on SSRIs as a class are conflicting and that if there is an association between paroxetine exposure and cardiovascular malformations, the absolute increase in risk appears to be small.[138]

Neonatal adaptation

In a systematic review of 17 studies, 15 of the studies reported some association between gestational exposure to antidepressants (mainly SSRIs) and neonatal adaptation difficulties, although it was difficult to quantify risk or distinguish between medications due to the diversity of different outcome measures used. Some outcomes included serious problems such as seizures and admission to intensive care units but the majority of cases were for self limiting problems.[136] One meta-analysis of cohort studies found that SSRI exposure in late pregnancy is associated with increased incidence of neonatal admission to special care nursery as well as poor neonatal adaptation.[137] The evidence for TCAs and serotonin-norepinephrine reuptake inhibitors (SNRIs) was weak with case reports suggesting an association with adaptation difficulties. **2+**

Persistent pulmonary hypertension of the newborn

A systematic review described three studies examining the association between persistent pulmonary hypertension of the newborn (PPHN) and SSRI exposure. One prospective study used the Swedish Birth Register information and found that PPHN was associated with early and late SSRI exposure. This was in partial agreement with a previous case control study which reported that SSRI use after the 20th week of gestation was found to be significantly associated with PPHN (OR 5.1, 95% CI 1.9 to 13.3). The third study described was a retrospective cohort study which found no increased risk of PPHN in 1,104 infants exposed to SSRIs in the third trimester.[136] **2++**

A subsequent case control study examined the potential association of a range of factors including SSRI use in PPHN and found that only mode of delivery was associated with PPHN.[139] **2+**

The UK Teratology Information Service recommends that SSRIs should be avoided in late pregnancy unless the indication is compelling.[138] **4**

Neurodevelopmental outcomes

Two systematic reviews and a subsequent population based observational study on the effect of antenatal antidepressant exposure on childhood developmental outcomes were identified.

One systematic review reported on seven studies and noted that only one reported a positive finding indicating that children of depressed mothers treated with SSRIs had a significantly lower overall score on a psychomotor development index but no difference in scores on individual items on the index.[136] The data from a subsequent observational study conducted in Denmark suggested that children exposed to antidepressants in the second and third trimester of pregnancy were able to sit unaided 15.9 days later (95% CI 6.8 to 25.0) and to walk 28.9 days later (95% CI 15.0 to 42.7) than children of women not exposed to antidepressants but were still within the normal range of development. Fewer children with exposure to antidepressants were able to sit unsupported at six months of age (OR 2.1, 95% CI 1.23 to 3.60) and fewer were able to occupy themselves at 19 months of age (OR 2.1, 95 % CI 1.09 to 4.02). In this study, it was not possible to ascertain which antidepressants were employed.[140] The second review focused on effects of SSRI exposure and included additional studies. It highlighted an examination of 12 outcome studies all indicating normal cognitive development with no effect found on the development of language skills of the exposed infants. Abnormal externalising or social behavioural abnormalities were reported in three of the studies.[138] **2++** **3**

Summary

The evidence on the harms associated with antidepressant exposure in pregnancy is conflicting and interpretation of results is made difficult due to variation in outcome measures and the range of potential confounding factors, including the underlying depressive illness. Absolute risk of harm, with the exception of poor neonatal adaptation, is small. A detailed systematic review analysed consistency of findings across studies and concluded that it would appear that individual antidepressants apart from paroxetine, are unlikely to be teratogenic.[136] It remains uncertain whether there is a class effect with SSRI.

✓ General practitioners should review antidepressant therapy as soon as possible in pregnancy to discuss whether the current medication should be continued and any other alternative pharmacological or non-pharmacological treatments initiated.

C **In view of the association with harms to the fetus and neonate, paroxetine should not generally be initiated as first line therapy in pregnancy. For women already prescribed paroxetine an evaluation of individual risks and benefits should be carried out before a decision is made to continue use or switch to another antidepressant.**

✓ Choice of antidepressant in pregnancy should take into account implications for breastfeeding.

✓ Since the evidence base for safety of antidepressant prescribing in pregnancy is a rapidly developing area, clinicians should update their knowledge frequently.

6.3.3 LITHIUM

Congenital malformation

A systematic review of birth outcomes following lithium exposure noted that with only small and primarily retrospective studies, it is not possible to determine effects of exposure on rates of major malformations. A trend towards an increase in Ebstein's anomaly was found.[141] **2++**

Neurological effects on neonate

A case series concluded that there is an increased risk of neonatal complications, in particular central nervous system, neuromuscular, respiratory and thyroid complications, for infants exposed to high levels of lithium during delivery. The rate of all complications, with the exception of gestational diabetes, was consistently higher in the high lithium exposure group (as measured for those with above median placental lithium concentration). In particular, the rates of central nervous system and neuromuscular complications were significantly higher, the duration of infant hospital stays was significantly longer, and 1-minute Apgar scores were significantly lower in the high lithium exposure group.[142] Stopping or reducing lithium prior to delivery may reduce the risk of complications in infants. There is an absence of evidence to assist decisions on whether to reduce or discontinue lithium in the time leading up to delivery. **3**

Other complications

There have been reports of other adverse effects associated with maternal lithium exposure including cardiotoxicity, feeding difficulties, hypotonia and cyanosis, thyroid problems and diabetes insipidus.[143] **2+**

Relapse

Women with bipolar disorder who stop lithium in pregnancy are at high risk of recurrence of illness.[79] Careful, individualised assessment needs to take place urgently when a woman taking lithium discovers that she is pregnant. To reduce the high relapse risk after delivery, women with bipolar disorder should be encouraged to resume prophylactic medication immediately after giving birth. Women with a pre-existing psychosis are at elevated risk in the postpartum period and must be referred and managed along 'high-risk' pathways in conjunction with specialist perinatal mental health services during the antepartum and postnatal periods.[87,89] **4**

See section 4.3 for discussion of lithium as prophylactic for postpartum psychosis.

6 Any woman taking lithium in pregnancy should have an individualised psychiatric care plan, involving maternity services and the woman herself, for lithium management throughout pregnancy and the peripartum. This should include consideration of:

- frequency of monitoring and dose adjustment
- potential for interaction with medications prescribed in pregnancy
- preparation for and mode of delivery
- risks to the neonate.

✓ Women taking lithium in early pregnancy should be offered detailed ultrasound scanning for fetal abnormality.

6 Where a woman is taking lithium in pregnancy, mental health services should provide maternity services with information on the recognition of lithium toxicity, lithium-drug interactions and pregnancy-related events which may precipitate toxicity.

Sample information on lithium use is provided in Annex 3.

6.3.4 ANTIEPILEPTIC DRUGS

Congenital malformation

The antiepileptic drugs (AEDs) carbamazepine, sodium valproate and lamotrigine are used as mood stabilisers particularly in the management of bipolar disorder. A systematic review of controlled cohort studies in women with epilepsy reported evidence that exposure to AEDs in early pregnancy increases the risk of congenital malformations and is associated with pregnancy and neonatal complications. The risk was greatest with valproate.[141] The review highlighted data from the North American, UK and Australian AED registries which found the overall major malformation rate to be 2.9% for carbamazepine, 8.7% for sodium valproate and 2.7% for lamotrigine. A large registry-based review failed to find evidence of a substantial increase in the combined risk of all major birth defects for lamotrigine.[144] **2+ 3**

Neurological effects on neonate

A systematic review of 11 studies examining the effect of sodium valproate exposure on child development consistently found an association with poorer outcomes across a diverse range of outcome measures for infant and child development such as intelligence quotient (IQ), verbal ability and attention. No effects on development were found for carbamazepine or lamotrigine. Polytherapy was associated with highest risks.[141] **2++**

C **In view of the risk of early teratogenicity and longer term neurobehavioural toxicity, valproate** (when used as a mood stabiliser) **should not be prescribed to women of childbearing potential.**

✓ If there is no alternative to valproate treatment for a woman of childbearing potential, long-acting contraceptive measures should be put in place. Check the Medicines and Healthcare products Regulatory Agency (MHRA) website for current advice.

C **Valproate should not be used as a mood stabiliser in pregnancy.**

Several AEDs are folate antagonists. Folic acid supplements are recommended for women on AEDs from preconception to the end of the first trimester.[145,146] The use of folic acid supplements even at 5 mg daily, will, however, not necessarily negate the risk of neural tube defects with AEDs.[147] **2+ 4**

D **All women taking antiepileptic drugs as mood stabilisers should be prescribed a daily dose of 5 mg of folic acid from preconception until at least the end of the first trimester.**

✓ Women taking antiepileptic drugs in early pregnancy should be offered detailed ultrasound scanning for fetal abnormality.

Additional guidance on the use of Vitamin K_1 peripartum supplementation in the management of women taking enzyme-inducing antiepileptic drugs can be found in SIGN 70, diagnosis and management of epilepsy in adults.[146]

Maternal drug metabolism

Lamotrigine is subject to significant alterations in metabolism in pregnancy with clearance increasing significantly as pregnancy progresses. There is a risk of postpartum maternal toxicity as clearance rates return to normal.[148] **2+**

✓ Maternal lamotrigine levels should be monitored throughout pregnancy and the early postpartum period.

6.3.5 ANTIPSYCHOTICS

Congenital malformation

Two systematic reviews provide no conclusive evidence that first or second generation antipsychotics are associated with structural teratogenicity, describing how the evidence base is too limited to draw definitive conclusions.[149,150] **2++**

Two observational studies found no association between the use of antipsychotic drugs in pregnancy and complications such as rates of stillbirth, gestational age at birth, and congenital abnormalities and perinatal syndromes. The two studies considered a total of 401 pregnancy outcomes between them for women taking antipsychotics, 299 on risperidone, 60 on olanzapine, 36 on quetiapine and six on clozapine. There was no increased rate of any major malformation for any drug. The studies were not clear on timing or duration of exposure.[151,152] **2+**

Neurological effects on neonate

There have been reports of self-limiting extra-pyramidal symptoms or possible withdrawal emergent syndromes in neonates exposed to risperidone in the third trimester.[152] **3**

Effects on fetal growth and pregnancy metabolism

A prospective observational study focusing on infant birth weight found an association between low birth weight and the use of first generation antipsychotics in pregnancy, and babies who were large for gestational age in the group of women taking second generation antipsychotics, especially olanzapine and clozapine.[153] **2+**
A systematic review reported an increased risk of gestational diabetes with olanzapine and clozapine.[149] **2++**

The evidence on potential adverse consequences from the use of antipsychotic drugs in pregnancy is conflicting and there is no clear link between individual antipsychotic medications and particular complications in pregnancy, during birth, or for the neonate. An exception is the possible link between olanzapine and clozapine and the risk of gestational diabetes and infants who are large for gestational age.

C **Women taking antipsychotics during pregnancy should be monitored for alterations in fetal growth. Additional monitoring for blood glucose abnormalities is required where olanzapine or clozapine are prescribed.**

6.3.6 HYPNOTICS AND SEDATIVES

Congenital malformation

While earlier studies suggested an increase in orofacial cleft defects following in utero exposure to benzodiazepines,[154] a more recent large prospective study found no significant association with birth defects.[155] **2+**

Neurological effects on neonate

Benzodiazepine use in the first trimester may increase the risk for pre-term birth and low birth weight. Third trimester use carries a higher risk of neonatal withdrawal symptoms such as 'floppy infant syndrome' which includes hypotonia, lethargy and sucking difficulties. These withdrawal symptoms can appear within a few days to three weeks after birth and can last up to several months.[156] **2+**

C **In women taking benzodiazepines the need for continued use in pregnancy should be reviewed and use should be restricted to short term and low dose where possible. Consideration should be given to tapering the dose prior to childbirth.**

One population cohort study examined pregnancy outcomes where women were taking the non-benzodiazepine (Z-drug) zolpidem. Women taking zolpidem had higher rates of low birth weight and small for gestational age babies, preterm deliveries and Caesarean section.[157] **2+**

No evidence was identified on the use of zopiclone or zaleplon in pregnancy.

6.4 PSYCHOTROPIC MEDICATIONS DURING BREAST FEEDING

✓ Breast feeding is an individual decision for each woman. Clinicians should support women in their choice and be mindful that taking prescribed psychotropic medication is not routinely a contraindication to commencing or continuing breast feeding.

The process of excretion of psychotropic medication is complex, with variation in milk/maternal plasma ratios for different drugs (and drug dose) and between foremilk and hindmilk, and time from ingestion to maximum concentration in breast milk. The level of exposure is a function of both the absolute dose and the ability of the neonate to cope with the drug. The level of metabolic maturity of the infant will influence any effect of a drug taken by the mother. Recommendations in this section apply to healthy full term infants. Because the limited evidence base generally relates to drugs prescribed at standard therapeutic doses, no inference can be made where drugs are prescribed at higher doses.

6.4.1 ANTIDEPRESSANTS

A systematic review of 31 small case series (12 of which were single case reports) found that for SSRIs the breast milk to infant plasma drug concentration ratios are elevated for fluoxetine, citalopram and escitalopram. The authors suggest that sertraline and paroxetine (among SSRIs) and nortriptyline and imipramine (among TCAs) have the best evidence base for use during breast feeding in terms of similar findings across multiple laboratories, usually undetectable infant serum levels and no reports of short term adverse events.[158] **3**

One study found no evidence to support the hypothesis that SSRIs with a milk to plasma ratio of less than one would be safer.[159] **2+**

A review of case reports concluded that, for most TCAs, the breast milk to infant plasma ratio is less than one with the exception of the metabolite of doxepin. The review highlighted that no adverse clinical effect has been reported with the use of venlafaxine. Breast milk excretion of trazodone is low. Very little information exists for other medications.[160] **4**

D **Avoid doxepin for treatment of depression in women who are breast feeding. If initiating selective serotonin reuptake inhibitor treatment in breast feeding, then fluoxetine, citalopram and escitalopram should be avoided if possible.**

✓ When initiating antidepressant use in women who are breastfeeding, both the absolute dose and the half life should be considered.

6.4.2 LITHIUM

Lithium is excreted in breast milk at a level of approximately 40% of maternal serum level. Lithium toxicity has been described in a breastfed infant and lithium is known to impair thyroid and renal function in adults.[161,162] A study of ten mother-infant pairs found limited adverse effects, but the authors emphasised caution regarding the generalisability of their findings and the potential for significant harm associated with renal or thyroid dysfunction.[163] **3**

D **In view of the potential risks to the infant of a breastfeeding mother taking lithium, mothers should be encouraged to avoid breast feeding. In mothers taking lithium who have decided to breast feed, close monitoring of the infant, including serum lithium levels, thyroid and renal monitoring should be provided.**

6.4.3 ANTIEPILECTIC DRUGS

Sodium valproate is excreted in breast milk in low levels and infant serum levels are between one and two per cent of the maternal serum level. No short term adverse clinical effects have been noted in breastfed children when mothers are taking sodium valproate.[161,164] **2-**

The evidence on carbamazepine suggests that it is excreted into breast milk in significant quantities and infant carbamazepine levels in serum range from 6-65% of maternal serum levels.[165]

One cohort study examined the level of exposure to lamotrigine in breastfed infants. Infant plasma concentrations four hours after breast feeding were 18.3% of the maternal dose. It concludes that infant exposure was similar to other antiepileptic drugs.[166] **3**

✓ Antiepileptic mood stabiliser prescription is not, of itself, a contraindication to breastfeeding, but decisions should be made individually with the woman, after full discussion of the risks and benefits.

6.4.4 HYPNOTICS AND SEDATIVES

Benzodiazepines are excreted in breast milk with a low milk/plasma ratio.[130,167] However, there are reports of sedation, poor feeding, weight loss and apnoea, which may be more likely to occur with longer-acting agents.[131] **4**

✓ If a benzodiazepine is required during breast feeding short-acting agents should be prescribed in divided doses. Mothers should be advised not to stop medication suddenly and to contact their doctor if the infant is observed to have sleepiness, low energy or poor suckling.

6.4.5 ANTIPSYCHOTICS

Most antipsychotic medications are excreted in breast milk but as yet there is no evidence to suggest that breastfed infants are at risk of toxicity or impaired development.[129,130, 167-169] There is little evidence on second generation antipsychotic drugs.[130,170] Clozapine is associated with agranulocytosis and is therefore not recommended in breast feeding.[149] **3**

D **Women who are taking clozapine should not breast feed.**

✓ All breastfed infants should be monitored for sedation and extra-pyramidal adverse effects where mothers are taking antipsychotic medications.

7 Provision of information

7.1 CHECKLIST FOR PROVISION OF INFORMATION

This section explains what information patients/carers can reasonably expect to be provided with at key stages of the patient journey. The checklist was designed by members of the guideline development group based on their experience and understanding of the evidence base. The checklist is neither exhaustive nor exclusive.

Any information provided, particularly when in written form, should take into account the woman's individual circumstances, particularly where English is not a first language or there are literacy problems.

All women taking psychotropic medications for mental health problems
• Discuss pregnancy planning and the role of contraception. • Discuss specific risks in relation to postnatal relapse of illness for women with bipolar disorder and schizophrenia. • When planning a pregnancy, discuss the risks and benefits of changing or stopping medication and emphasise the need to continue contraception where appropriate.
Pregnant women identified as at risk of postpartum psychosis
• Inform women who have a history of bipolar disorder, postpartum psychosis or schizophrenia that they should have assessment and support by a specialist during pregnancy. • Inform women who have a family history of bipolar disorder or postpartum psychosis that they should be reviewed by their GP during pregnancy and should tell their GP and maternity service if they develop any mood or anxiety problems. • Inform women that they should have an individualised plan for their care, including the management of any medication, in pregnancy and the early postpartum period, drawn up with them and shared with all services involved in their care. Inform them that this is especially important if taking lithium as the medication dose will need to be monitored as pregnancy progresses and a plan put in place for management of medication around the time of the birth. • Discuss the potential effects of medications on the fetus and infant and the monitoring, including detailed anomaly ultrasound scanning, which may be required. • Inform women that, with some exceptions, taking psychotropic drugs is not usually a contraindication to commencing or continuing to breast feed, providing the infant is healthy and term.
Pregnant women identified as at risk of depression
• Explain the symptoms of depression to women and their families. Inform them that although symptoms can be similar to 'baby blues' these common emotional upsets typically only last a few days and that women should speak to their health visitor, midwife or GP if symptoms persist or seem to be getting worse. • Advise women who have previously had postnatal depression, and their partners, that they may experience it again with subsequent pregnancies. • Discuss the importance of seeking help when signs and symptoms develop. • Discuss social support and provide information on local groups where they can meet other women, for example self help groups, breastfeeding groups, mother and baby groups.

Women who become depressed during pregnancy or after the birth of their baby

- Reassure women that depression is a common condition, affecting a large proportion of women and can be experienced by women of any age and social background.
- The following quality of life issues should be discussed with women:
  - stigma
  - difficulties relating to partner and family members
  - misconceptions about perinatal depression.
- Discuss social support and provide information on local groups where they can meet other women, for example self help groups, breastfeeding groups, mother and baby groups.
- Offer advice and reassurance about their birth experience and choice of infant feeding.
- Discuss any suicidal thoughts that a woman may have with her and advise her where she can find help should this be an issue at any time.
- Make women aware of books and websites available to help them and their families understand perinatal depression.
- Provide women with written information to help make partners and family members aware of their feelings and how they can get help.
- Discuss the risks and benefits of continuing/commencing antidepressant treatment during pregnancy and breast feeding and the most appropriate medication.
- Discuss potential side effects of medications with women.
- Provide information on treatments including talking therapies (CBT and IPT), and exercise.
- Advise women not to use St John's Wort or other herbal treatments during pregnancy and when breast feeding.
- Reassure women and their families that, with treatment, the majority of women have a positive outcome.

Women who experience symptoms of postpartum psychosis

- Explain that postpartum psychosis is an uncommon but severe postnatal mental illness.
- Explain the symptoms of postpartum psychosis to women and families including:
  - excessive anxieties
  - delusions
  - hallucinations
  - irrational thoughts.
- Advise women and families that postpartum psychosis develops quickly and needs urgent treatment, which may include admission to hospital. Offer reassurance that they should have the opportunity to have their baby with them during treatment in a specialised mother and baby unit.

7.2 SOURCES OF FURTHER INFORMATION

7.2.1 HELPLINES

Breathing Space
0800 838 587

Breathing Space is a free and confidential service to help you if you are feeling down or experiencing depression and need someone to talk to. Breathing Space also offers a free and confidential British Sign Language (BSL) service you can access using their website at www.breathingspacescotland.co.uk

CarersLine
Tel: 0808 808 7777

Carers UK's advice line is a free and confidential helpline, offering information to carers.

Cry-sis
Tel: 08451 228669

Cry-sis offers support for families with excessively crying, sleepless and demanding babies.

NHS24
Tel: 08454 24 24 24

NHS24 can answer questions and offer advice on health matters.

Samaritans
Tel: 0845 790 9090

Samaritans is available 24 hours a day to provide confidential and emotional support to people who are distressed and thinking about suicide.

SAMH (Scottish Association for Mental Health)
Tel: 0800 917 3466

SANEline
Tel: 0845 767 8000

This is a national out-of-hours helpline offering emotional support and information for people affected by mental health problems.

7.2.2 ORGANISATIONS

Action on Depression
11 Alva Street
Edinburgh EH2 4PH
Tel: 0808 802 2020
Email: admin@actionondepression.org
Website: www.actionondepression.org

A national charity for depression in Scotland offering a range of information including self-help groups, an information service by email and a wide range of leaflets and fact sheets.

Action on Postpartum Psychosis
Website: www.app-network.org

A patient organisation aimed at building up a pool of women who have experienced postpartum psychosis and are interested in helping with research. Aims to provide up to date research information to women who have experienced postpartum psychosis and their families.

Association for Post-Natal illness (APNI)
145 Dawes Road, Fulham
London SW6 7EB
Tel: 020 7386 0868
Website: www.apni.org

APNI is a charity which provides information and support to anyone affected by postnatal depression. They provide information leaflets which can be downloaded from their website.

Bipolar Scotland
Studio 1015, Mile End Mill, Abbeymill Business Centre, Seedhill Road
Paisley PA1 1T
Website: www.bipolarscotland.org.uk

Bipolar Scotland supports a network of self-help groups throughout Scotland.

Breaking the Silence
Mental Health Network
Templeton Business Centre, 62 Templeton St
Glasgow G40 1DA
Website: www.mhngg.org.uk

Breaking the Silence provides information on perinatal mental health issues.

CrossReach
Postnatal Depression Services
Wallace House, 3 Boswall Road
Edinburgh EH5 3RJ
Tel: 0131 538 7288
Fax: 0131 552 2319
Website: www.crossreach.org.uk

CrossReach aims to provide support for families where a mother or father is suffering from postnatal depression, through a range of services.

HAPIS (Highland Antenatal and Postnatal Illness Support)
Email: info@hapis.org.uk
Website: www.hapis.org.uk

HAPIS is an Inverness based support group for antenatal and postnatal mothers.

The National Childbirth Trust (NCT)
Alexandra House, Oldham Terrace, Acton
London W3 6NH
Tel: 0300 330 0770
Website: www.nctpregnancyandbabycare.com

The NCT provides information and support on all aspects of pregnancy, childbirth and early parenthood. There is individual and group support offered, and local groups around Scotland.

The Royal College of Psychiatrists
17 Belgrave Square
London SW1X 8PG
Tel: 020 7235 2351
Website: www.rcpsych.ac.uk/

The Royal College of Psychiatrists produces a leaflet on postnatal depression which can be downloaded from their website.

SAMH (Scottish Association for Mental Health)
Cumbrae House, 15 Carlton Court
Glasgow G5 9JP
Tel: 0141 568 7000
Email enquire@samh.org.uk
Website www.samh.org.uk

SAMH provides information and support to people who experience mental health problems. They also offer a range of leaflets and fact sheets on mental health conditions.

7.2.3 WEBSITES

www.breathingspace.co.uk

www.mind.org.uk

www.moodjuice.scot.nhs.uk

http://moodgym.anu.edu.au/welcome

www.moodcafe.co.uk

SIGN accepts no responsibility for the content of the websites listed and does not support the use of treatments which have not been proven to be effective using SIGN methodology.

8 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

8.1 RECOMMENDATIONS WITH POTENTIAL RESOURCE IMPLICATIONS

Recommendation		Section	Likely resource implication
✓	Given the importance of early intervention in a maternity context, services delivering psychological therapies should prioritise early response to pregnant and postnatal women.	5.2.1	*Primary care mental health services will require additional education and training in order to prioritise and deliver psychological interventions to pregnant and postnatal women.*
B	**Cognitive behavioural therapies should be considered for treatment of mild to moderate depression in the postnatal period.**	5.2.1	
D	**A national managed clinical network for perinatal mental health should be centrally established in Scotland. The network should be managed by a coordinating board of health professionals, health and social care managers, and service users and carers.**	5.4	*A managed clinical network will require central administrative support, and support in the development of educational and training resources.*
D	**All women of childbearing potential who take psychotropic medication should be made aware of the potential effects of medications in pregnancy. The use of reliable contraceptive methods should be discussed.**	6.2	*Adult mental health services will require additional education and training in order to assist women in pregnancy planning and provide advice on effective contraception.*

8.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- The proportion of women requiring admission to hospital within one year of childbirth who have access to specialist mother and baby inpatient admission facilities.
- The number of women who are at high risk of early major postpartum mental illness who are identified in pregnancy and have a joint management plan developed between maternity and mental health services.
- The proportion of women of childbearing potential who have a diagnosis of bipolar affective disorder or schizophrenia who have documented evidence of information on pregnancy planning, which includes risk of illness recurrence, effects of medication and contraception advice.

9 The evidence base

9.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using search strategies devised by a SIGN information specialist. Databases searched include Medline, Embase, CINAHL, PsycINFO, MIDIRS and the Cochrane Library. For most searches, the date range covered was 1999 to 2010. Internet searches were carried out on various websites including the US National Guideline Clearinghouse, NLH Guidelines Finder, and Guidelines International Network (GIN). The Medline version of the database search strategies for each key question can be found on the SIGN website. The main searches were supplemented by material identified by individual members of the guideline development group.

9.1.1 LITERATURE SEARCH FOR PATIENT ISSUES

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to management of perinatal mood disorders. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised and presented to the guideline development group.

9.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline *(see Annex 1)*. The following areas for further research have been identified:

- What risk reduction strategies in pregnancy or the early postnatal period are most likely to reduce the incidence of postnatal depression?
- What interventions are effective in preventing antenatal depression?
- Does prophylactic drug treatment reduce the risk of recurrence of postnatal depression?
- Does prophylactic drug treatment reduce the risk of postpartum psychosis?
- What interventions for postnatal depression improve outcomes for mother-infant relationship and infant development?
- What are the most effective treatments for antenatal anxiety?
- What interventions for antenatal anxiety improve outcomes for mother-infant relationship and infant development?
- How cost effective are mother and baby units, and which disorders are best helped by joint mother-baby admission?
- What are the most effective models of community mental health service provision in the antenatal and postnatal period, including Integrated Care Pathways and Managed Clinical Networks?
- How is information on risk in relation to pregnancy best communicated to women with mental illness?
- What risks are associated with SSRI prescribing in pregnancy?
- What is the role of physical activity in preventing and treating postnatal depression?

9.3 REVIEW AND UPDATING

This guideline was issued in 2012 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: **www.sign.ac.uk.**

10 Development of the guideline

10.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in SIGN 50: A Guideline Developer's Handbook, available at **www.sign.ac.uk**

10.2 THE GUIDELINE DEVELOPMENT GROUP

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive. All members of the SIGN Executive make yearly declarations of interest and further details of these are available on request.

Mr Euan Bremner	*Guideline Coordinator*
Mrs Lesley Forsyth	*Events Coordinator*
Mrs Karen Graham	*Patient Involvement Officer*
Ms Christine Hill	*Distribution and Office Coordinator*
Mr Stuart Neville	*Publications Designer*

10.2.1 ACKNOWLEDGEMENTS

SIGN would like to acknowledge the guideline development group responsible for the development of SIGN 60: postnatal depression and puerperal psychosis, on which this guideline is based and to thank the following former members of the guideline development group.

Ms Anna Gibbons	*Counselling Services Manager, Midlothian Sure Start*
Mrs Mary Thomson	*Public Health Team Leader, Coatbridge*

10.3 CONSULTATION AND PEER REVIEW

10.3.1 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Professor Marie-Paule Austin	*Chair Perinatal and Women's Mental Health, University of New South Wales, Sydney, Australia*
Miss Wendy Ackroyd	*Lead Clinical Pharmacist, Mental Health, Dumfries and Galloway Royal Infirmary on behalf of (NHS Scotland) Mental Health Pharmacy Strategy Group*
Ms Eleanor Forrest	*Midwifery Lecturer, Glasgow Caledonian University*
Miss Anna Gibbons	*Counselling Services Manager, Midlothian Sure Start*
Professor Dale Hay	*Professor of Psychology, Cardiff University*
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Sister Rose Sloan	*Special Needs in Pregnancy Midwife, Inverclyde Royal Hospital, Greenock*
Ms Carol Paton	*Chief Pharmacist, Oxleas NHS Foundation Trust*
Mrs Laura Patience	*Perinatal Mental Health Nurse, NHS Highland*
Mrs Christine Puckering	*Chartered Clinical Psychologist, Royal Hospital for Sick Children, Glasgow*

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Dr Judy Shakespeare	*General Practitioner, Oxford*
Dr Robby Steel	*Consultant Liaison Psychiatrist, Edinburgh Royal Infirmary*
Miss Mary Thomson	*Public Health Nurse/Health Visitor, Adam Avenue Health Centre, Airdrie*
Mrs Rosemary Whaley	*Patient Representative, Edinburgh*

The following expert referees commented collectively on behalf of the Royal College of Paediatrics and Child Health.

Dr James Moorcraft	*Consultant in Neonatal Medicine, Singleton Hospital, Swansea*
Dr Avril Washington	*Consultant Paediatrician, Homerton University Hospital, Londo*n
Dr Jane Hawdon	*Consultant Neonatologist, University College London Hospitals*
Dr Ian Maconochie	*Consultant in Paediatric Accident and Emergency Medicine, St Mary's Hospital, London*

10.3.2 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

Dr Keith Brown	*Chair of SIGN; Co-Editor*
Dr John Gillies	*Royal College of General Practitioners Scottish Council*
Dr Roberta James	*Acting Programme Director, SIGN; Co-Editor*
Ms Fiona McMillan	*Royal Pharmaceutical Society of Great Britain (Scottish Department)*
Dr Sara Twaddle	*Director of SIGN; Co-Editor*
Professor David Wilson	*Royal College of Paediatrics and Child Health*

Abbreviations

AED	antiepileptic drugs
ALPHA	Antenatal Psychosocial Health Assessment
APMH	Antenatal and Postnatal Mental Health
BNF	British National Formulary
CEMD	Confidential Enquiry into Maternal Deaths
CBT	cognitive behavioural therapy
CI	confidence interval
ECT	electroconvulsive therapy
EPDS	Edinburgh Postnatal Depression Scale
GP	general practitioner
HAM-D	Hamilton Depression Rating Scale
HIS	Healthcare Improvement Scotland
HTA	health technology assessment
IPT	interpersonal therapy
IQ	intelligence quotient
MTA	multiple technology appraisal
NICE	National Institute for Health and Clinical Excellence
NPV	negative predictive value
NSC	National Screening Committee
OR	odds ratio
PPHN	persistent pulmonary hypertension of the newborn
PPMD	postpartum mental disorder
PPV	positive predictive value
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
RR	relative risk
SIDS	Sudden Infant Death Syndrome
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SNRI	serotonin-norepinephrine reuptake inhibitor
SPC	summary of product characteristics
SSRI	selective serotonin reuptake inhibitor
TCAs	tricyclic antidepressants
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

Annex 1

Key questions addressed in this update

ASSESSMENT AND DIAGNOSIS	
Key question	**Guideline section**
1. What are the most effective epidemiology, detection and assessment tools for perinatal depression or anxiety, when should they be administered, and how should they be used? Consider: (a) in the antenatal period to: (i) identify current depression or anxiety (ii) predict postnatal depression (iii) predict postpartum psychosis. (b) in the postnatal period. Tools to consider to include: EPDS; Whooley; PHQ-9; Postpartum Depression Screening Scale	**3.1** **4.4** **4.5**
2. What evidence exists concerning the epidemiology, detection of and risk factors for postpartum psychosis? (Include: risks faced by patients with bipolar disorder)	**3.1** **3.2**
3. Which interventions have demonstrated effectiveness in reducing the incidence of perinatal depression or anxiety (prevention) in the general population or in high-risk groups? Consider: (a) antenatal education (b) social support (c) psychological interventions (d) gentle/mindful yoga based exercises	**4.1** **4.2** **4.3**
4. What epidemiological evidence exists concerning the effects of antenatal depression or anxiety on infant outcomes?	**1.1.3**
TREATMENT	
Key question	**Guideline section**
5. What are the risks and benefits of aerobic exercise (antenatal and postnatal) in symptom reduction in mothers with perinatal depression and anxiety? (Include: walking, running, swimming, sport, dance, yoga, T'ai Chi) Consider: maternal and infant outcomes.	**5.2.5**
6. What is the evidence of the effectiveness of counselling and psychotherapy (antenatal and postnatal) in reducing symptomatology in mothers with perinatal depression or anxiety and postpartum psychosis? Consider: maternal and infant outcomes; include self directed and computer based interventions.	**5.2.1**
7. What interventions to increase social support have demonstrated effectiveness in reducing symptomatology in mothers with perinatal depression or anxiety? Include: peer support, antenatal/postnatal support groups, provision of support by health visitors, web-based, texting, social groups, community initiatives. Consider: maternal and infant outcomes	**5.2.2**

8. What family-focused interventions have demonstrated effectiveness in reducing symptomatology in mothers with perinatal depression or anxiety? Consider: (a) home visiting (b) couple therapy (c) interventions directed at the partner (d) interventions directed at existing children (e) interventions to improve the mother-child relationship (f) infant massage (g) maternal and infant outcomes.	**5.2.3** **5.2.4**
9. What are the risks and benefits of mood stabilisers and antipsychotics in the prophylaxis and management of postpartum psychosis, and the management of bipolar disorder in pregnancy? Consider: (a) in the first trimester (b) in the second and third trimester (c) in lactation (d) in terms of long term consequences on child development (e) preconception counselling for patients on mood stabilisers and antipsychotics.	**5.3.3** **6.3.4** **6.3.5** **6.4.3** **6.4.5**
10. What are the risks and benefits of antidepressant and anxiolytic medications? Consider: (a) in the first trimester? (b) in the second and third trimesters? (c) in lactation? (d) in terms of long term consequences on child development? (e) preconception counselling for patients on antidepressant and anxiolytic medications.	**5.3.2** **6.3.2** **6.4.1**
What evidence exists concerning the benefits of specific elements of service design and delivery for patients with antenatal and postnatal mental health disorders? Consider: (a) mother and baby units (b) community services and maternity liaison (c) managed care networks and integrated care pathways.	**5.5**

Annex 2

Sample care plan

Pregnancy and early postnatal care pathway (to be completed between 28 and 32 weeks of gestation)

Name	DOB:
EDD:	Date plan agreed:

CPN:	Contact info:
Health visitor:	Contact info:
Midwife:	Contact info:
Social worker:	Contact info:
Obstetrician:	Contact info:
Psychiatrist:	Contact info:
GP:	Contact info:
Other professional:	Contact info:
Family member/named person:	Contact info:

Risk of illness:

Early warning signs:
1.
2.
3.

Current management:
1.
2.
3.

Planned antenatal changes:
1.
2.
3.

Immediate postnatal plan: Intention to breastfeed? ☐ Yes ☐ No
1.
2.
3.

Advance statement completed? ☐ Yes ☐ No

Sign/print name (PMHS worker): Date:

Sign/print name (patient): Date:

*Adapted from the Glasgow Pregnancy and Early Postpartum Care Pathway.

Annex 3

Lithium use in the perinatal period - guidance for maternity services.

Adapted from Glasgow Perinatal Mental Health Service

Lithium is a mood stabilising drug, used in the management of bipolar affective disorder. It is rarely used in pregnancy, because of teratogenicity and neonatal complications. However, it may be prescribed under specialist supervision. It has a narrow therapeutic to toxic ratio and must be monitored regularly by blood sampling. Dose range to achieve therapeutic blood levels is usually between 400 mg and 1,200 mg/day, but this is less important than the blood level. The dose required to achieve therapeutic levels may increase from mid-pregnancy, but high levels at delivery can be associated with toxicity in the mother and neonate. For this reason, the dose is usually reduced in advance of delivery. Lithium should not be administered once labour has commenced. Any woman taking lithium in pregnancy should have an individualised psychiatric care plan for lithium management throughout pregnancy and the peripartum.

Therapeutic levels are usually within the range 0.5–0.8 mmol/l

Toxicity is usually evident above 1.5 mmol/l

Symptoms of lithium toxicity include:

- **Early** - restlessness, apathy, nausea, coarse tremor
- **Later** - vomiting, diarrhoea, ataxia, dysarthria, confusion, convulsions, renal failure, coma

If such clusters of symptoms are noted at any clinical encounter, a blood sample should be taken for urgent lithium monitoring. Note the time of the last dose taken on the request card. Seek advice on the correct blood tube to use. Suspected toxicity requires immediate medical attention.

Toxicity can be precipitated by:

- dehydration
- impaired renal function
- sodium-restricted diet
- overdose
- drug interactions.

Drugs that interact with lithium to cause toxicity include:

- diuretics – particularly thiazides
- non-steroidal anti-inflammatory drugs (NSAIDs)
- ACE inhibitors
- calcium channel blockers.

Pregnancy-related conditions that increase the risk of lithium toxicity include:

- fluid loss at delivery
- hyperemesis
- pre-eclampsia

Remember: *If lithium toxicity is suspected, take a lithium level, noting the time when the sample was taken, and the time and amount of the last dose, and seek medical/psychiatric advice. Withhold further lithium until a satisfactory blood result is obtained.*

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