

Best Practice Guidelines for Mental Health Disorders in the Perinatal Period

*BC Reproductive
Mental Health Program
&
Perinatal Services BC*

March 2014



BC MENTAL HEALTH
& SUBSTANCE USE SERVICES
An agency of the Provincial Health Services Authority



Perinatal Services BC
An agency of the Provincial Health Services Authority



BEST PRACTICE GUIDELINES FOR MENTAL HEALTH DISORDERS IN THE PERINATAL PERIOD

(2014) is a manual for healthcare clinicians who care for women during their reproductive years. This guidance describes best practices for the care of women with depression, anxiety disorders, bipolar disorder and psychotic disorders, including postpartum psychosis, in the perinatal period (conception through to one year postpartum).

PRODUCED BY

BC Reproductive Mental Health Program, part of BC Mental Health and Substance Use Services and Perinatal Services BC. Both are agencies of the Provincial Health Services Authority in BC. In partnership with the BC Ministry of Health, Healthy Development and Women's Health: Population and Public Health.

PROJECT LEAD & MAJOR AUTHOR

Janet Williams BSN, MBA. Project Manager (Consultant).

BC REPRODUCTIVE MENTAL HEALTH PROGRAM

Author and Medical Advisor: **Dr Deirdre Ryan** MB, FRCPC, Psychiatrist & Medical Director.

Author and Editor: **Kate Thomas-Peter** BSc, MSc, Project Manager.

PERINATAL SERVICES BC

Editor: **Janet Walker** RN, MSN, Lead for Education and Quality.

MEDICATIONS TABLES

Author and Consultant: **Barbara Cadario** BSc(Hon), BScPharm, MSc, Clinical Associate Professor, Faculty of Pharmaceutical Sciences, University of British Columbia.

Author and Consultant (Anxiolytics medication section): **Dorothy Li** BScPharm, ACPR, CSPI. BC Drug and Poison Information Centre.

RESEARCH CONSULTANT

Gillian Hanley BSc, MA, PhD. Postdoctoral Fellow, University of British Columbia.



ADVISORY GROUP

Sarah Bell RN, MBA, CHE, Executive Director,
Children's and Women's Mental Health Programs,
BC Mental Health and Substance Use Services.

Joan Geber RN, BN, MPA, Executive Director, Healthy Development
and Women's Health, Population and Public Health, Ministry of
Health BC.

REVIEW GROUP

Tricia Bowering MD, FRCPC, Psychiatrist.

Diana Carter MB., BS, FRCPC, Psychiatrist.

Debbie Chaplain MPH, Director Child, Youth and Family, Island Health.

Sheryl Davis-Kahn MA, RCC, Clinical Counselor.

Patti Hallam BSN, RN, Knowledge Coordinator, Promotion and
Prevention, Interior Health Authority.

Andrea Kennedy MD, FRCPC, Psychiatrist.

Gerald Marquette MD, Obstetrician & Gynecologist.

Shaila Misri MD, FRCPC, Psychiatrist.

Pam Munro BScN, RN, MSN Clinical Nurse Specialist, Public Health.
Fraser Health Authority.

Pratibha Reebye MB, BS, Infant Psychiatrist.

Barbara Shulman MD, FRCPC, Psychiatrist.

Joanne Smrek BSN, RN, CIHS, Regional Knowledge Coordinator,
Promotion and Prevention, Interior Health Authority.

Jana H Wong MSW, RSW, Social Worker.

Leanne Yeates BHSc, BA, RM, Midwife.

FUNDED BY

BC Mental Health and Substance Use Services
and Perinatal Services BC,
both agencies of the Provincial Health Services Authority.

DESIGN AND PRODUCTION BY

George Rose.

COPYRIGHT

©2014 BC Reproductive Mental Health Program.

DOWNLOAD COPIES FROM

BC Reproductive Mental Health www.reproductivementalhealth.ca

BC Mental Health and Substance Use Services www.bcmhsus.ca
(Programs and Services)

Perinatal Services BC www.perinatalservicesbc.ca

PURCHASE HARD COPIES FROM

C&W Bookstore <http://bookstore.cw.bc.ca>

Table of Contents

Executive Summary and Recommendations	6
1.0 Introduction	11
2.0 Mental Health Disorders in the Perinatal Period	13
2.1 Prevalence	13
2.2 Clinical Significance.	14
2.2.1 Impact of Untreated Mental Health Disorders	14
2.2.2 Barriers to Seeking Help	15
2.3 Key Points	15
3.0 Perinatal Depression	17
3.1 Education and Prevention	17
3.1.1 What is Perinatal Depression?	17
3.1.2 Signs and Symptoms	17
3.1.3 Risk Factors.	18
3.2 Screening and Diagnosis.	19
3.2.1 Screening	19
3.2.2 Diagnosis	23
3.3 Treatment and Self-Management.	24
3.3.1 Psychoeducation.	24
3.3.2 Self-care: The NEST-S Program	25
3.3.3 Psychotherapies	26
3.3.4 Bright Light Therapy	29
3.3.5 Pharmacotherapy (Medications).	30
3.3.6 Electroconvulsive Therapy	31
3.4 Partners and Depression.	31
3.5 Key Points and Recommendations.	32
4.0 Anxiety Disorders	37
4.1 Education and Prevention	37
4.1.1 What is an Anxiety Disorder?	37
4.1.2 Signs and Symptoms	38
4.1.3 Risk Factors.	40
4.1.4 Prevention.	41
4.2 Screening and Diagnosis.	41
4.3 Treatment and Self-Management.	42
4.3.1 Summary of Treatments.	42
4.3.2 Medications for the Treatment of Anxiety Disorders	43
4.4 Key Points and Recommendations.	43
5.0 Bipolar Disorder	45
5.1 Education and Prevention	45
5.1.1 What is Bipolar Disorder?.	45
5.1.2 Signs and Symptoms	45
5.1.3 Risk Factors.	46
5.1.4 Prevention.	46
5.2 Screening and Diagnosis.	47
5.3 Treatment and Self-Management.	47
5.3.1 Summary of Treatments.	47
5.3.2 Medications used for the Treatment of Bipolar Disorder.	48
5.4 Key Points and Recommendations.	49

6.0	Psychotic Disorders and Postpartum Psychosis	52
6.1	Education and Prevention	52
6.1.1	What is a Psychosis; Relationship to Psychotic Disorders; Postpartum Psychosis.	52
6.1.2	Signs and Symptoms	52
6.1.3	Risk Factors.	54
6.1.4	Prevention.	54
6.2	Screening and Diagnosis.	54
6.3	Treatment and Self-Management.	55
6.3.1	Summary of Treatments.	55
6.3.2	Medications for the Treatment of Psychotic Disorders and Postpartum Psychosis	56
6.4	Key Points and Recommendations.	56
7.0	Suicide and Infanticide.	58
7.1	Suicide	58
7.2	Neonaticide and Infanticide	60
7.3	Key Points and Recommendations.	62
8.0	Coping and Support Networks	63
	Appendix 1: Edinburgh Postnatal Depression Scale (EPDS)	65
	Appendix 2: Diagnostic Assessment Interview in the Perinatal Period	66
	Appendix 3: Perinatal Suicide Risk Questions.	69
	Appendix 4: Perinatal Infanticide Risk Questions	70
	Appendix 5: Psychotropic Medications Used in the Perinatal Period	71
	Appendix 6: Suggested Actions/Monitoring for Women on Psychotropic Medications in the Perinatal Period	87
	Appendix 7: Types of Psychotic Disorders	90
	References.	91

List of Tables

Table 1: Prevalence of Depression, Anxiety, Bipolar Disorder & Schizophrenia in Perinatal & Non-Perinatal Populations.	13
Table 2: Common Depression Screening Tools	20
Table 3: EPDS Scores: Interpretation and Actions	22
Table 4: Common Treatments Used for the Treatment of PND	24
Table 5: EPDS Score, Interpretation & Action	34
Table 6: Guidelines for the Treatment of Depression during the Perinatal Period	35
Table 7: Treatments Commonly used to Treat Anxiety Disorders in the Perinatal Period	42
Table 8: Guidelines for the Treatment of Anxiety Disorders during the Perinatal Period	44
Table 9: Common Treatments for Bipolar Disorder in the Perinatal Period	48
Table 10: Guidelines for the Treatment of Bipolar Disorder	50
Table 11: Guidelines for the Prevention/Management of Psychotic Disorders & Postpartum Psychosis	57
Table 12: General Responses to Identified Suicide Risk	59
Table 13: Components of a Safety Plan.	60
Table 14: Sample Safety Plan.	60

Executive Summary and Recommendations

As many as one in five women in BC will experience a mental health disorder during the perinatal period (pregnancy up to one year postpartum). Such disorders affect all aspects of a woman's life, as well as that of her baby and family. The risks of untreated perinatal depression can include compromised prenatal care, increased risk of obstetrical complications, self-medication or substance use, compromised mother/infant interactions and cognitive, emotional and behavioural impairments in the developing child. The most tragic consequences of untreated perinatal depression are maternal suicide and infanticide.

Although mental illness is serious, with the right strategy and a coordinated approach, it can be detected early and effectively treated. The purpose of this guideline is to support healthcare clinicians in this early detection and coordinated treatment of pregnant and postpartum women with mental health challenges.

Four mental health disorders common in the perinatal period are reviewed in this guideline:

1. Depression
2. Anxiety disorders
3. Bipolar disorder
4. Psychotic disorders and postpartum psychosis

Each of the disorders is discussed in light of the four pillars of action identified in the 2006 Provincial Perinatal Depression Framework: education and prevention; screening and diagnosis; treatment and self-management and coping and support networks. Where sufficient evidence exists, best practice recommendations are noted.

There is a separate section on Suicide and Infanticide.

Recommendations common to all perinatal mental health disorders

The full discussion of mental health disorders in the perinatal period, including prevalence and clinical significance, can be found in Section 2 of these Guidelines.

1. Encourage women with a personal or family history of a mental health disorder to plan their pregnancy, ideally timed when their mood (and physical condition) is as stable as possible.
2. For women with a chronic mental health disorder:
 - a. Share decision-making with the woman and her healthcare providers before and during pregnancy to plan individualized treatment that takes into consideration the severity of her illness, previous response to medication and any supports that might be available to her.
 - b. Consider referral to a psychiatrist before or during pregnancy to assist with treatment planning and monitoring of the woman's mental health status.
 - c. Where a woman decides to stop taking medications before or during pregnancy without consultation, pay particular attention to her mental status throughout pregnancy and especially in the postpartum period because of the high risk of relapse.
3. For women requiring psychotropic medications in the perinatal period:
 - a. Support informed decision-making by discussing the risks and benefits of medications as well as the risks of not treating symptoms with the woman. Involve partners and other family members whenever possible and where appropriate.
 - b. Use the minimum number of psychotropic medications at the lowest effective dose.
4. Encourage women with severe mental health disorders requiring multiple psychotropic medications to deliver in a hospital (versus a home birth). This will facilitate closer monitoring of mother and baby. See Perinatal Services BC guideline on Antidepressant Use During Pregnancy: Considerations for the Newborn Exposed to SSRIs/SNRIs.
5. Where possible, encourage breastfeeding (psychotropic medications are not usually a contraindication to breastfeeding):
 - a. Maximize the breastfeeding support to women to increase the probability of success. Refer to a lactation consultant and/or public health nurse.

- b. Where exclusive breastfeeding is not possible (e.g., medical reasons for the mother/baby or challenges for the mother with breastfeeding, including significant psychological stress), support options that promote optimal nutrition for the baby and support the health and wellbeing of the mother. This may include supplementation with the mother's expressed breast milk, pasteurized donor milk, formula or fully formula feeding.
 - c. Women with premature babies or babies with significant health problems are encouraged to discuss their psychotropic medications with the baby's pediatrician if they want to breastfeed.
6. Educate partners and family members about recognizing the symptoms of mental health disorders and ways to support women during pregnancy and after the birth. Support should include ways to maximize the woman's opportunity for adequate sleep.

Perinatal Depression

The full discussion of Perinatal Depression, including education and prevention, screening and diagnosis, treatment and self-management, can be found in Section 3 of these Guidelines.

Key Points

These can be found in full in Section 3.5. Major depression occurs in up to 16% of women in the perinatal period and at greatest risk are those with a personal or family history of depression and those who have suffered depression in previous pregnancies. Whilst the literature does not support preventive measures in pregnancy, there are some steps that may be taken to prevent depression occurring or re-occurring in the postpartum period. (See discussion in Section 3).

Clinical experience is that early detection of mental health challenges and disorders improves outcomes for both mother and baby. In support, the 2006 Framework for BC "Addressing Perinatal Depression" recommends using the *Edinburgh Postnatal Depression Scale* (EPDS) screening tool where care pathways exist. However, the EPDS is not diagnostic, the "gold standard" being the diagnostic interview, confirmed with the criteria in DSM-V. It is important to note the discussion in Section 3.2 on current debates around screening. Where used, the EPDS is also relevant for fathers and adoptive parents. The diagnostic interview should always include an assessment of suicide risk and potential risks to the baby. Medical conditions and concurrent substance use that may cause similar symptoms should be excluded.

There are a range of treatments available for perinatal depression and combination treatments (both pharmacological and non-pharmacological) are most effective. See Section 3.3 for discussion on treatment and self-management and Appendix 5 for medication-related information. The risk of drug effects on the fetus/baby must be weighed against the risks associated with untreated depression (see Section 2.2).

Recommendations for perinatal depression

These can be found, including tables summarizing the interpretation of EPDS scores and Guidelines for the Treatment of Depression in Section 3.5. The recommendations focus on the Treatment Approach and Medication Management for:

- Women with chronic mental health disorders.
- Women requiring psychotropic medications.
- Breastfeeding and psychotropic medications.
- Education for women and their family members.
- Screening using the EPDS.
- Treatment regimens during the stages of care for women in the perinatal period.

Anxiety Disorders

The full discussion about Anxiety disorders, including education and prevention, screening and diagnosis, treatment and self-management, can be found in Section 4 of these Guidelines.

Key Points

Anxiety disorders and depression often co-exist and the prevalence of anxiety disorders is higher in perinatal than in non-perinatal populations. The most common types of anxiety disorders in the perinatal period are Generalized Anxiety Disorder (GAD), Obsessive Compulsive Disorder (OCD) and Panic Disorder. Major risk factors are a personal or family history of anxiety disorder or anxiety disorder in a previous pregnancy. Early intervention improves outcomes for the mother and her baby.

Unlike screening for depression, there has been little research on the use and validity of self report tools to screen for anxiety in the perinatal period. Where an anxiety disorder is suspected, a diagnostic interview and confirmation with DSM-V criteria should occur. Medical conditions and substance use that may be the cause of similar symptoms should be excluded.

Treatment and Self-Management is discussed at Section 4.3. Mild to moderate anxiety disorders may be successfully treated with a combination of non-pharmacological treatments and medications may be required for women with moderate to severe anxiety disorders. See Appendix 5 for medication-related information.

Recommendations for anxiety disorders

Promote early identification and treatment of anxiety disorders in perinatal women by enquiring about risk factors (e.g., personal and/or family history of anxiety disorders) and/or direct observation (e.g., excessive concerns about fetus/pregnancy or baby).

Utilize the guidelines in Table 8 in Section 4.4 (Guidelines for the Treatment of Anxiety Disorders during the Perinatal Period) for the treatment of women with anxiety disorders.

Bipolar Disorder

Bipolar disorder is one of the most serious mental health disorders that affect women in the perinatal period. The full discussion of Bipolar Disorder, including education and prevention, screening and diagnosis, treatment and self-management, can be found in Section 5 of these Guidelines.

Key Points

Whilst there is no increased prevalence of bipolar disorder during pregnancy, there is increased risk for development and relapse of bipolar disorder in the postpartum. (See Section 2.1 for prevalence.)

Women with existing bipolar disorder are at risk of developing postpartum manic episodes, postpartum depressive episodes and postpartum psychosis. **Postpartum psychosis is a psychiatric and obstetric emergency**, usually requiring hospitalization and intensive treatment. (See Section 6 for a discussion of postpartum psychosis and Section 7.0 for a discussion of Bipolar disorder, Psychosis and Suicide/Infanticide.) A woman with no previous psychiatric history who develops a postpartum psychosis will require close follow up as she is at increased risk of developing further mood episodes and eventually being diagnosed as having a bipolar disorder.

There are no easily implemented self-report screening tools for bipolar disorder and it is not preventable but risks and impacts can be successfully managed. Medications play a significant role in management but adding a psychosocial intervention can improve treatment outcomes, particularly during the depression phase of bipolar. See Section 5.3 for discussion of Treatment and Self-Management.

Recommendations for bipolar disorder

Promote early identification and treatment of bipolar disorder in perinatal women by enquiring about risk factors (personal or family history of bipolar disorder and/or postpartum psychosis) and/or direct observation or reports (e.g., unusual behavior, racing thoughts, distractible, inflated self-esteem or grandiosity, disorganized thoughts, erratic and impulsive behaviour, rapid speech, difficulty sleeping).

For women with bipolar disorder, develop an integrated treatment plan which involves the woman and her family supports, psychiatry, obstetrics (obstetrician, family physician, midwife), primary care, and public health nursing.

Refer to a psychiatrist or reproductive psychiatrist for a mental health assessment, assistance with development of the treatment plan, including medication management, and ongoing monitoring of the woman's mental health status during the perinatal period.

Utilize the Guidelines for the Treatment of Bipolar Disorder Table 10 in Section 5.4 and refer to Appendix 5 for medication-related information.

Women with bipolar disorder should be offered referral for genetic counselling to discuss family history and recurrence risk (i.e., risk of the disorder to their offspring). A referral would also be appropriate in situations where the baby's father has a severe mental health disorder.

Psychotic Disorders and Postpartum Psychosis

The full discussion of these disorders can be found in Section 6 of these guidelines, including education and prevention, screening and diagnosis, treatment and self-management.

Key Points

Psychosis is a generic term associated with a loss of contact with reality and is seen in the more severe forms of some psychiatric disorders, most commonly schizophrenia, schizoaffective disorder and bipolar disorder. It can also occur with a major depressive disorder.

Psychotic disorders are classified under the heading "Schizophrenia Spectrum and Other Psychotic Disorders" in the DSM-V. Distorted thoughts and behaviours may negatively involve the baby, creating additional risk (see 6.1.2 for Signs and Symptoms). Women with schizophrenia are at higher risk of poor perinatal and neonatal outcomes. Schizophrenia (and other serious maternal psychotic disorders) may have a devastating impact on mother-infant bonding and the baby's neurodevelopment may be affected by the mother's parenting difficulties.

The risks and impacts of psychotic disorders can be successfully managed through preconception counselling and appropriate perinatal planning, management and support. (See 6.3 for Treatment and Self Management).

Postpartum psychosis is rare (approximately 1-2 cases per 1000 live births). Onset of psychotic symptoms is usually unexpected and rapid (within hours), most often appearing within 72 hours to four weeks after delivery. Symptoms may last from one day and up to one month (or beyond), with eventual return to previous level of functioning. **Postpartum Psychosis is a psychiatric and obstetrical emergency.** Hospitalization is required for the safety of the woman and her baby and to start treatment with medication, including antipsychotic medication and possibly mood-stabilizing medication. Postpartum psychosis is strongly associated with bipolar disorder.

Psychotic disorders and postpartum psychosis are primarily managed using medications. Women unable to tolerate or take medications, where improvement needs to be quicker and where suicide is a possibility, may find ECT beneficial.

Recommendations for psychotic disorders and postpartum psychosis

Utilize the principles in "Guidelines for the Prevention/Management of Psychotic disorders and Postpartum Psychosis" Table 11 in Section 6.4 of these guidelines. Refer to Appendix 5 for medication-related information.

Suicide and Infanticide

The full discussion of suicide and infanticide can be found in Section 7 of these guidelines.

Key points

Suicide is the most common cause of death amongst women during pregnancy and the first postpartum year, although still rare. (See Section 7.1 for information on prevalence). Mental illness is a significant cause of suicide and concerns about suicide in women in the perinatal period should always be followed up, with

inquiry made about risk of harm to the baby. If using the EPDS, a positive score on question 10 should trigger a full risk assessment. Appendix 2 provides guidelines on areas of questioning to be included in a diagnostic assessment interview during the perinatal period and Appendices 3 and 4 provide specific questions to assess suicide and Infanticide risk.

When level of risk is assessed as “high”, immediate referral to the Emergency Room is recommended. Contact with partner/family should take place to inquire about arrangements for the baby and consideration given to making a referral to the Ministry of Child and Family Development (MCFD).

Neonaticide and infanticide are also very rare but a subset of women who commit these acts have a diagnosed mental health disorder that influences their behaviour. Postpartum psychosis is a risk factor and there is an associated risk between infanticide and maternal suicide.

Wherever a woman has a significant mental health disorder and/or there are observed difficulties with the mother-infant interaction, further enquiry is always warranted. Asking women about thoughts or images of harming their child or children is an essential part of a diagnostic assessment interview.

If concern about the safety of the infant is identified, there is a legal duty to report the situation to MCFD. Dial 310-1234 (no area code required). If needed, ministry services will be provided for the child and family. Refer to: www.mcf.gov.bc.ca/child_protection/keeping_kids_safe.htm

Recommendations related to suicide and infanticide

Assess women who are depressed and/or psychotic for suicide and infanticide risk (see Appendices 3, 4 and 5 for suggested questions). If present, develop a safety plan and refer for a specialist psychiatric assessment and follow-up. Hospitalization may be required. If there are concerns about the safety of the baby, involve other parties as appropriate (partner, extended family, MCFD).

1.0 Introduction

Pregnancy or the birth of a new baby does not protect against mental illness

Mental health disorders are a significant cause of disability for women in the perinatal period (conception through to one year postpartum). As many as one in five women in BC will experience significant depression and/or another mental health disorder during their pregnancy and/or in the postpartum period. Unfortunately, only a small proportion will seek help.

Mental illness affects all aspects of a woman's life and that of her baby and partner/family. Without treatment, it can contribute to compromised prenatal care, increased risk of obstetrical complications, self-medication and/or substance related disorders, compromised mother-infant interactions and cognitive/neuro behavioural impairments in the early years. The most tragic consequences are maternal suicide and infanticide.

Although mental illness is serious, with the right strategy and a coordinated approach, it can be detected early and effectively treated.

*Addressing Perinatal Depression: A Framework for BC's Health Authorities*¹ provides a framework to improve the recognition, diagnosis, treatment and follow-up care for women affected by perinatal depression. This guideline, *Best Practice Guidelines for Mental Health Disorders in the Perinatal Period*, applies the principles and pillars of action identified in the perinatal depression (PND) framework to other mental health disorders which occur in the perinatal period, namely anxiety disorders, bipolar disorder and psychotic disorders.

Four pillars of action identified in the Framework (see Figure 1):

1. Education and Prevention
2. Screening and Diagnosis
3. Treatment and Self-Management
4. Coping and Support Networks

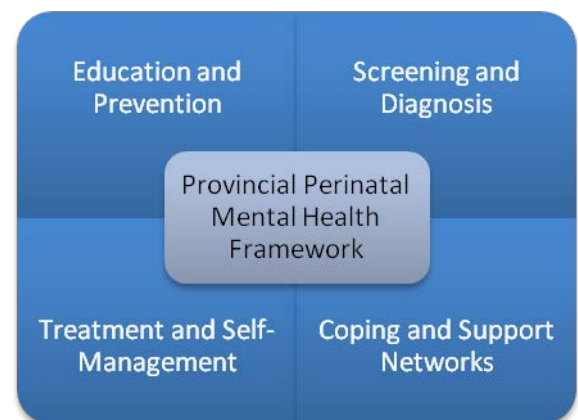
This guideline is intended for healthcare clinicians and describes best practices in each of the pillars for the care of women with depression, anxiety disorders, bipolar disorder and psychotic disorders in the perinatal period (conception through to one year postpartum), including postpartum psychosis.

The goal of the guideline is to promote collaborative and supportive care of women/mothers with mental health disorders and their babies and families by healthcare providers during this critical period of the life cycle.

This guideline is divided into 8 sections:

1. Introduction
2. Mental Health Disorders in the Perinatal Period (prevalence and clinical significance)
3. Perinatal Depression
4. Anxiety Disorders
5. Bipolar Disorder
6. Psychotic Disorders and Postpartum Psychosis
7. Suicide and Infanticide
8. Coping and Support Networks

Figure 1: BC Perinatal Mental Health Framework (adapted from the BC PND Framework)



Abbreviations/definitions used in this guideline:

ADHD	Attention Deficit Hyperactivity Disorder
aOR	adjusted Odds Ratio
CBT	Cognitive Behavioural Therapy
DSM-V	Diagnostic and Statistical Manual of Mental Disorders (published by the American Psychiatric Association or APA)
ECT	Electroconvulsive Therapy
EPDS	Edinburgh Postnatal Depression Scale
GAD	Generalized Anxiety Disorder
IM	Intramuscular
IPT	Interpersonal Therapy
LBW	Low Birth Weight
LGA	Large for Gestational Age
MCM	Major Congenital Malformations
MCFD	Ministry of Children and Family Development
M:P	Milk:Plasma Ratio
MRHD	Maximum Recommended Human Dose
NAS	Neonatal Adaptation Syndrome ⁱ
NEST_S	N utrition, E xercise, S leep and rest, T ime for self and S upport
NS	Not Statistically Significant
OCD	Obsessive-Compulsive Disorder
OR	Odds Ratio
Perinatal	In this guideline, refers to the period from conception to one year postpartum
PD	Panic Disorder
PDT	Psychodynamic Therapy
PPD	Postpartum Depression
PND	Perinatal Depression
PPHN	Persistent Pulmonary Hypertension of the Newborn
PRN	Pro re nata (latin term for “as the circumstances arise” or “as necessary”)
RID	Relative Infant Dose (estimated) compared with maternal dose
SAB	Spontaneous Abortions
SGA	Small for Gestational Age
SNRI	Serotonin Noradrenaline Reuptake Inhibitor
SS	Statistically Significant
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressant drug

ⁱ NAS is a set of neurobehavioral signs in infants born to mothers taking antidepressants during pregnancy. NAS generally presents a few hours after birth and may include a combination of respiratory distress, feeding difficulty, jitteriness, irritability, temperature instability, sleep problems, tremors, shivering, restlessness, jaundice, rigidity and hypoglycemia.

2.0 Mental Health Disorders in the Perinatal Period

2.1 Prevalence

Mental health disorders in the perinatal period are a significant health issue. Perinatal depression is the most commonly diagnosed, with the research reporting rates as high as 16%. Rates of PND and other mental health disorders vary widely in the published literature because:

- Sample characteristics differ (e.g., high-risk women, first time pregnant women, women with a history of depression, etc).
- Definitions and measures used to define mental health disorders differ (e.g., for depression, use of a screening tool such as the EPDS versus clinical interviews).
- Many studies use very small sample sizes, hampering generalization to the population at-large.
- It is often unclear if the researchers are reporting new cases of a mental health disorder or already existing cases.

The most important source of variation is whether researchers estimate prevalence rates based on a single point in time (e.g. at 24 weeks gestation) or over a period of time (e.g. the entire pregnancy). The majority of the research estimates prevalence at a single point in time, and researchers choose varying time points for their estimate. The prevalence of a major depressive disorder at 3 months postpartum is not the same as the prevalence at 9 months postpartum and nor would this be expected; however, both of these time points are in the first postpartum year and thus are both estimates of the prevalence of postpartum depression. Table 1 provides what we believe are reliable estimates of the prevalence rates of depression, anxiety disorders, bipolar disorder and schizophrenia (schizophrenia is the most well-known of the psychotic disorders) in perinatal and non-perinatal populations.

Current evidence suggests that the rates for depression are the same in perinatal and non-perinatal populations while the rates for anxiety disorders and bipolar disorder may be slightly higher in the perinatal population (the perinatal period is a vulnerable time for relapse).² The rate for schizophrenia is similar in perinatal and non-perinatal populations (i.e., the perinatal period is not a particularly vulnerable time for relapse).

Table 1: Prevalence of Depression, Anxiety, Bipolar Disorder & Schizophrenia in Perinatal & Non-Perinatal Populations

Disorder	Pregnancy	Postpartum	Non-Pregnant Adult Population
Depression			
Major depressive disorder (MDD)	Estimates suggest that between 5%–16% of women will experience MDD at some point during their pregnancy. ³⁻⁶	Estimates suggest that between 4.2%–9.6% ^{3,7-9} will experience a major depressive disorder between birth and 3 months postpartum and estimates vary between 9.3% and 31% ^{6,10,11} for the first year postpartum.	No evidence that there is a difference in prevalence between perinatal women and women of childbearing age.
Anxiety Disorders			
Generalized anxiety disorder (GAD)	Between 1.3-8.5% will experience GAD during pregnancy. ^{5,11,12}	4.4%–8.2% ^{4,8,13,14} will experience GAD in the first year postpartum.	In women of childbearing age, approx 3% ¹⁵ will experience GAD in a year.
Panic disorder (PD)	Prevalence during pregnancy and the first year postpartum: 1.3%–5.4%. ^{12-14,16-19}		In women of childbearing age, 1%–2% ²⁰ will experience PD in a year.
Obsessive compulsive disorder (OCD)	Between 0.2%–3.4% will experience OCD during pregnancy. ^{12-14,18,19}	2.7%–3.9% will experience OCD in the first year postpartum. ^{12-14,18,19}	In women of childbearing age, 1.5%–2.1% ²⁰ will experience OCD in a year.

Disorder	Pregnancy	Postpartum	Non-Pregnant Adult Population
Bipolar disorder	No reason to suspect increased prevalence, but there is a reported increase in exacerbation of symptoms. 45–50% of pregnant women with bipolar disorder report exacerbated symptoms. ²¹⁻²³	Increased risk for development of bipolar disorder or a psychotic episode. Women with existing bipolar disorder have a 25%–30% recurrence rate in the immediate postpartum ^{24,25} and relapse rates at 3-6 months postpartum of 67%–82%. ²¹⁻²³ Rate of postpartum psychosis is 10–20% among women with bipolar disorder. ²⁶⁻²⁸	Approximately 2.1% ²⁹ of Canadian women will experience bipolar disorder in their lifetime. About 0.5% ³⁰ experience bipolar disorder each year.
Schizophrenia (psychotic disorder)	No reason to suspect increased prevalence.	There is no evidence to suggest an increased risk of recurrence in patients who were previously stable, nor is there evidence that the risk of psychotic episodes increases in the postpartum period. ³¹⁻³⁴	Approx 1% in the general population including men and women. ³⁵

2.2 Clinical Significance

2.2.1 Impact of Untreated Mental Health Disorders

Mental health disorders in the perinatal period are particularly important because they occur at a critical time in the lives of the woman, her baby and her family. Failure to treat promptly may result in a prolonged, negative effect on the mother, the relationship between the mother and baby and on the child’s psychological, social and educational development. The relationship between the woman and her partner may also be negatively affected.³⁶

Because depression is the most diagnosed of the mental health disorders in the perinatal period, research on the impact of untreated mental health disorders is often based on studies of depressed women. It is likely that the impact of other mental health disorders is similar.

A. Potential impacts on women

- Negative views of motherhood & themselves as mothers.
- See their baby’s behaviour as “difficult”.
- May not recognize their baby’s cues & respond appropriately, with potential of negative consequences to baby’s development.
- May breastfeed for shorter period of time.
- May use alcohol, cigarettes or other substances.
- Increased risk of future episodes of depression and other mental health issues.
- Risk of suicide (rare but does occur, especially in cases of untreated postpartum psychosis). (refer to section 7.1 for information about suicide).

B. Potential impacts on babies

- Behaviour disturbances:
 - Quicker to cry & cry louder & longer.
 - Spend less time in the “quiet & alert” state when they learn the most about their environment.
- Development delays:
 - May walk & talk later than others.

- Social issues:
 - May have more difficulty establishing secure relationships.
 - May be socially withdrawn.
- Risk of infanticide (rare but does occur, especially in cases of untreated postpartum psychosis; refer to section 7.2 for information about infanticide).

C. Potential impacts on partners/families (see section 3.4 for a discussion on partners and depression)

- Relationship disruption (increased risk of separation/divorce).
- Partners may also be depressed and may need treatment.
- A meta-analysis³⁷ of depression rates in men (rates in same-sex couples have not been well studied) in the perinatal period reported:
 - Depression rates of about 10% (studies ranged from 1.2%–25.5%).
 - Rates were highest in the 3–6 month postpartum period.
 - A moderate positive correlation between paternal and maternal depression.
- Partner depression in the perinatal period has been shown to have many of the same negative impacts on relationships, family and the baby as maternal depression.³⁸

2.2.2 Barriers to Seeking Help

There are many barriers to women with perinatal mental health disorders seeking help. Similar to studies on the impact of untreated mental health disorders, most of the research on barriers to seeking help has been based on studies of depressed women. Similar factors are likely to affect women experiencing other mental health disorders.

Barriers to seeking help include (but are not limited to):

- Stigma (guilt, shame and judgement) associated with a mental illness or asking for help.
- Lack of knowledge of normal adjustment to becoming a parent and what is a mental health disorder that requires help.
- Minimizing symptoms and thinking they will just go away (denial).
- Lack of awareness about mental illness and that it is treatable.
- Lack of awareness of the implications of mental illness if not treated.
- Spoken and interpretive language limitations.
- Concerns about the baby being removed from parental care.
- Lack of child care & transportation to get to appointments.
- Lack of available services.

Most women need the support of health professionals, family and friends to seek assistance for a mental health disorder.

2.3 Key Points

Key points:

- As many as one in five women in BC will experience a mental health disorder during their pregnancy and/or in the postpartum period. Perinatal depression is the most diagnosed mental health disorder, with the research reporting rates as high as 16% (see Section 2.1 for specifics).
- Mental illness affects all aspects of a woman's life and that of her baby and partner/family. Without treatment, it can contribute to compromised prenatal care, increased risk of obstetrical complications, self-medication and/or substance related disorders, compromised mother-infant interactions and

cognitive/neuro behavioural impairments in the early preschool years. The most tragic consequences are maternal suicide and infanticide.

Although mental illness is serious, with the right strategy and a coordinated approach, it can be detected early and effectively treated. Most women need the support of health professionals, family and friends to seek assistance for a mental health disorder.

3.0 Perinatal Depression

3.1 Education and Prevention

3.1.1 What is Perinatal Depression?

Perinatal depression (PND) is a term used to describe a major depressive episode during pregnancy (also referred to as the antepartum or antenatal period) and/or after the birth (also referred to as the postpartum or postnatal period) or adoption of a baby. Perinatal depression is more than the “Baby Blues”.

Baby (Postpartum) Blues

- Occurs in up to 50%–80% of new mothers.
- Generally occurs between three and five days postpartum.
- May be characterized by crying for no apparent reason, rapid mood swings (happy one minute and sad the next) and feelings of anxiety.
- These are normal feelings and responses to the birth of a new baby.
- Symptoms usually resolve within a week or two and do not require treatment. Only a small percentage of these women progress to postpartum depression.

Perinatal Depression (PND)

- Occurs in up to 16% of perinatal women (see section 2.1 for details on prevalence).
- May occur anytime during pregnancy or within the first year after childbirth/adoption.
- May start with the same symptoms as the baby blues but the symptoms don’t resolve within two weeks and they become more severe.
- Unlike baby blues, the symptoms require treatment and, if not treated, can negatively impact the mother, baby and family.

3.1.2 Signs and Symptoms

Signs and symptoms of depression in the perinatal period are similar to those occurring at other times of life.

The American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders DSM V³⁹ defines PND as a sub-category of a major depressive disorder. It does not define PND as a discrete disorder.

The APA DSM-V criteria for a major depressive disorder include:

- At least one of the following must be present for at least a 2-week time period:
 - Depressed mood.
 - Anhedonia (loss of interest or pleasure).
- At least five or more of the following must be present over the same 2-week time period:
 - Feeling sad most of the time, nearly every day.
 - Decrease in pleasure or interest in all, or almost all, daily activities, nearly every day.
 - Changes in appetite (with marked weight gain or loss).
 - Sleep disturbance (insomnia, hypersomnia), nearly every day.
 - Psychomotor retardation or agitation nearly every day (observable by others).
 - Lack of energy or fatigue nearly every day.
 - Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
 - Difficulty concentrating, or making decisions, nearly every day.
 - Frequently occurring thoughts of death, suicide or suicidal plan.
- Symptoms must cause significant impairment or distress in social, occupational or other important daily living functions.

The DSM-V criteria for diagnosis of “depression with peripartum onset” (also referred to as PND) indicates that the onset of the depressive episode must occur during pregnancy or within four weeks after childbirth.³⁹ Clinical experience in BC has shown that symptoms can appear anytime up to one year postpartum.

3.1.3 Risk Factors

Major risk factors for perinatal depression include:

- Personal history of depression. This is the strongest risk factor for depression during pregnancy and a strong predictor of postpartum depression.^{40,41}
- Up to 50% of women who have a history of depression before conception and during pregnancy will experience depression during the postpartum period.^{40,42,43}
- History of postpartum depression with a previous pregnancy. More than 40% of women who experience postpartum depression will experience a recurrent episode after a subsequent pregnancy.⁴⁴
- Family history of depression. Up to 50% of women experiencing postpartum depression have a family history of psychiatric illness.⁴⁵⁻⁴⁷

Contributing risk factors include:

- Excessive anxiety during pregnancy.
- Poor social support – social isolation, recent move, poverty, cultural or language issues.
- Relationship or family conflict.
- Recent adverse life events (e.g., loss of close relative or friend).
- Maternal anxiety.
- Life/financial stress.
- Intimate partner violence.
- Unintended pregnancy/ambivalence towards pregnancy.
- Infants with health problems or perceived difficult temperaments.
- Chronic/acute maternal health problems.

3.1.4 Prevention

Antenatal depression:

- A systematic review published in Scotland (2012) concluded that in the absence of identified risk factors, the evidence doesn't support specific interventions for the prevention of depression during pregnancy.⁴⁸

Postpartum depression:

- With respect to non-pharmacotherapies, a 2013 Cochrane review⁴⁹ of 28 trials (n=17,000 women) covering a range of psychosocial and psychological interventions for preventing postpartum depression concluded that women who received a psychosocial or psychological intervention were significantly less likely to develop postpartum depression than those that received standard care. The Cochrane systematic review included studies that examined patient populations at no known risk and women who were identified as being at-risk of developing postpartum depression. They excluded trials where more than 20% of participants were depressed at trial entry.
 - The most promising interventions included (1) intensive, individualized postpartum home visits provided by public health nurses or midwives; (2) lay (peer)-based telephone support; and (3) interpersonal psychotherapy.
 - Interventions provided by health professionals and lay individuals were similarly beneficial. Single interventions were beneficial as were those that involved multiple contacts.
- With respect to pharmacotherapy, a 2012 Scottish review concluded there was insufficient evidence to make any recommendations for or against the use of antidepressants or estrogen hormonal therapies in the prevention of postpartum depression. They reported there was some evidence that progestins may worsen outcomes.⁴⁸

3.2 Screening and Diagnosis

3.2.1 Screening

3.2.1.1 Screening and Early Detection

Perinatal depression has broad-reaching consequences on the mother, baby and family (see section 2.2.1 Impact of Untreated Mental Health Disorders). Early detection and treatment can help to eliminate or reduce these impacts.

The literature describes three basic approaches to the early detection of depression:

1. Screen all pregnant and postpartum women for depression at periodic intervals during the perinatal period (universal screening). If the screen is positive, conduct a diagnostic assessment interview (see section 3.2.2) to determine if depression is present.
2. Screen pregnant and postpartum women with known risk factors and/or exhibiting clinical clues of depression at periodic intervals during the perinatal period (targeted screening). If the screen is positive, conduct a diagnostic assessment interview (see section 3.2.2) to determine if depression is present.
3. Do not screen pregnant and postpartum women for depression but, if symptoms of depression are apparent, conduct a diagnostic assessment interview (see section 3.2.2) to confirm the diagnosis.

In May 2013, the Canadian Task Force on Preventive Health Care⁵⁰ recommended screening only when symptoms are apparent. However, they acknowledge that this recommendation is not a strong one, based on the weak evidence available in the studies that met their review criteria.

There are, however, three fair or good-quality randomized trials from the US, UK, and Hong Kong that demonstrate that routine screening with follow-up by low-intensity interventions is associated with modest improvements in maternal depression.^{52-54,55} These authors and others conclude there are benefits to universal screening.^{56,57} In addition, there is an impact on the child and the mother/child relationship when the mother is suffering depression (see section 2.2.1). A BC Provincial Position Statement⁵⁸, supported by BC Reproductive Mental Health Program, Perinatal Services BC and the BC Ministry of Health, recommends universal screening of perinatal women for depression. This was developed following a Provincial Consensus Meeting which considered expert opinion and a broad range of perinatal-specific literature, including evidence on the impact of depression on the mother/baby dyad.

Although there is conflict about the value of universal screening, there is consensus about the importance of healthcare providers being aware of, and alert to, clinical clues⁵⁰ and regularly enquiring about depressive symptoms⁵⁹ in perinatal women. Despite the consensus that healthcare providers should be alert to clinical cues of depression in perinatal women, research has shown that many perinatal women with high levels of depressive symptoms are not recognized as depressed by their healthcare providers.⁶⁰⁻⁶³ In fact, studies have suggested that major depressive episodes go undiagnosed more often in pregnant women than in non-pregnant women.⁶² When a screening tool, such as the EPDS is used, significantly more women are accurately diagnosed with depression.^{61,63,64} Many healthcare providers report that screening tools are useful in providing a non-threatening mechanism for initiating the discussion of emotional issues.

Some exceptions may apply such as situations in which the healthcare provider and woman have a long-standing relationship and there are no apparent symptoms or risk factors for depression. Nonetheless, even in these circumstances many clinicians feel perinatal women are less likely to report depressive symptoms because of social expectations and feel that the systematic use of a self-administered screening tool enables women to express these feelings more easily.

There are many tools available that can be used to screen for depression. Most of the tools can be completed in less than 10 minutes and have a sensitivityⁱⁱ ranging from 45 – 100% and a specificityⁱⁱⁱ ranging from 72– 100%. With a few exceptions (e.g., Edinburgh Postnatal Depression Scale and the Postpartum Depression Screening Scale), the tools were developed for general populations and in many cases, have not been validated in perinatal populations. See Table 2 for examples of depression screening tools and their characteristics.⁶⁵

Table 2: Common Depression Screening Tools

Screening Tool	Number of Items	Time to Complete	Sensitivity ⁱⁱ	Specificity ⁱⁱⁱ
Edinburgh Postnatal Depression Scale (EPDS)	10	<5 min	59 – 100%	49–100%
Postpartum Depression Screening Scale (PDSS)	35	5 – 10 min	91–94%	72–98%
Patient Health Questionnaire-9 (PHQ-9)	9	<5 min	75%	90%
Beck Depression Inventory (BDI)	21	5 – 10 min	48 – 82%	86 – 89%
Beck Depression Inventory-II (BDI-II)	21	5 – 10 min	56 – 57%	97 – 100%
Centre for Epidemiologic Studies Depression Scale (CES-D)	20	5 – 10 min	60%	92%
Zung Self-Rating Depression Scale (Zung SDS)	20	5 – 10 min	45 – 89%	77 – 88%

Source: American College of Obstetricians and Gynecologists, 2010.

3.2.1.3 *Edinburgh Postnatal Depression Scale (EPDS)*

In BC, the Edinburgh Postnatal Depression Scale (EPDS) is the recommended depression screening tool for the perinatal period.¹ It is one of the most common tools used world-wide to screen for depression in perinatal women. It has been specifically validated in perinatal populations and several studies have demonstrated its acceptability to women.

The Tool

- Developed by Cox and colleagues in 1987 specifically to screen for depression in the postpartum period.⁶⁶
- It has subsequently been validated for use during pregnancy.
- Ten-item self-report questionnaire in which women are asked to rate how they have felt in the previous seven days (this is the only validated time period).
- EPDS is a screening tool and is designed to provide guidance on which women require further assessment by a trained healthcare provider. **A positive screen on the EPDS is not the same as a diagnosis of depression.** A process for further assessment and follow-up of women who score positive is integral to a depression screening program.
- The EPDS is validated as a screening tool for perinatal depression but not for perinatal anxiety. However, because many women with PND also experience anxiety, screening women for depression and directing those with positive scores for further assessment/treatment will also help women with co-existing depression and anxiety.
- See Appendix 1 for the English version of the EPDS. Translated versions of the tool are available at www.perinatalservicesbc.ca/ForHealthcareProviders/Resources/ProfessionalToolbox/EPDSScale.

ii Sensitivity (true positive rate): the percentage of depressed women who are captured in the positive screen group (i.e., correctly identified as having depression).

iii Specificity (true negative rate): the percentage of non-depressed women who are not captured in the positive screen group (i.e., correctly identified as not having depression).

How to administer the EPDS

- The literature supports the administration of the EPDS by telephone, face-to-face, mail-in and internet administration. All forms of administration have been shown to be valid.
- Self-administration (mail-in, internet administration) has been shown to result in more positive screens and higher overall EPDS scores. While we currently cannot explain why self-administration results in higher EPDS scores, it is something to be aware of when reviewing scores. Possible reasons include:
 - Higher rates of false positives.
 - More honest responses.
 - Participation from a different group of women.
- Regardless of the method of administration (self or provider administered), the tool should be provider-scored so that proper follow-up is offered when women screen positive and/or have a positive score on question 10 (suicidality).

When to administer the EPDS

During pregnancy:

- There is no research evidence recommending a specific timeframe for screening during pregnancy. In BC, screening between 28 and 32 weeks gestation is suggested for practical reasons but the tool is valid anytime.
- Earlier screening promotes earlier identification of depression and increases the likelihood of improving outcomes for mothers and babies; however, screening very early in pregnancy can be challenging and may lead to missing depression that develops later in pregnancy.

Postpartum:

- The EPDS has been shown to be valid as a postpartum depression screening tool anytime between three days and two years postpartum (although the postpartum period is usually considered up to one year postpartum in the organization of services in BC). The onset of PND is highest in the first three months postpartum, but it can begin anytime up to 12 months.
- If the EPDS is to be universally administered only once during the postpartum period, the suggested timeframe is between six and 16 weeks postpartum. This timeframe balances the benefits of early treatment for women who experience early onset PND with the risk of screening out women who experience late onset PND.
- An alternative approach would be to universally administer the EPDS before eight weeks postpartum and repeat the screening between four and six months for women with moderate scores on the early screen.

Scoring the EPDS and follow-up

- Each question is scored 0 (normal), 1, 2 or 3 (severe), giving a maximum score of 30 for all ten questions.
- Choice of a cut-off score (the score used to determine when you will refer a woman for further assessment) is about maximizing sensitivity (capturing the largest number of depressed women in the positive screen group) while maintaining a high level of specificity (avoiding the inclusion of non-depressed women in the positive screen group).
- The literature provides guidance on validated scores for detecting depression that maximize sensitivity and maintain a high level of specificity.
 - To screen for **probable** depression:
 - 15 or more in antenatal women⁶⁷
 - 13 or more in postpartum women⁶⁸⁻⁷²
 - To screen for **possible** depression:
 - 13 or more in antenatal women⁶⁷
 - 10 or more in postpartum women⁶⁸⁻⁷²

Table 3 interprets the findings from the literature and makes recommendations on follow-up actions based on EPDS scores. To avoid the complexities associated with different cut-off scores for pregnant and postpartum women, it is recommended that the lower threshold score for postpartum women be used.

Table 3: EPDS Scores: Interpretation and Actions

EPDS Score	Interpretation	Action
Less than 8	Depression not likely	Continue support
9–11	Depression possible	Support, re-screen in 2–4 weeks. Consider referral to primary care provider (PCP).
12–13	Fairly high possibility of depression	Monitor, support and offer education. Refer to PCP.
14 and higher (positive screen)	Probable depression	Diagnostic assessment and treatment by PCP and/or specialist.
Positive score (1, 2 or 3) on question 10 (suicidality risk)		Immediate discussion required. Refer to PCP ± mental health specialist or emergency resource for further assessment and intervention as appropriate. Urgency of referral will depend on several factors including: whether the suicidal ideation is accompanied by a plan, whether there has been a history of suicide attempts, whether symptoms of a psychotic disorder are present and/or there is concern about harm to the baby.

Linguistic/cultural considerations in administering the EPDS

- Translated versions of the EPDS are valid for depression screening for the most common non-English speaking groups in BC, including Chinese, Punjabi, Vietnamese, Korean and Farsi.
- Translated versions are not a direct translation, but account for differences in use of language and cultural considerations.
- A cut-off score of 10 has been validated for all groups when screening for **possible** depression. Studies have not provided a cut-off score when screening for **probable** depression; however, there is no evidence to suggest it would be different than for English-speaking women.
- The EPDS has been validated for use in Hindi women during pregnancy with a cut-off score of 13 or more. It has not been validated in the postpartum period.
- The EPDS has not been validated in Tagalog. This translation should be used with caution, along with any other translation that has not been properly validated.
- The EPDS has been validated in Aboriginal populations in Saskatchewan and Aboriginal populations in Australia. Thus, it is most likely also valid for use in Aboriginal populations in BC. Some level of caution is required, however, as it has not been directly validated in BC Aboriginal populations.
- Translated versions of the EPDS are available at www.perinatalervicesbc.ca <http://www.perinatalervicesbc.ca/ForHealthcareProviders/Resources/ProfessionalToolbox/EPDSScale/default.htm>

Use of the EPDS for partners, adopted parents and step parents

Partners (see section 3.4 for a discussion of partners and depression):

- The EPDS is valid for depression screening for new biological fathers (there is nothing in the literature regarding the validity in same-sex partners).
- The valid and reliable timeframe for offering the EPDS to new fathers is similar to new mothers.
- The literature suggests it may be appropriate to use a lower cut-off score for fathers than mothers: 10 in fathers versus 13 in mothers for probable depression (men tend to answer lower on the questions about crying and self-harm).

- Targeted screening could be offered to fathers with partners who are depressed as there has been shown to be a moderate correlation between partner and maternal depression.³⁷

Parents of adopted babies:

- The EPDS is valid for mothers/parents of adopted babies.
- There is no reason to adjust the method, timing of administration or the cut-off score for use with adopted versus biological parents.

Step parents:

- Although it has not been directly validated, there is evidence to suggest that the EPDS can also be used in step parents.

3.2.2 Diagnosis

Before diagnosing a mental health disorder, it is important to exclude medical conditions that might cause symptoms that mimic a mental health disorder. Concurrent substance related disorders should also be ruled out.

Assuming medical conditions have been excluded, the BC Practice Support Program^{iv} recommends the following steps for diagnosing depression (or any other mental health disorder):⁷³

1. Diagnostic assessment interview (see Appendix 2 for guidelines for a diagnostic assessment interview in the perinatal period).
2. Confirmation of the suspected diagnosis with the DSM-V criteria.

Diagnosing depression in the perinatal period can be challenging. Normal emotional changes and responses may be mistaken for depression or, conversely, may mask depressive symptoms:

- Pregnancy: Somatic symptoms of pregnancy and depression may overlap. e.g., insomnia, decreased energy, poor concentration, appetite changes and nausea.
- Postpartum: Symptoms of normal adjustment, “baby blues” and/or sleep deprivation may overlap.

Areas of focus that help to distinguish depression from normal emotional changes and responses in the perinatal period include:

- Persistent and marked depressed mood/sadness/irritability/loss of pleasure.
- Persistent and marked decrease in concentration/decision-making.
- Feelings of hopelessness and being constantly overwhelmed by the responsibilities of parenthood.
- Statements about being a “bad” or “terrible” mother.
- Statements of guilt or worthlessness as a parent.
- Withdrawing from family, friends and social contacts.
- Co-existence of symptoms of anxiety (depression and anxiety often co-exist in the perinatal period):
 - Physical symptoms such as muscle tension, shortness of breath, rapid heartbeat, dizziness, dry mouth and nausea.
 - Feeling restless, on edge or irritable.
 - Thoughts of unrealistic or excessive worry about the baby or others.
 - Unable to sleep even when the baby is sleeping.
 - Frequent physician visits for various physical complaints about their health or that of their baby.

^{iv} The BC Practice Support Program (PSP) provides training and support (learning modules) for physicians and their medical office assistants designed to improve clinical and practice management and to support enhanced delivery of patient care. The PSP began as an initiative of the General Practice Services Committee (GPSC), a partnership between the BC Medical Association (BCMA) and Ministry of Health (MOH). The Program now receives additional direction, support and funding from the Shared Care Committee and the Specialist Services Committee (also a partnership between the BCMA and MOH).

- Thoughts or images of harm to self and/or baby, either accidental or intentional.
- Suicidal ideation/passive need to “escape”.

3.3 Treatment and Self-Management

This section reviews the most common treatments for perinatal depression. Most are also appropriate for the treatment of anxiety disorders and as adjuncts to pharmacotherapy in the treatment of bipolar disorder and psychotic disorders.

The treatment recommended for a specific woman will depend on several factors including:

1. The nature of the mental health disorder.
2. The severity of symptoms.
3. Her previous response to treatment.
4. The support, resources and desires of the woman.

General guidelines in terms of the order in which treatments are offered:

- For women with mild to moderate symptoms, non-pharmacological treatments are recommended before pharmacological treatments. If non-pharmacological treatments are not effective, medication may be required.
- For women with severe symptoms, medications may be initiated as the first-line therapy and non-pharmacological treatments added when the time is appropriate. Women who are acutely suicidal will require intensive home treatment or hospitalization.

Table 4: Common Treatments Used for the Treatment of PND

Severity of Symptoms	Treatment & Self-Management
Mild to moderate	A. Psychoeducation B. Self-care: The NEST-S Program C. Psychotherapies <ol style="list-style-type: none"> i. Cognitive behavioural therapy (CBT) ii. Interpersonal therapy (IPT) iii. Psychodynamic therapy (PDT) iv. Group therapy (therapist and/or peer led) v. Parent-infant psychotherapy vi. Couples and family therapy D. Bright light therapy
Moderate to severe or at high risk of relapse	Treatments listed above plus: E. Pharmacotherapy (medications) (see Appendix 5) F. Electroconvulsive therapy (ECT) (if unable to tolerate/take medications or in whom a rapid response is required – e.g., psychosis or suicide risk)

3.3.1 Psychoeducation

The goal of psychoeducation is to help women and their families understand their symptoms and the underlying disorder, learn about available treatments and reinforce effective coping strategies.

Psychoeducation has been shown to be effective in both individual and group settings.^{74,75}

In the case of PND (similarly with other mental health disorders), specific topics important to cover in psychoeducation include:

- Information about the disorder (e.g., PND).
- Prevalence.

- Signs and symptoms.
- Risk factors.
- Benefits of early treatment.
- Possible treatments.
- Expected progress during treatment.

3.3.2 Self-care: The NEST-S Program

Self-care is often neglected by women in the perinatal period, particularly postpartum when they are focused on caring for their baby and/or other family members. Self-care is about making positive changes in one’s life that will help to lessen depression.⁷⁶ In BC, a common acronym used to help women remember the basic steps in self-care is “NEST-S”.⁷⁶

Each letter in NEST-S stands for one area of self-care:

- **Nutrition:** Eating nutritious foods throughout the day.
- **Exercise:** Getting regular exercise. There is considerable research on the benefits of exercise for improving depression.⁷⁷
- **Sleep & rest:** Sleep is very important for both physical and mental health. Getting enough in the perinatal period can be challenging.
- **Time for self:** Taking self-time is an area that new mothers often neglect. This is a particular concern in women who are depressed and/or experiencing other mental health disorders.
- **Support:** Social support plays an important role in helping new mothers adjust to the life changes that go along with being a mother. Healthy relationships are a protective factor against depression and other mental health disorders and are an important factor in recovery.

*Coping with depression during pregnancy & following the birth*⁷⁶ and *Coping with anxiety during pregnancy & following the birth*⁷⁸ are both helpful resources for women with depression and/or anxiety. They provide practical information on depression and anxiety in the perinatal period, as well as different exercises and activities (self-care strategies) that will help lead to positive changes. The guides utilize the principles of cognitive behavioural therapy to guide women in making changes. Both can be downloaded at www.bcmhsus.ca or www.reproductivementalhealth.ca.

Mind-Body Modalities

Mind-Body Modalities are useful in many ways because they can link together aspects of the NEST-S Program for women. They might be “Exercise”, “Time for self”, the “rest” part of “Sleep and rest” and also the “Support” area too. Increasing numbers of women practice one or more mind-body modalities for the feelings of symptom relief and sense of wellness that they provide.

Although many other cultures’ traditions and beliefs are based on mind-body connections, western cultures have more recently acknowledged these complex links and the ability to change mind states through integrative body work. “Mind” encompasses thoughts, emotions, beliefs and images. “Mind-Body Modalities” (MBM) are endorsed by The National Center for Complementary and Alternative Medicine (NCCAM) and include, but are not limited to,

- Meditation
- Mindfulness
- Tai Chi
- Qigong
- Yoga
- Biofeedback
- Guided imagery
- Creative therapies e.g., Art therapy
- Relaxation
- Hypnosis
- Prayer

Mind-body interventions have been shown to help in reducing stress and improving overall mood in perinatal women. Mind-body techniques such as yoga, meditation and breathing exercises may also help to increase birth weight and reduce preterm births.⁷⁹

Mindfulness Meditation and Relaxation

Mindfulness, based on Buddhist tradition, teaches non-judgmental focus on present thoughts and emotions from a state of conscious awareness. It is regarded as useful in the treatment of stress, anxiety, depressive relapse, disordered eating and addiction.⁸⁰⁻⁸⁴

- Mindfulness may be useful in treating mild to moderate depression or as an adjunct to pharmacotherapy for perinatal depression and/or anxiety. Research suggests it may reduce pregnancy-related anxiety, stress and depression as well as improving maternal-infant interactions in the postpartum period.^{85,86}
- Mindfulness can induce states of relaxation but is not considered a relaxation technique.⁸⁷

Relaxation techniques help to reduce stress and anxiety by promoting a calm physiological (body) response. The three basic relaxation techniques are diaphragmatic breathing, progressive muscle relaxation, and guided imagery. Developing these relaxation skills over time can improve overall health and stress management. Research suggests benefits may include lowered heart rate, improved patience, decreased irritability, increased energy, improved memory and concentration, better sleep, fewer headaches, decreased pain and overall mental and physical improvement.⁸⁷

Mindfulness Meditation & Relaxation are complimentary & interchangeable. They involve emptying the mind of “clutter” and being in the moment, free of distracting negative thoughts and emotions. These techniques are essential building blocks in the self management of stress and anxiety.

3.3.3 Psychotherapies

Research supports the use of psychotherapies (sometimes referred to as “talk therapies”) as effective for the treatment of depression and other mental health disorders in the perinatal period.

- Therapies may focus on one or both parents or the mother/baby dyad or parent/baby relationship.
- Wider family may sometimes be involved.
- Therapies are effective when provided one-on-one or in a group setting.

Psychotherapies should be conducted by providers trained in the specific treatment(s). For example, CBT, IPT and PDT are effective in the treatment of PND and may be used on their own or in combination. However, not all therapists/counsellors or psychologists have training in all forms of therapy and practical considerations may determine the treatment offered.

All of these therapies are effective in treating perinatal depression. However, the relationship between the therapist/counsellor and woman is more important than the specific therapeutic approach.

3.3.3.1 Cognitive Behavioural Therapy

- Cognitive Behavioral Therapy (CBT) focuses on how thoughts can affect emotions which, in turn, can affect behaviour and body (physiological) responses. A hallmark feature of depression/anxiety is “negative, distorted thinking”. CBT teaches women to:
 - Identify upsetting, negative, distorted thoughts/assumptions.
 - Understand how their negative, distorted thoughts & assumptions influence their mood and behaviour.
 - Challenge and replace negative, distorted thoughts/assumptions with more realistic and accurate thoughts/assumptions.
 - Reduce behaviours that contribute to depression/anxiety.
 - Increase behaviours that contribute to greater physical and mental well-being.
 - Prevent relapse of symptoms.
 - Lessen overall symptoms of depression/anxiety.
- CBT is effective in treating a variety of mental health disorders such as depression, anxiety and panic attacks, obsessive-compulsive disorder and eating disorders in the general population, with a reported success rate of 52 to 97%.⁸⁸⁻⁹¹

- There is also evidence suggesting that CBT is effective in treating depression during pregnancy and postpartum.⁹²⁻⁹⁴
- In the treatment of mild to moderate depression in the perinatal period, CBT has been shown to be effective in combination with psychoeducation and self-care. In the treatment of moderate to severe depression, it is a helpful adjunct to pharmacotherapy.
- Several studies have reported that:
 - CBT is as effective as antidepressant medication for mild to moderate depression.^{89,91}
 - CBT provided in combination with an antidepressant medication yields more enduring results than does either treatment alone.^{93,95-97}
 - CBT may be provided individually or in groups.⁹⁸

3.3.3.2 *Interpersonal Psychotherapy*

- Interpersonal psychotherapy (IPT) focuses on role transitions, including changing roles and relationships with other people. It teaches the skills that are needed to adjust to changing roles and to improve interactions.
- IPT is effective in reducing depressive symptoms and increasing social adjustment in women with mild to moderate depression.^{89,91,99} IPT has also been shown to be effective in treating depression in the perinatal period.^{89,91,101-105}
- IPT provided in combination with an antidepressant medication is more effective than interpersonal psychotherapy alone.^{95,97,110}
- There is some suggestion, based on meta-analyses of other research studies, that IPT may be slightly more effective in treating depression than other forms of psychotherapies.⁹⁷
- IPT is a short-term therapy.
- IPT may be provided individually or in groups.^{111,112}

3.3.3.3 *Psychodynamic Therapy*

- Psychodynamic therapy (PDT) is also referred to as insight-oriented therapy.
- The goal of PDT is to increase self-awareness and understanding of the influence of the past on present behaviour. It focuses on unconscious processes as they manifest in present behaviour (e.g., trauma in early life that may have led to the present depression).
- In its brief form, PDT helps a person examine unresolved conflicts from past dysfunctional relationships and their impact on present behaviour (including parenting).
- PDT is often used in combination with other psychological techniques (most commonly CBT) to effect change.^{100,113}
- PDT has been shown to be effective in treating depression in the general population.^{100,113-117}
- There is less published research about the effectiveness of PDT in the perinatal period.
- The research that has been done suggests that PDT decreases rates of PPD when compared to a control group.^{92,118}
- Little or no research has been done on the effectiveness of PDT during pregnancy.
- PDT may be provided individually or in groups.⁹⁸

3.3.3.4 *Group therapy*

- Group therapy may be provided on its own or as an adjunct to other therapies.
- Group therapy may be therapist or peer led and may have continual intake (open group) or fixed intake (closed group). Group therapy usually occurs in person but is increasingly available through technological means (e.g., teleconference, videoconference or online).

- Group therapy provides a safe and accepting place to vent frustration and fears and receive comfort and encouragement from others. It may use any number of therapeutic approaches, including CBT, IPT and PDT.^{91,119,120}
- When group therapy is used in combination with antidepressant medications, patients experience better outcomes than when using antidepressant medications alone.¹²¹
- Group therapy has been shown to be an effective treatment for depression in the general population.^{122,123}
- There is also a large amount of random controlled trial evidence indicating that group therapy is effective for treating postpartum depression.^{108,124-129}
- Research has been done to determine whether PPD may be preventable using group therapy during pregnancy among a group of mothers deemed to be at high risk for PPD. Currently the evidence suggests that group therapy is not effective in preventing PPD in these groups.^{130,131}

3.3.3.5 Parent-Infant Psychotherapy

- Functional disorders (sleep and feeding disorders) and behavioural disorders are the most frequent reasons for psychiatric consultation for children under three years.¹³²
- Many studies have shown a significant association between these early disorders in babies and toddlers and the presence of depressive symptoms in their mothers.¹³³⁻¹³⁶
- Perinatal depression can cause an altered state of mind (sadness, apathy, preoccupation and/or psychotic thinking) which may impact the mother's capacity to be attuned to the world, including her capacity to look after her baby. Familiar alternate caregivers/partners can minimize these effects if they are intimately and consistently involved with the baby, until the mother is able to resume her parenting/maternal role if she desires to do so.
- Even after a mother's postpartum depression resolves, the developmental trajectory for many infants is derailed. This is seen both in physiological and other regulatory functions.
- Parent-infant psychotherapy is a therapeutic intervention which aims to improve the quality of the parent-infant interaction and the socio-emotional functioning of the baby. It focuses on the:
 - History of the parent(s), particularly their view of their own attachment experiences.
 - Mother/baby connections before the baby is born.
 - Observable and deducible parent/child interactional experiences.
- Questions, worries and concerns of mothers and parents are acknowledged and further studied.
- The therapist works with the parent(s) and the baby to help the parent(s) understand the relationship and develop a healthy attachment.
- The therapeutic connection between the mother and the therapist is critical in assisting the mother/infant dyad.
- The therapist may help the parent(s) to learn how to observe the baby and then ponder over her reactions and what is happening in the baby's mind.
- The mother's new way of being with the baby is charted with the help of the therapist.
- Situations in which parent-infant psychotherapy is most likely to benefit the baby and mother with perinatal depression disorders include:
 - Babies that are having difficulty regulating their eating, sleeping and emotions (crying).
 - Mothers that have concerns about their feelings toward their baby.
 - Mothers that have concerns about the way their baby reciprocates their expression of love and warmth.
- Despite considerable interest, there has been only a small amount of research in the area of parent-infant psychotherapy. The evidence that is available suggests that the outcomes are positive and generally persist for six months or more after the end of treatment.¹³⁷⁻¹⁴⁰

- Parent-infant psychotherapy has been shown to improve a child's symptoms of functional or behavioural disorder, mother-child interactions, maternal self-esteem, parenting stress and mother-infant conflict.^{137,138,140}
- Interventions involving both parents appear to be more effective and a supportive partner is an important predictor of success in parent-infant psychotherapy.¹⁴¹⁻¹⁴³
- Improvement in maternal outcomes are less pronounced when there is separation from the child's father, higher initial maternal anxiety and depression scores and more serious behavioral issues in the baby/children.¹³²
- Length of treatment, mother's educational status, presence of environmental risk factors, sex of the child and parental age and occupation had no effect on the effectiveness of parent-infant psychotherapy.^{132,141,144,145}
- In preventive interventions with depressed mothers, two meta-analyses showed that the most effective interventions:
 - Focused on sensitizing mothers to their baby's behavioural signals.
 - Lasted less than 16 sessions.
 - Started after babies were six months of age.^{141,142}

3.3.3.6 *Couples and/or Family Therapy*

- Strain in a couple's relationship has been shown to be a key factor in the development and outcome of PPD. Women who report poor quality relationships with their partner are both at higher risk for PPD¹⁴⁶⁻¹⁵⁰ and likely to suffer from more severe depression for a longer duration.¹⁵¹⁻¹⁵³
- While there has been limited research examining the effectiveness of couples and/or family therapy in the treatment of PND, there have been several randomized controlled trials that have examined its effectiveness on relationship distress and depression in the non-perinatal (general) population. Their results suggest that, compared to individual therapy, couples and/or family therapy is just as effective in improving depression symptoms¹⁵⁴⁻¹⁵⁷ and more effective in reducing relationship distress.^{154,155}
- The results from a small number of couples-based interventional trials demonstrate that the partner relationship plays an important role in both prevention and recovery from PPD.¹⁵⁸⁻¹⁶⁰
- Further, reports of a few case studies (based on very small numbers of couples or families) examining couples and/or family therapy as treatment for PPD suggest that this type of therapy has the potential to improve both maternal depressive symptoms as well as overall couple and/or family relationship dynamics.^{161,162}

3.3.4 *Bright Light Therapy*

- There is substantial evidence from non-perinatal populations (general population) that bright light therapy (BLT) is effective in treating seasonal affective disorder.¹⁶³⁻¹⁶⁵
- Research also suggests that BLT can be an effective treatment for depression in the perinatal period. Further, there is no evidence of adverse effects of light therapy on pregnancy.¹⁶⁶⁻¹⁶⁸
- Two small randomized controlled trials found evidence that bright white light treatment for five weeks significantly improved depression in a population of pregnant women with major depressive disorder, with treatment effects similar to those seen in antidepressant drug trials.^{166,167}
- Another trial suggested that depression ratings had improved by 49% among a group of pregnant women with major depression following three weeks of bright light therapy. These benefits lasted through five weeks of treatment.¹⁶⁸
- The effectiveness of BLT in a perinatal population was recently confirmed in a systematic review on the topic.¹⁶⁹

3.3.5 Pharmacotherapy (Medications)

3.3.5.1 Psychotropic Medications in the Perinatal Period

Psychotropic medications, in combination with psychoeducation, self-care and psychotherapies, are often necessary to treat women with moderate to severe PND and/or other mental health disorders. Prescribing psychotropic medications in pregnant or breastfeeding women, however, is very challenging. The risks of drug effects on the fetus/baby must be weighed against the risk of depression (or other mental health disorder) in the woman.

There is a substantial amount of negative commentary/messages on the internet, in newspapers and on television, about the risks of psychotropic medications in pregnancy or while breastfeeding. Women and their families who are exposed to such commentary may be understandably frightened by the thought that taking medications while pregnant or breastfeeding may harm their baby. Many assume that stopping or avoiding all medications while they are pregnant or breastfeeding is the right decision. In fact, the decision to abruptly stop all psychotropic medications and/or to not take medications in situations of serious mental health disorders may lead to a worsening of the disorders, which can negatively affect the developing fetus or new baby (see section 2.2.1 for a discussion of the impact). By contrast, a psychologically healthy mom can provide an emotionally secure relationship and environment for her baby to flourish.

Research on the effects of psychotropic medication exposure during pregnancy and breastfeeding is **ongoing and evolving**. Appendix 5 provides **current** information (as of March 2013) about the relative safety of medications currently used for the treatment of depression, anxiety disorders, bipolar disorder and psychotic disorders in the perinatal period. As more experience is gained, the guidelines will be updated accordingly. The tables included in this document compare risks of medication use during the perinatal period to the background risks of prematurity, spontaneous abortion, major congenital malformations, low birth weight, cardiac defects and neural tube defects.

The American Food and Drug Administration (FDA)-assigned pregnancy categories are used to classify the risk of the medications to the developing fetus. The Hale risk classification categories are used to classify the risk of the medications to the baby through exposure to breast milk. These categories may be subject to change over the coming years. The Motherisk website (Canadian) at www.motherisk.org (phone: 1-877-439-2744) provides additional medication-related information.

Refer to section 3.5 for key points and recommendations related to prescribing psychotropic medications in the perinatal period.

3.3.5.2 Medications for the Treatment of Perinatal Depression

The first-line medications used for the treatment of depression are antidepressants. If a co-existing anxiety disorder is present, benzodiazepines may also be beneficial. Benzodiazepines and hypnotics (non-benzodiazepines) may be useful on a PRN (as needed) basis to help with intermittent insomnia.

Of the antidepressants, selective serotonin reuptake inhibitors (SSRIs) are the most commonly used in the perinatal period, followed by serotonin-norepinephrine reuptake inhibitors (SNRIs) and then tricyclic antidepressants (TCAs).

While most newborns born to women who continue SSRI or SNRI treatment during pregnancy are healthy, approximately one third will experience Neonatal Adaptation Syndrome (NAS). This generally presents within a few hours following birth and may include a combination of respiratory distress, feeding difficulty, jitteriness, irritability, temperature instability, sleep problems, tremors, and restlessness. Typically NAS symptoms are **mild and transient**, generally resolving without treatment within two to three weeks of delivery.

There is a slightly increased risk of persistent pulmonary hypertension of the newborn (PPHN) in newborns exposed to SSRIs in utero; however, the absolute risk is very small and has not been very well-defined. PPHN is a rare condition defined as a failure of the normal relaxation in the fetal pulmonary vascular bed during the circulatory transition that occurs shortly after birth. A recent guideline (2013) from Perinatal Services BC, an agency of the Provincial Health Services Authority, recommends the use of pulse oximetry to test oxygen saturation every 4 hours for the first 24 hours following delivery to screen for this condition.¹⁷⁰

First trimester use of SSRIs/SNRIs is associated with a slightly increased risk of congenital heart defects (especially paroxetine). The recent guideline (2013) from Perinatal Services BC recommends the use of pulse oximetry after delivery to screen for the presence of congenital heart defects.¹⁷⁰

Refer to section 3.5 for key points and recommendations related to prescribing antidepressants in the perinatal period.

Refer to Appendix 5 for current information (as of March 2013) about specific medications commonly used in the perinatal period for the treatment of depression.

3.3.6 Electroconvulsive Therapy

Electroconvulsive therapy (ECT) is reported in the literature to be safe and effective in the treatment of severe mental illness during pregnancy and in the postpartum period. It is generally used for women experiencing severe depression who have not responded to medications.^{41,171,172}

It is also used when a rapid or higher probability of response is needed, such as women experiencing an episode of acute psychosis and/or who are suicidal.¹⁷³ For women in the postpartum period, ECT offers a treatment option that is safe for the baby and allows for continuation of the breastfeeding schedule with only minor disruptions at the time of the treatment.¹⁷⁴

During pregnancy, ECT should be provided in a hospital with the ability to manage maternal and fetal emergencies. Consultation with an obstetrician is recommended.¹⁷³

3.4 Partners and Depression

A recent meta-analysis (43 studies, 28,004 participants and 16 countries)¹⁷⁵ reported:

- Prenatal and postpartum depression was evident in about 10% of men during the perinatal period in the reviewed studies. This is a higher rate than for men in the general population.
- The highest risk period was between three to six months after the birth.
- There was a moderate positive correlation between partner and maternal depression.
- There was no causal role found between maternal and partner depression.

Risk factors:

Many of the same risk factors that contribute to depression in new mothers apply to partners including:

- Previous history of depression.
- Family history of depression.
- Worries about being a parent.
- Unintended pregnancy/ambivalence towards pregnancy.
- Life/financial stress.
- Poor social support.
- Poor partner relationship/conflict.
- Baby with health problems or perceived difficult temperaments.

Risk factors that seem to play a more prominent role for partners than new mothers include:

- Changing roles and responsibilities in the family.
- Feeling excluded when the attention from friends and family is on the mom and new baby.
- Missing pre-baby relationship with partner.
- Missing sexual relationship.
- Feeling overwhelmed with work pressures, expectations to provide financially for the family and being at home to participate in baby care.

Signs and symptoms:

Partners experiencing depression after the birth of a baby may have a multitude of symptoms, many of which are similar to those of new mothers and may include:¹⁷⁶

- Depressed, sad mood.
- Loss of interest or pleasure.
- Significant weight loss or gain.
- Trouble sleeping or over-sleeping.
- Fatigue, loss of energy or tired all the time.
- Restless feelings and inability to sit still or slow down.
- General anxiety and/or panic attacks.
- Problems with concentration and motivation.
- Increased anger/conflict in relationship.
- Significantly and persistently less productive at school, work, or in the home.
- Difficulty concentrating and making decisions.
- Increased use of alcohol or drugs.
- Physical symptoms such as headaches, digestive problems and pain.
- Feelings of worthlessness or guilt about parenting ability.
- Recurrent thoughts of death or suicide.

Screening:

The EPDS is valid for depression screening for new biological fathers (studies have not reported on the use for same-sex partners).

The valid and reliable timeframe for offering the EPDS to new fathers is similar to new mothers. A lower cut-off score may be considered for men as men tend to answer lower on the questions about crying and self-harm (cut-off score of 10 versus 13 for probable depression).

Treatment and support:

Effective treatments for partners with postpartum depression are similar to those used for new mothers.

The range of potential medications is broader because the risk to the fetus or baby is non-existent.

3.5 Key Points and Recommendations

Key Points

- Rates of depression are the same in perinatal women and (non-perinatal) women of childbearing age (~ 16%). (see Section 2.1 on prevalence).
- Major risk factors for perinatal depression include: personal history of depression,^{40,41} history of depression with a previous pregnancy⁴⁴ and family history of depression.⁴⁵⁻⁴⁷
- In the absence of identified risk factors, there is no evidence to support specific interventions for the prevention of depression during pregnancy.⁴⁸ There is, however, evidence to support specific interventions for the prevention of postpartum depression.
- Early detection of depression facilitates early intervention and treatment and is more likely to result in a favourable outcome for the mother, baby and partner/family.
- The Edinburgh Postnatal Depression Scale (EPDS) is a common, simple to administer, effective tool used to screen for perinatal depression.⁶⁶
- Translated versions have been validated for use in English-speaking and many of the common non-English speaking groups in BC (Chinese, Punjabi, Vietnamese, Korean and Farsi). The tool has also been validated with fathers and mothers/parents of adopted babies. The literature supports the administration of the tool by telephone, face-to-face, mail-in and internet.
- The EPDS is not a diagnostic tool. The gold standard for diagnosis is a diagnostic assessment interview and confirmation of the suspected diagnosis with the DSM-V criteria. Assessing the risk of suicide and potential risk to the baby are important components of the diagnostic assessment interview.
- Before diagnosing a mental health disorder, it is important to exclude medical conditions that might cause symptoms that mimic a mental health disorder. Concurrent substance use disorders should also be ruled out.
- A multi-prong treatment strategy for depression is the most effective. Mild and moderate depression is often successfully treated with a combination of non-pharmacological treatments. Depression that does

not respond to non-pharmacological treatments and/or severe depression may require medication. The risks of drug effects on the fetus/baby must be weighed against the risk of untreated depression in the woman.

- Non-pharmacologic treatments shown to be successful include psychoeducation, self-care, psychotherapies (also called “talk therapies”) and bright light therapy. With respect to psychotherapies, cognitive behavioural therapy, interpersonal therapy and psychodynamic therapy are all effective (psychodynamic therapy has been less well studied) and may be used on their own or in combination and with individuals, groups and couples/families. Parent-infant psychotherapy may be helpful in situations in which the mother’s depression has negatively impacted her relationship with her baby and affected aspects of the baby’s development.
- Electroconvulsive therapy (ECT) is reported in the literature to be safe and effective in the treatment of severe depression for those who have not responded to medications and/or who require a rapid or higher probability of response (e.g., acutely psychotic or suicidal).^{21,177,178}
- Perinatal depression is also a significant health issue for male partners. Rates are estimated to be about 10%.¹⁷⁵ This is a higher rate than for men in the general population. Signs and symptoms and the impact of the depression are similar to that for maternal perinatal depression, although the range of treatments is broader because the risk to the fetus or baby is non-existent.

Recommendations

Common to all perinatal mental health disorders:

1. Encourage women with a history or family history of a mental health disorder to plan their pregnancy, ideally timed when their mood (and physical condition) is as stable as possible.
2. For women with a chronic mental health disorder:
 - a. Work with the woman and other healthcare providers pre- and during pregnancy to develop an individualized treatment plan which optimizes the woman’s mental health during the perinatal period.
 - b. Consider referring the woman to a psychiatrist pre- or during pregnancy to assist with treatment planning and ongoing monitoring of the woman’s mental health status during the perinatal period.
 - c. If a woman decides to stop taking her medications prior to or upon discovery of her pregnancy without consulting a healthcare provider, pay particular attention to her mental status throughout the pregnancy and especially in the postpartum period (high risk of relapse).
3. For women requiring psychotropic medications in the perinatal period:
 - a. Support informed decision-making by discussing the risks and benefits of the medications with the woman as well as the risks of not treating her symptoms. Involve the woman’s partner and other family members whenever possible and where appropriate.
 - b. Use the minimum number of psychotropic medications at the lowest effective dose.
 - c. When breastfeeding while taking psychotropic medications, monitor the baby for any adverse effects.
4. Encourage women with severe mental health disorders that require multiple psychotropic medications to deliver in a hospital (versus a home birth). This will facilitate closer monitoring of the mother and baby. See PSBC guideline on Antidepressant Use During Pregnancy: Considerations for the Newborn Exposed to SSRIs/SNRIs.
5. Where possible, encourage breastfeeding (psychotropic medications are not usually a contraindication to breastfeeding):
 - a. Maximize the breastfeeding support provided to women to increase the probability of success (e.g., refer to a lactation consultant and/or public health nurse).
 - b. In situations where exclusive breastfeeding is not possible (e.g., medical reasons for the mother/baby or there are challenges with breastfeeding, including significant psychological stress for the mother), support infant feeding options that promote optimal nutrition for the baby and consider

the health and wellbeing of the mother. This may include supplementation with the mother's expressed breast milk, pasteurized donor milk, formula or fully formula feeding.

- c. Encourage women wanting to breastfeed but whose babies are premature or have significant health problems to discuss their psychotropic medications with their baby's pediatrician.
6. Educate partners and family members about recognizing the symptoms of mental health disorders and ways to support women during pregnancy and after the birth. Support should include ways to maximize the woman's opportunity for adequate sleep.

Specific to perinatal depression:

- 7. Assuming care pathways are established, screen all women for perinatal depression.^v
 - a. Screen using the EPDS at least once during pregnancy and once in the postpartum period. Suggested timeframes for administering the EPDS are: 28 to 32 weeks gestation (although the tool is valid anytime during pregnancy), 6 to 16 weeks postpartum and anytime concerns are identified.
 - b. Interpret the EPDS score for both pregnant and postpartum women using the guidelines in Table 5:

Table 5: EPDS Score, Interpretation & Action

EPDS Score	Interpretation	Action
Less than 8	Depression not likely	Continue support
9–11	Depression possible	Support, re-screen in 2–4 weeks. Consider referral to Primary Care Provider (PCP).
12–13	Fairly high possibility of depression	Monitor, support and offer education. Refer to PCP.
14 and higher (positive screen)	Probable depression	Diagnostic assessment and treatment by PCP and/or specialist.
Positive score (1, 2 or 3) on question 10 (risk of suicidality)		Immediate discussion required. Refer to PCP ± mental health specialist or emergency resource for further assessment and intervention as appropriate. Urgency of referral will depend on several factors including: whether the suicidal ideation is accompanied by a plan, whether there has been a history of suicide attempts, whether symptoms of a psychotic disorder are present and/or there is concern about harm to the baby.

^v Some exceptions may apply such as situations in which the healthcare provider and woman have a long-standing relationship and there are no apparent symptoms or risk factors for depression. In these situations, clinical judgement best guides the course of action.

- c. Utilize the guidelines in Table 6 for the treatment of women with mild, moderate and severe depression:

Table 6: Guidelines for the Treatment of Depression during the Perinatal Period

	Clinically Stable for 4–6 Months & Risk of Relapse is Low	Currently Symptomatic &/or Clinically Stable but Risk of Relapse is High
Treatment approach		
Pregnancy & Postpartum	<p>Mild to Moderate Depression: Focus on psychoeducation, self-care &/or psychotherapies. Medications are usually not required.</p> <p>Moderate to Severe Depression: Focus on psychoeducation, self-care &/or psychotherapies. Medications may also be required.</p>	<p>Mild to Moderate Depression: Focus on psychoeducation, self-care &/or psychotherapies. Medications may not be required.</p> <p>Moderate to Severe Depression: Medications are frequently required in addition to psychoeducation, self-care &/or psychotherapies.</p>
Medication management		
Preconception & Pregnancy	<p>If taking an antidepressant, consider a trial of gradually discontinuing the medication prior to pregnancy if the risk of relapse is low.</p> <p>If unable to discontinue the antidepressant, continue with the current (effective) medication.</p> <p>See Appendix 6 for recommended monitoring and folic acid supplementation guidelines for women taking antidepressants during pregnancy.</p>	<p>If taking an antidepressant, continue with the current (effective) medication.</p> <p>If not taking an antidepressant and one is required during pregnancy, consider an SSRI (1st option, most researched) or SNRI (2nd option). If possible, avoid paroxetine (SSRI) in the first trimester (risk of cardiac defects may be higher than with other SSRIs, although risk is still very small¹⁷⁹⁻¹⁸¹).</p> <p>See Appendix 6 for recommended monitoring and folic acid supplementation guidelines for women taking antidepressants during pregnancy.</p>
At birth	<p>Maintain therapeutic dose of antidepressant at the time of delivery and in the immediate postpartum period.</p> <p>See Appendix 6 for recommended monitoring guidelines for women taking antidepressants at the time of delivery.</p>	<p>Maintain therapeutic dose of antidepressant at the time of delivery and in the immediate postpartum period.^{vii}</p> <p>See Appendix 6 for recommended monitoring guidelines for women taking antidepressants at the time of delivery.</p>

vi Some clinicians advocate tapering the dose of antidepressants close to delivery and restarting them postpartum in the belief that this will reduce symptoms of Neonatal Adaptation Syndrome (NAS) following the birth. There are no studies that support this position. In addition, it would be very difficult to implement as most women do not know when they are going to deliver and thus may be off their medication for a significant period of time and put them at high risk of experiencing a relapse in their mood at the time of delivery or in the immediate postpartum period. The recommendation from the BC Reproductive Mental Health Program is for women to remain on a therapeutic dose of antidepressant at the time of delivery to reduce the risk of postpartum relapse.

	Clinically Stable for 4–6 Months & Risk of Relapse is Low	Currently Symptomatic &/or Clinically Stable but Risk of Relapse is High
Postpartum	<p>If an antidepressant is required in the postpartum period, continue with the current (effective) medication (postpartum is a vulnerable period for recurrence). Dose adjustments may be necessary postpartum.</p> <p>If not taking an antidepressant and one is required during postpartum, consider an SSRI. Citalopram is a good option (the infant plasma levels are lower than with some other SSRIs). Paroxetine is also a good option if the woman is not planning a pregnancy within the next year.</p> <p>See Appendix 6 for recommended monitoring guidelines for women taking antidepressants while breastfeeding.</p> <p>Continue treatment with antidepressants:</p> <ul style="list-style-type: none"> • If the first episode, treat for at least six to twelve months after achieving full symptom remission. • If three or more episodes have occurred, treat up to two years but consider indefinite/lifelong treatment if the illness is severe. 	
All phases	<p>Benzodiazepines and other hypnotics (non-benzodiazepines) may be useful on a PRN basis for intermittent insomnia.</p> <p>If co-existing anxiety disorder is present, concurrent treatment with benzodiazepines may be necessary. See section 4.4 on treatment recommendations related to anxiety disorders.</p>	

4.0 Anxiety Disorders

4.1 Education and Prevention

4.1.1 What is an Anxiety Disorder?

Everyone experiences anxiety from time to time. At low levels, anxiety can be helpful in increasing motivation, giving focus to solving everyday problems and avoiding dangerous situations. However, when anxiety becomes intense, lasts for a long time and/or is overwhelming and disruptive to daily life, it is referred to as an anxiety disorder. Anxiety disorders are common in the perinatal period.

Anxiety disorders are a group of related conditions rather than a single disorder. All are characterized by persistent or severe fear or worry in situations where most people wouldn't feel threatened. The situations causing the irrational fear or worry may be real or imaged. More than one type of anxiety disorder may be experienced at the same time.

The most common types of anxiety disorders occurring in the perinatal period are:

1. Panic disorder (PD)
2. Generalized anxiety disorder (GAD)
3. Obsessive compulsive disorder (OCD)
4. Post-traumatic stress disorder (PTSD)

Anxiety disorders in the perinatal period:

- The clinical features of anxiety disorders in pregnancy are similar to those in non-pregnant women except that concerns over the pregnancy and fetus may present as the predominant feature. e.g., women with panic disorders may interpret a panic attack as something being wrong with the fetus.
- Rates for anxiety disorders in the perinatal population are relatively high and may be as high as those for depression. Anxiety disorders and depression often co-exist. This is partly because feeling anxious all the time can cause people to feel depressed. As well, anxiety disorders are often linked to feelings of inadequacy because people with these conditions can feel their behaviour is irrational and damaging. These feelings of inadequacy can lead to depression.
- In an Australian study, two-thirds of women identified with an anxiety disorder had a co-morbid depression. Of women identified with a major depressive episode, 40% had a co-morbid anxiety disorder.⁵⁹ These findings are similar or slightly higher to the findings in other studies.¹⁸²⁻¹⁸⁴
- Overlapping symptoms of anxiety and depression include sleep and concentration difficulties, tension, excessive worry, fear and the onset of panic attacks.
- Despite the known high prevalence of anxiety disorders, they are diagnosed less often than depression in the perinatal period. The belief that new mothers are “naturally anxious” contributes to this under-diagnosis. Fortunately, this is starting to change and more attention and research is being focused on anxiety.¹⁸³

Generalized anxiety disorder (GAD):

- GAD is described as a persistent and excessive anxiety about a number of events or activities which cause the person significant distress or impairment (e.g., worry over work, money, children and health). There is no one specific source of worry.
- Age of onset is variable – from childhood to late adulthood with a mean and median age in the early 30s (coincides with peak childbearing years). GAD is more common in women than men.
- GAD is more prevalent in perinatal women than in the general population of childbearing women (see section 2.1 for details on prevalence).
- Up to 60% of GAD sufferers have a co-existing mental health condition (panic disorder and major depressive disorder are the most common).¹⁸⁵

Obsessive compulsive disorder (OCD):

- OCD is when recurrent and unwelcome thoughts, ideas or doubts (obsessions) give rise to distress. Some people may respond to these obsessional anxieties with excessive behaviours or mental acts (compulsions). Other people experience compulsions in the absence of obsessions.¹⁸⁶
- The obsessions and compulsions are very distressing and time consuming and significantly interfere with daily life. The person recognizes that their obsessions and compulsions are excessive and unreasonable.
- Age of onset of OCD is typically during adolescence or early adulthood.
- OCD is more prevalent in perinatal women than in the general population of childbearing women (see section 2.1 for details on prevalence).

Panic disorder (PD):

- PD is described as an unreasonable level of fear brought on by the presence or anticipation of a specific situation which leads to unexpected and recurrent panic attacks.
- PD may be accompanied by agoraphobia. Agoraphobia is an anxiety about, and subsequent avoidance of, being in places or situations from which escape might be difficult or in which help may not be available in the event of a panic attack (e.g. public places).
- Onset is typically during the mid-twenties (coincides with peak childbearing years). Panic disorders are more common in women than men.
- PD is more prevalent in perinatal women than in the general population of childbearing women (see section 2.1 for details on prevalence).
- Panic attacks that do not occur frequently enough to meet the criteria for a PD may also occur in the context of other mood disorders (e.g., major depression and some of the other anxiety disorders).

Post-traumatic stress disorder (PTSD):

- PTSD occurs when a person has persistent symptoms after a traumatic event (e.g., physical, sexual and/or psychological abuse, natural disaster, accident). A history of unresolved trauma may increase the risk of PTSD in the perinatal period.
- PTSD symptoms cause clinically significant distress and/or impairment in social, occupational or other important areas of functioning.
- Symptoms include: persistent “reliving” of the traumatic event (e.g., flashbacks or nightmares); avoidance of feelings, people or places associated with the event (e.g., emotional “numbing”, feeling detached, showing less emotions); and hyper arousal or a high general level of anxiety (e.g., insomnia, difficulty concentrating, startling easily, feeling irritable and/or having outbursts of anger).
- Treatment for PTSD includes psychoeducation, peer support, trauma-focused psychotherapy (e.g., CBT and “desensitization” therapy) and pharmacotherapy. Antidepressants, including SSRIs, have been shown to be effective.
- PTSD is less common than GAD, PD and OCD in the perinatal period. It will not be detailed further in this guideline but it is important to consider in women with anxiety symptoms.

4.1.2 Signs and Symptoms

Signs and symptoms of anxiety disorders vary depending on the type of disorder. Common to most is a subjective experience of distress with accompanying disturbances of sleep, concentration and lower levels of social and/or occupational functioning.

The clinical features of anxiety disorders in the perinatal period are similar to those in the non-perinatal period. Women with anxiety disorders often present with complaints of poor physical health as their primary concern which can temporarily distract from the underlying anxiety symptoms. In the perinatal period, women commonly present with excessive concerns about their pregnancy, fetus and/or baby.¹⁸⁷ Some women turn to alcohol or drugs to deal with their anxiety. It is important to ask about any substance use and to refer the woman for treatment if necessary.

Despite the similarities amongst anxiety disorders, the disorders often differ in presentation, course and treatment.

GAD:

- Anxious and excessive worry about everyday matters such as money, health, family, relationships and work.
- Anxiety that things will go wrong or that they can't cope, even when there are no signs of trouble.
- Other symptoms may include feeling restless, agitated and/or irritable, difficulty concentrating, difficulty falling or staying asleep, fatigue and physical symptoms such as muscle tension, shortness of breath, rapid heartbeat, dizziness, dry mouth, difficulty swallowing and rashes.
- Examples of worries and feelings that are common in women with GAD in the perinatal period include:⁷⁸
 - During pregnancy:
 - What if the foods or drinks I ingested before I realized I was pregnant hurt the baby?
 - What if I miscarry?
 - Will I be a good mother?
 - What if the baby isn't developing normally?
 - What if I can't cope with the pain of childbirth?
 - What if I can't afford this baby?
 - Postpartum:
 - What if my baby gets sick? What if this symptom is a sign of serious illness?
 - What if something happens if I leave the baby with someone else?
 - What if the baby is abducted? Abused?
 - What if my baby stops breathing while asleep?
- These worries may be associated with uncomfortable physical sensations.
- These worries often affect the woman's behaviour. e.g., afraid of having the baby out of her sight, waking up at night to check if the baby is still breathing and frequent visits to the physician about the baby's health.
- For a formal diagnosis of GAD, symptoms must be consistent, ongoing and have been persistent for at least six months.

OCD:

- Repetitive obsessive thoughts such as:
 - Unwanted aggressive/horrific thoughts or urges (e.g., visions of the baby with injuries).
 - Thoughts of harming someone else.
 - Fear of contamination (e.g., germs, bacteria, dirt, etc).
 - Fear of forgetting to do things (e.g., locking doors or turning off the stove).
 - Needing to do things in an exact way.
 - Fear of illness or disease.
- Repetitive compulsions such as:
 - Washing or cleaning (hands, clothes, kitchen, food, etc).
 - Checking (the baby, locks, appliances, etc).
 - Repeating actions.
 - Requesting or demanding assurances from others.
 - Tidying things in a particular way.

- When new obsessions occur in the perinatal period, it is common for them to relate to the possibility of harm coming to the developing fetus or new baby.⁷⁸ One study (n=17) reported this obsession to be present in 54% of perinatal women with OCD.¹⁸⁸
 - During pregnancy, the most common obsessions concern the possibility of harm coming to the unborn baby. e.g., worry about their baby becoming contaminated by toxins. Because these thoughts are upsetting, the woman may do things she believes will minimize the risks (e.g., avoiding all potential toxins or washing/cleaning excessively).
 - After the birth of a baby, worries about the baby getting sick are common. Even women without OCD can experience fleeting, unwanted thoughts about harm coming to their baby (e.g., accidentally or purposely drowning the baby while bathing, stabbing the baby with a knife, dropping the baby over the balcony, etc). In most cases, although frightening, these thoughts are temporary, harmless and disappear without causing great distress. For some new mothers, however, the unwanted thoughts become obsessions (repetitive and highly distressing). The obsessional thoughts are described as ego-dystonic, meaning they are subjectively felt to be unacceptable and distressing. Women with ego-dystonic thoughts are typically aware that their thoughts are irrational. They commonly try to avoid situations which may trigger these thoughts (e.g., avoid bathing their baby or using knives, avoid being alone with their baby). For the most part, women with OCD do not act on their thoughts of harming their children.
- Thoughts of harm coming to their baby are not unique to women with OCD – they can be present in postpartum women with no mental health disorder or they can be present in women experiencing postpartum psychosis and/or severe PND. In women where these thoughts are present, further assessment is warranted to ensure the safety of the baby/family. See section 7.0 for a discussion of neonaticide and infanticide.

Panic disorder:

- A panic attack is a period of intense fear or discomfort which develops suddenly and peaks usually within 10 minutes. Symptoms may include: chest pain or discomfort, chills or hot flushes, feelings of unreality or depersonalization (being detached from oneself), fear of losing control, feeling dizzy, unsteady, lightheaded, or faint, feeling of choking, nausea or abdominal distress, palpitations or tachycardia, paresthesias, sensations of shortness of breath or smothering, sense of impending doom, sweating and/or trembling or shaking.³⁹
- Panic attacks can start during pregnancy or after the birth of the baby and may be triggered by different factors:⁷⁸
 - During pregnancy: Often triggered by changes in women's bodies which may cause uncomfortable physical symptoms and cause them to worry excessively about their own health and/or the health of their unborn baby and about how they will be as mothers.
 - After the birth of a baby, panic attacks may occur in the context of sleep deprivation and the increased stress and responsibility of parenting a child. Common triggers include worries about one's own health, the health of the baby and/or one's parenting skills. Panic attacks can also be triggered by the baby crying uncontrollably or needing to feed. A common response for mothers that experience panic attacks is to fear being left alone with the baby because of the possibility of having a panic attack and losing control and not being able to care for their baby. Some women also fear going out of the home with the baby.

4.1.3 Risk Factors

Many of the risk factors for anxiety disorders are similar to those for PND.

Major factors:

- Personal history of anxiety disorder with a previous pregnancy.
- Personal history of an anxiety disorder not related to the perinatal period.
- Family history (first degree relative) of an anxiety disorder in the perinatal period.

Contributing factors:

- Life stressors.
- Lack of social support.
- Poor relationships.
- Family history of anxiety disorders.
- Babies with health problems or perceived difficult temperaments.
- Chronic or acute maternal health problems such as thyroid disease and diabetes.
- Smoking and caffeine intake.

4.1.4 Prevention

No biologic markers are specific enough at this time to detect anxiety disorders early, and there is no research to show that current medications are effective in preventing these disorders.

4.2 Screening and Diagnosis

Unlike screening for depression, there has been little research on the use and validity of self-report tools to screen for anxiety in the perinatal period.¹⁸²

- The only anxiety screening tool that has been developed specifically for the perinatal population is the Pregnancy Anxiety Scale. There have been no studies done to validate this tool since its creation in 1991.
- While some studies have been done on utilizing standard self-report anxiety tools in the perinatal population, methodological differences limit comparisons across studies. Suitability and validity of the tools need to be further studied in the perinatal population, as do appropriate cut-off rates.
- Standard self-report anxiety tools do not contain any measures specific to the perinatal population (unlike the EPDS for depression). This is problematic as there are many overlapping physiological symptoms of anxiety and pregnancy/postpartum. Anxiety tools are therefore only useful if they can differentiate anxiety from depression.
- At this point the literature is inconclusive in recommending a specific tool to screen for anxiety in the perinatal period.

Some authors have suggested that items 3 – 5 on the EPDS could be utilized as a separate subscale to screen for anxiety (called the anxiety subscale). The research evidence available at this time suggests caution in using this approach because:

- While it is true that the score on the anxiety subscale correlates with external measures of anxiety, so does the total EPDS score.^{189,190}
- There is no consensus in the literature regarding the cut-off point to be used with the anxiety subscale. One study recommends a cut-off point of 6¹⁹¹ while another recommends a cut-off point of 4.¹⁹²
- Many of the women who will score positive on the anxiety related questions will score positive on the total EPDS. Directing women with positive EPDS scores for further assessment/treatment will identify women with co-existing depression and anxiety.

In the absence of a commonly accepted screening tool for anxiety in the perinatal period, it is important to screen for specific risk factors such as a personal and/or family history of an anxiety disorder to facilitate identification and treatment as early as possible.

The steps in diagnosing an anxiety disorder are the same as for depression: diagnostic assessment interview and confirmation of the suspected diagnosis with the DSM-V criteria. Appendix 2 provides guidelines for a diagnostic assessment interview in the perinatal period.

4.3 Treatment and Self-Management

4.3.1 Summary of Treatments

For the most part, the treatments utilized for women with anxiety disorders are similar to those used for depression with the exception of bright light therapy and ECT. See Table 7 for a list of treatments commonly used to treat anxiety disorders.

Table 7: Treatments Commonly used to Treat Anxiety Disorders in the Perinatal Period

Severity of Symptoms	Treatment & Self-Management
Mild to moderate	A. Psychoeducation B. Self-care: The NEST-S Program C. Psychotherapies <ol style="list-style-type: none"> i. Cognitive behavioural therapy (CBT) ii. Interpersonal therapy (IPT) iii. Psychodynamic therapy (PDT) iv. Group therapy (therapist and/or peer led)
Moderate to severe or at high risk of relapse	Treatments for mild to moderate symptoms plus: D. Pharmacotherapy (medications)

Section 3.3 provides an overview of each of the treatments with a focus on the treatment of depression. Similar principles apply to the treatment of anxiety disorders, with specific characteristics discussed in this section. Medications used for the treatment of anxiety disorders are discussed in section 4.3.2.

For the treatment of anxiety disorders:

- For mild to moderate anxiety in perinatal women, psychoeducation, self-care and psychotherapies are recommended as first-line interventions. Pharmacotherapy may also be required for women with moderate to severe anxiety disorders.
- Psychoeducation and self-care:
 - The goals are the same as for the treatment of depression.
 - Relaxation training (e.g., progressive muscle relaxation or thinking of relaxing scenes or places), as a form of self-care has been shown to be effective in the treatment of anxiety disorders, especially the treatment of GAD and panic disorders (less evidence of effectiveness for OCD). Relaxation techniques can be learned through self-help or from a professional.⁷⁸
 - Other therapies such as mindfulness and meditation are an increasingly important part of Self-care and research has shown that they are helpful in the reduction of stress and anxiety.⁸⁰⁻⁸⁶
 - See the discussion in section 3.3.2.
- Psychotherapies:
 - Cognitive behavioural therapy (CBT) has been studied more than other psychotherapies and has been shown to be effective for the treatment of anxiety disorders.
 - CBT has been shown to be effective in treating adult anxiety¹⁹³⁻¹⁹⁶ and group CBT has also been shown to effectively treat anxiety.^{197,198}
 - In the general population, CBT has been shown to be effective in treating obsessive-compulsive and panic disorder. Improvements in panic frequency, panic-related cognitions, phobia avoidance, anxiety and depression were maintained at follow-up.^{194,199-201}
 - Several authors have suggested CBT as the psychotherapy of choice in treating pregnant and postpartum women suffering from anxiety.^{78,202,203}
 - Interpersonal therapy (IPT) has not been as well studied for the treatment of anxiety as it has for the treatment of depression; however, the limited research that has been done shows promising results that suggest it can be an effective form of therapy^{204,205} for the treatment of anxiety disorders.

- CBT with an IPT component does not appear to significantly improve long-term outcomes compared to CBT treatment alone for generalized anxiety disorder.²⁰⁶
- There is some evidence to suggest that psychodynamic therapy (PDT) can be useful in treating anxiety; however, the evidence base is currently stronger for CBT and IPT.^{207,208}
- Family or couples therapy can be effective in circumstances where relationships are identified as an issue (poor couple relationships and lack of social support are consistent psychosocial predictors of anxiety symptoms in the perinatal period).
- There is no evidence to support the use of bright light therapy in the treatment of anxiety.
- While there are some case studies suggesting that ECT might be useful for treating refractory OCD,²⁰⁹ further research needs to be done before recommending the use of ECT for refractory OCD.²⁰⁸
- There is no evidence to support the use of ECT for other forms of anxiety.

4.3.2 Medications for the Treatment of Anxiety Disorders

SSRIs and SNRIs (antidepressants) are first line treatment for women who require regular treatment for anxiety disorders.

Benzodiazepines may be useful on a PRN or regularly scheduled but time-limited basis. Long term use is discouraged as tolerance readily develops and withdrawal symptoms are common upon discontinuation.

Benzodiazepines and other hypnotics (non-benzodiazepines) may be useful on a PRN basis for intermittent insomnia.

Quetiapine (Seroquel XR®), an atypical antipsychotic medication, may be considered for women with a **severe** anxiety disorder who have had only a partial response to antidepressants and benzodiazepines. This can be particularly helpful for women with **severe** obsessive compulsive disorder.

Key points and recommendations related to prescribing antidepressant medications in the perinatal period are provided in section 4.4.

Refer to Appendix 5 for current information (as of March 2013) about specific medications commonly used in the perinatal period for the treatment of anxiety disorders.

4.4 Key Points and Recommendations

Key points

- Anxiety disorders and depression often co-exist.
- Rates for anxiety disorders are higher in the perinatal population than non-perinatal population, both in terms of new onsets and worsening of existing symptoms. (see Section 2.1 on prevalence).
- The most common types of anxiety disorders in the perinatal period are generalized anxiety disorder, obsessive compulsive disorder and panic disorder.
- Clinical features of anxiety disorders in perinatal women are similar to those in non-perinatal women (e.g., subjective experience of distress with accompanying disturbances of sleep, reduced concentration and lower levels of social and/or occupational functioning). In the perinatal period, women commonly present with excessive concerns about their pregnancy, fetus and/or baby.¹⁸⁷
- Major risk factors for an anxiety disorder during the perinatal depression include: history of an anxiety disorder with a previous pregnancy, personal history of an anxiety disorder not related to the perinatal period, and family history of an anxiety disorder in the perinatal period.
- There is no evidence to support specific interventions for the prevention of anxiety disorders in the perinatal period.
- Unlike the EPDS for depression, there is no commonly accepted, validated self-report tool to screen for anxiety disorders.¹⁸²
- Screening for risk factors will assist with early identification and treatment.²¹⁰

- The steps for diagnosing anxiety disorders are the same as for depression: diagnostic assessment interview and confirmation of the suspected diagnosis with the DSM-V criteria. Before diagnosing a mental health disorder, it is important to exclude medical conditions, including substance use, which might cause symptoms that mimic a mental health disorder.
- The treatments used for anxiety disorders in the perinatal period are similar to those used for depression. Mild to moderate anxiety disorders are often successfully treated with a combination of non-pharmacological treatments. Medications may also be required for women with moderate to severe anxiety disorders.
- Effective non-pharmacologic treatments include psychoeducation, self-care and psychotherapies (also called “talk therapies”). Of the psychotherapies, CBT has been studied the most in the treatment of anxiety disorders and shown to be effective. While the research is limited, IPT also shows promising results.^{211,212}
- The evidence is currently stronger for CBT and IPT^{207,208} than for psychodynamic therapy.
- There is little or no evidence to support the use of bright light therapy or ECT in the treatment of anxiety disorders.

Recommendations

1. Promote early identification and treatment of anxiety disorders in perinatal women by enquiring about risk factors (e.g., personal and/or family history of anxiety disorders) and/or direct observation (e.g., excessive concerns about fetus/pregnancy or baby).
2. Utilize the guidelines in Table 8 for the treatment of women with anxiety disorders:

Table 8: Guidelines for the Treatment of Anxiety Disorders during the Perinatal Period

Treatment approach	
Pregnancy & Postpartum	<p>Mild to Moderate Anxiety Disorder: Focus on psychoeducation, self-care &/or psychotherapies. Medications are usually not required.</p> <p>Moderate to Severe Anxiety Disorder: Medications are frequently required in addition to focusing on psychoeducation, self-care &/or psychotherapies.</p>
Medication management	
Pregnancy & Postpartum	<p>SSRIs and SNRIs are first line treatment for women who require regular treatment for anxiety disorders (see section 3.5, table 6 for guidelines related to antidepressant use).</p> <p>Benzodiazepines may be useful on a PRN or regularly scheduled but time-limited basis. Long term use is discouraged as tolerance readily develops and withdrawal symptoms are common upon discontinuation.</p> <p>Benzodiazepines and other hypnotics (non-benzodiazepines) may be useful on a PRN basis for intermittent insomnia.</p>
Pregnancy	Minimize the use of benzodiazepines and other hypnotics (non-benzodiazepines) close to delivery, if possible, to reduce the likelihood of NAS. Monitor baby for NAS.
Postpartum	<p>SSRIs and SNRIs are not contraindicated with breastfeeding.</p> <p>If required, use short-acting benzodiazepines in divided doses during lactation. Monitor for adverse effects in the baby (e.g., sedation, poor feeding and irritability).</p>

5.0 Bipolar Disorder

5.1 Education and Prevention

5.1.1 What is Bipolar Disorder?

Bipolar disorder is one of the most serious mental health disorders that affect women in the perinatal period. It is a mood disorder in which people experience disruptive mood swings which are so intense that they interfere with their daily life. Bipolar disorder usually lasts a lifetime. If not treated, bipolar disorder tends to worsen with more frequent and severe episodes. Proper treatment helps to reduce the frequency and severity of the episodes.

Women with existing bipolar disorder are at risk of developing postpartum manic episodes, postpartum depressive episodes and postpartum mixed states and postpartum psychosis. **Postpartum psychosis is a psychiatric and obstetric emergency**, usually requiring hospitalization and intensive treatment. (See Section 6 for a discussion of postpartum psychosis and Section 7.0 for a discussion of Bipolar disorder, Psychosis and Suicide/Infanticide.) A woman with no previous psychiatric history who develops a postpartum psychosis will require close follow up as she is at increased risk of developing further mood episodes during times of stress, including subsequent pregnancies. An eventual diagnosis of bipolar disorder may be made.

5.1.2 Signs and Symptoms

The two most common forms of bipolar disorder are:

- Bipolar Disorder 1 (historically known as manic–depressive disorder or manic depression)
- Bipolar Disorder 2

Bipolar Disorder 1 (DSM-V³⁹):

- Disruptive mood swings characterized by episodes of either mania or hypomania which often (but may not) alternate with major depressive episodes (see below for definitions of mania, hypomania and depressive episodes). Episodes are intense and significantly interfere with daily functioning.
- If manic and depressive symptoms occur in the same episode, this is called a “mixed state”.

Bipolar Disorder 2 (DSM-V³⁹):

- Characterized by at least one episode of hypomania and one major depressive episode.
- Episodes of hypomania and depression frequently alternate and cause clinically significant distress and interfere with daily functioning.

Manic episode:

- Distinct period of abnormally and persistently elevated, expansive or irritable mood and abnormally and persistently increased goal-directed activity or energy, lasting at least one week and present most of the day, nearly every day (or any duration if hospitalization is necessary).
- Several of the following symptoms are usually present:
 - Inflated self-esteem or grandiosity.
 - Decreased need for sleep (e.g., feels rested after only 3 hours of sleep).
 - Flight of ideas or subjective experience that thoughts are racing.
 - More talkative than usual or pressure to keep talking.
 - Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli).
 - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless non-goal-directed activity).
 - Excessive involvement in high-risk activities (e.g., engaging in unrestrained buying sprees, sexual indiscretions, foolish or ill-advised business investments).
- Mood disturbance is severe enough to significantly interfere with social or occupational functioning or to necessitate hospitalization to prevent harm to self or others.
- Psychotic features may be present.

Hypomanic episode:

- Similar to a manic episode but shorter lasting (at least four consecutive days) and less severe.
- While the mood disturbance and change in functioning is observable by others, hypomanic episodes do not cause marked interference with social or occupational functioning and do not necessitate hospitalization.
- Psychotic symptoms are not present.

Depressive episode:

- Signs of depression are similar to those listed in the section on perinatal depression.
- Psychotic features may be present.

5.1.3 Risk Factors

Although the causes are not well understood, bipolar disorder (with or without psychotic features) often runs in families and is exacerbated by stressful life events (e.g., childbirth).

Bipolar disorder in the perinatal period:

- During pregnancy, there is no reason to suspect increased prevalence of bipolar disorder but there is an increase in exacerbation of symptoms in many women.
- The postpartum period is a period of increased risk for development and relapse of bipolar disorder (see section 2.1 for details on prevalence). Psychotic features may be present—see section 6.0 for a discussion of psychotic disorders during pregnancy.
- Hypomanic symptoms can be overlooked in the immediate postpartum period and attributed to the elation that follows the birth of the baby. These women may present weeks or months later with a major depressive episode but in fact have an underlying bipolar disorder.

5.1.4 Prevention

While bipolar disorder is not preventable, the risks and impacts can be successfully managed through preconception counselling and appropriate perinatal planning, management and support.

Preconception counselling includes:

- Discussing risks and ways to minimize the symptoms of bipolar disorder if contemplating pregnancy.
- Reviewing and potentially changing medications prior to becoming pregnant.
- Reinforcing the importance of seeking early help once becoming pregnant.

Planning, management and support includes:

- Asking all pregnant women about a personal and/or family history of bipolar disorder, major depressive episodes and/or postpartum psychosis.
- For at-risk women:
 - Developing a management plan which involves the woman and her family supports, psychiatry, obstetrics (obstetrician, family physician, midwife), primary care, and public health nursing. Planning needs to incorporate ongoing monitoring and, if necessary, adjustment of psychotropic medications throughout the perinatal period. Referring at-risk women to a psychiatrist or reproductive psychiatrist for a mental health assessment and assistance with development of the management plan is recommended.
 - Addressing factors that might increase risk such as sleep deprivation in late pregnancy and the early postpartum period.
 - For high-risk women, planning for a longer postpartum stay in hospital (at least three nights) to monitor mood and maximize sleep.

5.2 Screening and Diagnosis

There are no self-report screening tools for bipolar disorder that can be easily implemented. Observation and/or report of changes in appearance and activity usually prompt the need for a thorough assessment.

Before diagnosing bipolar disorder, it is important to exclude medical conditions that might cause symptoms that mimic the disorder. Observation of women for substance related disorders is also important as substance use and bipolar disorder may coexist and/or substance use may mimic a manic episode in the absence of a bipolar disorder.

The diagnostic assessment interview is the gold standard for diagnosis of bipolar disorder (see Appendix 2 for guidelines for a diagnostic assessment interview in the perinatal period). Tools such as the Standardized Mini-Mental State Examination (SMMSE), Brief Psychiatric Rating Scale (BPRS), Mood Disorder Questionnaire (MDQ) and HIGHS Scale may provide additional information. These tools and others are available on the internet.

5.3 Treatment and Self-Management

5.3.1 Summary of Treatments

Acute phase:

- Bipolar disorder is primarily managed with medications, which may be augmented with non-pharmacological therapies. Hospitalization may be required.
- Rates of relapse of bipolar disorder are high when women stop taking their mood stabilizer/anti-psychotic medications during pregnancy^{213,214} while maintenance treatment during pregnancy has proved to be protective against relapse.²¹⁵
- Rates of relapse of bipolar disorder are lower in women with bipolar disorder taking anti-psychotic/mood stabilizer medications than among those who do not.^{214,216}
- There is some evidence from a general population study suggesting that adding a psychosocial intervention such as CBT or couples and/or family therapy to pharmacotherapy can improve treatment outcomes, particularly in the depression phase of bipolar disorder.²¹⁷⁻²²⁰
 - These adjunct therapies have been shown to reduce hospitalizations and improve psychosocial outcomes.²¹⁷⁻²²⁰
 - The benefits have been apparent in the treatment of depression but not the treatment of acute hypomania or mania.²¹⁷
- For women who are unable to tolerate/take medications, or in whom the medication fails to reach a timely response and where suicide is a possibility, ECT may be beneficial.²²¹

Recovery phase:

- Psychoeducation, self-care and psychotherapies by themselves are not effective for the acute treatment of bipolar disorder, but they are useful adjuncts to medications during the recovery phase when the focus is on maintenance of well-being and learning ways to cope with the disorder. See section 3.3 for an overview of these adjunct (non-pharmacological) treatments.

Table 9: Common Treatments for Bipolar Disorder in the Perinatal Period

Severity of Symptoms	Treatment & Self-Management
Acute phase	A. Pharmacotherapy (medications) B. Electroconvulsive therapy (ECT) (if unable to tolerate/take medications or in whom a rapid response is required – e.g., suicide risk)
Recovery phase	Used as an adjunct to pharmacotherapy or ECT: A. Psychoeducation B. Self-care: The NEST-S Program C. Psychotherapies i. Cognitive behavioural therapy (CBT) ii. Interpersonal therapy (IPT) iii. Group therapy (therapist and/or peer led) iv. Parent-infant psychotherapy v. Couples and/or family therapy (also referred to as family-focused therapy in the literature on bipolar disorder)

Psychoeducation, self-care and psychotherapies are discussed in section 3.3.

5.3.2 Medications used for the Treatment of Bipolar Disorder

Women with bipolar disorder will require pharmacological treatment. Mood stabilizers and antipsychotics (neuroleptics) and are the most commonly used medications. Benzodiazepines may be utilized on a short-term basis to help control manic symptoms until mood-stabilizing or anti-psychotic medications take effect. Antidepressants may be useful in the treatment of Bipolar Disorder 2.

Mood stabilizers:

- Lithium is the oldest and best-known mood-stabilizing medication and is considered the “gold standard” for the treatment of bipolar disorder. Other commonly used mood stabilizers include carbamazepine, gabapentin, lamotrigine, topiramate and valproic acid/divalproex. With the exception of lithium, most mood stabilizers fall within the sub-classification of “anticonvulsants”.
- Mood stabilizers are effective for the treatment of acute manic episodes and for long-term control or prophylaxis against relapse. With the exception of lamotrigine, they are less effective at treating depression, although they may help to prevent depression by preventing mania and subsequent mood cycling.
- The main concern about treating with mood stabilizers during pregnancy is the risk of teratogenicity. Lithium use is associated with an increased risk of cardiac anomalies although the absolute risk is considered low. Where clinically possible, avoid lithium in the first trimester. Valproic acid/divalproex and carbamazepine are associated with increased risk of neural tube defects. Valproic acid/divalproex is not recommended in pregnancy unless the woman has a severe illness that ONLY responds to valproic acid. Carbamazepine should be avoided in the first trimester where clinically possible. Numerous large registry studies have found no increased risk of major congenital malformations with lamotrigine. Other mood stabilizers have been less well studied.
- Women who abruptly stop their mood stabilizing medications when they find out that they are pregnant are at risk of experiencing a relapse during the pregnancy but especially in the postpartum period. Women with more severe illness or those who have had multiple hospitalizations should remain on their mood stabilizers when it is clear that the benefits of remaining on treatment outweigh any exposure effects to the fetus.

Antipsychotics (neuroleptics):

- Antipsychotics are classified as atypical (newer) and typical antipsychotics.
- Atypical antipsychotics may be used as first-line treatment for bipolar disorder during pregnancy because of their mood stabilizing properties and a potentially lower rate of teratogenicity than the mood stabilizers (although they have been less well studied as they are relatively new).
- Typical (older) antipsychotics are no longer considered to be first-line treatment because the atypical (newer) antipsychotics are more effective and have a lower risk of side effects.

Key points and recommendations related to prescribing mood stabilizers in the perinatal period are provided in section 5.4. Key points and recommendations related to prescribing antidepressants, benzodiazepines and antipsychotics are provided in sections 3.5, 4.4 and 6.4 respectively.

Refer to Appendix 5 for current information (as of March 2013) about specific medications commonly used in the perinatal period for the treatment of bipolar disorder and/or psychosis.

5.4 Key Points and Recommendations

Key points

- Bipolar disorder is one of the most serious mental health disorders that affect women in the perinatal period. Women with existing bipolar disorder are at risk of developing postpartum manic episodes, postpartum depressive episodes, postpartum mixed episodes and postpartum psychosis. Postpartum psychosis is a psychiatric and obstetric emergency, usually requiring hospitalization and intensive treatment. (See Section 6 for a discussion of post partum psychosis and Section 7.0 for a discussion of Bipolar disorder, Psychosis and Suicide/Infanticide.)
- A woman with no previous psychiatric history who develops a postpartum psychosis will require close follow up as she is at increased risk of developing further mood episodes and eventually being diagnosed as having a bipolar disorder.
- During pregnancy, there is no reason to suspect increased prevalence of bipolar disorder but there is an increase in exacerbation of symptoms in many women. The postpartum period is a period of increased risk for development and relapse of bipolar disorder (see section 2.1 for details on prevalence).
- While bipolar disorder is not preventable, the risks and impacts can be successfully managed through preconception counselling and appropriate perinatal planning, management and support. There are no self-report screening tools for bipolar disorder that can be easily implemented.
- While mood stabilizing medications have been associated with an increased risk of teratogenicity, some women with more severe illness and with multiple hospitalizations, may need to remain on their mood stabilizing medications during pregnancy. Women should be educated about the risks and benefits of treatment.
- Bipolar disorder is primarily managed using pharmacotherapy (medications). For women who are unable to tolerate/take medications, or in whom the medication fails to reach a timely response and where suicide is a possibility, ECT may be beneficial.²²¹
- There is some evidence to suggest that adding a psychosocial intervention to pharmacotherapy can improve treatment outcomes, particularly during the depression phase of bipolar disorder.

Recommendations

1. Promote early identification and treatment of bipolar disorder in perinatal women by enquiring about risk factors (personal or family history of bipolar disorder and/or postpartum psychosis) and/or direct observation or reports (e.g., unusual behavior, racing thoughts, distractible, inflated self-esteem or grandiosity, disorganized thoughts, erratic and impulsive behaviour, rapid speech, difficulty sleeping).
2. Offer women who have severe bipolar disorder or another mental health disorder a referral for genetic counselling to discuss family history and recurrence risk (i.e., risk of the disorder to their offspring). A referral would also be appropriate in situations where the baby's father has a severe mental health

disorder. Genetic counselling is available through the department of medical genetics at BC Women's Hospital and Health Centre (Vancouver) and Victoria General Hospital.

3. For women with bipolar disorder, develop an integrated treatment plan which involves the woman and her family supports, psychiatry, obstetrics (obstetrician, family physician, midwife), primary care, and public health nursing. Refer at-risk women to a psychiatrist or reproductive psychiatrist for a mental health assessment, assistance with development of the treatment plan and ongoing monitoring of the woman's mental health status and response to treatment during the perinatal period. This plan may include a recommendation that the woman remain in hospital for at least three days after the delivery to help her establish a sleep routine and for close monitoring of her mood.
4. Utilize the guidelines in Table 10 for the treatment of women with bipolar disorder:

Table 10: Guidelines for the Treatment of Bipolar Disorder

Treatment of Bipolar Disorder	
Treatment approach	<p>Women with diagnosed or pre-existing bipolar disorder (including psychosis) require individualized treatment planning which considers the frequency/severity of previous episodes and response to medication.</p> <p>Women whose illness is in remission (i.e., clinically stable) often need to remain on medication because of vulnerability to relapse and the possibility of psychosis in the perinatal period.</p> <p>Symptomatic women require medication because of the high risk of relapse.</p> <p>Consider ECT for pregnant women with moderate/severe mania or mixed episodes who do not respond to medication.</p> <p>Psychoeducation, self-care &/or psychotherapies helpful as adjunct therapies.</p>
Medication management	
Preconception & Pregnancy	<p>If taking a mood stabilizer or antipsychotic medication and clinically stable for 4–6 months and the relapse risk is low, consider a trial of gradually discontinuing medication prior to pregnancy.</p> <p>If the woman has a severe illness and a history of relapse after discontinuing medication and it is to be continued, prescribe current (effective) medication unless medication is valproic acid/divalproex. Valproic acid/divalproex has a higher risk than other medications for multiple congenital malformations including neural tube defects. If possible, substitute atypical antipsychotic (risk of major congenital malformation is lower²²²⁻²²⁷) or another mood stabilizer.</p> <p>If the woman is currently medication free but a medication is required during pregnancy (e.g., new onset and/or relapse), consider atypical antipsychotic or mood stabilizer (not valproic acid/divalproex, see above). If possible, avoid carbamazepine and lithium in first trimester (risk of major congenital malformations).</p> <p>See Table 11 for information on the use of antipsychotics and Appendix 6 for recommended monitoring and folic acid supplementation guidelines for women taking mood stabilizers and/or atypical antipsychotics during pregnancy.</p>
At Birth	See Appendix 6 for recommended monitoring guidelines for women taking mood stabilizers and/or atypical antipsychotics at the time of delivery.

Postpartum	<p>Women taking medication, still required postpartum, prescribe current (effective) antipsychotic, mood stabilizer or atypical antipsychotic. Dose adjustments may be necessary.</p> <p>Women not taking medication who require postpartum treatment, any mood stabilizer or atypical antipsychotic (excluding clozapine) may be considered.</p> <p>Women taking lithium, breastfeeding not recommended due to reports of high infant plasma levels and toxicity.</p> <p>Women taking medications with high levels reported in nursing infants and/or where there are reported toxicities, caution is advised for breastfeeding. See Appendices 5 & 6 for details.</p> <p>Women taking mood stabilizers and/or atypical antipsychotics postpartum, see Appendix 6 for monitoring guidelines.</p>
All phases	Benzodiazepines may be utilized on a short-term basis to help control manic symptoms until mood-stabilizing or anti-psychotic medications take effect.

6.0 Psychotic Disorders and Postpartum Psychosis

6.1 Education and Prevention

6.1.1 What is a Psychosis; Relationship to Psychotic Disorders; Postpartum Psychosis.

Psychosis is a generic term used to describe conditions that affect the mind in which there has been some loss of contact with reality. It is characterized by changes in ways of thinking, believing, perceiving and/or behaving. Psychosis is associated with more severe forms of some psychiatric disorders, most commonly schizophrenia, schizoaffective disorder and bipolar disorder. It can also occur with a major depressive disorder.

Psychotic disorders are classified under the heading “Schizophrenia Spectrum and Other Psychotic Disorders” in the DSM-V.³⁹ They include a range of disorders, all of which are defined by the presence of psychotic symptoms and/or other abnormalities. Psychotic disorders include: schizotypal personality disorder, delusional disorder, brief psychotic disorder, schizophreniform disorder, schizoaffective disorder and schizophrenia. Diagnosis of a particular psychotic disorder depends on the type and duration of symptoms. Appendix 7 provides a brief description of each of the psychotic disorders.

Postpartum psychosis is a term that refers to the sudden onset of psychotic symptoms following childbirth. It is most commonly associated with bipolar disorder (acute manic episode or a major depressive episode), a brief psychotic disorder or a major depressive disorder. While the first episode of postpartum psychosis can also be a presentation of schizoaffective disorder or schizophrenia, it is much less likely.²²⁸ Postpartum psychosis requires rapid and intensive psychiatric treatment and hospitalization (sometimes requiring involuntary hospital admission).

6.1.2 Signs and Symptoms

Psychotic disorders:

The onset for most psychotic disorders is between ages 15 and 35²²⁹ (coincides with the childbearing years). Psychotic disorders affect roughly equal numbers of men and women. They differ, however, in their expression and subsequently in their treatment requirements. Women tend to experience more mood symptoms, more rapid cycling, a briefer duration of symptoms and a later onset of symptoms than men.²³⁰

Psychotic disorders are defined by abnormalities in at least one of the following five areas (DSM-V):³⁹

1. **Delusions:** False beliefs that often manifest according to a consistent theme. Common themes include paranoia (e.g., being followed or plotted against; baby is possessed by the devil), grandiosity (e.g., having special abilities or “powers”) and control (e.g, being controlled by forces or other individuals).
2. **Hallucinations:** Person perceives experiences (sees, hears, feels, smells or tastes things) in the absence of an external stimulus. Auditory (hearing) and visual (seeing) hallucinations are the most common.
3. **Disorganized speech:** May move quickly from one topic to the next or speech may be garbled and incomprehensible.
4. **Grossly disorganized or abnormal motor behaviour:** May result in difficulties concentrating, following a conversation, or performing activities of daily living (e.g., cooking, self-care). May also display inappropriate behaviours (e.g, inappropriate sexual behaviour, untriggered agitation, laughing while describing a personal tragedy) and/or catatonic behaviours (muscle tightness or rigidity and lack of response to the environment which may alternate with periods of excited or hyperactive behaviour).
5. **Negative symptoms** such as social withdrawal, loss of motivation, sleep disturbances and diminished emotional expression.

Psychotic disorders and the perinatal period:

- Most of the studies about psychotic disorders in the perinatal period focus on women with schizophrenia. This learning is likely relevant to other psychotic disorders.

- In recent decades, there has been an increase in the pregnancy rates of women with schizophrenia. This is likely a result of several factors including: deinstitutionalization, changing attitudes towards conception amongst those with psychiatric disorders, a shift to the newer atypical antipsychotics in the treatment of psychotic disorders (fertility rates are higher with the newer atypical antipsychotics than the older typical antipsychotics) and improved preconception and prenatal care.²³¹
- It is estimated that 50-60% of women with schizophrenia will become pregnant. Of these, 50% will be unplanned or unwanted,²³² a rate which is significantly higher than for the general population.²³³
- Women with schizophrenia that become pregnant are typically older than the general population of pregnant women, have fewer social supports and are more likely to engage in unhealthy behaviours (e.g., smoking, poor diet, alcohol and/or substance use). Many seek prenatal care late in pregnancy and some do not seek prenatal care at all.²³⁴
- All of these factors make women with schizophrenia at higher risk of poor perinatal and neonatal outcomes than women in the general population.
- Schizophrenia has been associated with multiple perinatal and neonatal complications including low APGAR scores, prematurity, low birth weights, small-for-gestational age babies, stillbirth and death.^{235,236} It is unclear whether these outcomes are due to the illness itself, the treatment (antipsychotics) and/or characteristics of the women themselves.²³²
- Schizophrenia (and other serious maternal psychotic disorders) may also have a devastating impact on the quality of the mother-infant bonding and, as a result, on the baby's neurodevelopment.²³¹
- Mother-infant bonding may be compromised by the psychopathology of the mother's illness (e.g., delusions and/or negative symptoms such as apathy or difficulty expressing emotion) as well as the reality of their psychosocial situation.²³⁷
- Postpartum psychosis, while the incidence is lower than for women with bipolar disorder, can further impact mother-infant bonding and potentially present a danger to the baby and/or the woman herself. See section 7.2 for a discussion of postpartum psychosis and neonaticide/infanticide.
- Studies have shown that mothers with schizophrenia are more likely to experience difficulties with parenting and thus to lose custody of their children than mothers in general.²³¹ It is reported that approximately 50% of mothers with schizophrenia temporarily or permanently lose custody of their children.^{238,239} Mothers with schizophrenia are also most likely to have poorer interactions with their babies than mothers with affective disorders (e.g., bipolar disorder).^{240,241}

Postpartum psychosis:

- Onset is usually unexpected and rapid (within hours) and symptoms most often appear within 72 hours to four weeks after delivery.²⁴²
- Psychotic episode lasts at least one day and may last up to one month (or beyond), with eventual return to previous level of functioning.
- Symptoms are similar to psychotic symptoms experienced at other times of life. The distorted thoughts and behaviours may involve the baby, creating additional risk for the baby. See section 7.2 for a discussion of postpartum psychosis and neonaticide/infanticide.
- Women who present acutely with symptoms of a postpartum psychosis usually have little insight into the seriousness of their condition. They will require hospitalization for their safety, for their babies' safety and to start treatment with antipsychotic ± mood stabilizing medication.
- The postpartum period is a time of increased risk for development and relapse of bipolar disorder and/or a psychotic episode. While the risk of relapse for schizophrenia is no higher than at other times of a woman's life, vigilance in monitoring is important given the potentially devastating impact of psychosis during this period. (see section 2.1 for details on prevalence)
- Postpartum psychosis is rare – approximately 1–2 per 1000 live births.²⁴³
- **Psychosis in the perinatal period is a psychiatric and obstetrical emergency.**

6.1.3 Risk Factors

Psychotic disorders:

- The causes of psychotic disorders are not well understood. Most theories suggest that psychotic disorders are an interplay between genetic (familial) and environmental risk factors.²⁴⁴
- Psychotic disorders run in families. For example, the risk of illness in an identical twin of a person with schizophrenia is 40%-50%. A child of a parent with schizophrenia has a 10% chance of developing the illness as compared to a 1% risk in the general population.²⁴⁵

Postpartum psychosis:

Women at increased risk of developing postpartum psychosis include:

- Women with a personal history of psychosis with previous pregnancies – relapse rates of 50%–60% have been reported.²⁴⁶
- Women with bipolar disorder – rates of 25-50% of women who gave birth and have a history of bipolar disorder have been reported.^{247,248}
- Family history (first degree relative) of postpartum psychosis – rates as high as 74% have been reported for women with bipolar disorder who also have a family history of postpartum psychosis.²⁴⁸
- Women with a family history (first degree relative) of bipolar disorder.
- Use of drugs – i.e., drug-induced psychosis.

Women with schizophrenia are less likely to have an acute relapse in the postpartum period, but instead display a more chronic course throughout the entire perinatal period.²⁴⁹

One study found that women with bipolar disorder were four times more likely to be hospitalized during the first month postpartum than women with schizophrenia.²⁵⁰

6.1.4 Prevention

Psychotic disorders:

Similar to bipolar disorder, psychotic disorders are not preventable. The risk and impacts of schizophrenia, however, can be successfully managed through preconception counselling and appropriate management and support, especially in the postpartum period. The principles are similar to the care of women with bipolar disorder (see section 5.1.4).

Postpartum psychosis:

In women with pre-existing bipolar disorder, the impact of a postpartum psychotic episode can be lessened through appropriate preconception counselling and appropriate management and support (see section 5.1.4).

In rare cases, women with no previous psychiatric history will develop a postpartum psychosis after the birth of their baby. These women have a greater than 50% risk of developing another postpartum psychotic episode after subsequent deliveries. Any woman who experiences a postpartum psychosis needs to be educated about her risk and, in all subsequent pregnancies, an integrated treatment plan be in place which involves the woman, her family supports and her healthcare providers. If possible, she should remain in hospital for at least three days after the delivery to help her establish a sleep routine and for close monitoring of her mood. Childcare supports should be in place prior to discharge from hospital.

6.2 Screening and Diagnosis

Similar to bipolar disorder, there are no self-report screening tools for psychotic disorders or postpartum psychosis that can be easily implemented. Observation and/or reports of changes in appearance and activity usually prompt the need for a thorough assessment.

Before diagnosing psychotic disorders or perinatal psychosis, it is important to exclude medical conditions that might cause psychotic symptoms. Observation of women for substance related disorders is also important as substance use and psychotic disorders may coexist and/or substance use may cause psychotic symptoms in the absence of a psychotic disorder.

The gold standard for diagnosis of psychotic disorders and/or postpartum psychosis is the diagnostic assessment interview (see Appendix 2 for guidelines for a diagnostic assessment interview in the perinatal period). Tools such as the Standardized Mini-Mental State Examination (SMMSE), Brief Psychiatric Rating Scale (BPRS), Mood Disorder Questionnaire (MDQ) and HIGHS Scale may provide additional information. These tools and others are available on the internet.

When addressing psychotic symptoms in women during the perinatal period, it is important to distinguish between women who have a pre-existing psychotic disorder and those who develop a first-onset psychotic disorder. The course of the disorder and treatment issues will vary significantly in these two populations. First-onset psychotic disorders that develop during the perinatal period require a diagnostic assessment similar to that performed for non-pregnant women.²⁵¹

6.3 Treatment and Self-Management

6.3.1 Summary of Treatments

Psychotic disorders:

- Care of women with severe psychotic disorders is complex and requires an integrated multidisciplinary approach. Education before conception to reduce unhealthy behaviours and use of contraception to avoid unplanned pregnancies is an important component of the care.
- Psychotic disorders are primarily managed with medication (usually antipsychotics)²³¹ which may be augmented with non-pharmacological therapies. Hospitalization may be required.
- Rates of relapse of schizophrenia are about 50% within two years for those that stop taking their medication. This compares to 15% in those that continue to take their medication.²³²
- Women with schizophrenia require a lot of support during the perinatal period. Healthcare providers can help by assisting women to look after their own health, to self-monitor for signs of relapse, to seek out help as needed (e.g., family, parent groups) and to develop a crisis plan in the event that their ability to care for their baby/children is temporarily impaired.²⁵²
- Close follow-up, especially in the postpartum period, is important to identify psychotic symptoms and/or inattention to the baby which may put the baby at risk. Ongoing assessment of parental capacity is important in offsetting the risk to the baby/children.²⁵²
- The decision to breastfeed needs to be made after an individual risk-benefit analysis that includes a review of the severity and frequency of symptoms, level of family support, general cooperation with treatment and ability to monitor the newborn and identify early warning signs related to antipsychotic exposure.²³⁴

Postpartum psychosis:

- Psychotic disorders are primarily managed with medication (usually antipsychotics),²⁵³ which may be augmented with non-pharmacological therapies. Hospitalization may be required.
- For women experiencing a psychotic episode who are unable to tolerate/take medications, or in whom the medication fails to reach a timely response and where suicide is a possibility, ECT may be beneficial.²²¹
 - During pregnancy, the safety record of ECT in situations where a woman is manic or suffering from psychotic depression with suicidal thoughts or disorganized thinking (clinical situations that are associated with danger from impulsivity and self-harm) has been well documented.^{254,255} ECT during pregnancy tends to be underused because of concerns that the treatment will harm the fetus; however, considerable evidence supports its safe use in severely ill pregnant women.^{256,257}
 - Although more evidence is likely warranted, it may be feasible to consider ECT as first-line treatment for postpartum psychosis.^{258,259}
 - The safety and efficacy of ECT in the treatment of women with postpartum psychosis has been established through individual case reports and small case-controlled studies.^{260,261}

6.3.2 Medications for the Treatment of Psychotic Disorders and Postpartum Psychosis

First-line medication treatment for women with psychotic disorders, including those experiencing postpartum psychosis, is antipsychotics (neuroleptics). Benzodiazepines may also be utilized on a short-term basis to help control symptoms until the anti-psychotic medications take effect.

For women with schizoaffective disorder (symptoms of both schizophrenia and a major mood episode – major depressive or manic episode), a mood stabilizer ± an antidepressant may also be required to treat the symptoms of the mood disorder.

Refer to section 6.4 for key points and recommendations related to prescribing antipsychotics in the perinatal period. Sections 3.5, 4.4 and 5.4 provide key points and recommendations related to prescribing antidepressants, benzodiazepines and mood stabilizers respectively.

Refer to Appendix 5 for current information (as of March 2013) about specific medications commonly used in the perinatal period for the treatment of psychotic disorders and/or postpartum psychosis.

6.4 Key Points and Recommendations

Key points

- **Psychosis** is a generic term used to describe conditions that affect the mind in which there has been some loss of contact with reality. Psychosis is associated with more severe forms of some psychiatric disorders, most commonly schizophrenia, schizoaffective disorder and bipolar disorder. It can also occur with a major depressive disorder.
- **Psychotic disorders** are classified under the heading “Schizophrenia Spectrum and Other Psychotic Disorders” in the DSM-V.³⁹
 - They include a range of disorders, all of which are defined by the presence of psychotic symptoms and/or other abnormalities. Schizophrenia is the most well-known.
 - Symptoms of psychotic disorders in the perinatal period are similar to those experienced at other times of life, although the distorted thoughts and behaviours may involve the baby, creating additional risk for the baby.
 - For a variety of reasons (e.g., deinstitutionalization, changing attitudes, changes to the medications²³¹), there has been an increase in the pregnancy rates of women with schizophrenia. Unfortunately, a significant proportion (estimated to be 50%²³²) of these pregnancies are unplanned or unwanted, a rate which is significantly higher than for the general population.²³³
 - Women with schizophrenia that become pregnant are typically older than the general population of pregnant women, have fewer social supports and are more likely to engage in unhealthy behaviours (e.g., smoking, poor diet, alcohol and/or substance use). Many seek prenatal care late in pregnancy and some do not seek prenatal care at all.²³⁴ All of these factors make women with schizophrenia at higher risk of poor perinatal and neonatal outcomes than women in the general population.
 - Schizophrenia (and other serious maternal psychotic disorders) may also have a devastating impact on the quality of the mother-infant bonding and, as a result, on the baby’s neurodevelopment.²³¹ Bonding may be compromised by the psychopathology of the mother’s illness (e.g., delusions and/or negative symptoms such as apathy or difficulty expressing emotion) as well as the reality of their psychosocial situation.²³⁷
 - Studies have shown that mothers with schizophrenia are more likely to experience difficulties with parenting and thus to lose custody of their children than mothers in general.²³¹
 - The risks and impacts of psychotic disorders can be successfully managed through preconception counselling and appropriate perinatal planning, management and support.
- **Postpartum psychosis** is a term that refers to the sudden onset of psychotic symptoms following childbirth.
 - It is usually unexpected and rapid (within hours) and symptoms most often appear within 72 hours to four weeks after delivery.²⁴²

- Psychotic episode lasts at least one day and may last up to one month (or beyond), with eventual return to previous level of functioning.
- It is most commonly associated with bipolar disorder (acute manic episode or a major depressive episode), a brief psychotic disorder or a major depressive disorder. While the first episode of postpartum psychosis can also be a presentation of schizoaffective disorder or schizophrenia, it is much less likely.²²⁸
- Women who present acutely with symptoms of a postpartum psychosis usually have little insight into the seriousness of their condition. They will require hospitalization for their safety, for their babies' safety and to start treatment with antipsychotic ± mood stabilizing medication.
- Postpartum psychosis is rare – approximately 1–2 per 1000 live births.²⁴³
- Psychotic disorders and postpartum psychosis are primarily managed using medications. For women experiencing a psychotic episode who are unable to tolerate/take medications, or in whom the medication fails to reach a timely response and where suicide is a possibility, ECT may be beneficial.²²¹

Recommendations

See recommendations under bipolar disorder. Referring to genetic counselling, enquiring about risk factors and developing an integrated treatment plan are the same for women with psychotic disorders and/or a history of postpartum psychosis.

1. Utilize the principles in Table 11 for the treatment of women with psychotic disorders and/or a history of postpartum psychosis.

Table 11: Guidelines for the Prevention/Management of Psychotic Disorders & Postpartum Psychosis

Prevention/Management of Postpartum Psychotic illnesses	
Treatment approach	<p>Individualized treatment plan, taking into account frequency and severity of previous episodes and response to medication.</p> <p>Severe psychotic disorders (e.g., schizophrenia) will need continued antipsychotic medication(s) throughout pregnancy.</p> <p>Less severe disorders may also require medication, especially postpartum which is a vulnerable period for psychosis.</p>
Medication management	
Preconception & Pregnancy	<p>If taking antipsychotic medication, clinically stable for 4-6 months and relapse risk is low, consider trial of gradually discontinuing medication prior to pregnancy.</p> <p>If antipsychotic medication needs to be continued, prescribe current (effective) medication.</p> <p>If currently not using antipsychotic medication but experience a relapse in pregnancy, avoid clozapine if possible (cases of maternal agranulocytosis have been reported).</p> <p>For monitoring and folic acid supplementation guidelines for women taking atypical antipsychotics during pregnancy, see Appendix 6</p>
At birth	See Appendix 6 for recommended monitoring guidelines for women taking atypical antipsychotics at the time of delivery.
Postpartum	<p>Women taking antipsychotic medication, still required postpartum, continue current (effective) medication. Dose adjustments may be necessary.</p> <p>Women not taking antipsychotic medication who requires postpartum treatment, avoid clozapine if possible if the woman is breastfeeding. (Sedation and agranulocytosis have been reported in nursing infants).</p> <p>Women taking atypical antipsychotics in the postpartum period ± breastfeeding, see Appendix 6 for recommended monitoring guidelines.</p>

7.0 Suicide and Infanticide

7.1 Suicide

Pregnancy-related maternal mortality is rare. However, suicide is the most common cause of death during pregnancy and in the first postpartum year. BC data from 2001 to 2010 presented to the Maternal Mortality Review Committee of Perinatal Service BC (unpublished, 2013) showed that of women in the perinatal period, there were:

- 10 documented suicides (3 during pregnancy and 7 during the first year postpartum).
- 3 accidental poisonings “suggestive” of suicide.
- 1 “traumatic” death.
- 3 deaths involving trauma and/or drugs where suicide could not be ruled out.

In BC in 2008, the estimated pregnancy-related mortality rate was 7.6 per 100,000 births^{vii} (BC Maternity Mortality Review Committee, 2008; www.perinataleservicesbc.ca). If suicides and deaths suspicious for suicide were to be included, this rate could increase to as high as 11.6 per 100,000.

Additional insights reported in the literature on suicidal deaths amongst perinatal women include:

- Suicide is four times more likely to occur in the nine months after childbirth than during pregnancy.²⁶²
- Psychiatric illness leading to suicide was a significant factor in at least 28% of maternal deaths in the United Kingdom.²⁶²
- Women who have had a postpartum psychiatric admission have a 70 times greater risk of suicide in their first postpartum year.^{263,264}
- Violent suicides appear more common in childbearing women who commit suicide than in the population generally.

It is important that women who are depressed and have suicidal thoughts in the perinatal period be assessed for suicide risk and, if present, appropriate actions taken.

Assessing the risk

The gold standard for assessment of a mental health disorder, including suicide risk, is a diagnostic assessment interview (see Appendix 2 for guidelines for a diagnostic assessment interview in the perinatal period). If concerns about suicidality are identified, further assessment is warranted. While there are multiple tools to assist with this assessment, the Provincial Suicide Clinical Framework²⁶⁵ does not recommend one tool over another. When the clinical situation allows, suggested areas of focus include (see Appendix 3 for specific questions):

- Current presentation of suicidality.
- Psychiatric diagnosis.
- History of current illness.
- Current medications.
- Psychosocial situation.
- Current alcohol and drug use.
- Individual strengths and vulnerabilities.

When the clinical situation does not allow for a full assessment, efforts should focus on the most salient and relevant issues and other factors followed-up at a later time. This includes:²⁶⁵

1. **Assessing suicidal ideation:** The nature, timing and persistence of the desire and intent of these ideas.
2. **Assessing suicide plan:** The lethality the woman expects from the plan, the level of detail and violence and access to means. e.g., access to a weapon or store of medication.

vii Obstetrical deaths up to one year postpartum, excluding suicide.

3. **Assessing current or previous attempts:** The timing, intent, method and consequences of the attempts.
4. **Estimating suicide risk:** Knowledgeable assessment of acute and chronic risk and protective factors and determination of methods to mitigate or strengthen those risks or protective factors.







Whenever assessing a woman for risk of suicide, enquiry should be made about the risk of harm to her baby and appropriate follow-up initiated as required.⁵⁹

Further guidance on assessing suicide risk and follow-up actions can be found in the document “Working with the Client Who is Suicidal: A tool for Adult Mental Health and Addiction Services” at www.health.gov.bc.ca/mhd/publications.html or from www.carmha.ca.

Managing immediate risk

Suicide risk assessment and response needs to be adapted for local circumstances and resources and be informed by clinical judgment. An overview of general responses is provided in Table 12.

Table 12: General Responses to Identified Suicide Risk

Ask • Suicidal thoughts • Plan • Lethality • Means Consider risk to the infant at all times		
 Suicidal ideation or thoughts <u>only</u>, without a plan  Low Risk	 Suicidal ideation with a plan or history of suicide attempt, without immediate intent  Medium Risk	 Suicidal ideation with an imminent plan  High Risk
<ul style="list-style-type: none"> • Refer to primary care provider (PCP) as soon as possible for further assessment &/or mental health referral • Provide information about crisis/urgent telephone lines e.g., 1 800-SUICIDE (1-800-784- 2433) • Develop a Safety Plan with the woman (see section on Developing a Safety Plan) 	<ul style="list-style-type: none"> • Contact PCP to discuss need for urgent mental health assessment • Provide information about crisis/urgent telephone lines • Develop a Safety Plan with the woman (see section on Developing a Safety Plan) 	<ul style="list-style-type: none"> • Refer immediately to local Emergency Room • If family unable to take woman to ER, call 911 (or other immediate response such as “car 87” in Vancouver)

Concern about harm to the baby

The baby’s safety is paramount. Ask who will be responsible for the care of the baby or supervision of the mother’s care of the baby and, if appropriate, make contact with the partner or other family member(s). A Social Worker at the Ministry of Child and Family Development should also be contacted (phone: 310-1234, no area code required) for their assessment of the suitability of alternative carers or supervisors and the home circumstances. Good communication between all agencies is vital to the safety of the baby as well as the mother.

Developing a safety plan

A healthcare provider should develop a safety plan in collaboration with the woman and a responsible family member or friend. A safety plan is a prioritized list of coping strategies and sources of support that women can use when they experience suicidal thoughts. See Table 13 for components of a safety plan.⁵⁹

Table 13: Components of a Safety Plan

Safety Plan:

1. Warning signs of the risk of imminent suicide (e.g., feeling trapped, worthless, hopeless, talking about death, writing a will, hoarding medications).
2. Coping strategies that decrease the woman's level of risk (activities that calm or comfort the woman such as deep breathing, meditation, taking a bath, a walk, etc).
3. People within the woman's network who can assist in times of need (friends/family).
4. Health professionals, agencies and crisis lines that can be contacted for help.

Safety plans need to be frequently revisited and modified as needed.

Table 14: Sample Safety Plan

Example of a Safety Plan:

Mary told her public health nurse that she was having thoughts that "she would be better off dead". She had no definite plan and no immediate intention to end her life. Through discussion and identifying the issues for her, the public health nurse helped Mary to draw up her safety plan.

Mary's Safety Plan

1. Warning signs to look out for: **Hoarding my antidepressants. Feeling like a failure.**
2. Coping strategies: **Going for a walk with neighbour, Ann. Practising mindfulness meditation.**
3. Phone numbers of friends who can be called on: **Ann: XXX-XXX-XXXX. Joan: XXX-XXX-XXXX.**
4. Supportive Health Professionals: **Family Physician: Dr A, XXX XXX XXXX. Crisis Line: 1-800-784-2433. Emergency: 911.**

7.2 Neonaticide and Infanticide

Neonaticide is the killing of an infant within 24 hours of the birth. Infanticide is the killing of young children, most commonly in the first year of life. Both neonaticide and infanticide are distinguishable within the more general term of filicide which is the killing by a parent of their own child(ren) of any age. While not all cases of filicide are perpetrated by mothers with mental health disorders, untreated mental illness can be a rare but devastating cause of infanticide. When supporting women during the perinatal period, healthcare providers need to pay attention to the risks for both mother and baby/child(ren).

Estimates from seven incidence studies between 1994 and 2006 of neonaticide and infanticide in industrialized countries vary from rates of 2.4 to 7.0 per 100,000 births. In Canada, the rate is reported to be less than 3.0 per 100,000.²⁶⁶ Fortunately these rates demonstrate that maternal killing of babies/children is a rare event.

Neonaticide

- Women who commit neonaticide are typically younger than 25 years old, emotionally immature, single, often living with their parents, unemployed and may still be attending school. Mothers who commit neonaticide often do not seek prenatal care, are usually no longer involved with the baby's father and often give birth at home (rather than in hospital). The baby is typically unwanted.²⁶⁶
- The majority of these women are not mentally ill at the time of the murder and maternal suicide after neonaticide is rare.²⁶⁶

- Typically, perinatal healthcare providers will not come into contact with neonaticide mothers during first pregnancies or after the birth, but clearly, any mother with a history of neonaticide needs to be closely monitored and supported in subsequent pregnancies.

Infanticide

- As with neonaticide, many women who commit infanticide do not have a severe mental illness that precludes them from being aware of the wrongfulness of their actions.²⁶⁷ There are a number of motivations for infanticide.
- A subset of women who commit infanticide, however, do have a definitive mental illness that can be shown to have strongly influenced their behavior.²⁶⁶ Postpartum psychosis is a risk factor, although it is noted that psychosis-related infanticide is extremely rare (as is the underlying illness) and estimated at less than 1 case per 1,000 births.^{266,268}

Assessing the risk

The gold standard for assessment of a mental health disorder, including risk to the baby/children, is a diagnostic assessment interview (see Appendix 2 for guidelines for a diagnostic assessment interview in the perinatal period). If concerns about potential risk to the baby/children are identified, a careful, in-depth assessment is required.

In very rare cases, a woman suffering a severe postpartum depression or psychosis may believe that her baby would be better off dead. Typically, thoughts of ending her baby's life would not cause her distress. These thoughts are described as ego-syntonic. Women with ego-syntonic thoughts of harming their baby pose a threat to their baby's (and potentially other children's) safety and need to be hospitalized immediately for treatment of their mental illnesses and to ensure the safety of their baby/children.

Women with OCD postpartum may also report recurrent thoughts or images of harming their baby (e.g., drowning or stabbing their baby with a knife). In most cases, although frightening, these thoughts are temporary, harmless and disappear without causing great distress. For some new mothers, however, these unwanted thoughts become obsessions (repetitive and highly distressing) and are described as ego-dystonic. Women with ego-dystonic thoughts are typically aware that their thoughts are irrational and do not want to act on them. They commonly try to avoid situations which may trigger these thoughts (e.g., avoid bathing their baby or using knives). For the most part, women with OCD do not act on their thoughts of harming their children.⁷⁸

Despite the rarity and complexity of infanticide, if a woman has a significant mental health disorder and/or there are observed difficulties with the mother-infant interaction, further enquiry is **always** warranted. In some situations, hospitalization may be required.

Examples of questions that may be asked to assess risk to the baby include:²⁶⁹

- Have you felt irritated by your baby?
- Have you had significant regrets about having this baby?
- Does the baby feel like it's not yours at times?
- Have you wanted to shake or slap your baby?
- Have you ever harmed your baby?

Examples of supplementary questions include:

- Do you have thoughts of harming your baby or putting him or her in harm's way?
- Do you think the baby would be better off dead?
- Have you ever felt you should end your life and the baby's life too?

Specific questions for exploring the risk of infanticide are listed in Appendix 4.

Women who commit infanticide are also at risk of committing suicide. Between 16% and 29% of mothers who commit filicide, commit suicide.²⁷⁰ This is particularly true of women who kill their older children. Unfortunately,

women who have psychiatric illnesses and who kill their children usually do not get treatment until after their children are dead.

Reporting concerns about harm to the baby

If concern about the safety of the infant is identified, there is a legal duty to report the situation to MCFD. Dial 310-1234 (no area code required). If needed, ministry services will be provided for the child and family. Refer to: http://www.mcf.gov.bc.ca/child_protection/keeping_kids_safe.htm.

7.3 Key Points and Recommendations

Key points

Suicide:

- Pregnancy-related maternal mortality is rare. However, of the causes, suicide is the most common cause of death during pregnancy and in the first postpartum year.
- Suicide is four times more likely to occur in the nine months after childbirth than during pregnancy. Mental illness is a significant cause of suicide.
- If concerns about suicidality are identified (e.g., positive score on question 10 of the EPDS and/or direct observation), it is important that a risk assessment be undertaken. Appendix 2 provides guidelines on areas of questioning to be included in a diagnostic assessment interview during the perinatal period and Appendices 3 and 4 provide specific questions to assess suicide and infanticide risk.
- Whenever assessing a woman for risk of suicide, enquiry should be made about the risk of harm to her baby and appropriate follow-up initiated as required.⁵⁹
- Suicide risk assessment and response needs to be adapted for local circumstances and resources and be informed by clinical judgment. The guideline provides suggested actions in low, medium and high risk situations. Providing information about crisis/urgent telephone lines and development of a safety plan is integral to follow-up at all risk levels.
- When risk is assessed as “high”, immediate referral to the Emergency Room is recommended. Contact with the partner/family is important and consider making a referral to MCFD.

Neonaticide and infanticide:

- Neonaticide and infanticide are very rare.
- A subset of women who commit neonaticide and infanticide have a diagnosed mental health disorder that influences their behaviour. Postpartum psychosis is a risk factor.
- Women who commit infanticide are also at risk of committing suicide.
- Despite the rarity and complexity of infanticide, if a woman has a significant mental health disorder and/or there are observed difficulties with the mother-infant interaction, further enquiry is always warranted. Asking women about thoughts or images of harming their child or children is an essential part of a diagnostic assessment interview.
- If concern about the safety of the infant is identified, there is a legal duty to report the situation to MCFD. Dial 310-1234 (no area code required). If needed, ministry services will be provided for the child and family. Refer to: www.mcf.gov.bc.ca/child_protection/keeping_kids_safe.htm

Recommendations

1. Assess women who are depressed and/or psychotic for suicide and infanticide risk (see Appendices 3, 4 and 5 for areas of questioning). If present, develop a safety plan and refer for a specialist psychiatric assessment and follow-up. If there are concerns about the safety of the baby, involve other parties as appropriate (partner, extended family, MCFD).

8.0 Coping and Support Networks

Community Resources for Moms

- Family Physician/Midwife/Nurse Practitioner
- Local Public Health Nurse
- Local Mental Health Team
- Emergency Room
- HealthLink BC at 811 (24/7). Provides non-emergency health information. www.healthlinkbc.ca
- Mental Health Support/Crisis Line at 310-6789 (no area code) (24/7). Provides mental health support, information and resources
- Suicide Line at 1-800-784-2433 or 1-800-SUICIDE (24/7). Provides skilled suicide assessment and intervention. www.crisiscentre.bc.ca

Self-Care Guides for Moms

- Coping with Depression during Pregnancy & Following the Birth: A Cognitive Behaviour Therapy-based Self-Management Guide for Women. Download from www.bcmhsus.ca or www.reproductivementalhealth.ca.
- Coping with Anxiety during Pregnancy and Following the Birth: A Cognitive Behaviour Therapy-based Resource and Self-Management Guide for Women and Healthcare Providers, 2013. www.bcmhsus.ca or www.reproductivementalhealth.ca
- Celebrating the Circle of Life: coming back to Balance and Harmony. A guide to emotional health in pregnancy and early motherhood for Aboriginal women and their families. Download from www.bcmhsus.ca, www.reproductivementalhealth.ca or www.perinatalservicesbc.ca.
- PPD & anxiety: a self-help guide for mothers (small cost). Order from www.postpartum.org

Websites for Dads

- Postpartum Dads: www.postpartumdads.org
- Postpartum Men: www.postpartummen.com
- 24 hour Cribside Assistance for New Fathers (Postpartum Support International): www.newdadmanual.ca
- Boot Camp for New Dads: www.bootcampfornewdads.org

Resources for BC Physicians

- Psychiatrist from BC Reproductive Mental Health available M-F 09:00-16:30 @ 604-875-2025
- Reproductive Mental Health Programs:
 - BC Reproductive MH (BC Women's): 604-875-2025; www.bcmhsus.ca or www.reproductivementalhealth.ca
 - St Paul's: 604-806-8589
 - Richmond: 604-244-5488
 - Royal Columbian: 604-520 4662
 - Surrey Memorial: 604-582-4558
 - Victoria General: 250-737-4529
 - Kamloops Perinatal Support Services: 250-377-6500
- Best Practice Guidelines for Mental Health Disorders in the Perinatal Period. www.bcmhsus.ca or www.reproductivementalhealth.ca or www.perinatalservicesbc.ca
- Motherisk (information for physicians and patients regarding medication safety in pregnancy and while breastfeeding from the Hospital for Sick Children in Ontario). www.motherisk.org

- BC Psychosis Program (UBC Hospital): Inpatient services to patients with psychotic illness (referral required). www.vch.ca
- Edinburgh Postnatal Depression Scale (PEDS) is available in multiple languages at www.perinatalservicesbc.ca
- Medical Genetics Programs
 - BC Women's (genetic counselling); ph: 604-875-2000, ext 4733.
 - Victoria General Hospital: ph: 250-727-4461.

Websites for Moms

- Pacific Post Partum Support Society (includes help-line, PND Journey, support groups). www.postpartum.org
- Postpartum Support International (includes help-line and weekly telephone chat groups for moms and for dads). www.postpartum.net
- BC Reproductive Mental Health. www.bcmhsus.ca (Programs & Services→Reproductive Mental Health) or www.reproductivementalhealth.ca
- Best Chance. www.bestchance.gov.bc.ca (Feeling Blue Section)
- BC Psychological Association. 1-800-730-0522. www.psychologists.bc.ca
- BC Association of Clinical Counsellors. www.bc-counsellors.org
- Doula Services Association (birth and postpartum doulas available in BC—for a fee). 604-515-5588 or 1-877-365-5588. www.bcdoulas.org
- BC Schizophrenia Society (includes information and on-line support for people with schizophrenia and their families). www.bcscs.org
- Mood Disorders Association of BC (provides support and education for those living with a mood disorder or other mental illness. Support groups are available in cities and towns across BC). 604-873-0103. www.mdabc.net
- Canadian Mental Health Association. www.cmha.ca
- Bounce Back (telephone coaching and DVD video of practical tips on recognizing and dealing with depression). www.cmha.bc.ca/bounceback
- Here to Help (self-help information website sponsored by BC Partners for Mental Health and Addictions). www.heretohelp.bc.ca
- Aboriginal Organizations and Services in BC (provincial listing of First Nation, Métis and Aboriginal organizations, communities and community services) www.gov.bc.ca/arr/services/guide.html
- BC Association of Pregnancy Outreach Programs. www.bcapop.ca
- VictimLink BC (domestic violence). 1-800-563-0808 (24/7). www.bc211.ca/victimlink.html



Perinatal Services BC

An agency of the Provincial Health Services Authority

Edinburgh Perinatal/Postnatal Depression Scale (EPDS)

For use between **28–32 weeks** in all pregnancies and **6–8 weeks** postpartum

Name: _____ Date: _____ Gestation in Weeks: _____

As you are having a baby, we would like to know how you are feeling. Please mark “X” in the box next to the answer which comes closest to how you have felt in the **past 7 days**—not just how you feel today.

In the past 7 days:

- | | |
|--|---|
| <p>1. I have been able to laugh and see the funny side of things</p> <p>0 <input type="checkbox"/> As much as I always could</p> <p>1 <input type="checkbox"/> Not quite so much now</p> <p>2 <input type="checkbox"/> Definitely not so much now</p> <p>3 <input type="checkbox"/> Not at all</p> | <p>6. Things have been getting on top of me</p> <p>3 <input type="checkbox"/> Yes, most of the time I haven't been able to cope</p> <p>2 <input type="checkbox"/> Yes, sometimes I haven't been coping as well as usual</p> <p>1 <input type="checkbox"/> No, most of the time I have coped quite well</p> <p>0 <input type="checkbox"/> No, I have been coping as well as ever</p> |
| <p>2. I have looked forward with enjoyment to things</p> <p>0 <input type="checkbox"/> As much as I ever did</p> <p>1 <input type="checkbox"/> Rather less than I used to</p> <p>2 <input type="checkbox"/> Definitely less than I used to</p> <p>3 <input type="checkbox"/> Hardly at all</p> | <p>7. I have been so unhappy that I have had difficulty sleeping</p> <p>3 <input type="checkbox"/> Yes, most of the time</p> <p>2 <input type="checkbox"/> Yes, sometimes</p> <p>1 <input type="checkbox"/> Not very often</p> <p>0 <input type="checkbox"/> No, not at all</p> |
| <p>3. I have blamed myself unnecessarily when things went wrong</p> <p>3 <input type="checkbox"/> Yes, most of the time</p> <p>2 <input type="checkbox"/> Yes, some of the time</p> <p>1 <input type="checkbox"/> Not very often</p> <p>0 <input type="checkbox"/> No, never</p> | <p>8. I have felt sad or miserable</p> <p>3 <input type="checkbox"/> Yes, most of the time</p> <p>2 <input type="checkbox"/> Yes, quite often</p> <p>1 <input type="checkbox"/> Not very often</p> <p>0 <input type="checkbox"/> No, not at all</p> |
| <p>4. I have been anxious or worried for no good reason</p> <p>0 <input type="checkbox"/> No, not at all</p> <p>1 <input type="checkbox"/> Hardly ever</p> <p>2 <input type="checkbox"/> Yes, sometimes</p> <p>3 <input type="checkbox"/> Yes, very often</p> | <p>9. I have been so unhappy that I have been crying</p> <p>3 <input type="checkbox"/> Yes, most of the time</p> <p>2 <input type="checkbox"/> Yes, quite often</p> <p>1 <input type="checkbox"/> Only occasionally</p> <p>0 <input type="checkbox"/> No, never</p> |
| <p>5. I have felt scared or panicky for no very good reason</p> <p>3 <input type="checkbox"/> Yes, quite a lot</p> <p>2 <input type="checkbox"/> Yes, sometimes</p> <p>1 <input type="checkbox"/> No, not much</p> <p>0 <input type="checkbox"/> No, not at all</p> | <p>10. The thought of harming myself has occurred to me</p> <p>3 <input type="checkbox"/> Yes, quite often</p> <p>2 <input type="checkbox"/> Sometimes</p> <p>1 <input type="checkbox"/> Hardly ever</p> <p>0 <input type="checkbox"/> Never</p> |

Total Score

Talk about your answers to the above questions with your health care provider.

Translations for care-provider use available on PSBC website: perinatalservicesbc.ca.

The Royal College of Psychiatrists 1987. From Cox, JL, Holden, JM, Sagovsky, R (1987). Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*. 150, 782–786. Reprinted with permission.

Appendix 2: Diagnostic Assessment Interview in the Perinatal Period

This section identifies topics that are important to include in taking a mental health history from a pregnant or postpartum woman.

1. Identifying information:

- Age. Occupation. Marital status.
- Partner's age and occupation (If applicable).
- Living situation.
- If children—number and ages. If newborn, date of birth and type of delivery.
- If pregnant, number of weeks pregnant and EDC.

2. Chief complaint: What is the woman's major concern at the time of assessment?

3. History of present illness:

- If the woman is pregnant,
 - Was it planned or unplanned?
 - How does she feel about it?
 - Note any complications
- If the patient is postpartum,
 - How is she adjusting to motherhood?
 - How is breastfeeding going?
 - Is she feeling bonded to her baby?
- Assess present illness and determine
 - Is this the first episode of a depressive, manic, anxiety, psychotic or substance related disorder? or
 - Is it a relapse or exacerbation of an underlying psychiatric illness in the context of pregnancy or having given birth?
- Thoroughly review and record symptoms of the disorder
 - Woman's description of her mood, sleep pattern, eating pattern, energy level, ability to focus, memory
 - Feelings of guilt or worthlessness, hopelessness
 - Psychotic symptoms (if present)
 - Suicidal ideation or plans (See Appendix 3 for specific suicide risk questions)
 - Fears of harming the baby (if postpartum) (See Appendix 4 for specific infanticide risk questions)
 - Screen for symptoms of co-morbid anxiety e.g., recurrent worries, panic attacks, obsessional thoughts or images or compulsive behaviours
 - Screen for manic symptoms e.g., irritability, grandiosity, high energy, decreased need for sleep or increased talkativeness
 - When did the symptoms first appear?
 - What has been done to manage the symptoms? What has helped?
 - What are the woman's expectations at this time?

4. Past psychiatric illness:

- Has the woman been diagnosed with a psychiatric illness in the past? If so, what is the diagnosis and what treatments have been used. Was remission achieved?
- Does she have a history of previous postpartum depression or PMDD?
- Has she ever attempted to harm herself in the past?
- Has she attempted suicide? If so, what method did she use? Were substances involved?

- Has she been hospitalized for treatment of a psychiatric illness? Which hospital and for how long? What treatments were tried?
- 5. Family psychiatric illness:**
- Psychiatric history of family of origin: maternal, paternal, siblings and extended family
 - Include diagnoses, treatment and response to treatment
 - Has anyone in the family committed suicide? If so, record method used
- 6. Past medical history:**
- Include previous hospitalizations for medical or surgical reasons. Is there a chronic illness?
 - Is there a history of head injury or seizure disorder?
 - Is there a history of thyroid or endocrine disorder?
 - Is there a cardiac history?
 - Obstetrical history, including number of pregnancies, pregnancy losses, complications and method of deliveries
- 7. Alcohol history:**
- Frequency, quantity and when last used
 - Is there a history of problematic drinking?
 - Has woman sought treatment in the past? What has been effective?
 - Is she currently getting treatment?
- 8. Drug history:**
- Is there a history of MJ, ecstasy, stimulant, opiate or other street drug use or abuse?
 - Is there current use of illegal drugs? Frequency, quantity and when last used
 - Has the woman sought treatment in the past? What has been effective?
 - Is she currently receiving treatment?
- 9. Current medications:**
- All medications being taken with dosages
 - Include non-prescription medications and supplements
- 10. Allergies:**
- Record allergies to medications
- 11. Social history:**
- Place of birth, labour and delivery, growth and development
 - Relationship with other family members
 - Temperament as child
 - History of physical, emotional or sexual abuse
 - School experiences, academic and social
 - Post-secondary education, employment and vocational training
 - Relationship history, including current relationship
 - Support systems
 - Current stresses
- 12. Mental status exam:** (your recorded observation of the woman during interview)
- Appearance, rapport, behaviour during interview

- Speech
- Affect
- Suicidal or infanticidal ideation
- Thought form, thought content, perception
- Presence of psychotic symptoms (delusions or hallucinations)
- Cognitive ability
- Insight and judgment

13. Multi-axial diagnosis:

After completing the history, formulate a multi-axial diagnosis and develop a treatment plan.

Multi-axial diagnosis classifications:

AXIS I:	Psychiatric Disorder/s
Axis II:	Personality Disorders/Traits
Axis III:	Pregnant or postpartum
	Other co-morbid medical conditions
Axis IV	Current Stresses
Axis V:	Global Assessment of Functioning Score: (1-100)

Note: DSM-5 will move to a non-axial documentation of diagnosis, combining the former Axes I, II, and III, with separate notations for psychosocial and contextual factors (formerly Axis IV) and disability (formerly Axis V).

Appendix 3: Perinatal Suicide Risk Questions

Begin the discussion with: “Sometimes when women are depressed, they have thoughts about harming themselves”. Then proceed to the following questions:

1. Have you had any thoughts of harming yourself?

If yes:

- Can you describe your thoughts of harming yourself?
- How frequent and persistent are these thoughts?
- Do you have a definite plan to harm yourself?
- Do you have a definite plan to end your life?
- Do you have the means to carry out your plan?
- How close have you come to acting on this plan?
- What stopped you from acting on this plan?

If no:

- Do you ever wish that you were dead?
- Do you ever wish that you could escape or disappear or not wake up in the morning?

2. Have you attempted to harm yourself in the past?

If yes:

- Can you tell me about it?
- Did you want to die at that time?
- Were you drinking alcohol or using drugs at that time?
- Were you admitted to hospital?
- How did you feel after the attempt?

3. Is there a family history of suicide?

If yes:

- Can you tell me about it?

If you are concerned that the patient is a suicide risk, develop a safety plan and refer immediately for psychiatric care (see section 7.0 for a discussion of suicide and infanticide).

Appendix 4: Perinatal Infanticide Risk Questions

Begin the discussion with: “Sometimes when women are depressed after giving birth, they have thoughts about harming their babies”. Then proceed to the following questions:

1. Have you had any thoughts of harming your baby?

If yes:

- Can you describe your thoughts of harming your baby?
- How frequent and persistent are these thoughts?
- Are you having images of harming the baby?
- How frequent and persistent are these images?
- Do these thoughts or images distress you or frighten you?
- Do you have a definite plan to harm your baby?
- Do you think that your baby would be better off dead?
- Do you have a definite plan to end your baby’s life?
- Do you have the means to carry out your plan?
- How close have you come to acting on this plan?
- What stopped you from acting on this plan?

If no: Do you ever wish that you had never become pregnant?

2. Do you have thoughts of harming both yourself and the baby?

If yes:

- Can you describe your thoughts of harming both of you?
- How frequent and persistent are these thoughts?
- Do you think that you would both be better off dead?
- Do you have a definite plan to harm both yourself and your baby?
- Do you have a definite plan to end both your lives?
- Do you have the means to carry out your plan?
- How close have you come to acting on this plan?
- What stopped you from acting on this plan?

3. Have you attempted to harm your baby in the past?

If yes:

- Can you tell me about it?
- Did the baby require any medical treatment?
- Were you drinking alcohol or using drugs at that time?
- How did you feel after the event?

If you are concerned about any risk to the baby or other children, ensure partner or extended family are involved, contact the MCFD (telephone 310-1234, no area code required) as necessary and ensure the woman has access to psychiatric care (see section 7.0 for a discussion of suicide and infanticide).

Appendix 5: Psychotropic Medications Used in the Perinatal Period

This Appendix provides current information (as of March 2013) about the relative safety of medications currently used for the treatment of depression, anxiety disorders, bipolar disorder and psychotic disorders in the perinatal period. As more experience is gained, the guidelines will be updated accordingly. It is also noted that there are contradictory findings in different studies that use psychotropic medications in the literature. This guideline attempts to incorporate the most comprehensive up-to-date research.

General principles for women requiring psychotropic medications in the perinatal period:

- Support informed decision-making by discussing the risks and benefits of the medications with the woman ± partner as well as the risks of not treating her symptoms.
- Use the minimum number of psychotropic medications at the lowest effective dose.
- Women with severe psychiatric illness with multiple hospitalizations and a history of relapse after discontinuing their medication are advised to remain on their medication in pregnancy if the risk of discontinuing is greater than the risk of fetal exposure to medication.
- Encourage women with premature babies or babies with significant health problems to discuss their psychotropic medications with their baby's pediatrician if they want to breastfeed.

Appendix 6 summarizes suggested actions/monitoring for women on psychotropic medications during the perinatal period. The goal is to minimize the risks to the woman and fetus/baby.

Background Risk

The concept of “background risk” is frequently referred to in the medication tables in this Appendix. Background risk refers to the risk of a particular clinical problem occurring in the general population (in the case of this guideline, the general population refers to the population of pregnant women). It provides a useful reference point for evaluating the risk to the fetus/baby of women taking psychotropic medications during the perinatal period.

Background risks of clinical problems discussed in the medication tables are approximately:

- Major congenital malformation (MCM): 3%²⁷¹
- Clinically recognized spontaneous abortion (SAB): 15%²⁷¹
- Prematurity: 4%²⁷¹
- Low birth weight (LBW): 8%²⁷²
- Cardiac defects: 1%²⁷³
- Neural tube defects: 0.1%²⁷⁴
- Persistent Pulmonary Hypertension of the Newborn: 0.1–0.2%³⁰⁸

Risk Categories

The American Food and Drug Administration (FDA)-assigned pregnancy categories are used to classify the risk of relevant medications to the developing fetus. The Hale categories are used to classify the risk to the baby through exposure to breast milk. It is noteworthy that these categories may be changed over the coming years.

FDA Pregnancy Risk Categories

Category A: Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters) and the possibility of fetal harm appears remote.

Category B: Either animal reproduction studies have not demonstrated a fetal risk, but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).

Category C: Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal, or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.²⁷⁵

Category D: There is positive evidence of human fetal risk, but the benefits of use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

Category X: Studies in animals or human beings have demonstrated fetal abnormalities, or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Hale Lactation Risk Categories

L1 Safest: Drug which has been taken by a large number of breastfeeding mothers without any observed increase in adverse effects in the infant. Controlled studies in breastfeeding women fail to demonstrate a risk to the infant and the possibility of harm to the breastfeeding infant is remote; or the product is not orally bioavailable in an infant.

L2 Safer: Drug which has been studied in a limited number of breastfeeding women without an increase in adverse effects in the infant, and/or the evidence of a demonstrated risk which is likely to follow use of this medication in breastfeeding women is remote.

L3 Probably Safe: There are no controlled studies in breastfeeding women; however, the risk of untoward effects to a breastfed infant is possible, or controlled studies show only minimal non-threatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk to the infant.

L4 Possibly Hazardous: There is positive evidence of risk to a breastfed infant or to breast milk production, but the benefits from use in breastfeeding mothers may be acceptable despite the risk to the infant (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

L5 Hazardous: Studies in breastfeeding mothers have demonstrated that there is a significant and documented risk to the infant based on human experience, or it is a medication that has a high risk of causing significant damage to an infant. The risk of using the drug in breastfeeding women clearly outweighs any possible benefit from breastfeeding. The drug is contraindicated in women who are breastfeeding an infant.

Medications

Medications in this Appendix are grouped according to drug classes: antidepressants, anxiolytics (benzodiazepines), hypnotics (non-benzodiazepines), mood stabilizers and antipsychotics. For each medication, information is provided on dosage range, FDA pregnancy risk category and fetal risks, including the risk of developing NAS (Neonatal Adaptation Syndrome, see page 30), Hale lactation risk category and breastfeeding risks.

For specific disorders, the relevant drug classes are as follows:

Disorder	Relevant Drug Class
Depression	<ul style="list-style-type: none"> • Antidepressants • Anxiolytics (benzodiazepines), if co-existing anxiety disorder • Hypnotics (non-benzodiazepines)
Anxiety disorders	<ul style="list-style-type: none"> • Antidepressants • Anxiolytics (benzodiazepines) • Hypnotics (non-benzodiazepines)
Bipolar disorder	<ul style="list-style-type: none"> • Mood stabilizers • Antipsychotics (neuroleptics) • Antidepressants • Anxiolytics (benzodiazepines)
Psychotic disorders (schizophrenia & postpartum psychosis)	<ul style="list-style-type: none"> • Antipsychotics (neuroleptics) • Anxiolytics (benzodiazepines)

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Antidepressants					
SSRIs					
Citalopram (Celexa®)	10–40 mg per day. ²⁷⁶	C ²⁷⁷	<p>SSRIs in general: Small increased risk of SAB (OR 1.8)²⁷⁸, prematurity (aOR 1.4)²⁷⁹ and LBW (aOR 1.2)²⁷⁸⁻²⁸⁸ For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM.^{278,288,289}</p> <p>SSRIs have been associated with a very slight risk of cardiac defects.^{279,290-292} For citalopram: possible small increase in the risk of septal heart defects (incidence 1.1%, expected 0.5%, also reported for other SSRIs).^{278,279,284,292-297} NAS has been reported in up to 30% of infants.^{283,287,298-307} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk.³⁰⁸</p>	L2	M:P ratio up to 3. Infant serum levels up to 17% of maternal levels. Sedation reported. ^{305,309-314} Monitor baby.
Escitalopram (Cipralex®)	5–20 mg per day. ²⁷⁶	C ²⁷⁷	<p>SSRIs in general: Small increased risk of SAB (OR 1.8),²⁷⁸ prematurity (aOR 1.4)²⁷⁹ and LBW (aOR 1.2).^{276,278-288,299,315} Insufficient data on escitalopram to determine risk of teratogenicity.^{286,307} For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM.^{278,288,289} SSRIs have been associated with a very slight risk of cardiac defects.^{279,290-292} See Citalopram. Based on data from other SSRIs, NAS may occur in up to 30% of infants.^{283,298,300,301} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk.³⁰⁸</p>	L2	Limited data (10 cases). ^{178,316,317} M:P ratio up to 2.5. Escitalopram levels in nursing infants have ranged from undetectable up to 20% of maternal levels. No toxicity reported.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Fluoxetine (Prozac®)	20–80 mg per day. ³¹⁸	C ³¹⁹	SSRIs in general: Small increased risk of SAB (OR 1.8), ²⁷⁸ prematurity (aOR 1.4) ²⁷⁹ and LBW (aOR 1.2). ^{276,278-288,299,319-321} For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM. ^{278,288,289} SSRIs have been associated with a very slight risk of cardiac defects. ^{279,290-292} For fluoxetine: Small increased risk of cardiac defects (incidence up to 3%, expected 1%); for septal defects specifically, incidence up to 1%, expected 0.5%). ^{279,288,291,292,322} Well-documented risk of NAS in up to 30% of neonates, including rare cases of cardiac events. ^{300,309,320,323-329} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk. ³⁰⁸	L2	Fluoxetine and its active metabolite desmethylfluoxetine are found at variable levels in the plasma of nursing infants, ranging from undetectable to levels in the therapeutic range. ^{309,314,330-336} Few reports of toxicity; some reports of colic and decreased weight gain. SSRIs with lower infant plasma levels are preferred.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Fluvoxamine (Luvox®)	50–300 mg per day. ³³⁷	C ²⁷⁵	No specific data on risk of SAB, prematurity, LBW or long-term neurodevelopmental effects with fluvoxamine. SSRIs in general: Small increased risk of SAB (OR 1.8), ²⁷⁸ prematurity (aOR 1.4) ²⁷⁹ and LBW (aOR 1.2). ^{276,278-288,299,319-321} For fluvoxamine: Insufficient data to determine risk of teratogenicity; no evidence of an increased risk of MCM. ^{285,291,293,322,338,339} For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM. ^{278,288,289} SSRIs have been associated with a very slight risk of cardiac defects. ^{279,290-292} See Citalopram; Fluoxetine; Paroxetine; Sertraline. Based on data from other SSRIs, NAS may occur in up to 30% of infants. ^{283,298,300,301,340} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk. ^{308,341,342}	L2	Very limited information (10 cases). ³⁴³⁻³⁴⁷ Infant levels have reached 45% of maternal levels. ³⁴⁵ Alternatives with more safety data and lower plasma levels in the neonate are preferred.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Paroxetine (Paxil®)	20–60 mg per day. ³⁴⁸	D ³⁴⁹	SSRIs in general: Small increased risk of SAB (OR 1.8) ²⁷⁸ , prematurity (aOR 1.4) ²⁷⁹ and LBW (aOR 1.2). ^{276,278-288,299,319-321} For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM. ^{278,288,289} SSRIs have been associated with a very slight risk of cardiac defects. ^{279,290-292} For paroxetine: Controlled studies indicate a small, dose-related increased risk of cardiac malformations following paroxetine exposure in the first trimester (2–4% incidence, 1% expected) particularly in septal defects. ^{180,181,279,289,291,296,297,341,350-352} Well-documented risk of NAS in up to 30% of neonates. ^{300,309,320,323,325-329,340,353-357} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk. ^{308,320,341,342}	L2	Well researched. Low levels in milk. Most infants have undetectable paroxetine levels. No toxicity reported (one case of irritability). ^{314,346,358-360}
Sertraline (Zoloft®)	25–200 mg per day. ³⁶¹	C ³⁶²	SSRIs in general: Small increased risk of SAB (OR 1.8) ²⁷⁸ prematurity (aOR 1.4) ²⁷⁹ , and LBW (aOR 1.2). ^{276,278-288,299,319-321} For SSRIs the risk of teratogenicity is not large, with an expectation that most exposed infants would be born without a MCM. ^{278,288,289} SSRIs have been associated with a very slight risk of cardiac defects. ^{279,290-292} For sertraline: possible small risk of cardiac malformations (incidence 2%, expected 1%) specifically in septal defects (incidence 1.5%, expected 0.5%). ^{278,279,290,292,296,338,352} NAS may occur in up to 30% of infants. ^{283,298,300,301,340,357,363-368} Small risk of PPHN for all SSRIs (incidence 0.3%; expected 0.1–0.2%), approximately double the background risk. ^{308,341}	L2	Extensively researched. ^{314,346,358,369-374} M:P 0.4–4.8. Infant plasma levels are usually low, although there have been a few cases of elevated levels. Monitor baby and if concerns, check serum levels.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
SNRIs					
Duloxetine (Cymbalta®)	30–120 mg per day. ³⁷⁵	C ^{2,375}	A relatively new drug with little data. Insufficient data to assess risk of teratogenicity. One small controlled study found no evidence of teratogenicity. ³⁷⁶ NAS has been reported. ^{377,378} Limited evidence of altered behaviour in animals exposed in utero; implications for humans are unknown. ^{375,375,379}	L3	Minimal data. ^{378,380,381} M:P ratio up to 1.3. No toxicity reported. Poor oral absorption, therefore levels may be low in nursing infants. ^{275,375,379,382} However, drugs with more evidence of safety are preferred
Desvenlafaxine (Pristiq®)	50–100 mg per day. ³⁸³	C ³⁸⁴	No specific data on desvenlafaxine. Desvenlafaxine is the active metabolite of venlafaxine. See Venlafaxine.	L3	Limited specific data on desvenlafaxine. ^{385,386} M:P ratio up to 2.7. RID estimated as up to 8.1% of maternal dose. Infant plasma levels up to 6.2% of maternal levels. Monitor. See also Venlafaxine.
Venlafaxine (Effexor®)	37.5–225 mg per day. ³⁸³	C ³⁸⁴	Possible dose-related increased risk of SAB. ^{280,387-389} Prematurity is possible. ^{388,390} Most controlled studies find no increase in the risk of MCM. ^{339,387,390-392} One case-control study found an elevated risk of MCM but confirmation is needed. ³⁹² NAS has been reported with venlafaxine (many cases). ^{300,328,388-390,393-398}	L3	Relatively high levels of exposure in nursing infants. ^{358,399-402} M:P ratio up to 7 (venlafaxine plus active metabolite). Detected in infant plasma as active metabolite at up to 37% of maternal level. Monitor the baby.
Tricyclic Antidepressants (TCAs)					
Amitriptyline (Elavil®)	75–200 mg per day. ⁴⁰³	C ²⁷⁵	For TCAs in general: Possible small risk of SAB; ⁴⁰⁴ possible 2-fold increased risk of premature birth and LBW; ^{295,405} insufficient data to determine the risk of teratogenicity, including limb anomalies in humans. ^{298,405-410} NAS is possible with TCAs; seizures are rare. ^{295,405,411-414} Minimal information is available on amitriptyline or its metabolite nortriptyline.	L2	Very limited data. Present in milk. No toxicities reported. ⁴¹⁵⁻⁴¹⁷ Monitor baby.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Clomipramine (Anafranil®)	25–200 mg per day. ⁴¹⁸	C ²⁷⁵	For TCAs in general: Possible small risk of SAB; ⁴⁰⁴ possible 2-fold increased risk of premature birth and LBW, ^{295,405} insufficient data to determine the risk of teratogenicity in humans. One controlled study reported a 2-fold increased risk of cardiovascular defects with Clomipramine specifically (incidence 1.8%, expected 0.9%, OR 2.03 (1.22–3.40)). ⁴¹⁹ A possible association of TCAs with limb anomalies requires further research. ^{298,405-410} NAS is possible with TCAs especially clomipramine; seizures are rare. ^{295,405,411-414,420}	L2	Very limited data (1 case). Detected in infant plasma. No toxicity reported. ⁴²⁰ Monitor baby.
Nortriptyline (Aventyl®)	75–150 mg per day. ⁴²¹	D275 / Unassigned ⁴²²	For TCAs in general: Possible small risk of SAB; ⁴⁰⁴ possible 2-fold increased risk of premature birth and LBW, ^{295,405} insufficient data to determine the risk of teratogenicity in humans. A possible association of TCAs with limb anomalies requires further research. ^{298,405-410} NAS is possible with TCAs; seizures are rare. ^{295,405,411-414} Minimal information is available on nortriptyline or the related drug amitriptyline.	L2	Nortriptyline is the active metabolite of amitriptyline. Possibly concentrated in milk. Minimal information indicates low levels in the infant and no toxicities have been reported. ^{423,424} Monitor baby.

Other Antidepressants

Bupropion (Wellbutrin®, Zyban®)	150–300 mg per day. ^{425,426}	C ⁴²⁷	Possible increased risk of SAB. ^{428,429} Small absolute increase in the risk of cardiovascular malformations (left ventricular outflow tract obstruction (LVOTO) heart defects) associated with first trimester exposure to bupropion monotherapy (incidence 0.279% vs. 0.07% with exposure to other antidepressants). ^{179,293,391,428-431} NAS has been reported rarely: one case of arrhythmia and one case of seizures due to prolonged hypoglycemia. ^{432,433} Further research is needed to clarify possible increased risk of ADHD. ⁴³⁴	L3	Limited data (18 cases). ^{298,435-438} Variable and at times high levels in milk: M:P ratio range 0.09 up to 8.7. One seizure reported in a nursing infant. Monitor baby.
---------------------------------	--	------------------	---	----	--

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Mirtazapine (Remeron®)	15–45 mg per day. ⁴³⁹	C ⁴⁴⁰	Possible increase in SAB (limited data) ^{441,442} and preterm births. ^{390,441,442} No evidence of teratogenicity (limited data <500 documented exposures). ^{293,390,441-446} NAS has been reported. ^{390,447,448}	L3	Limited data (10 cases). ⁴⁴⁹⁻⁴⁵¹ M:P ratio up to 1.5. Low levels in infant plasma. No toxicity reported. Monitor baby.
Anxiolytics (benzodiazepines)^{viii}					
Alprazolam	Anxiety: 0.5–3 mg per day in 2-3 divided doses. Panic Disorder: 0.5–10 mg per day in divided doses. ⁴⁵²	D ⁴⁵³	A controlled study indicated increased risk of SAB. ⁴⁵⁴ Controlled studies indicate no or small increased risk of prematurity and LBW. ^{454,455} Controlled studies indicate no increased risk for major malformation, oral clefts or cardiovascular malformations for benzodiazepines as a group (conflicting data). ^{339,455-460} Combined with SSRI may increase the risk for cardiac malformations. ³³⁹ NAS has been reported including respiratory depression. ^{455,461,462} Consider reducing dose close to delivery, if possible.	L3 ⁴⁶³	M:P ratio 0.36.464 RID estimated as 3-8.5%. ^{463,464} Reports of sedation, withdrawal (also in-utero exposure). ^{461,465,466} Increased risk for CNS depression if mother is taking > 1 CNS depressive drug. ⁴⁶⁶ Monitor infant for sedation, poor feeding, irritability.
Clonazepam	Panic Disorder: 0.50 to 1 mg per day in divided doses. Maximum 4 mg per day. ⁴⁶⁷	D ⁴⁶⁷	A controlled study indicated increased risk of SAB. ⁴⁵⁴ Controlled studies indicate no increased risk for major malformation, oral clefts or cardiovascular for benzodiazepines as a group (conflicting data). ^{339,456-458,460,468} Combining clonazepam with antiepileptic drugs may increase risk for major malformation. ⁴⁶⁸ Combination with SSRI may increase the risk for cardiac malformations and NAS. ^{339,357} NAS has been reported including respiratory depression. ^{357,469,470} Consider reducing dose close to delivery, if possible.	L3 ⁴⁶³	M:P ratio 0.33.471 RID estimated at: 2.5%. ⁴⁷² Low plasma concentrations in infants. ^{469,471-473} Reports of mild depression, apnea (also in-utero exposure). ^{466,469,471} Increased risk for CNS depression if mother is taking > 1 CNS depressive drug. ⁴⁶⁶ Monitor infant for sedation, poor feeding, irritability.

viii Many of the controlled trials on teratogenicity of benzodiazepines focus on diazepam. For alprazolam, clonazepam and lorazepam, much of the teratogenicity safety information comes from controlled trials which combined benzodiazepines.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Diazepam	Anxiety: 2–10 mg two to four times daily. ⁴⁷⁴	D ⁴⁷⁵	A controlled study indicated increased risk of SAB. ⁴⁵⁴ Controlled studies indicate a slight risk of prematurity and LBW associated with exposure in the 2nd & 3rd trimesters. ^{339,454,455,476,477} Combined with SSRI may increase risk of prematurity and cardiac malformation. ^{339,478} Controlled studies indicate no increased risk for major malformation, oral clefts or cardiovascular malformations with benzodiazepines as a group (conflicting data). ^{339,455-458,476,479-483} NAS has been reported including respiratory depression. ^{455,476,478,484-487} Consider reducing dose close to delivery, if possible.	L3 L4 (chronic use) ⁴⁶³	Wide range of M:P (0.13-0.50). 488-490 RID estimated as 2.7-7.1%. ^{463,489} Reports of lethargy, weight loss. ^{490,491} Increased risk for CNS depression if mother is taking > 1 CNS depressive drug. ⁴⁶⁶ Monitor infant for sedation, poor feeding, irritability. Increased risk of drug accumulation if premature or very low birth weight. ^{475,492,493}
Lorazepam (Ativan®)	Anxiety: 2–4 mg per day in divided doses. Max 6 mg per day. ⁴⁹⁴	D ⁴⁹⁵	One controlled study indicated a small increased risk of SAB. ⁴⁵⁴ Controlled studies indicate no increased risk for major malformation, oral clefts or cardiovascular malformations with first trimester exposure to benzodiazepines as a group (conflicting data). ^{339,456-458,496} Combined with SSRIs may increase the risk for cardiac malformations. ³³⁹ NAS has been reported including respiratory depression. ^{476,497,498} Consider tapering the dose close to delivery, if possible.	L3 ⁴⁶³	M:P ratio 0.22499 RID estimated at: 2.9 & 3.6%. ^{463,497} No data on infant serum concentrations. Limited reports of adverse effects. Increased risk for CNS depression if mother is taking > 1 CNS depressive drug. ⁴⁶⁶ Monitor infant for sedation, poor feeding, irritability.
Hypnotics (non-benzodiazepines)					
Trazodone (Oleptro®, Trazorel®) (also used for depression but less common)	Insomnia: 25–200 mg per day. ⁵⁰⁰ Depression: 150–600 mg per day. ^{500,501}	C ⁵⁰²	Very limited data. Small controlled studies found no evidence of malformations. ^{293,503-505}	L2	Limited data (7 cases). ^{503,506} M:P ratio low (0.14). RID estimated as 0.6%. No toxicity reported. Monitor baby.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Zolpidem (Sublinox®, Ambien®)	10 mg per day. ⁵⁰⁷	C ⁵⁰⁸	Controlled studies indicate a small 1.5 to 2-fold increased risk of prematurity ^{509,510} and LBW. ^{509,510} No evidence of an increased risk of malformations. ⁵⁰⁹⁻⁵¹² A possible link with intestinal malformations requires further research. ⁵¹¹ NAS has been reported, including severe respiratory depression. ^{507,509,513}	L3	Very limited data. ²⁷⁵ Low levels in milk. Sedation and decreased appetite have been reported. May inhibit milk secretion, based on animal data. ⁵⁰⁷ Monitor for sedation and lack of weight gain.
Zopiclone (Imovane®)	5–7.5 mg per day. ⁵¹⁴	C ⁵¹⁵	LBW is possible. ^{514,516} Controlled studies have not found an increased risk of malformations in humans or animals. ^{511,514,516,517} A possible link with intestinal malformations requires further research. ⁵¹¹ No reports of NAS at therapeutic doses. ^{516,517} However, since a withdrawal syndrome has been reported in neonates following high maternal doses, ⁵¹⁸ minimize use at delivery if possible.	L2	Very limited data. ^{518,519} M:P ratio up to 0.7. RID estimated as 1.4% of maternal dose. No data on infant plasma levels following maternal therapeutic doses. Monitor baby for sedation.

Mood Stabilizers

Carbamazepine (Tegretol®)	100 to 1600 mg per day ⁵²⁰	D ⁵²¹	Teratogenicity is possible with an incidence of MCM of 3–5% (2-fold increased risk), mainly neural tube defects. ⁵²²⁻⁵²⁷ The majority of infants will therefore be born without defects. Risk increases with increasing doses. ⁵²⁸ A “fetal carbamazepine syndrome” of minor facial defects, fingernail dysplasia and cognitive defects has been described. ⁵²³ Folic acid supplementation is recommended, along with an 18-20 wk detailed ultrasound. ^{529,530} Prematurity and LBW are possible. ^{522,531} Long-term neurodevelopmental effects have been found in some studies but not in others; more research is needed. ^{523,531-537} Avoid if clinically possible in the first trimester.	L2	Well-studied. M:P ratio < 1 and few toxicities reported in nursing infants (case reports of liver dysfunction and seizures). Infant level was 69% of maternal level in one study. Monitor baby. ^{298,538-543}
---------------------------	---------------------------------------	------------------	--	----	--

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Gabapentin (Neurontin®)	900–3600 mg/day. ⁵⁴⁴	C ⁵⁴⁵	Low birth weight is possible. ^{546,547} Insufficient data to assess risk of teratogenicity. Based on small controlled studies, gabapentin has not shown teratogenicity in humans. ^{298,525,546,548-550}	L2	Very limited data. ^{275,551,552} M:P ratio 0.7-1.3. Low plasma levels in nursing infants, approximately 6–12% of maternal plasma levels. No toxicities reported. Monitor for sedation and unusual effects.
Lamotrigine (Lamictal®)	25–500 mg per day. ⁵⁵³	C ⁵⁵⁴	Numerous large registry studies find no evidence of an increased risk of MCM. ^{224,226,549,550} Major malformations may be more likely with higher lamotrigine doses above 200–300 mg/day ^{524,525,528,555} or if combined with valproic acid. ^{524,555} Conflicting evidence of increased risk of oral clefts and the absolute risk is small (7 oral clefts in 1000 exposures). ^{536,556}	L3	Infant plasma levels have been 25–43% of maternal plasma ratios and close to the therapeutic range. Few adverse effects have been documented; one case of apnea and cyanosis in a nursing infant. ⁵⁵⁷⁻⁵⁶² Monitor baby and consider monitoring plasma levels.
Lithium (Carbolith®, Lithane®)	900–1800 mg per day. ⁵⁶³	D ⁵⁶⁴	Older evidence indicates a risk of MCM varying from no increased risk to a 12% incidence, ⁵⁶⁵⁻⁵⁶⁷ mainly an increased risk of cardiac anomalies (incidence 0-7%). ^{295,565,567,568} Many authorities consider the absolute risk of cardiac defects to be small and contrary to earlier estimates, ^{569,570} there is only a small absolute risk, if any, of Ebstein's anomaly ⁵⁷¹ (incidence 0.05–0.1% (5–10 in 10,000) ⁵⁷¹⁻⁵⁷³ (expected incidence 0.005% (1 in 20,000)). ⁵⁶⁹ Avoid in the first trimester if clinically possible, or do a detailed ultrasound and echocardiography at 18–20 weeks. ^{572,574} NAS is possible but the risk is unknown. There have been case reports of floppy baby syndrome, goiter, diabetes insipidus, cardiac defects and hepatomegaly in the neonate. ^{563,565,567,572,574-576} Hold lithium at time of delivery. ^{577,578} Maintain hydration.	L3 with close observation ²⁷⁵	Infant plasma levels are in the range of 10–100% of maternal levels. ^{275,570,576,579,580} Other than one case of floppy infant syndrome, lethargy and T wave inversion, and cases of poor feeding, no toxicities reported. Monitor the baby's lithium levels. Avoid infant dehydration. Monitor thyroid function if symptoms occur (lithium can decrease thyroxine production).

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Topiramate (Topamax®)	Up to 400mg per day. ⁵⁸¹	D ⁵⁸²	Low birth weight is possible; ^{581,583,584} Overall low risk of teratogenicity. ^{525,549,550,584-587} Small increased risk of MCM. ^{550,585} Approximately 95% of infants have been born without major abnormalities. Increased risk of oral cleft but the absolute risk is small (incidence 1.2–2.2%, versus expected 0.12–0.2%). ^{550,581,583,585} A small increased risk of hypospadias (incidence 1.1% versus expected 0.33%). ^{525,550,583,586} Possible NAS including rare hypocalcemic seizures. ^{588,589} One small study has reported long-term neurobehavioural deficiencies; more research is needed. ⁵⁸⁸	L3	Very limited data. M:P ratio 0.67-1.1. Estimated RID 3–23% of maternal dose. Infant plasma levels 10–20% of maternal levels. No toxicities reported. Monitor baby. ⁵⁹⁰
Valproic Acid and Divalproex Sodium (Depakene®, Epival®)	15–60 mg/kg per day. ⁵⁹¹	D ⁵⁹²	Valproic acid has been identified as a human teratogen. ²²²⁻²²⁷ Risk of MCM increases with increasing dose (3–5% at doses below 1400 mg/day, up to 8–35% at higher doses). ^{227,528,593,594} The most common malformation is spina bifida, incidence 1–2% (expected 0.14%–0.2%), ^{591,592,595} but other anomalies are also reported. ^{526,595-597} The “Fetal Valproate Syndrome” includes distinctive facial abnormalities, neural tube defects, long thin fingers and toes, hypospadias and possibly poor neurobehavioural development. ^{298,596} NAS has been common in some studies. ⁵⁹⁸⁻⁶⁰⁰ Reduced IQ and autism are suspected; more research is needed. ^{533,534,543,601,602} Avoid in pregnancy, if possible.	L3	Low levels in milk (M:P ratio 0.05–0.10). Neonatal drug levels 0.9–40% of maternal levels. ⁶⁰³⁻⁶⁰⁵ Thrombocytopenia and anemia have been reported. ⁶⁰⁶

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Antipsychotics (Neuroleptics)					
Atypical Antipsychotics					
Aripiprazole (Abilify®)	10–30 mg per day. ⁶⁰⁷	C ⁶⁰⁸	A relatively new drug. Insufficient data to determine risk of teratogenicity in humans. Animal studies suggest a possible risk of teratogenicity, LBW and long-term neurodevelopmental effects. ^{607,608} Gestational diabetes may complicate pregnancy. ⁶⁰⁹ NAS has been reported. ⁶¹⁰⁻⁶¹²	L3	Very limited data. Low levels in milk. ^{613,614} Sedation has been reported. ²⁷⁵
Asenapine	Sublingual: 10–20 mg per day. ⁶¹⁵	C ⁶¹⁶	A relatively new drug with no human data. Insufficient data to determine risk of teratogenicity in humans. Animal data describe embryotoxicity, decreased fetal weight and delayed growth. The risk of NAS is probably similar to other atypical antipsychotic drugs. ^{615,616}	L3	No human data. Very low oral absorption when swallowed ⁶¹⁵ – it is unlikely that a nursing infant would be exposed to large amounts of the drug. Monitor baby.
Clozapine (Clozaril®)	12.5–600 mg per day. ⁶¹⁷	B ⁵²⁰	Insufficient data to determine risk of teratogenicity in humans. ^{391,618,619} Monitor for maternal agranulocytosis. NAS has been reported. ⁶¹⁹⁻⁶²² Gestational diabetes may complicate pregnancy. ^{609,609,623} Possible risk of LGA. ⁶²⁴ Insufficient data on risk of SAB and long-term neurodevelopmental effects.	L3	May concentrate in milk (very limited data). Sedation and agranulocytosis have been reported in nursing infants. ^{619,620} Other drugs are preferred.
Olanzapine (Zyprexa®)	Oral: 5–20 mg per day. IM injection: 5–10 mg per dose, maximum 20 mg per day. ⁶²⁵	C ⁶²⁶	Limited data. No evidence of teratogenicity. ^{625,627} NAS has been reported, including one seizure. ⁶²⁸⁻⁶³⁰ Gestational diabetes may complicate pregnancy. ^{609,631-633} Possible risk of LGA. ^{623,634} No evidence of SAB or prematurity. ^{609,635}	L2	Olanzapine has not been detectable in the plasma of nursing infants. ^{636,637} However, extrapyramidal reactions have occurred ³⁰⁷ and there are a few reports of developmental effects. ⁶²⁹
Paliperidone (Invega®)	Oral: 3–12 mg per day. IM injection: 50–150 mg once a month. ⁶³⁸	C ⁶³⁹	No data on paliperidone. See risperidone (paliperidone is the major active metabolite of risperidone).	L3	No data on paliperidone. Following administration of risperidone, its active metabolite paliperidone is detected in milk and infant plasma. ⁶⁴⁰⁻⁶⁴³ See risperidone.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Quetiapine (Seroquel®)	50–800 mg per day. ⁶⁴⁴	C ⁶⁴⁵	No evidence of teratogenicity in humans but data is limited. ^{391,627,644,645} The risk of NAS is probably similar to other atypical antipsychotic drugs. ⁶⁴⁵ Gestational diabetes may complicate pregnancy. ⁶⁰⁹ LBW is possible. ^{623,627,645} No increased risk of SAB or long-term neurodevelopmental effects reported in humans. ⁶²⁷	L2	Very little information. Low levels in milk. Detected in infant plasma and developmental delay has been reported (unclear causality). ^{506,646,647}
Risperidone (Risperdal®)	Oral: 1–8 mg per day. IM injection: 25–50 mg once every two weeks. ⁶⁴⁸	C ⁶⁴⁹	Very limited information. No evidence that this drug is a teratogen. ^{627,648,650-652} NAS has been reported. ⁶⁵² Gestational diabetes may complicate pregnancy. ⁶⁰⁹ Possible small risk of LBW. ⁶²⁷ Insufficient data on the risk of SAB, prematurity or long-term neurodevelopmental effects.	L3	Low levels in milk and in infant plasma (limited data). ⁶⁴⁰⁻⁶⁴³ Some concerns of developmental effects in animals. ^{648,653}
Ziprasidone (Zeldox®)	40–160 mg per day. ⁶⁵⁴	C ⁶⁵⁵	A relatively new drug. Insufficient data to determine risk of teratogenicity in humans. Animal studies suggest a possible risk of teratogenicity, LBW and long-term neurodevelopmental effects. ⁶⁵⁴ Gestational diabetes may complicate pregnancy. ⁶⁰⁹ The risk of NAS is probably similar to other atypical antipsychotic drugs. ⁶⁵⁴	L2	The number of documented exposures is too small to determine risk. Very limited data suggest low exposure. ⁶⁵⁶

Typical Antipsychotics

Fluphenazine (Modectate®)	Injection: Fluphenazine decanoate: 2.5–25 mg every 2–4 weeks. ^{657,658} Oral fluphenazine: 2.5–20 mg per day. ⁶⁵⁹	C unassigned ^{275,659}	Very limited data specifically on fluphenazine. Rare case reports of malformations, ^{298,660,661} but controlled studies of phenothiazines have not shown an increased risk of teratogenicity. ^{661,662} Gestational diabetes may complicate pregnancy. ⁶⁰⁹ NAS has been reported; symptoms may include extrapyramidal effects and may be delayed and persistent. ⁶⁶³⁻⁶⁶⁶	L3	No data. Because of high protein binding (> 90%) and high molecular weight, ⁶⁵⁷ milk levels may be low. Monitor baby for sedation and extrapyramidal effects.
---------------------------	--	------------------------------------	---	----	--

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Drug Class	Dosage Range	FDA Pregnancy Risk Category	Fetal Risks	Hale Lactation Risk Category	Breastfeeding
Haloperidol (Haldol®)	Oral: 1.5–20 mg per day. ^{1,2} Immediate-acting IM Injection: 2–5 mg per dose, maximum 20 mg per day. ² Haloperidol decanoate Long-acting IM Injection: 50–200 mg every 4 weeks. ^{667,668}	C ⁶⁶⁹	Not considered a major teratogen. One controlled study found no increased risk of teratogenicity for butyrophenones such as haloperidol, ⁶⁷⁰ in contrast to earlier case reports of limb defects. ^{661,662,670-673} Gestational diabetes may complicate pregnancy. ⁶⁰⁹ NAS has been reported. ^{324,630,674-676} No increased risk of SAB. ⁶⁷⁰ Possible risk of prematurity and LBW. ^{630,670,677}	L3	M:P ratio 0.5–3.6. Infant plasma levels have ranged from undetectable up to levels in the therapeutic range. One report of developmental concerns at high doses. Use the lowest effective dose and monitor for sedation. ⁶⁷⁸⁻⁶⁸¹
Loxapine (Loxapac®)	Oral: 20–100 mg per day. Intra-muscular: 12.5–50 mg every 4–6 hours. ⁶⁸²	C Unclassified ^{275,683}	Insufficient data to assess risk of teratogenicity. Conflicting data in animals. ^{683,684} Drugs with evidence of safety are preferred. The risk of NAS is probably similar to other atypical antipsychotic drugs. ^{685,686}	L3	No information. Well-studied alternatives are preferred. Monitor for sedation.

aOR = adjusted Odds Ratio	MRHD = Max recom'd human dose	SAB = Spontaneous abortion
LBW = Low Birth Weight	NAS = Neonatal adaptation syndrome	SGA = Small for gestational age
LGA = Large for Gestational Age	NS = Not statistically significant	SS = Statistically significant
MCM = Major congenital malformations	OR = Odds Ratio	
M:P = Milk:Plasma ratio	RID = Est. relative infant dose compared with maternal dose	
FDA Pregnancy Risk Category – refer to pages 71 & 72		Hale Lactation Risk Category – refer to page 71

Appendix 6: Suggested Actions / Monitoring for Women on Psychotropic Medications in the Perinatal Period

This table summarizes suggested actions/monitoring for women on psychotropic medications during the perinatal period. The goal of the actions/monitoring is to minimize risk to the woman and fetus/baby.

Notes re folic acid and second trimester ultrasound:

1. Folic Acid supplementation is recommended for all pregnant women: 0.4 mg – 1 mg per day throughout pregnancy. 5 mg per day is recommended for at risk women during the first 14 weeks, including women on certain types of anticonvulsant medications.⁶⁸⁷
2. A detailed second trimester ultrasound (18 – 20 weeks) is recommended for all pregnant women.⁶⁸⁷

Psychotropic Medication	Pregnancy	At Birth	Breastfeeding
Antidepressants			
SSRIs (except Paroxetine) SNRIs	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.	Monitor for Neonatal Adaptation Syndrome (NAS). Take baby's vital signs post-delivery q4 hr x 24 hr. If possible, measure O ₂ sat using pulse oximeter 1 hr post-delivery & q4 hr with vital signs x 24 hrs. If O ₂ sat low, consult with pediatrician (to rule out rare congenital heart defects or PPHN).	Considered safe; however: Monitor baby for adverse effects (e.g., sedation, poor feeding & irritability). If concerns, check baby's serum drug level (if possible).
Paroxetine (SSRI)	Avoid if possible in 1st trimester Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.	Same as other SSRIs.	Considered safe. Low infant plasma levels.
Tricyclic antidepressants	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.	Monitor for NAS.	No concerns reported (limited data).
Other antidepressants (bupropion & mirtazapine)	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.	Monitor for NAS.	Monitor baby for adverse effects. (e.g., sedation, poor feeding & irritability). If concerns about possible exposure effects in baby, check baby's serum drug level.
Anxiolytics (benzodiazepines) & Hypnotics (non-benzodiazepines)	Folic acid (0.4–1 mg daily). Detailed ultrasound at 18–20 weeks.	Minimize use close to delivery, if possible. Monitor for withdrawal symptoms.	Monitor baby for adverse effects (e.g., sedation, poor feeding & irritability), with particular attention if administered with other CNS sedating medications (e.g., opioids).

Psychotropic Medication	Pregnancy	At Birth	Breastfeeding
Mood Stabilizers			
Carbamazepine	Avoid if possible in 1st trimester (increased risk of major congenital malformation – esp neural tube defects). Folic acid 5 mg daily for the first 14 weeks of pregnancy, then folic acid 0.4–1 mg daily. Detailed ultrasound at 18–20 weeks.		Compatible with breastfeeding. Monitor baby for adverse effects. If concerns, check serum drug level & refer to pediatrician.
Gabapentin (limited data)	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.		Monitor baby for adverse effects (e.g., sedation &/or unusual behavior). (limited data).
Lamotrigine (limited data)	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.		Use with caution. Monitor baby for adverse effects (apnea & cyanosis reported). Check serum drug level if concerns noted. Monitor for skin rash (life-threatening skin rashes reported in adults).
Lithium	Avoid if clinically possible in 1st trimester (slight increased risk of cardiac defects). Folic acid (0.4–1 mg daily). Monthly maternal serum lithium levels. Adjust lithium dose as necessary. Ensure hydration. Detailed ultrasound & fetal echocardiogram at 18–20 weeks.	Ensure hydration. Hold lithium for 24 hours before a scheduled Cesarean section or induction. If spontaneous vaginal delivery, hold lithium from start of labour until after the birth. Then recommence at usual time at the preconception dose. Monitor for NAS, floppy baby syndrome & goiter in the baby.	Mother: Check serum lithium levels within first 5 days postpartum, then weekly until stable. Once stable, check lithium levels q 1–3 mos. Breastfeeding not recommended (high infant plasma levels & toxicity reported). Baby (if mother chooses to breastfeed): Use with caution. Check baby's serum drug level within 5 days of starting treatment or after delivery if baby exposed in utero. Check again if concerns noted and/or baby becomes dehydrated (e.g., vomiting). Monitor baby for adverse effects (restlessness, low muscle tone & lethargy reported). Refer to pediatrician if concerns.

Psychotropic Medication	Pregnancy	At Birth	Breastfeeding
Topiramate (limited data)	Folic acid (0.4–1 mg daily). Detailed ultrasound 18–20 weeks.	Monitor for NAS.	Use with caution. Monitor baby for adverse effects (electrolyte abnormalities reported). (limited data).
Valproic Acid/ Divalproex	Avoid if possible throughout pregnancy (increased risk of major congenital malformations & developmental effects). Folic acid 5 mg daily for the first 14 weeks of pregnancy, then folic acid 0.4–1 mg daily. Detailed ultrasound at 18–20 weeks.	Monitor for NAS.	Mother: Check serum drug levels within 1 week of starting treatment. Once stable, check serum levels q3–6 mos. Baby: Is compatible with breastfeeding but monitor baby for adverse effects (sedation, thrombocytopenia & anemia reported). If concerns, check serum levels & refer to pediatrician.
Antipsychotics (typical & atypical)	Avoid clozapine if possible (cases of maternal agranulocytosis reported). Folic acid (0.4–1 mg daily). Detailed ultrasound at 18–20 weeks. Monitor blood glucose levels (may increase risk of gestational diabetes & babies who are LGA) & fasting serum lipid levels.	Monitor for NAS & extrapyramidal signs.	If possible, avoid clozapine (sedation & agranulocytosis have been reported in nursing infants). Use with caution. Monitor baby for adverse effects (sedation, extrapyramidal symptoms & developmental delays). (limited data).

Appendix 7: Types of Psychotic Disorders

Diagnosis of a particular psychotic disorder depends on the type and duration of symptoms. The common denominator is the presence of **at least** one psychotic symptom for a time-defined period. The descriptions below are based on the DSM-V39 classifications.

1. **Schizotypal (personality) disorder:** Persistent pattern of social and interpersonal deficits, including reduced capacity for close relationships, cognitive or perceptual distortion (not delusions or hallucinations) and eccentric behaviour.
2. **Delusional disorder:** Presence of delusions for one month or more but no other psychotic symptoms. Delusions may be erotomanic (person believes another person – usually a stranger, high-status or famous person—is in love with them), grandiose, jealous, persecutory (person believes they are being conspired against, cheated, followed, etc) or somatic (affects the body).
3. **Brief psychotic disorder:** Sudden onset of psychotic symptoms which, at a minimum, includes delusions, hallucinations or disorganized speech. Symptoms last for more than one day and less than one month. This disorder can occur within four weeks postpartum (postpartum psychosis) and cause significant emotional turmoil and overwhelming confusion. The level of impairment may be severe and supervision will be required if the mother has difficulty looking after her baby. Emergency hospitalization and treatment will be required.
4. **Schizophreniform disorder:** Presence of psychotic symptoms lasting more than one month but less than 6 months.
5. **Schizoaffective disorder:** Symptoms of both a major mood episode (major depressive or manic) and schizophrenia which is preceded or followed by at least two weeks of delusions or hallucinations without prominent mood symptoms.
6. **Schizophrenia:** Presence of psychotic symptoms lasting for at least six months and including at least one month of active symptoms. At a minimum, delusions, hallucinations or disorganized speech is present. Behaviour may be grossly disorganized and negative symptoms may also be present. Level of functioning in work, interpersonal relations and/or self-care is significantly impaired. Onset of symptoms is slow and gradual, usually between the late teens and mid-thirties. Approximately 20% will have a favourable course but most individuals will require formal or informal daily living supports.

References

1. BC Reproductive Mental Health Program, BC Ministry of Health. *Addressing perinatal depression: A framework for BC's health authorities*. Vancouver; 2006.
2. Abramowitz JS, Schwartz SA, Moore KM, Luenzman KR. Obsessive-compulsive symptoms in pregnancy and the puerperium: A review of the literature. *Anxiety Disord*. 2003;17:461-478.
3. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: A systematic review of prevalence and incidence. *Obstetrics & Gynecology*. 2005;106(5, Part 1):1071-1083.
4. Watson JP, Elliott SA, Rugg AJ, Brough DL. Psychiatric disorder in pregnancy and the first postnatal year. *Br J Psychiatry*. 1984;144:453-462.
5. Giardinelli L, Innocenti A, Benni L, et al. Depression and anxiety in perinatal period: Prevalence and Risk factors in an Italian sample. *Archives of Women's Mental Health*. 2012;15(1):21-30.
6. Banti S, Mauri M, Oppo A, et al. From the third month of pregnancy to 1 year postpartum. Prevalence, incidence, recurrence, and new onset of depression. Results from the perinatal Depression-Research & screening unit study. *Compr Psychiatry*. 2011;52(4):343-351.
7. Kumar R, Robson KM. A prospective study of emotional disorders in childbearing women. *The Br J Psychiatry*. 1984;144(1):35-47.
8. Pop VJ, Essed GG, de Geus CA, van Son MM, Komproe IH. Prevalence of postpartum depression-or is it post-puerperium depression? *Acta Obstet Gynecol Scand*. 1993;72:354-358.
9. Cooper PJ, Campbell EA, Day A, Kennerley H, Bond A. Non-psychotic psychiatric disorder after childbirth. A prospective study of prevalence, incidence, course and nature. *The Br J Psychiatry*. 1988;152(6):799-806.
10. Areias ME, Kumar R, Barros H, Figueiredo E. Comparative incidence of depression in women and men during pregnancy and after childbirth: Validation of the Edinburgh Postnatal Depression Scale, and assessment of risk factors for postnatal depression. *J Affect Disord*. 1996;169:30-35.
11. Vesga-Lopez O, Blanco C, Keyes K, Olfson M, Grant BF. Psychiatric disorders in pregnant and postpartum women in the United States. *Arch Gen Psychiatry*. 2008;65(7):805-815.
12. Sutter-Dallay A. Women with anxiety disorders during pregnancy are at increased risk of intense postnatal depressive symptoms: A prospective survey of the MATQUID cohort. *Eur Psychiatry*. 2004;19:459-463.
13. Wenzel A, Haugen EN, Jackson LC, Brendle JR. Anxiety symptoms and disorders at eight weeks postpartum. *J Anxiety Disord*. 2005;19(3):295-311.
14. Ross LE, McLean LM. Anxiety disorders during pregnancy and the postpartum period: A systematic review. *J Clin Psychiatry*. 2006.
15. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. American Psychiatric Publishing, Inc.; 2000.
16. Smith MV, R. Screening for and detection of depression, panic disorder, and PTSD in public-sector obstetric clinics. *Psychiatr Serv*. 2004;55:407-414.
17. Wenzel A, H. Prevalence of generalized anxiety at eight weeks postpartum. *Archives of Women's Mental Health*. 2003;6:43-49.
18. Wenzel A, G. The occurrence of panic and obsessive compulsive symptoms in women with postpartum dysphoria: A prospective study. *Archives of Women's Mental Health*. 2001;4(1):5-12.
19. Zar M, W. Relations between anxiety disorders and fear of childbirth during late pregnancy. *Clinical Psychology & Psychotherapy*. 2002;9:122-130.
20. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. Fourth edition. 1984.
21. Blehar MC, D. Women with bipolar disorder: Findings from the NIMH genetics initiative sample. *Psychopharmacol Bull*. 1998;34:239-243.
22. Freeman MP, S. The impact of reproductive events on the course of bipolar disorder in women. *J Clin Psychiatry*. 2002;63(4):284-287.
23. Viguera AC, N. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. *Am J Psychiatry*. 2000;157:179-84.

24. Grof P, R. Protective effect of pregnancy in women with lithium-responsive bipolar I disorder. *J Affect Disord.* 2000;61:31-39.
25. Hunt N, S. Does puerperal illness distinguish a subgroup of bipolar patients? *J Affect Disord.* 1995;34:101-107.
26. Tomruk NB, Saatcioglu O, Ugurlu E, Hacıoglu M. ECT use in refractory obsessive-compulsive disorder. *Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology.* 2010;20(2):167-170.
27. Chabrol H, Teissedre F, Saint-Jean M, Teisseyre N, Roge B, Mullet E. Prevention and treatment of postpartum depression: A controlled randomized study on women at risk. *Psychol Med.* 2002;32:1039-1047.
28. Brockington IF, C. Puerperal psychosis: Phenomena and diagnosis. *Arch Gen Psychiatry.* 1981;38:829-33.
29. Schaffer A, Cairney J, Cheung A, Veldhuizen S, Levitt A. Community survey of bipolar disorder in Canada: Lifetime prevalence and illness characteristics. *The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie.* 2006;51(1):9-16.
30. Baldessarini RJ, Tondo L, Hennen J. Treatment delays in bipolar disorders. *Am J Psychiatry.* 1999; 5:811.
31. Harlow B, Vitonis AF, Sparen P, Cnattingius S, Joffe H, Hultman CM. Incidence of hospitalization for postpartum psychotic and bipolar episode in women with and without prior prepregnancy or prenatal psychiatric hospitalizations. *Arch Gen Psych.* 2007;64:42-48.
32. Pfullmann B, Stoeber G, Beckmann H. Postpartum psychosis: Prognosis, risk factors and treatment. *Curr Psychiatry Rep.* 2002;4:185-190.
33. Schopf J, Rust B. Follow-up and family study of postpartum psychosis. *Eur Arch Psychiatry Clin Neurosci.* 1994;244:101-111.
34. Terp IM, Mortenson PB. Postpartum psychosis: Clinical diagnoses and relative risk of admission after parturition. *Br J Psychiatry.* 1998;172:521-526.
35. Hafner H, an der Heiden W. Epidemiology of schizophrenia. *Can J Psychiatry.* 1994;42:139-151.
36. Scottish Intercollegiate Guidelines Network. Management of perinatal mood disorders: A national clinical guideline. 2012; SIGN publication no. 127.
37. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression. *JAMA: the Journal of the American Medical Association.* 2010;303(19):1961-1969.
38. Kim P, Swain JE. Sad dads: Paternal postpartum depression. *Psychiatry (Edgmont).* 2007;4(2):35.
39. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders.* Fifth edition ed. Arlington, VA: American Psychiatric Association; 2013.
40. Dietz P, Williams S, Callaghan W, Bachman D, Whitlock E, Hornbrook M. Clinically identified maternal depression before, during, and after pregnancies ending in live births. *Am J Psychiatry.* 2007; 164(10):1515-1520.
41. Stewart DE. Depression during pregnancy. *N Engl J Med.* 2011;365(17):1605-1611.
42. Gotlib IH, W. Prevalence rates and demographic characteristics associated with depression in pregnancy and the postpartum period. *J Consult Clin Psychol.* 1989;57:269-274.
43. Chaudron LH, Klein M, Remington P, Palta M, Allen C, Essex M. Predictors, prodromes and incidence of postpartum depression. *Journal of Psychosomatic Obstetrics & Gynecology.* 2001; 22(2):103-112.
44. Wisner KL, Perel JM, Peindl KS, Hanusa BH. Timing of depression recurrence in the first year after birth. *J Affect Disord.* 2004;78(3):249-252.
45. Driscoll JW. Postpartum depression: The state of the science. *J Perinat Neonatal Nurs.* 2006; 20(1):40-42.
46. Forty L, Jones L, Macgregor S, et al. Familiarity of postpartum depression in unipolar disorder: Results of a family study. *Am J Psychiatry.* 2006; 163(9):1549-1553.
47. Steiner M. Postnatal depression: A few simple questions. *Fam Pract.* 2002; 19(5):469-470.
48. Scottish Intercollegiate Guidelines Network. Management of perinatal mood disorders: A national clinical guideline. *SIGN Publication.* 2012;127.
49. Dennis C, Doswell T. *Psychosocial and psychological interventions for preventing postpartum depression.* The Cochrane Collaboration; 2013.
50. Joffres M, et. al. Recommendations on screening for depression in adults. *CMAJ.* 2013.

51. Myers E, Aubuchon-Endsley N, Bastian L, et al. Efficacy and safety of screening for postpartum depression. Comparative effectiveness review 106. Prepared by the Duke Evidence-based Practice Center under contract no. 290-2007-10066-I. 2013;AHRQ Publication No. 13-EHC064-EF.
52. Leung S, Leung C, Lam T, et al. Outcome of a postnatal depression screening programme using the Edinburgh Postnatal Depression Scale: A randomized controlled trial. *J Public Health*. 2011; 33(2):292-301.
53. Yawn B, Dietrich A, Wollan P, et al. TRIPPD: A practice-based network effectiveness study of postpartum depression screening and management. *Ann Fam Med*. 2012;10(4):320-329.
54. Morrell C, Slade P, Warner R, et al. Clinical effectiveness of health visitor training in psychologically informed approaches for depression in postnatal women: Pragmatic cluster randomised trial in primary care. *BMJ*. 2009; 338(7689):276-279.
55. Leung SSK, Lam TH. Group antenatal intervention to reduce perinatal stress and depressive symptoms related to intergenerational conflicts: A randomized controlled trial. *Int J Nurs Stud*. 2012; 49(11):1391-1402.
56. Horowitz JA, Murphy CA, Gregory KE, Wojcik J. A community-based screening initiative to identify mothers at risk for postpartum depression. *Journal of Obstetric, Gynecologic, & Neonatal Nursing: Clinical Scholarship for the Care of Women, Childbearing Families, & Newborns*. 2011; 40(1):52-61.
57. Buist A, Barnett EW, Milgrom J, et al. To screen or not to screen: That is the question in perinatal depression. *MJA*. 2002; 177:s101-s105.
58. BC Reproductive Mental Health Program, Perinatal Services BC, BC Ministry of Health. BC Position Statement 'Screening for Depression in the Perinatal Period'. 2014. www.reproductivementalhealth.ca; www.perinatalservicesbc.ca
59. Austin M-P, Higher N and the Guidelines Expert Advisory Committee. Clinical practice guideline for depression and related disorders - anxiety, bipolar disorder and puerperal psychosis - in the perinatal period. *Melbourne: Australian Government: Beyond Blue: the National Depression Initiative*. 2011.
60. Heneghan A, Silver E, Bauman L, Stein R. Do pediatricians recognize mothers with depressive symptoms? *Pediatrics*. 2000; 106:1367-1373.
61. Georgiopoulos A, Bryan T, Wollan P ea. Routine screening for postpartum depression. *J Fam Pract*. 2001; 50:117-122.
62. Ko JY, Farr SL, Dietz PM, Robbins CL. Depression and treatment among U.S. pregnant and nonpregnant women of reproductive age, 2005 - 2009. *Journal of Women's Health*. 2012; 21:830-836.
63. Evins G, Theofrastous J, Galvin S. Postpartum depression: A comparison of screening and routine clinical evaluation. *Am J Obstetr Gynecol*. 2000; 182:1080-1082.
64. des Rivières-Pigeon C, Saurel-Cubizolles M, Lelong N. Considering a simple strategy for detection of women at risk of psychological distress after childbirth. *Birth: Issues in Perinatal Care*. 2004; 31:34-42.
65. The American College of Obstetricians and Gynecologists. Screening for depression during and after pregnancy. *Obstet Gynecol 2010*; . 2010; 115:394-5.
66. Cox JL, Holden J, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *The British Journal of Psychiatry*. 1987; 150(6):782-786.
67. Matthey S, Henshaw C, Elliott S, Barnett B. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale - implications for clinical and research practice. *Arch Womens Ment Health*. 2006; 9(6):309-315.
68. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *The Br J Psychiatry*. 1987;150:782-786.
69. Boyce P, Stubbs J, Todd A. The Edinburgh Postnatal Depression Scale: Validation for an Australian sample. *Aust N Z J Psychiatry*. 1993; 27(3):472-476.
70. Harris B, Huckle P, Thomas R, Johns S, Fung H. The use of rating scales to identify post-natal depression. *The Br J Psychiatry*. 1989; 154(6):813-817.
71. Murray L, Carothers AD. The validation of the Edinburgh Post-natal Depression Scale on a community sample. *The Br J Psychiatry*. 1990; 157(2):288-290.

72. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EDDS). *Journal of Reproductive and Infant Psychology*. 1990;8(2):99-107.
73. Practice Support Program. Mental health - making in real practice guide. *Impact BC*. 2009.
74. Goodman JH, Santangelo G. Group treatment for postpartum depression: A systematic review. *Archives of Women's Mental Health*. 2011;14(4):277-293.
75. Sockol LE, Epperson CN, Barber JP. A meta-analysis of treatments for perinatal depression. *Clin Psychol Rev*. 2011;31(5):839-849.
76. Haring M. Coping with depression during pregnancy and following the birth: A cognitive behaviour therapy-based resource and self-management guide for women and health care providers. *BC Mental Health and Addiction Services*. 2011.
77. Rimer J, Dwan K, Lawlor DA, et al. Exercise for Depression. *Cochrane Database Syst Rev*. 2012;7.
78. M H, JE S, D B, S M, RM L, D. R. *Coping with anxiety during pregnancy and following the birth: A cognitive behaviour therapy-based resources and self-management guide for women and health care providers*. BC Mental Health and Addiction Services. 2013.
79. Narendran S, Nagarathna R, Narendran V, Gunasheela S, Nagendra H. Efficacy of yoga on pregnancy outcome. *J Altern Complement Med*. 2005;11:237-244.
80. Kabat-Zinn J. An outpatient program in behavioural medicine for chronic pain patients based on the practice of mindfulness meditation : Theoretical considerations and preliminary results. *Gen Hosp Psychiatry*. 1982(4):33-47.
81. Kabat-Zinn J, Massion A, Kristeller J, et al. Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *Am J Psychiatry*. 1992;149:936-943.
82. Kristeller J, Hallett C. An exploratory study of a meditation-based intervention for binge eating disorders. *Journal of Health Psychology*. 1999;4(3):357-363.
83. Shapiro S, Schwartz G, Bonner G. Effects of mindfulness-based stress reduction on medical and pre-medical students. *Journal of Behavioural Medicine*. 1998;139:267-274.
84. Teasdale J, Segal Z, Williams J, Ridgeway V, Soulsby J, Lau M. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol*. 2000; 68:615-623.
85. Duncan L, Bardacke N. Mindfulness-based childbirth and parenting education. *Journal of Child and Family Studies*. 2010;19(2):190-202.
86. Folkman S, Moskowitz J. Positive affect and the other side of coping. *Am Psychol*. 2000; 55:647-654.
87. Wiegartz P, Gyoerkoe K. *Practical skills to help you overcome anxiety, worry, panic attacks, obsessions and compulsions*. Raincoast Books (Canada distributor); 2000.
88. Butler AC, Chapman JE, Forman EM, Beck AT. The empirical status of cognitive-behavioral therapy: A review of meta-analyses. *Clin Psychol Rev*. 2006; 26(1):17-31.
89. Cuijpers P, Geraedts AS, van Oppen P, Andersson G, Markowitz JC, van Stratten A. Interpersonal psychotherapy of depression: A meta-analysis. *Am J Psychiatry*. 2011;168:581-592.
90. Gloaguen V, Cottraux J, Cucherat M, Blackburn I. A meta-analysis of the effects of cognitive therapy in depressed patients. *J Affect Dis*. 1998; 49:59-72.
91. Cuijpers P, Andersson G, Donker T, van Straten A. Psychological treatment of depression: Results of a series of meta-analyses. *Nordic Journal of Psychiatry*. 2011; 65(6):354-364.
92. Cooper PJ, Murray L, Wilson A, Romaniuk H. Controlled trial of the short- and long-term effect of psychological treatment of post-partum depression. 1. Impact on maternal mood. *The Br J Psychiatry*. 2003;182(5):412-419.
93. Bledsoe SE, Grote NK. Treating depression during pregnancy and the postpartum: A preliminary meta-analysis. *Research on Social Work Practice*. 2006; 16(2):109-120.
94. Chabrol H, Teissedre F, Saint-Jean M, Teisseyre N, Roge B, Mullet E. Prevention and treatment of post-partum depression: A controlled randomized study on women at risk. *Psychol Med*. 2002;32:1039-1047.
95. Cuijpers P, Geraedts AS, van Oppen P, Andersson G, Markowitz JC, van Stratten A. Interpersonal psychotherapy of depression: A meta-analysis. *Am J Psychiatry*. 2011;168:581-592.

96. Appleby L, Warner R, Whitton A, Faragher B. A controlled study of fluoxetine and cognitive-behavioural counseling in the treatment of postnatal depression. *BMJ*. 1997; 314:932-936.
97. Cuijpers P, Andersson G, Donker T, van Straten A. Psychological treatment of depression: Results of a series of meta-analyses. *Nordic Journal of Psychiatry*. 2011;65(6):354-364.
98. Huntley AL, Araya R, Salisbury C. Group psychological therapies for depression in the community: Systematic review and meta-analysis. *The Br J Psychiatry*. 2012; 200(3):184-190.
99. Ekers D, Richards D, Gilbody S. A meta-analysis of randomized trials of behavioural treatment of depression. *Psychol Med*. 2008;38(5):611-623.
100. Ekers D, Richards D, Gilbody S. A meta-analysis of randomized trials of behavioural treatment of depression. *Psychol Med*. 2008;38(5):611-623.
101. Bledsoe SE, Grote NK. Treating depression during pregnancy and the postpartum: A preliminary meta-analysis. *Research on Social Work Practice*. 2006;16(2):109-120.
102. Grote NK, Swartz HA, Bledsoe SE, Frank E. Treating depression in low-income pregnant patients: The role of brief interpersonal psychotherapy. *Res Social Work Prac*. 2004; 14:397-406.
103. O'Hara MW, Stuart S, Gorman L, Wenzel A. Efficacy of interpersonal psychotherapy for postpartum depression. *Arch Gen Psychiatry*. 2000;57:1039-1045.
104. Mulcahy R, Reay RE, Wilkonson RB, Owen C. A randomised control trial for effectiveness of group interpersonal psychotherapy for postnatal depression. *Arch Womens Ment Health*. 2010;13:125-139.
105. Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. *Am J Psychiatry*. 2003;160:555-562.
106. Grote NK, Swartz HA, Bledsoe SE, Frank E. Treating depression in low-income pregnant patients: The role of brief interpersonal psychotherapy. *Res Social Work Prac*. 2004; 14:397-406.
107. O'Hara MW, Stuart S, Gorman L, Wenzel A. Efficacy of interpersonal psychotherapy for postpartum depression. *Arch Gen Psychiatry*. 2000; 57:1039-1045.
108. Mulcahy R, Reay RE, Wilkonson RB, Owen C. A randomised control trial for effectiveness of group interpersonal psychotherapy for postnatal depression. *Arch Womens Ment Health*. 2010;13:125-139.
109. Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. *Am J Psychiatry*. 2003; 160:555-562.
110. Schramm E, Schneider D, Zobel I, et al. Efficacy of interpersonal psychotherapy plus pharmacotherapy in chronically depressed inpatients. *J Affect Disord*. 2008;109(1-2):65-73.
111. Leung SSK, Lam TH. Group antenatal intervention to reduce perinatal stress and depressive symptoms related to intergenerational conflicts: A randomized controlled trial. *Int J Nurs Stud*. 2012;49(11):1391-1402.
112. Reay RE, Mulcahy R, Wilkinson RB, Owen C, Shadbolt B, Raphael B. The development and content of an interpersonal psychotherapy group for postnatal depression. *Int J Group Psychother*. 2012;62(2):221-251.
113. Driessen E, Cuijpers P, de Maat SCM, Abbass AA, Dekker JJ. The efficacy of short-term psychodynamic psychotherapy for depression: A meta analysis. *Clin Psychol Rev*. 2010;30(1):25-36.
114. Gallagher D, T. Treatment of major depressive disorder in older adult outpatients with brief psychotherapies. *Psychotherapy*. 1982.
115. McLean PD, H. Clinical depression: Comparative efficacy of outpatient treatments. *J Consult Clin Psychol*. 1979;47:818-836.
116. Thompson L, G. Comparative effectiveness of psychotherapies for depressed elders. *J Consult Clin Psychol*. 1987;55:385-390.
117. Jakobsen JC, Hansen JL, Simonsen E, Gluud C. The effect of adding psychodynamic therapy to antidepressants in patients with major depressive disorder. A systematic review of randomized clinical trials with meta-analyses and trial sequential analyses. *J Affect Disord*. 2012;137(1-3):4-14.
118. Kurzweil S. Psychodynamic therapy for depression in women with infants and young children. *Am J Psychother*. 2012;66(2):181-199.
119. Cuijpers P, van Straten A, Andersson G, van Oppen P. Psychotherapy for depression in adults: A meta-analysis of comparative outcome studies. *J Consult Clin Psychol*. 2008;76:909-922.

120. Huntley AL, Araya R, Salisbury C. Group psychological therapies for depression in the community: Systematic review and meta-analysis. *The Br J Psychiatry*. 2012;200(3):184-190.
121. Levkovitz Y, S. Group interpersonal psychotherapy for patients with major depression disorder: Pilot study. *J Affect Dis*. 2000;60:191-195.
122. Hauser Bowen A. *Antenatal depression: Prevalence and determinants in a high-risk sample of women in saskatoon*. ProQuest Information & Learning; 2008.
123. Hayes BA. From 'postnatal depression' to 'perinatal anxiety and depression': Key points of the national perinatal depression plan for nurses and midwives in Australian primary health care settings. *Contemp Nurse*. 2010;35(1):58-67.
124. Goodman JH, Santangelo G. Group treatment for postpartum depression: A systematic review. *Archives of Women's Mental Health*. 2011;14(4):277-293.
125. Honey KL, Bennett P, Morgan M. A brief psycho-educational group intervention for postnatal depression. *British Journal of Clinical Psychology*. 2002;41(4):405-409.
126. Chen C, Tseng Y, Chou F, Wang S. Effects of support group intervention in postnatally distressed women: A controlled study in Taiwan. *J Psychosom Res*. 2000;49(6):395-399.
127. Meager I, Milgrom J. Group treatment for postpartum depression: A pilot study. *Australasian Psychiatry*. 1996;30(6):852-860.
128. Puckering C, McIntosh E, Hickey A, Longford J. Mellow babies: A group intervention for infants and mothers experiencing postnatal depression. *Counselling Psychology Review*. 2010;25(1):28-40.
129. Lane B, Roufeil LM, Williams S, Tweedie R. It's just different in the country: Postnatal depression and group therapy in a rural setting. *Soc Work Health Care*. 2001;34:333-348.
130. Austin M, Frilingos M, Lumley J, et al. Brief antenatal cognitive behaviour therapy group intervention for the prevention of postnatal depression and anxiety: A randomised controlled trial. *J Affect Disord*. 2008;105(1-3):35-44.
131. Austin M. Targeted group antenatal prevention of postnatal depression: A review. *Acta Psychiatr Scand*. 2003;107(4):244-250.
132. Herve MJ, Paradis C, Rattaz S, et al. Predictors of outcome in infant and toddlers functional or behavioral disorders after a brief parent-infant psychotherapy. *Eur Child Adolesc Psychiatry*. 2009;18:737-746.
133. Cowan P, Cowan CP. A couple perspective on the transmission of attachment patterns. In: Clulow C, ed. *Adult attachment and couple psychotherapy*. London: Brunner-Routledge; 2001:62-82.
134. Hopkins J. Infant-parent psychotherapy. *Journal of Child Psychotherapy*. 1992;18(1):5-17.
135. Marchand JF, Hock E. The relation of problem behaviors in preschool children to depressive symptoms in mothers and fathers. *J Genet Psychol*. 1998;159:353-366.
136. Thome M, Skuladottir A. Evaluating a family-centered intervention for infant sleep problems. *J Adv Nurs*. 2005;50:5-11.
137. Cohen NJ, Muir E, Lojkasek M, et al. Watch, wait, and wonder: Testing the effectiveness of a new approach to mother-infant psychotherapy. *Infant Mental Health Journal*. 1999;20(4):429-451.
138. Cohen NJ, Lojkasek M, Muir E, Muir R, Parker CJ. Six-month follow-up of two mother-infant psychotherapies: Convergence of therapeutic outcomes. *Infant Mental Health Journal*. 2002;23(4):361-380.
139. Cramer B, Robert-Tissot C, Stern DN, et al. Outcome evaluation in brief mother-infant psychotherapy: A preliminary report. *Infant Mental Health Journal*. 1990;11(3):278-300.
140. Robert-Tissot C, Cramer B, Stern DN, et al. Outcome evaluation in brief mother-infant psychotherapies: Report on 75 cases. *Infant Mental Health Journal*. 1996;17(2):97-114.
141. Bakermans-Kranenburg MJ, Van Ijzendoorn MH, Juffer F. Less is more: Meta-analyses of sensitivity and attachment interventions in early childhood. *Psychol Bull*. 2003;129(2):195.
142. Jzendoorn MH, Juffer F, Duyvesteyn MG. Breaking the intergenerational cycle of insecure attachment: A review of the effects of Attachment-based interventions on maternal sensitivity and infant security. *Journal of Child Psychology and Psychiatry*. 1995;36(2):225-248.

143. Heinicke CM, Goorsky M, Moscov S, et al. Relationship-based intervention with at-risk mothers: Factors affecting variations in outcome. *Infant Mental Health Journal*. 2000;21(3):133-155.
144. Cicchetti D, Rogosch FA, Toth SL. The efficacy of toddler-parent psychotherapy for fostering cognitive development in offspring of depressed mothers. *J Abnorm Child Psychol*. 2000;28(2):135-148.
145. Cicchetti D, Toth SL, Rogosch FA. The efficacy of toddler-parent psychotherapy to increase attachment security in offspring of depressed mothers. *Attachment & Human Development*. 1999;1(1):34-66.
146. Barnett B, L. Mood disorders among mothers of infants admitted to a mothercraft hospital. *J Paediatr Child H*. 1993;29:270-275.
147. Beck CT. Predictors of postpartum depression: An update. *Nursing Researches*. 2001;50:275-285.
148. Boyce P, H. Psychosocial factors associated with depression: A study of socially disadvantaged women with young children. *J Nerv Ment Dis*. 1998;186:3-11.
149. Marks M, W. How does marriage protect women with histories of affective disorders from postpartum relapse? *Br J Med Psychol*. 1996;69:329-342.
150. Morinaga K, Y. Childbirth and changes of women's social support network and mental health. *Shinrigaku Kenkyu*. 2003;74:412-419.
151. Patel V, R. Gender, poverty, and postnatal depression: A study of mothers in goa. *India Am J Psychiatry*. 2002;159:43-47.
152. Campbell SB, C. Course of correlates of postpartum depression during the transition to parenthood. *Dev Psychopathol*. 1992;4:29-47.
153. Fisher J, F. Nature, severity and correlates of psychological distress in women admitted to a private hospital mother baby unit. *J Paediatr Child H*. 2002;38:140-145.
154. Barbato A, D'A. Efficacy of couple therapy as a treatment for depression: A meta-analysis. *Psychiatr Q*. 2008;79:121-132.
155. Beach SRH, O'L. Treating depression in the context of marital discord: Outcome and predictors of response of marital therapy versus cognitive therapy. *Behavior Therapy*. 1992;23:507-528.
156. Emanuels-Zuurveen L. Spouse-aided therapy with depressed patients. *Behav Modif*. 1997;21:62-77.
157. Jacobson NS, D. Marital therapy as a treatment for depression. *J Consult Clin Psychol*. 1991;59:547-557.
158. Matthey S, K. Prevention of postnatal distress or depression: An evaluation of an intervention at preparation for parenthood classes. *J Affect Disord*. 2004;79:113-126.
159. Misri S, K. The impact of partner support in the treatment of postpartum depression. *Canadian Journal of Psychiatry*. 2000;45:554-558.
160. Schulz MS, C. Promoting healthy beginnings: A randomized control trial of a preventative intervention to preserve marital quality during the transition to parenthood. *J Consult Clin Psychol*. 2006;74:20-31.
161. Carter W, Grigoriadis S, Ross LE. Relationship distress and depression in postpartum women: Literature review and introduction of a conjoint interpersonal psychotherapy intervention. *Archives of Women's Mental Health*. 2010;13(3):279-284.
162. Calvert CA. *Structural family therapy as a treatment modality to decrease depressive symptoms for women suffering from postpartum depression and improve family functioning*. ProQuest Information & Learning; 2009.
163. Rosenthal NE, Sack DA, Gillin JC, et al. Seasonal affective disorder: A description of the syndrome and preliminary findings with light therapy. *Arch Gen Psychiatry*. 1984;41(1):72.
164. Terman M, Terman JS, Ross DC. A controlled trial of timed bright light and negative air ionization for treatment of winter depression. *Arch Gen Psychiatry*. 1998;55(10):875.
165. Reeves GM, Nijjar GV, Langenberg P, et al. Improvement in depression scores after 1 hour of light therapy treatment in patients with seasonal affective disorder. *J Nerv Ment Dis*. 2012;200(1):51-55.
166. Wirz-Justice A, Bader A, Frisch U, et al. A randomized, double-blind, placebo-controlled study of light therapy for antepartum depression. *J Clin Psychiatry*. 2011;72(7):986-993.
167. Epperson CN, Terman M, Terman JS, et al. Randomized clinical trial of bright light therapy for antepartum depression: Preliminary findings. *J Clin Psychiatry*. 2004;65(3):421-425.

168. Oren DA, Wisner KL, Spinelli M, et al. An open trial of morning light therapy for treatment of antepartum depression. *Am J Psychiatry*. 2002;159(4):666-669.
169. Krysta K, Krzystanek M, Janas-Kozik M, Krupka-Matuszczyk I. Bright light therapy in the treatment of childhood and adolescence depression, antepartum depression, and eating disorders. *J Neural Transm*. 2012;119(10):1167-1172.
170. Perinatal Services BC. Antidepressant use during pregnancy: Considerations for the newborn exposed to SSRI's/SSNIs (guideline). 2013.
171. Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: A report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. *Gen Hosp Psychiatry*. 2009;31(5):403.
172. Anderson EL, R. ECT in pregnancy: A review of the literature from 1941 to 2007. *Psychosom Med*. 2009;71:235-42.
173. Saatcioglu O, Tomruk NB. The use of electroconvulsive therapy in pregnancy: A review. *Isr J Psychiatry Relat Sci*. 2011;48(1):6.
174. Nielsen RE, Damkier P. Pharmacological treatment of unipolar depression during pregnancy and breast-feeding-A clinical overview. *Nordic Journal of Psychiatry*. 2012;66(3):159-166.
175. Paulson JF, Bazemore SD. Prenatal and postpartum depression in fathers and its association with maternal depression. *JAMA: the journal of the American Medical Association*. 2010;303(19):1961-1969.
176. Cochran SV, Rabinowitz FE. Gender-sensitive recommendations for assessment and treatment of depression in men. *Professional Psychology: Research and Practice*. 2003;34(2):132.
177. Villegas L, McKay K, Dennis C, Ross LE. Postpartum depression among rural women from developed and developing countries: A systematic review. *The Journal of Rural Health*. 2011;27(3):278-288.
178. Rampono J, Hackett LP, Kristensen JH, Kohan R, Page-Sharp M, Ilett KF. Transfer of escitalopram and its metabolite demethylescitalopram into breastmilk. *Br J Clin Pharmacol*. 2006;62(3):316-322.
179. Cole JA, Ephross SA, Cosmatos IS, Walker AM. Paroxetine in the first trimester and the prevalence of congenital malformations. *Pharmacoepidemiol Drug Saf*. 2007;16(10):1075-1085.
180. Bar-Oz B, Einarson T, Einarson A, et al. Paroxetine and congenital malformations: Meta-analysis and consideration of potential confounding factors. *Clin Ther*. 2007;29(5):918-926.
181. Källén B. Antidepressant drugs during pregnancy and infant congenital heart defect. *Reproductive toxicology (Elmsford, NY)*. 2006;21(3):221.
182. Meades R, Ayers S. Anxiety measures validated in perinatal populations: A systematic review. *J Affect Disord*. 2011;133(1):1-15.
183. Ross LE, M. Anxiety disorders during pregnancy and the postpartum period: A systematic review. *J Clin Psychiatry*. 2006;67:1285-98.
184. Wenzel A, H. Anxiety symptoms and disorders at 8 weeks post partum. *J Anxiety Disord*. 2005;19:295-311.
185. Roney J, Hermida T, Malone D. Definition and etiology. *Anxiety*. 2010.
186. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM-IV-TR*. American Psychiatric Publishing, Inc.; 2000.
187. Vythilingum B. Anxiety disorders in pregnancy and the postnatal period. *Continuing Medical Education*. 2009;27(10).
188. Labad J, Menchon JM, Alonso P, Segalas C, Jimenez S, Vallejo J. Female reproductive cycle and obsessive-compulsive disorder. *J Clin Psychiatry*. 2005;66(4):428-435.
189. Evans J, H. Cohort study of depressed mood during pregnancy and after childbirth. *Br Med J*. 2001;323:257-260.
190. Adouard F, Glangeaud-Freudenthal N, Golse B. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in a sample of women with high-risk pregnancies in France. *Arch Women Ment Health*. 2005;8(2):89-95.
191. Bowen A, Bowen R, Maslany G, Muhajarine N. Anxiety in a socially high-risk sample of pregnant women in Canada. *The Canadian Journal of Psychiatry / La Revue canadienne de psychiatrie*. 2008;53(7):435-440.

192. Brouwers EPM, van Baar AL, Pop VJM. Does the Edinburgh Postnatal Depression Scale measure anxiety? *J Psychosom Res.* 2001;51(5):659-663.
193. Clark DM, E. Cognitive therapy versus fluoxetine in generalized social phobia: A randomized placebo controlled trial. *J Consult Clin Psychol.* 2003;71:1058-1067.
194. Clark DM, S. Brief cognitive therapy for panic disorder: A randomized controlled trial. *J Consult Clin Psychol.* 1999;67:583-9.
195. Mörtberg E, Clark DM, Sundin Ö, Åberg Wistedt A. Intensive group cognitive treatment and individual cognitive therapy vs. treatment as usual in social phobia: A randomized controlled trial. *Acta Psychiatr Scand.* 2007;115:142-154.
196. Stangier U, H. Cognitive therapy for social phobia: Individual versus group treatment. *Behav Res Ther.* 2003;41:991-1007.
197. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioral therapy: A review of meta-analyses. *Cognitive Therapy and Research.* 2012;36(5):427-440.
198. Davidson JR. Fluoxetine, comprehensive cognitive behavioral therapy, and placebo in generalized social phobia. *Arch Gen Psychiatry.* 2004;61:1005-1013.
199. Barlow JH, Ellard DR, Hainsworth JM, Jones FR, Fisher A. A review of self-management interventions for panic disorders, phobias and obsessive-compulsive disorders. *Acta Psychiatr Scand.* 2005;111(4):272-285.
200. Ito LM. Self-exposure therapy for panic disorder with agoraphobia. Randomised controlled study of external v. interoceptive self-exposure. *Br J Psychiatry.* 2001;178:331-336.
201. Murphy MT, M. The role of self-directed in vivo exposure in combination with cognitive therapy, relaxation training, or therapist-assisted exposure in the treatment of panic disorder with agoraphobia. *J Anxiety Disord.* 1998;12:117-138.
202. Newman MG, Castonguay LG, Borkovec TD, et al. A randomized controlled trial of cognitive-behavioral therapy for generalized anxiety disorder with integrated techniques from emotion-focused and interpersonal therapies. *J Consult Clin Psychol.* 2011;79(2):171-181.
203. Tolin DF. Is cognitive-behavioral therapy more effective than other therapies? : A meta-analytic review. *Clin Psychol Rev.* 2010;30(6):710-720.
204. Lipsitz JD, G. A randomized trial of interpersonal therapy versus supportive therapy for social anxiety disorder. *Depress Anxiety.* 2008;25:542-553.
205. Lipsitz JD, M. Open trial of interpersonal psychotherapy for the treatment of social phobia. *American Journal of Psychiatry.* 1999;156:1814-1816.
206. Newham JJ, Westwood M, Aplin JD, Wittkowski A. State-Trait anxiety inventory (STAI) scores during pregnancy following intervention with complementary therapies. *J Affect Disord.* 2012;142(1-3):22-30.
207. Crits-Christoph P, Crits-Christoph K, Wolf-Palacio D, Fichter M, Rudick D. Brief supportive-expressive psychodynamic therapy for generalized anxiety disorder. In: Barber JP, Crits-Christoph P, eds. New York, NY US: Basic Books; 1995:43-83.
208. Reavley NJ, Allen NB, Jorm AF, Purcell R. A guide to what works for anxiety disorders. 2010.
209. Shi S, Tang Y, Cheng L. An investigation of the prevalence of anxiety or depression and related risk factors in women during pregnancy and postpartum. *Chinese Mental Health Journal.* 2007;21(4):254-258.
210. Network SIG. Management of perinatal mood disorders: A national clinical guideline. 2012 (SIGN publication no. 127).
211. Lipsitz JD, G. A randomized trial of interpersonal therapy versus supportive therapy for social anxiety disorder. *Depress Anxiety.* 2008;25:542-553.
212. Lipsitz JD. Open trial of interpersonal psychotherapy for the treatment of social phobia. *American Journal of Psychiatry.* 1999;156:1814-1816.
213. Cohen LS. Treatment of bipolar disorder during pregnancy. *J Clin Psychiatry.* 2007;68:4-9.
214. Viguera AC, N. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. *Am J Psychiatry.* 2000;157:179-84.

215. Viguera AC. Women and bipolar disorder: Morbidity risk during pregnancy and the postpartum. *Women and bipolar disorder: morbidity risk during pregnancy and the postpartum*. 2003.
216. Freeman MP, Smith KW, Freeman SA, et al. The impact of reproductive events on the course of bipolar disorder in women. *J Clin Psychiatry*. 2002;63(4):284.
217. Sylvia LG, Tilley CA, Lund HG, Sachs GS. Psychosocial interventions: Empirically-derived treatments for bipolar disorder. *Current Psychiatry Reviews*. 2008;4(2):108-113.
218. Miklowitz DJ. Adjunctive psychotherapy for bipolar disorder: State of the evidence. *Am J Psychiatry*. 2008;165:1408-19.
219. Benyon S, S. Psychosocial interventions for the prevention of relapse in bipolar disorder: Systematic review of controlled trials. *Br J Psychiatry*. 2008;192:5-10.
220. Scott J, C. A meta-analysis of relapse rates with adjunctive psychological therapies compared to usual psychiatric treatment for bipolar disorders. *The International Journal of Neuropsychopharmacology*. 2007;10(1):123-129.
221. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. *Journal of Women's Health*. 2006;15(4):352-368.
222. Wide K, Winbladh B, Källén B. Major malformations in infants exposed to antiepileptic drugs in utero, with emphasis on carbamazepine and valproic acid: A nation-wide, population-based register study. *Acta Paediatrica*. 2004;93(2):174-176.
223. Wyszynski D, Nambisan M, Surve T, Alsdorf R, Smith C, Holmes L. Increased rate of major malformations in offspring exposed to valproate during pregnancy. *Neurology*. 2005;64(6):961-965.
224. Meador K, Baker G, Finnell R, et al. In utero antiepileptic drug exposure: fetal death and malformations. *Neurology*. 2006;67(3):407-412.
225. Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: A systematic review and meta-analysis of published pregnancy registries and cohorts. *Epilepsy Res*. 2008;81(1):1.
226. Vajda F, Graham J, Hitchcock A, O'Brien T, Lander C, Eadie M. Is lamotrigine a significant human teratogen? Observations from the Australian Pregnancy Register. *Seizure*. 2010;19(9):558-561.
227. Mawhinney E, Campbell J, Craig J, et al. Valproate and the risk for congenital malformations: Is formulation and dosage regime important? *Seizure*. 2012;21(3):215-218.
228. Kendell R, Chalmers J, Platz C. Epidemiology of puerperal psychoses. *The Br J Psychiatry*. 1987;150(5):662-673.
229. Kessler R, Amminger P, Ustun B. Age of onset of mental disorders: A review of recent literature. *Current Opin Psychiatry*. 2007;20(4):359-364.
230. Seeman M. Women and schizophrenia. *Medscape Women's Health*. 2000;5(2).
231. Gentile S. Antipsychotic therapy during early and late pregnancy. A systematic review. *Schizophrenia Bulletin*. 2010;36(3):518-544.
232. Robinson G. Treatment of schizophrenia in pregnancy and postpartum. *J Popul Ther Clin Pharmacol*. 2012;19(3):e380-e386.
233. Wikipedia. Pregnancy. <http://en.wikipedia.org/wiki/Pregnancy>. Updated 2013. Accessed August 26, 2013, 2013.
234. Matevosyan N. Pregnancy and postpartum specifics in women with schizophrenia: A meta-study. *Arch Gynecol Obstet*. 2011(283):1706-1708.
235. Howard L. Fertility and pregnancy in women with psychotic disorders. *Eur J Obstet Gynecol Reprod Biol*. 2005;119:3-10.
236. Nilsson E, Lichtenstein P, Cnattingius S, Murray R, Hultman C. Women with schizophrenia: Pregnancy outcome and infant death among their offspring. *Schizophr Res*. 2002;58:221-229.
237. Miller L. Psychotic denial of pregnancy: Phenomenology and clinical management. *Hosp Community Psychiatry*. 1990;41:1233-1237.
238. Hollingsworth L. Child custody loss among women with persistent severe mental illness. *Soc Work Res*. 2004;28:199-209.

239. Mason C, Subedi S, David R. Clients with mental illness and their children: Implications for clinical practice. *Issues Ment Health Nurs*. 2007;28:1105-1123.
240. McIntosh A, Homes S, Gleeson Sea. Maternal recall bias, obstetric history and schizophrenia. *Br J Psychiatry*. 2002;181:520-525.
241. Lerum C, Lo-Biondo-Wood G. The relationship of maternal age, quickening, and physical symptoms of pregnancy to the development of maternal-fetal attachment. *Birth*. 1989;16:13-17.
242. Cohen LS, Wang B, Nonacs R, Viguera AC, Lemon EL, Freeman MP. Treatment of mood disorders during pregnancy and postpartum. *Psychiatr Clin North Am*. 2010;33(2):273-293.
243. Kendell R, Chalmers J, Platz C. Epidemiology of puerperal psychoses. *Br J Psychiatry*. 1987;150:662-673.
244. Meli G, Otti B, Paladini A, Cataldi L. Prenatal and perinatal risk factors of schizophrenia. *The Journal of Maternal-Fetal and Neonatal Medicine*. 2012;25(12):2559-2563.
245. Edwards R, Stoppler M. Psychotic disorders. MedicineNet.com Web site. http://www.medicinenet.com/psychotic_disorders/article.htm. Updated 2013. Accessed August 26, 2013.
246. Robertson E, Jones I, Hague S, Holder R, Craddock N. Risk of puerperal and non-puerperal recurrence of illness following bipolar affective puerperal (post-partum) psychosis. *Br J Psychiatry*. 2005;186:258-259.
247. Brockington I. *Motherhood and mental health*. Oxford: Oxford University Press; 1996.
248. Jones I, Craddock N. Familiarity of the puerperal trigger in bipolar disorder: Results of a family study. *Am J Psychiatry*. 2001;158:913-918.
249. Kumar R, Marks MN, Platz C, Yoshida K. Clinical survey of a psychiatric mother and baby unit: Characteristics of 100 consecutive admissions. *Journal of Affective Disorders*. 1995;33(1):11-22.
250. Munk-Olsen T, Laursen T, Pedersen C, Mors O, Mortensen P. New parents and mental disorders: A population-based register study. *JAMA*. 2006;296:2582-2589.
251. Altshuler L, Cohen L, Szuba M, Burt V, Gitlin M, Mintz J. Pharmacologic management of psychiatric illness during pregnancy: Dilemmas and guidelines. *American Journal of Psychiatry*. 1996;153:592-606.
252. Seeman M. Clinical interventions for women with schizophrenia: Pregnancy. *Acta Psychiatr Scand*. 2013(127):12-22.
253. Doucet S, Jones I, Letourneau N, Dennis C, Blackmore ER. Interventions for the prevention and treatment of postpartum psychosis: A systematic review. *Archives of Women's Mental Health*. 2011;14(2):89-98.
254. Impasato DJ, G. Electric and insulin shock therapy during pregnancy. *Dis Nerv Syst*. 1964;25:542-546.
255. Remick RA, M. ECT in pregnancy. *Am J Psychiatry*. 1978;135:761-762.
256. Anderson EL, R. ECT in pregnancy: A review of the literature from 1941 to 2007. *Psychosom Med*. 2009;71:235-42.
257. Ferrill MJ, K. ECT during pregnancy: Physiologic and pharmacologic considerations. *Convuls Ther*. 1992;8:186-200.
258. Forray A, O. The use of electroconvulsive therapy in the treatment of postpartum affective disorders. *JECT*. 2007;23(3):188-193.
259. Reed P, Sermin N, Appleby L, Faragher B. A comparison of clinical response to electroconvulsive therapy in puerperal and non-puerperal psychoses. *J Affect Disord*. 1999;54(3):255-260.
260. Forray A, O. The use of electroconvulsive therapy in the treatment of postpartum affective disorders. *JECT*. 2007;23(3):188-193.
261. Martin ME. Puerperal mental illness; a follow-up study of 75 cases. *Br Med J*. 1958;2(5099):773-777.
262. Lewis G, Drife JO, Botting BJ, Ireland N. *Why mothers die: The fifth report of the confidential enquiries into maternal deaths in the United Kingdom 1997-1999*. RCOG Press; 2001.
263. Appleby L, Mortensen PB, Faragher EB. Suicide and other causes of mortality after post-partum psychiatric admission. *The Br J Psychiatry*. 1998;173(3):209-211.
264. Oates M. Suicide: The leading cause of maternal death. *Br J Psychiatry*. 2003;183:279-281.
265. BC Mental Health & Addiction Services. Provincial suicide clinical framework. www.bcmhsus.ca/global-resources. Updated 2011 2013.

266. Porter T, Gavin H. Infanticide and neonaticide: A review of 40 years of research literature on incidence and causes. *Trauma, Violence, & Abuse*. 2010;11(3):99-112.
267. Friedman SH, Resnick PJ. Neonaticide: Phenomenology and considerations for prevention. *Int J Law Psychiatry*. 2009;32(1):43.
268. Terp I, Mortensen P. Post-partum psychoses. Clinical diagnoses and relative risk of admission after parturition. *The Br J Psychiatry*. 1998;172(6):521-526.
269. Brockington I, Fraser C, Wilson D. The postpartum bonding questionnaire: A validation. *Archives of Women's Mental Health*. 2006;9(5):233-242.
270. Friedman SH, Holden CE, Hrouda DR, Resnick PJ. Maternal filicide and its intersection with suicide. *Brief Treatment and Crisis Intervention*. 2008;8(3):283.
271. Brent RL. Environmental causes of human congenital malformations: The pediatrician's role in dealing with these complex clinical problems caused by a multiplicity of environmental and genetic factors. *Pediatrics*. 2004;113(Supplement 3):957-968.
272. Review guidance: Evaluating the risks of drug exposure in human pregnancies. US Department of Health and Human Sciences Web site. Updated 2005.
273. Paroxetine (paxil) and pregnancy. Organization of Teratology Information Specialists Web site. <http://www.mothersbaby.org/files/paroxetine.pdf>. Updated 2010. Accessed June 4, 2013.
274. Surveillance for anencephaly and spina bifida and the impact of prenatal diagnosis. *MMWR (CDC)*. 1996(44):1-13.
275. Hale TW. *Medications and mothers' milk*. 15th ed. Amarillo, TX: Hale Publishing; 2012.
276. Lundbeck Canada Inc., ed. *Citalopram (celexa®) product monograph*; June 12, 2012.
277. Forest Pharmaceuticals Inc, ed. *Citalopram (celexa®) product monograph*; December, 2012.
278. Nikfar S, Rahimi R, Hendoiee N, Abdollahi M. Increasing the risk of spontaneous abortion and major malformations in newborns following use of serotonin reuptake inhibitors during pregnancy: A systematic review and updated meta-analysis. *DARU Journal of Pharmaceutical Sciences*. 2012;20(1):75.
279. Colvin L, Slack-Smith L, Stanley FJ, Bower C. Dispensing patterns and pregnancy outcomes for women dispensed selective serotonin reuptake inhibitors in pregnancy. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2011;91(3):142-152.
280. Nakhai-Pour HR, Broy P, Bérard A. Use of antidepressants during pregnancy and the risk of spontaneous abortion. *Can Med Assoc J*. 2010;182(10):1031-1037.
281. Rahimi R, Nikfar S, Abdollahi M. Pregnancy outcomes following exposure to serotonin reuptake inhibitors: A meta-analysis of clinical trials. *Reproductive Toxicology*. 2006;22(4):571-575.
282. Wisner KL, Sit DK, Hanusa BH, et al. Major depression and antidepressant treatment: Impact on pregnancy and neonatal outcomes. *Focus*. 2009;7(3):374.
283. Oberlander TF, Warburton W, Misri S, Aghajanian J, Hertzman C. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. *Arch Gen Psychiatry*. 2006;63(8):898.
284. Ericson A, Källén B, Wiholm B. Delivery outcome after the use of antidepressants in early pregnancy. *Eur J Clin Pharmacol*. 1999;55(7):503-508.
285. Nordeng H, van Gelder MM, Spigset O, Koren G, Einarson A, Eberhard-Gran M. Pregnancy outcome after exposure to antidepressants and the role of maternal depression: Results from the Norwegian mother and child cohort study. *J Clin Psychopharmacol*. 2012;32(2):186-194.
286. Klieger-Grossmann C, Weitzner B, Panchaud A, et al. Pregnancy outcomes following use of escitalopram: A prospective comparative cohort study. *The Journal of Clinical Pharmacology*. 2012;52(5):766-770.
287. Sivojelezova A, Shuhaiber S, Sarkissian L, Einarson A, Koren G. Citalopram use in pregnancy: Prospective comparative evaluation of pregnancy and fetal outcome. *Obstet Gynecol*. 2005;193(6):2004-2009.
288. Diav-Citrin O, Shechtman S, Weinbaum D, et al. Paroxetine and fluoxetine in pregnancy: A prospective, multicentre, controlled, observational study. *Br J Clin Pharmacol*. 2008;66(5):695-705.

289. Bérard A, Ramos E, Rey É, Blais L, St-André M, Oraichi D. First trimester exposure to paroxetine and risk of cardiac malformations in infants: The importance of dosage. *Birth Defects Research Part B: Developmental and Reproductive Toxicology*. 2007;80(1):18-27.
290. Kornum JB, Nielsen RB, Pedersen L, Mortensen PB, Nørgaard M. Use of selective serotonin-reuptake inhibitors during early pregnancy and risk of congenital malformations: Updated analysis. *Clinical Epidemiology*. 2010;2:29.
291. Merlob P, Birk E, Sirota L, et al. Are selective serotonin reuptake inhibitors cardiac teratogens? Echocardiographic screening of newborns with persistent heart murmur. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2009;85(10):837-841.
292. Pedersen LH, Henriksen TB, Vestergaard M, Olsen J, Bech BH. Selective serotonin reuptake inhibitors in pregnancy and congenital malformations: Population based cohort study. *BMJ: British Medical Journal*. 2009;339.
293. Einarson A, Choi J, Einarson TR, Koren G. Incidence of major malformations in infants following antidepressant exposure in pregnancy: Results of a large prospective cohort study. *Canadian Journal of Psychiatry*. 2009;54(4):242-246.
294. Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med*. 2007;356(26):2684-2692.
295. Kallen B. Neonate characteristics after maternal use of antidepressants in late pregnancy. *Arch Pediatr Adolesc Med*. 2004;158(4):312.
296. Bellantuono C, Migliarese G, Gentile S. Serotonin reuptake inhibitors in pregnancy and the risk of major malformations: A systematic review. *Hum Psychopharmacol Clin Exp*. 2007;22:121-128.
297. Källén BA, Otterblad Olausson P. Maternal use of selective serotonin re-uptake inhibitors in early pregnancy and infant congenital malformations. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2007;79(4):301-308.
298. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in pregnancy and lactation: A reference guide to fetal and neonatal risk*. 9th ed. Lippincott Williams & Wilkins; 2011.
299. Davidson S, Prokonov D, Taler M, et al. Effect of exposure to selective serotonin reuptake inhibitors in utero on fetal growth: Potential role for the IGF-I and HPA axes. *Pediatr Res*. 2009;65(2):236-241.
300. Levinson-Castiel R, Merlob P, Linder N, Sirota L, Klinger G. Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. *Arch Pediatr Adolesc Med*. 2006;160(2):173.
301. Sanz EJ, De-las-Cuevas C, Kiuru A, Bate A, Edwards R. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: A database analysis. *Lancet*. 2005;365(9458):482.
302. Nordeng H, Lindemann R, Perminov K, Reikvam A. Neonatal withdrawal syndrome after in utero exposure to selective serotonin reuptake inhibitors. *Acta Paediatrica*. 2001;90(3):288-291.
303. Laine K, Heikkinen T, Ekblad U, Kero P. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. *Arch Gen Psychiatry*. 2003;60(7):720.
304. Anderson GM, Czarkowski K, Ravski N, Epperson CN. Platelet serotonin in newborns and infants: Ontogeny, heritability, and effect of in utero exposure to selective serotonin reuptake inhibitors. *Pediatr Res*. 2004;56(3):418-422.
305. Franssen E, Meijjs V, Ettaher F, Valerio P, Keessen M, Lameijer W. Citalopram serum and milk levels in mother and infant during lactation. *Ther Drug Monit*. 2006;28(1):2-4.
306. Kwon P, Lefkowitz W. Neonatal extrapyramidal movements. neonatal withdrawal due to maternal citalopram and ondansetron use. *Pediatr Ann*. 2008;37(3):128-130.
307. Gentile S. Infant safety with antipsychotic therapy in breast-feeding: A systematic review. *J Clin Psychiatry*. 2008;69(4):666-673.
308. Kieler H, Artama M, Engeland A, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of persistent pulmonary hypertension in the newborn: Population based cohort study from the five Nordic countries. *BMJ*. 2012;344.

309. Heikkinen T, Ekblad U, Palo P, Laine K. Pharmacokinetics of fluoxetine and norfluoxetine in pregnancy and lactation. *Clinical Pharmacology & Therapeutics*. 2003;73(4):330-337.
310. Spigset O, Carleborg L, Öhman R, Norström Å. Excretion of citalopram in breast milk. *Br J Clin Pharmacol*. 1997;44(3):295-298.
311. Jensen PN, Olesen OV, Bertelsen A, Linnet K. Citalopram and desmethylcitalopram concentrations in breast milk and in serum of mother and infant. *Ther Drug Monit*. 1997;19(2):236-239.
312. Rampono J, Kristensen JH, Hackett LP, Paech M, Kohan R, Ilett KF. Citalopram and demethylcitalopram in human milk; distribution, excretion and effects in breast fed infants. *Br J Clin Pharmacol*. 2000;50(3):263-268.
313. Schmidt K, Olesen OV, Jensen PN. Citalopram and breast-feeding: Serum concentration and side effects in the infant. *Biol Psychiatry*. 2000;47(2):164-165.
314. Weissman AM, Levy BT, Hartz AJ, et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. *Am J Psychiatry*. 2004;161(6):1066-1078.
315. Heikkinen T, Ekblad U, Kero P, Ekblad S, Laine K. Citalopram in pregnancy and lactation. *Clinical Pharmacology & Therapeutics*. 2002;72(2):184-191.
316. Gentile S. Escitalopram late in pregnancy and while breast-feeding. *Ann Pharmacother*. 2006;40(9):1696-1697.
317. Castberg I, Spigset O. Excretion of escitalopram in breast milk. *J Clin Psychopharmacol*. 2006;26(5):536-538.
318. Eli Lilly Canada Inc., ed. *Fluoxetine (prozac®) product monograph*; November 21, 2012.
319. Lilly USA LLC., ed. *Fluoxetine (prozac®) product monograph*; January 3, 2013.
320. Chambers CD, Johnson KA, Dick LM, Felix RJ, Jones KL. Birth outcomes in pregnant women taking fluoxetine. *N Engl J Med*. 1996;335(14):1010-1015.
321. Hendrick V, Stowe ZN, Altshuler LL, Hwang S, Lee E, Haynes D. Placental passage of antidepressant medications. *Am J Psychiatry*. 2003;160(5):993-996.
322. Malm H, Artama M, Gissler M, Ritvanen A. Selective serotonin reuptake inhibitors and risk for major congenital anomalies. *Obstetrics & Gynecology*. 2011;118(1):111-120.
323. Spencer MJ. Fluoxetine hydrochloride (prozac) toxicity in a neonate. *Pediatrics*. 1993;92(5):721-722.
324. Mohan MS, Patole SK, Whitehall JS. Severe hypothermia in a neonate following antenatal exposure to haloperidol. *J Paediatr Child Health*. 2000;36(4):412-413.
325. Mohan CG, Moore JJ. Fluoxetine toxicity in a preterm infant. *J Perinatol*. 2000;20(7):445-446.
326. Abebe-Campino G, Offer D, Stahl B, Merlob P. Cardiac arrhythmia in a newborn infant associated with fluoxetine use during pregnancy. *Ann Pharmacother*. 2002;36(3):533-534.
327. Dubnov G, Fogelman R, Merlob P. Prolonged QT interval in an infant of a fluoxetine treated mother. *Arch Dis Child*. 2005;90(9):972-973.
328. Rampono J, Proud S, Hackett LP, Kristensen JH, Ilett KF. A pilot study of newer antidepressant concentrations in cord and maternal serum and possible effects in the neonate. *The International Journal of Neuropsychopharmacology*. 2004;7(3):329-334.
329. Alehan F, Saygi S, Tarcan A, Gürakan B. Prolonged neonatal complications after in utero exposure to fluoxetine. *Journal of Maternal-Fetal and Neonatal Medicine*. 2008;21(12):921-923.
330. Kristensen J, Ilett K, Hackett L, Yapp P, Paech M, Begg E. Distribution and excretion of fluoxetine and norfluoxetine in human milk. *Br J Clin Pharmacol*. 1999;48:521-527.
331. Kim J, Riggs KW, Misri S, et al. Stereoselective disposition of fluoxetine and norfluoxetine during pregnancy and breast-feeding. *Br J Clin Pharmacol*. 2006;61(2):155-163.
332. Chambers CD, Anderson PO, Thomas RG, et al. Weight gain in infants breastfed by mothers who take fluoxetine. *Pediatrics*. 1999;104(5):e61-e61.
333. Epperson CN, Jatlow PI, Czarkowski K, Anderson GM. Maternal fluoxetine treatment in the postpartum period: Effects on platelet serotonin and plasma drug levels in breastfeeding mother-infant pairs. *Pediatrics*. 2003;112(5):e425-e425.

334. Hendrick V, Stowe ZN, Altshuler LL, et al. Fluoxetine and norfluoxetine concentrations in nursing infants and breast milk. *Biol Psychiatry*. 2001;50(10):775-782.
335. Yoshida K, Smith B, Craggs M, Kumar R. Fluoxetine in breast-milk and developmental outcome of breast-fed infants. *The Br J Psychiatry*. 1998;172(2):175-178.
336. Lester BM, Cucca J, Andreozzi L, Flanagan P, Oh W. Possible association between fluoxetine hydrochloride and colic in an infant. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1993;32(6):1253-1255.
337. Abbott Laboratories Ltd., ed. *Fluvoxamine (Luvox®) product monograph*; July 30, 2012.
338. Kulin NA, Pastuszak A, Sage SR, et al. Pregnancy outcome following maternal use of the new selective serotonin reuptake inhibitors. *JAMA: the Journal of the American Medical Association*. 1998;279(8):609-610.
339. Oberlander TF, Warburton W, Misri S, Riggs W, Aghajanian J, Hertzman C. Major congenital malformations following prenatal exposure to serotonin reuptake inhibitors and benzodiazepines using population-based health data. *Birth Defects Research Part B: Developmental and Reproductive Toxicology*. 2008;83(1):68-76.
340. Moses-Kolko EL, Bogen D, Perel J, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors. *JAMA: the Journal of the American Medical Association*. 2005;293(19):2372-2383.
341. Reis M, Källén B. Delivery outcome after maternal use of antidepressant drugs in pregnancy: An update using Swedish data. *Psychol Med*. 2010;40(10):1723-1733.
342. Chambers CD, Hernandez-Diaz S, Van Marter LJ, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med*. 2006;354(6):579-587.
343. Wright S, Dawling S, Ashford J. Excretion of fluvoxamine in breast milk [letter]. *Br J Clin Pharmacol*. 1991;31(2):209-196.
344. Hägg S, Granberg K, Carleborg L. Excretion of fluvoxamine into breast milk. *Br J Clin Pharmacol*. 2000;49(3):286-288.
345. Arnold LM, Suckow R, Lichtenstein PK. Fluvoxamine concentrations in breast milk and in maternal and infant sera. *J Clin Psychopharmacol*. 2000;20(4):491-493.
346. Hendrick V, Fukuchi A, Altshuler L, Widawski M, Wertheimer A, Brunhuber MV. Use of sertraline, paroxetine and fluvoxamine by nursing women. *The Br J Psychiatry*. 2001;179(2):163-166.
347. Kristensen JH, Hackett LP, Kohan R, Paech M, Ilett KF. The amount of fluvoxamine in milk is unlikely to be a cause of adverse effects in breastfed infants. *Journal of Human Lactation*. 2002;18(2):139-143.
348. GlaxoSmithKline Inc., ed. *Paroxetine (paxil®) product monograph*; October 11, 2012.
349. GlaxoSmithKline, ed. *Paroxetine (paxil®) product monograph*; January 2013.
350. Wurst KE, Poole C, Ephross SA, Olshan AF. First trimester paroxetine use and the prevalence of congenital, specifically cardiac, defects: A meta-analysis of epidemiological studies. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2010;88(3):159-170.
351. Bakker MK, Kerstjens-Frederikse WS, Buys CH, de Walle HE, de Jong-van den Berg L. First-trimester use of paroxetine and congenital heart defects: A population-based case-control study. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2010;88(2):94-100.
352. Louik C, Lin AE, Werler MM, Hernández-Díaz S, Mitchell AA. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *N Engl J Med*. 2007;356(26):2675-2683.
353. Knoppert DC, Nimkar R, Principi T, Yuen D. Paroxetine toxicity in a newborn after in utero exposure: Clinical symptoms correlate with serum levels. *Ther Drug Monit*. 2006;28(1):5-7.
354. Laine K, Kytölä J, Bertilsson L. Severe adverse effects in a newborn with two defective CYP2D6 alleles after exposure to paroxetine during late pregnancy. *Ther Drug Monit*. 2004;26(6):685-687.
355. Duijvestijn Y, Kalmeijer MD, Passier AL, Dahlem P, Smiers F. Neonatal intraventricular haemorrhage associated with maternal use of paroxetine. *Br J Clin Pharmacol*. 2003;56(5):581-582.
356. Jaiswal S, Coombs RC, Isbister GK. Paroxetine withdrawal in a neonate with historical and laboratory confirmation. *Eur J Pediatr*. 2003;162(10):723-724.

357. Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure. *J Clin Psychiatry*. 2004;65(2):230-237.
358. Berle JØ, Steen VM, Aamo TO, Breilid H, Zahlsten K, Spigset O. Breastfeeding during maternal antidepressant treatment with serotonin reuptake inhibitors: Infant exposure, clinical symptoms, and cytochrome p450 genotypes. *J Clin Psychiatry*. 2004;65(9):1228-1234.
359. Merlob P, Stahl B, Sulkes J. Paroxetine during breast-feeding: Infant weight gain and maternal adherence to counsel. *Eur J Pediatr*. 2004;163(3):135-139.
360. Misri S, Kim J, Riggs KW, Kostaras X. Paroxetine levels in postpartum depressed women, breast milk, and infant serum. *J Clin Psychiatry*. 2000;61(11):828-832.
361. Pfizer Canada Inc., ed. *Sertraline (zoloft®) product monograph*; October 9, 2012.
362. Pfizer Inc., ed. *Sertraline (zoloft®) product monograph*; December, 2012b.
363. Oberlander TF, Grunau RE, Fitzgerald C, et al. Prolonged prenatal psychotropic medication exposure alters neonatal acute pain response. *Pediatr Res*. 2002;51(4):443-453.
364. Oberlander TF, Grunau RE, Fitzgerald C, Papsdorf M, Rurak D, Riggs W. Pain reactivity in 2-month-old infants after prenatal and postnatal selective serotonin reuptake inhibitor medication exposure. *Pediatrics*. 2005;115(2):411-425.
365. Kent L, Laidlaw J. Suspected congenital sertraline dependence. *The Br J Psychiatry*. 1995;167(3):412-413.
366. Vanhaesebrouck P, De Bock F, Zecic A, et al. Phototherapy-mediated syndrome of inappropriate secretion of antidiuretic hormone in an in utero selective serotonin reuptake inhibitor-Exposed newborn infant. *Pediatrics*. 2005;115(5):e508-e511.
367. Santos RP, Pergolizzi JJ. Transient neonatal jitteriness due to maternal use of sertraline (zoloft®). *Journal of perinatology*. 2004;24(6):392-394.
368. Oca MJ, Donn SM. Association of maternal sertraline (zoloft) therapy and transient neonatal nystagmus. *J Perinatol*. 1999;19(6 Pt 1):460-461.
369. Stowe ZN, Owens M, Landry JC, et al. Sertraline and desmethylsertraline in human breast milk and nursing infants. *Am J Psychiatry*. 1997;154(9):1255-1260.
370. Wisner KL, Perel JM, Blumer J. Serum sertraline and N-desmethylsertraline levels in breast-feeding mother-infant pairs. *Am J Psychiatry*. 1998;155(5):690-692.
371. Kristensen J, Ilett K, Dusci L, et al. Distribution and excretion of sertraline and N-desmethylsertraline in human milk. *Br J Clin Pharmacol*. 1998;45(5):453-458.
372. Epperson N, Czarkowski KA, Ward-Oâ D, et al. Maternal sertraline treatment and serotonin transport in breast-feeding mother-infant pairs. *Am J Psychiatry*. 2001;158(10):1631-1637.
373. Dodd S. Sertraline analysis in the plasma of breast-fed infants. *Aust N Z J Psychiatry*. 2001;35(4):545-546.
374. Stowe ZN, Hostetter AL, Owens MJ, et al. The pharmacokinetics of sertraline excretion into human breast milk: Determinants of infant serum concentrations. *J Clin Psychiatry*. 2003;64(1):73-80.
375. Eli Lilly Canada Ltd., ed. *Duloxetine (Cymbalta) product monograph*; December 5, 2012.
376. Einarson A, Smart K, Vial T, et al. Rates of major malformations in infants following exposure to duloxetine during pregnancy: A preliminary report. *J Clin Psychiatry*. 2012;73(11):1471-1471.
377. Eyal R, Yaeger D. Poor neonatal adaptation after in utero exposure to duloxetine. *Am J Psychiatry*. 2008;165(5):651. doi: 10.1176/appi.ajp.2008.07071194; 10.1176/appi.ajp.2008.07071194.
378. Boyce PM, Hackett LP, Ilett KF. Duloxetine transfer across the placenta during pregnancy and into milk during lactation. *Archives of women's mental health*. 2011;14(2):169-172.
379. Lilly USA., ed. *Duloxetine (Cymbalta) product monograph*; November 9, 2012.
380. Lobo ED, Loghin C, Knadler MP, et al. Pharmacokinetics of duloxetine in breast milk and plasma of healthy postpartum women. *Clin Pharmacokinet*. 2008;47(2):103-109.
381. Briggs GG, Ambrose PJ, Ilett KF, Hackett LP, Nageotte MP, Padilla G. Use of duloxetine in pregnancy and lactation. *Ann Pharmacother*. 2009;43(11):1898-1902.

382. Wells KA, Losin WG. In vitro stability, potency, and dissolution of duloxetine enteric-coated pellets after exposure to applesauce, apple juice, and chocolate pudding. *Clin Ther*. 2008;30(7):1300-1308.
383. Wyeth Pfizer Canada Inc, ed. *Desvenlafaxine (Pristiq®) product monograph*; 2012.
384. Pfizer - Wyeth Pharmaceuticals USA, ed. *Desvenlafaxine (Pristiq®) product monograph*; 2012.
385. Rampono J, Teoh S, Hackett LP, Kohan R, Ilett KF. Estimation of desvenlafaxine transfer into milk and infant exposure during its use in lactating women with postnatal depression. *Archives of women's mental health*. 2011;14(1):49-53.
386. Ilett KF, Watt F, Hackett LP, Kohan R, Teoh S. Assessment of infant dose through milk in a lactating woman taking amisulpride and desvenlafaxine for treatment-resistant depression. *Ther Drug Monit*. 2010;32(6):704-707.
387. Einarson A, Fatoye B, Sarkar M, et al. Pregnancy outcome following gestational exposure to venlafaxine: A multicenter prospective controlled study. *Am J Psychiatry*. 2001;158(10):1728-1730.
388. Ferreira E, Carceller AM, Agogué C, et al. Effects of selective serotonin reuptake inhibitors and venlafaxine during pregnancy in term and preterm neonates. *Pediatrics*. 2007;119(1):52-59.
389. Hoppenbrouwers CJ, Bosma J, Wennink HJ, Hilgevoord AA, Heres M, Honig A. Neonatal seizures on EEG after in utero exposure to venlafaxine. *Br J Clin Pharmacol*. 2010;70(3):454-456.
390. Lennestål R, Källén B. Delivery outcome in relation to maternal use of some recently introduced antidepressants. *J Clin Psychopharmacol*. 2007;27(6):607-613.
391. Einarson A, Boskovic R. Use and safety of antipsychotic drugs during pregnancy. *Journal of Psychiatric Practice®*. 2009;15(3):183-192.
392. Polen KN, Rasmussen SA, Riehle-Colarusso T, Reefhuis J, National Birth Defects Prevention Study. Association between reported venlafaxine use in early pregnancy and birth defects, national birth defects prevention study, 1997-2007. *Birth Defects Res A Clin Mol Teratol*. 2013;97(1):28-35. doi: 10.1002/bdra.23096; 10.1002/bdra.23096.
393. Boucher N, Koren G, Beaulac-Baillargeon L. Maternal use of venlafaxine near term: Correlation between neonatal effects and plasma concentrations. *Ther Drug Monit*. 2009;31(3):404-409.
394. Yaris F, Kadioglu M, Kesim M, et al. Newer antidepressants in pregnancy: Prospective outcome of a case series. *Reproductive Toxicology*. 2004;19(2):235-238.
395. Pakalapati RK, Bolisetty S, Austin M, Oei J. Neonatal seizures from in utero venlafaxine exposure. *J Paediatr Child Health*. 2006;42(11):737-738.
396. Koren G, Moretti M, Kapur B. Can venlafaxine in breast milk attenuate the norepinephrine and serotonin reuptake neonatal withdrawal syndrome. *J Obstet Gynaecol Can*. 2006;28(4):299-301.
397. Treichel M, Schwendener Scholl K, Kessler U, Joeris A, Nelle M. Is there a correlation between venlafaxine therapy during pregnancy and a higher incidence of necrotizing enterocolitis? *World Journal of Pediatrics*. 2009;5(1):65-67.
398. Jordan AE, Jackson GL, Deardorff D, Shivakumar G, McIntire DD, Dashe JS. Serotonin reuptake inhibitor use in pregnancy and the neonatal behavioral syndrome. *Journal of Maternal-Fetal and Neonatal Medicine*. 2008;21(10):745-751.
399. Ilett K, Hackett L, Dusci L, et al. Distribution and excretion of venlafaxine and O-desmethylvenlafaxine in human milk. *Br J Clin Pharmacol*. 1998;45(5):459-462.
400. Hendrick V, Altshuler L, Wertheimer A, Dunn WA. Venlafaxine and breast-feeding. *Am J Psychiatry*. 2001;158(12):2089-a-2090.
401. Newport DJ, Ritchie JC, Knight BT, Glover BA, Zach EB, Stowe ZN. Venlafaxine in human breast milk and nursing infant plasma: Determination of exposure. *J Clin Psychiatry*. 2009;70(9):1304-1310.
402. Ilett KF, Kristensen JH, Hackett LP, Paech M, Kohan R, Rampono J. Distribution of venlafaxine and its O-desmethyl metabolite in human milk and their effects in breastfed infants. *Br J Clin Pharmacol*. 2002;53(1):17-22.
403. AA Pharma Inc., ed. *Amitriptyline (elavil®) product monograph*; July 10, 2010.
404. Ban L, Tata LJ, West J, Fiaschi L, Gibson JE. Live and non-live pregnancy outcomes among women with depression and anxiety: A population-based study. *PloS one*. 2012;7(8):e43462.

405. Davis RL, Rubanowice D, McPhillips H, et al. Risks of congenital malformations and perinatal events among infants exposed to antidepressant medications during pregnancy. *Pharmacoepidemiol Drug Saf.* 2007;16(10):1086-1094.
406. Crombie D, Pinsent R, Fleming D. Imipramine in pregnancy. *Br Med J.* 1972;1(5802):745.
407. Sim M. Imipramine and pregnancy. *Br Med J.* 1972;2(5804):45.
408. Rachelefsky G, William Flynt J, Ebbin A, et al. Possible teratogenicity of tricyclic antidepressants. *The Lancet.* 1972;299(7755):838-839.
409. Barson A. Malformed infant. *Br Med J.* 1972;2(5804):45.
410. Kuenssberg E, Knox J. Imipramine in pregnancy. *Br Med J.* 1972;2(5808):292.
411. Shearer WT, Schreiner RL, Marshall RE. Urinary retention in a neonate secondary to maternal ingestion of nortriptyline. *J Pediatr.* 1972;81(3):570-572.
412. ter Horst PG, van der Linde S, Smit JP, et al. Clomipramine concentration and withdrawal symptoms in 10 neonates. *Br J Clin Pharmacol.* 2012;73(2):295-302.
413. ter Horst PG, Jansman FG, van Lingen RA, Smit J, Brouwers JR. Pharmacological aspects of neonatal antidepressant withdrawal. *Obstet Gynecol Surv.* 2008;63(4):267-279.
414. Cowe L, Lloyd DJ, Dawling S. Neonatal convulsions caused by withdrawal from maternal clomipramine. *Br Med J (Clin Res Ed).* 1982;284(6332):1837.
415. Bader T, Newman K. Amitriptyline in human breast milk and the nursing infant's serum. *Am J Psychiatry.* 1980;137(7):855-856.
416. Brixen-Rasmussen L, Halgrener J, Jørgensen A. Amitriptyline and nortriptyline excretion in human breast milk. *Psychopharmacology (Berl).* 1982;76(1):94-95.
417. Breyer-Pfaff U, Nill K, Entenmann KN, Gaertner HJ. Secretion of amitriptyline and metabolites into breast milk. *Am J Psychiatry.* 1995;152(5):812-813.
418. Sunovion Pharmaceuticals Canada Inc., ed. *Clomipramine (Anafranil®) product monograph* ; June 7, 2012.
419. Källén BA, Otterblad Olausson P. Maternal drug use in early pregnancy and infant cardiovascular defect. *Reproductive Toxicology.* 2003;17(3):255-261.
420. Schimmell MS, Katz EZ, Shaag Y, Pastuszak A, Koren G. Toxic neonatal effects following maternal clomipramine therapy. *Clin Toxicol.* 1991;29(4):479-484.
421. Pendopharm Division of Pharmascience Inc., ed. *Nortriptyline (aventyl®) product monograph*; January 4, 2012.
422. Mallinckrodt Inc., ed. *Nortriptyline (pamelor®) product monograph*; January 2013.
423. Wisner KL, Perel JM. Serum nortriptyline levels in nursing mothers and their infants. *Am J Psychiatry.* 1991;148(9):1234-1236.
424. Matheson I, Skjaeraasen J. Milk concentrations of flupenthixol, nortriptyline and zuclopenthixol and between-breast differences in two patients. *Eur J Clin Pharmacol.* 1988;35(2):217-220.
425. Valeant Canada LP, ed. *Bupropion (Zyban) product monograph*; January 2013.
426. Valeant Canada LP, ed. *Wellbutrin SR product monograph*; Dec 12, 2012.
427. Glaxo SmithKline, ed. *Bupropine (Wellbutrin SR) product monograph*; Aug 2011.
428. Bupropion pregnancy registry - final report Sept 1, 1997 - March 31, 2008. <http://pregnancyregistry.gsk.com/bupropion.html>. Accessed Feb, 2013.
429. Chun-Fai-Chan B, Koren G, Fayez I, et al. Pregnancy outcome of women exposed to bupropion during pregnancy: A prospective comparative study. *Obstet Gynecol.* 2005;192(3):932-936.
430. Alwan S, Reefhuis J, Botto LD, Rasmussen SA, Correa A, Friedman JM. Maternal use of bupropion and risk for congenital heart defects. *Obstet Gynecol.* 2010;203(1):52. e1-52. e6.
431. Thyagarajan V, Robin Clifford C, Wurst KE, Ephross SA, Seeger JD. Bupropion therapy in pregnancy and the occurrence of cardiovascular malformations in infants. *Pharmacoepidemiol Drug Saf.* 2012;21(11):1240-1242.
432. Leventhal K, Byatt N, Lundquist R. Fetal cardiac arrhythmia during bupropion use. *Acta Obstet Gynecol Scand.* 2010;89(7):980-981.

433. Gisslen T, Nathan B, Thompson T, Rao R. Hyperinsulinism associated with gestational exposure to bupropion in a newborn infant. *Journal of Pediatric Endocrinology and Metabolism*. 2011;24(9-10):819-822.
434. Figueroa R. Use of antidepressants during pregnancy and risk of attention-deficit/hyperactivity disorder in the offspring. *Journal of Developmental & Behavioral Pediatrics*. 2010;31(8):641-648.
435. Haas J, Kaplan C, Barenboim D, Jacob P, Benowitz N. Bupropion in breast milk: An exposure assessment for potential treatment to prevent post-partum tobacco use. *Tob Control*. 2004;13(1):52-56.
436. Baab SW, Peindl KS, Piontek CM, Wisner KL. Serum bupropion levels in 2 breastfeeding mother-infant pairs. *J Clin Psychiatry*. 2002;63(10):910-911.
437. Chaudron LH, Schoenecker CJ. Bupropion and breastfeeding: A case of a possible infant seizure. *J Clin Psychiatry*. 2004;65(6):881-882.
438. Davis MF, Miller HS, Nolan Jr PE. Bupropion levels in breast milk for 4 mother-infant pairs: More answers to lingering questions. *J Clin Psychiatry*. 2009;70(2):297.
439. Merck Canada Inc., ed. *Mirtazapine (Remeron) product monograph*; September 13, 2012.
440. Organon Inc., ed. *Mirtazapine (Remeron) product monograph*; 2004.
441. Djulus J, Koren G, Einarson TR, et al. Exposure to mirtazapine during pregnancy: A prospective, comparative study of birth outcomes. *J Clin Psychiatry*. 2006;67(8):1280.
442. Biswas PN, Wilton LV, Shakir SA. The pharmacovigilance of mirtazapine: Results of a prescription event monitoring study on 13 554 patients in England. *Journal of Psychopharmacology*. 2003;17(1):121-126.
443. Kesim M, Yaris F, Kadioglu M, Yaris E, Kalyoncu NI, Ulku C. Mirtazapine use in two pregnant women: Is it safe? *Teratology*. 2002;66(5):204-204.
444. Rohde A, Dembinski J, Dorn C. Mirtazapine (remergil) for treatment resistant hyperemesis gravidarum: Rescue of a twin pregnancy. *Arch Gynecol Obstet*. 2003;268(3):219-221.
445. Saks B. Mirtazapine: Treatment of depression, anxiety, and hyperemesis gravidarum in the pregnant patient. A report of 7 cases. *Archives of Women's Mental Health*. 2001;3(4):165-170.
446. Guclu S, Gol M, Dogan E, Saygili U. Mirtazapine use in resistant hyperemesis gravidarum: Report of three cases and review of the literature. *Arch Gynecol Obstet*. 2005;272(4):298-300.
447. Schwarzer V, Heep A, Gembruch U, Rohde A. Treatment resistant hyperemesis gravidarum in a patient with type 1 diabetes mellitus: Neonatal withdrawal symptoms after successful antiemetic therapy with mirtazapine. *Arch Gynecol Obstet*. 2008;277(1):67-69.
448. Sokolover N, Merlob P, Klinger G. Neonatal recurrent prolonged hypothermia associated with maternal mirtazapine treatment during pregnancy. *Can J Clin Pharmacol*. 2008;15(2):e188-90.
449. Aichhorn W, Whitworth AB, Weiss U, Stuppaeck C. Mirtazapine and breast-feeding. *Am J Psychiatry*. 2004;161(12):2325-2325.
450. Klier C, Mossahed N, Lee A, Zernig G. Mirtazapine and breastfeeding: Maternal and infant plasma levels. *American Journal of Psychiatry*. 2007;164(2):348.
451. Kristensen J, Ilett KF, Rampono J, Kohan R, Hackett LP. Transfer of the antidepressant mirtazapine into breast milk. *Br J Clin Pharmacol*. 2007;63(3):322-327.
452. Pfizer Canada Inc., ed. *Xanax and xanax TS (Alprazolam) product monograph*. Quebec: Kirkland; May 3, 2012.
453. Pfizer Pharmacia & Upjohn Co., ed. *Xanax (Alprazolam) product monograph*. NY(NY): Pfizer Pharmacia & Upjohn Co; August 2011.
454. Ornoy A, Arnon J, Shechtman S, Moerman L, Lukashova I. Is benzodiazepine use during pregnancy really teratogenic? *Reproductive Toxicology*. 1998;12(5):511-515.
455. Wikner BN, Stiller C, Bergman U, Asker C, Källén B. Use of benzodiazepines and benzodiazepine receptor agonists during pregnancy: Neonatal outcome and congenital malformations. *Pharmacoepidemiol Drug Saf*. 2007;16(11):1203-1210.
456. Enato E, Moretti M, Koren G. The fetal safety of benzodiazepines: An updated meta-analysis. *J Obstet Gynaecol Can*. 2011;33(1):46-48.

457. Enato E, Moretti M, Koren G. The fetal safety of benzodiazepines: An updated meta-analysis. erratum. *J Obstet Gynaecol Can.* 2011;33(4):319.
458. Dolovich LR, Addis A, Vaillancourt J, Power J, Koren G, Einarson TR. Benzodiazepine use in pregnancy and major malformations or oral cleft: Meta-analysis of cohort and case-control studies. *BMJ.* 1998;317(7162):839-843.
459. Gidai J, Acs N, Bánhidly F, Czeizel A. An evaluation of data for 10 children born to mothers who attempted suicide by taking large doses of alprazolam during pregnancy. *Toxicol Ind Health.* 2008;24(1-2):53-60.
460. Eros E, Czeizel AE, Rockenbauer M, Sorensen HT, Olsen J. A population-based case-control teratologic study of nitrazepam, medazepam, tofisopam, alprazolam and clonazepam treatment during pregnancy. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2002;101(2):147-154.
461. Anderson P, McGuire G. Neonatal alprazolam withdrawal--possible effects of breast feeding. *DICP: the annals of pharmacotherapy.* 1989;23(7-8):614.
462. Barry W, St Clair S. Exposure to benzodiazepines in utero. *Lancet.* 1987;1(8547):1436.
463. Hale TW. *Medications and mothers' milk.* 14th ed. Amarillo, TX: Hale Publishing; 2010.
464. Oo C, Kuhn R, Desai N, Wright C, McNamara P. Pharmacokinetics in lactating women: Prediction of alprazolam transfer into milk. *Br J Clin Pharmacol.* 1995;40(3):231-236.
465. Ito S, Blajchman A, Stephenson M, Eliopoulos C, Koren G. Prospective follow-up of adverse reactions in breast-fed infants exposed to maternal medication. *Am J Obstet Gynecol.* 1993;168(5):1393-1399.
466. Kelly LE, Poon S, Madadi P, Koren G. Neonatal benzodiazepines exposure during breastfeeding. *J Pediatr.* 2012.
467. Barr Laboratories Inc, ed. *Clonazepam tablet, orally disintegrating. product monograph.* Daily Med Current Medication Information, US National Library of Medicine; 2012.
468. Samrén EB, Van Duijn CM, Lieve Christiaens G, Hofman A, Lindhout D. Antiepileptic drug regimens and major congenital abnormalities in the offspring. *Ann Neurol.* 1999;46(5):739-746.
469. Kriel RL, Pharmed JC. Clonazepam and pregnancy. *Ann Neurol.* 1982;11(5):544-544.
470. Weinstock L, Cohen LS, Bailey JW, Blatman R, Rosenbaum JF. Obstetrical and neonatal outcome following clonazepam use during pregnancy: A case series. *Psychother Psychosom.* 2001;70(3):158-162.
471. Fisher JB, Edgren BE, Mammel MC, Coleman JM. Neonatal apnea associated with maternal. clonazepam therapy: A case report. *Obstetrics & Gynecology.* 1985;66(3):36S.
472. Söderman P, Matheson I. Clonazepam in breast milk. *Eur J Pediatr.* 1988;147(2):212-213.
473. Birnbaum CS, Cohen LS, Bailey JW, Grush LR, Robertson LM, Stowe ZN. Serum concentrations of antidepressants and benzodiazepines in nursing infants: A case series. *Pediatrics.* 1999;104(1).
474. Ltd HR, ed. *Valium (diazepam) product monograph;* 2008; No. 13.
475. Roche Pharmaceuticals, ed. *Valium product monograph.* Nutley (New Jersey): Roche Pharmaceuticals, January; 2008.
476. Laegreid L, Hagberg G, Lundberg A. The effect of benzodiazepines on the fetus and the newborn. *Neuropediatrics.* 1992;23(1):18.
477. Czeizel A, Szegal B, Joffe J, Racz J. The effect of diazepam and promethazine treatment during pregnancy on the somatic development of human offspring. *Neurotoxicol Teratol.* 1999;21(2):157-167.
478. Källén B, Reis M. Neonatal complications after maternal concomitant use of SSRI and other central nervous system active drugs during the second or third trimester of pregnancy. *J Clin Psychopharmacol.* 2012;32(5):608-614.
479. Laegreid L, Olegård R, Conradi N, Hagberg G, Wahlström J, Abrahamsson L. Congenital malformations and maternal consumption of benzodiazepines: a case-control study. *Developmental Medicine & Child Neurology.* 1990;32(5):432-441.
480. Bracken MB, HOLFORD TR. Exposure to prescribed drugs in pregnancy and association with congenital malformations. *Obstetrics & Gynecology.* 1981;58(3):336-344.
481. Bracken MB. Drug use in pregnancy and congenital heart disease in offspring. *N Engl J Med.* 1986;314(17):1120.

482. Czeizel A. Letter: Diazepam, phenytoin, and aetiology of cleft lip and/or cleft palate. *Lancet*. 1976;1(7963):810.
483. Rothman KJ, Fyler DC, Goldblatt A, Kreidberg MB. Exogenous hormones and other drug exposures of children with congenital heart disease. *Am J Epidemiol*. 1979;109(4):433-439.
484. Czeizel AE, Erös E, Rockenbauer M, Sørensen HT, Olsen J. Short-term oral diazepam treatment during pregnancy. *Clinical drug investigation*. 2003;23(7):451-462.
485. Gillberg C. "Floppy infant syndrome" and maternal diazepam. *Lancet*. 1977;2(8031):244.
486. Rementería JL, Bhatt K. Withdrawal symptoms in neonates from intrauterine exposure to diazepam. *J Pediatr*. 1977;90(1):123-126.
487. Speight AN. Floppy-infant syndrome and maternal diazepam and/or nitrazepam. *Lancet*. 1977;2(8043):878.
488. Brandt R. *Passage of diazepam and desmethyl diazepam into breast milk*. *Arzneim Forsch*; 1976.
489. Dusci L, Good S, Hall R, Ilett K. Excretion of diazepam and its metabolites in human milk during withdrawal from combination high dose diazepam and oxazepam. *Br J Clin Pharmacol*. 1990;29(1):123-126.
490. Wesson DR, Camber S, Harkey M, Smith DE. Diazepam and desmethyl diazepam in breast milk. *J Psychoactive Drugs*. 1985;17(1):55-56.
491. Patrick MJ, Tilstone WJ, Reavey P. Diazepam and breast-feeding. *Lancet*. 1972;1(7749):542-543.
492. Cree JE, Meyer J, Hailey DM. Diazepam in labour: Its metabolism and effect on the clinical condition and thermogenesis of the newborn. *Br Med J*. 1973;4(5887):251.
493. Gamble J, Moore J, Lamki H, Howard P. A study of plasma diazepam levels in mother and infant. *BJOG: An International Journal of Obstetrics & Gynaecology*. 1977;84(8):588-591.
494. Pfizer Canada Inc., ed. *Ativan (lorazepam) product monograph*. Kirkland, QC: Pfizer Canada Inc., October 18; 2012.
495. Hospira Inc, ed. *Lorazepam injection, USP. package insert*; March 2007.
496. Bonnot O, Vollset SE, Godet PF, D'Amato T, Robert E. Maternal exposure to lorazepam and anal atresia in newborns: Results from a hypothesis-generating study of benzodiazepines and malformations. *J Clin Psychopharmacol*. 2001;21(4):456-458.
497. Whitelaw A. Effect of maternal lorazepam on the neonate. *Br Med J (Clin Res Ed)*. 1981;282(6280):1973.
498. Erkkola R, Kero P, Kanto J, Aaltonen L. Severe abuse of psychotropic drugs during pregnancy with good perinatal outcome. *Ann Clin Res*. 1983;15(2):88-91.
499. Sommerfield R, Nielsen M. Excretion of lorazepam into breast milk. *Br J Anaesth*. 1985;57(10):1042-1043.
500. Canadian Pharmacists Association, ed. *Trazodone monograph* ; November 2012.
501. Teva Canada Ltd., ed. *Trazodone (Teva-trazodone) product monograph* ; May 29, 2011.
502. Keltman Pharmaceuticals Inc, ed. *Trazodone (Desyrel) product monograph*; January 2010.
503. Verbeeck R, Ross S, McKenna E. Excretion of trazodone in breast milk. *Br J Clin Pharmacol*. 1986;22(3):367-370.
504. Einarson A, Bonari L, Voyer-Lavigne S, et al. A multicentre prospective controlled study to determine the safety of trazodone and nefazodone use during pregnancy. *Canadian journal of psychiatry*. 2003;48(2):106-110.
505. Einarson TR, Einarson A. Newer antidepressants in pregnancy and rates of major malformations: A meta-analysis of prospective comparative studies. *Pharmacoepidemiol Drug Saf*. 2005;14(12):823-827.
506. Misri S, Corral M, Wardrop AA, Kendrick K. Quetiapine augmentation in lactation: A series of case reports. *J Clin Psychopharmacol*. 2006;26(5):508-511.
507. MEDA AB., ed. *Zolidem (Sublinox) product monograph*; August 16, 2012.
508. Sanofi-Aventis US LLC., ed. *Zopiclone (Ambien CR) product monograph*; May 2012.
509. Juric S, Newport DJ, Ritchie JC, Galanti M, Stowe ZN. Zolpidem (Ambien®) in pregnancy: Placental passage and outcome. *Archives of women's mental health*. 2009;12(6):441-446.

510. Wang L, Lin H, Lin C, Chen Y. Increased risk of adverse pregnancy outcomes in women receiving zolpidem during pregnancy. *Clinical Pharmacology & Therapeutics*. 2010;88(3):369-374.
511. Wikner BN, Källén B. Are hypnotic benzodiazepine receptor agonists teratogenic in humans? *J Clin Psychopharmacol*. 2011;31(3):356.
512. Wilton L, Pearce G, Martin R, Mackay F, Mann R. The outcomes of pregnancy in women exposed to newly marketed drugs in general practice in England. *BJOG: An International Journal of Obstetrics & Gynaecology*. 1998;105(8):882-889.
513. Askew JP. Zolpidem addiction in a pregnant woman with a history of Second-trimester bleeding. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2007;27(2):306-308.
514. Ratiopharm Inc., ed. *Zopiclone (Ratio-zopiclone) product monograph*; December 2, 2005.
515. Sanofi Limited, ed. *Zopiclone (Imovane) australian product monograph*; October 14, 2009.
516. Diav-Citrin O, Okotore B, Lucarelli K, Koren G. Pregnancy outcome following first-trimester exposure to zopiclone: A prospective controlled cohort study. *Am J Perinatol*. 1999;16(4):157-160. doi: 10.1055/s-2007-993850.
517. Diav-Citrin O, Okotore B, Lucarelli K, Koren G. Zopiclone use during pregnancy. *Canadian Family Physician*. 2000;46(1):63-64.
518. Mathieu O, Masson F, Thompson MA., et al. Case report: In utero exposure and safe breastfeeding in two premature twins of a chronically treated mother with high doses of zopiclone. abstract. *Fundam Clin Pharmacol*. 2010;24(Suppl. S1):424.
519. Matheson I, Sande H, Gaillot J. The excretion of zopiclone into breast milk. *Br J Clin Pharmacol*. 1990;30(2):267-271.
520. Novartis Inc., ed. *Clozapine (Clozaril®) product monograph*; October 2011.
521. Actavis Elizabeth LLC., ed. *Carbamazepine tablets USP. product monograph*; 2006.
522. Matalon S, Schechtman S, Goldzweig G, Ornoy A. The teratogenic effect of carbamazepine: A meta-analysis of 1255 exposures. *Reproductive toxicology*. 2002;16(1):9-17.
523. Ornoy A, Cohen E. Outcome of children born to epileptic mothers treated with carbamazepine during pregnancy. *Arch Dis Child*. 1996;75(6):517-520.
524. Holmes LB, Mittendorf R, Shen A, Smith CR, Hernandez-Diaz S. Fetal effects of anticonvulsant polytherapies: Different risks from different drug combinations. *Arch Neurol*. 2011;68(10):1275.
525. Morrow J, Russell A, Guthrie E, et al. Malformation risks of antiepileptic drugs in pregnancy: A prospective study from the UK epilepsy and pregnancy register. *Journal of Neurology, Neurosurgery & Psychiatry*. 2006;77(2):193-198.
526. Werler MM, Ahrens KA, Bosco JL, et al. Use of antiepileptic medications in pregnancy in relation to risks of birth defects. *Ann Epidemiol*. 2011;21(11):842-850.
527. Jentink J, Dolk H, Loane MA, et al. Intrauterine exposure to carbamazepine and specific congenital malformations: Systematic review and case-control study. *BMJ: British Medical Journal*. 2010;341.
528. Tomson T, Battino D, Bonizzoni E, et al. Dose-dependent risk of malformations with antiepileptic drugs: An analysis of data from the EURAP epilepsy and pregnancy registry. *The Lancet Neurology*. 2011;10(7):609-617.
529. Kennedy D, Koren G. Identifying women who might benefit from higher doses of folic acid in pregnancy. *Canadian Family Physician*. 2012;58(4):394-397.
530. Matlow J, Koren G. Is carbamazepine safe to take during pregnancy? *Canadian Family Physician*. 2012;58(2):163-164.
531. Galbally M, Roberts M, Buist A. Mood stabilizers in pregnancy: A systematic review. *Aust N Z J Psychiatry*. 2010;44(11):967-977.
532. Meador K, Baker G, Browning N, et al. Effects of fetal antiepileptic drug exposure outcomes at age 4.5 years. *Neurology*. 2012;78(16):1207-1214.
533. Meador KJ, Baker GA, Browning N, et al. Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs. *N Engl J Med*. 2009;360(16):1597-1605.

534. Banach R, Boskovic R, Einarson T, Koren G. Long-term developmental outcome of children of women with epilepsy, unexposed or exposed prenatally to antiepileptic drugs. *Drug Safety*. 2010;33(1):73-79.
535. Forsberg L, Wide K, Källén B. School performance at age 16 in children exposed to antiepileptic drugs in utero—A population-based study. *Epilepsia*. 2011;52(2):364-369.
536. Meador KJ, Baker GA, Browning N, et al. Fetal antiepileptic drug exposure and verbal versus non-verbal abilities at three years of age. *Brain*. 2011;134(2):396-404.
537. Bromley RL, Mawer G, Love J, et al. Early cognitive development in children born to women with epilepsy: A prospective report. *Epilepsia*. 2010;51(10):2058-2065.
538. Pynnonen S, Kanto J, Sillanpaa M, Erkkola R. Carbamazepine: Placental transport, tissue concentrations in foetus and newborn, and level in milk. *Acta Pharmacol Toxicol (Copenh)*. 1977;41(3):244-253.
539. Niebyl JR, Blake DA, Freeman JM, Luff RD. Carbamazepine levels in pregnancy and lactation. *Obstetrics & Gynecology*. 1979;53(1):139-140.
540. Froescher W, Eichelbaum M, Niesen M, Dietrich K, Rausch P. Carbamazepine levels in breast milk. *Ther Drug Monit*. 1984;6(3):266-271.
541. Shimoyama R, Ohkubo T, Sugawara K. Monitoring of carbamazepine and carbamazepine 10, 11-epoxide in breast milk and plasma by high-performance liquid chromatography. *Ann Clin Biochem*. 2000;37(2):210-215.
542. Kaneko S, Sato T, Suzuki K. The levels of anticonvulsants in breast milk. *Br J Clin Pharmacol*. 1979;7(6):624-627.
543. Meador K, Baker G, Browning N, et al. Effects of breastfeeding in children of women taking antiepileptic drugs. *Neurology*. 2010;75(22):1954-1960.
544. Pfizer Canada Inc., ed. *Gabapentin (Neurontin) product monograph*; July 30, 2012.
545. Pfizer Inc., ed. *Gabapentin (Neurontin) product monograph*; July 2012b.
546. Montouris G. Gabapentin exposure in human pregnancy: Results from the gabapentin pregnancy registry. *Epilepsy & Behavior*. 2003;4(3):310-317.
547. Almgren M, Källén B, Lavebratt C. Population-based study of antiepileptic drug exposure in utero—Influence on head circumference in newborns. *Seizure*. 2009;18(10):672-675.
548. Wilton LV, Shakir S. A postmarketing surveillance study of gabapentin as Add-on therapy for 3,100 patients in England. *Epilepsia*. 2002;43(9):983-992.
549. Mølgaard-Nielsen D, Hviid A. Newer-generation antiepileptic drugs and the risk of major birth defects. *JAMA: The Journal of the American Medical Association*. 2011;305(19):1996.
550. Hernández-Díaz S, Smith C, Shen A, et al. Comparative safety of antiepileptic drugs during pregnancy. *Neurology*. 2012;78(21):1692-1699.
551. Kristensen JH, Ilett KF, Hackett LP, Kohan R. Gabapentin and breastfeeding: A case report. *Journal of Human Lactation*. 2006;22(4):426-428.
552. Öhman I, Vitols S, Tomson T. Pharmacokinetics of gabapentin during delivery, in the neonatal period, and lactation: Does a fetal accumulation occur during pregnancy? *Epilepsia*. 2005;46(10):1621-1624.
553. Glaxo SmithKline Inc., ed. *Lamotrigine (lamictal) product monograph*; January 27, 2012.
554. Glaxo SmithKline Inc., ed. *Lamotrigine (lamictal) product monograph*; December 2011.
555. Cunnington M, Weil J, Messenheimer J, Ferber S, Yerby M, Tennis P. Final results from 18 years of the international lamotrigine pregnancy registry. *Neurology*. 2011;76(21):1817-1823.
556. Holmes L, Baldwin E, Smith C, et al. Increased frequency of isolated cleft palate in infants exposed to lamotrigine during pregnancy. *Neurology*. 2008;70(22 Part 2):2152-2158.
557. Rambeck B, Kurlemann G, Stodieck S, May T, Jürgens U. Concentrations of lamotrigine in a mother on lamotrigine treatment and her newborn child. *Eur J Clin Pharmacol*. 1997;51(6):481-484.
558. Tomson T, Öhman I, Vitols S. Lamotrigine in pregnancy and lactation: A case report. *Epilepsia*. 1997;38(9):1039-1041.
559. Ohman I, Vitols S, Tomson T. Lamotrigine in pregnancy: Pharmacokinetics during delivery, in the neonate, and during lactation. *Epilepsia*. 2000;41(6):709-713.

560. Liporace J, Kao A, D'Abreu A. Concerns regarding lamotrigine and breast-feeding. *Epilepsy & Behavior*. 2004;5(1):102-105.
561. Newport DJ, Pennell PB, Calamaras MR, et al. Lamotrigine in breast milk and nursing infants: Determination of exposure. *Pediatrics*. 2008;122(1):e223-e231.
562. Nordmo E, Aronsen L, Wasland K, Småbrekke L, Vorren S. Severe apnea in an infant exposed to lamotrigine in breast milk. *Ann Pharmacother*. 2009;43(11):1893-1897.
563. Valeant Canada Ltd, ed. *Lithium (cabolith) product monograph*; February 22, 2007.
564. Roxane Laboratories., ed. *Lithium carbonate product monograph*; 2011.
565. Cohen LS, Friedman J, Jefferson JW, Johnson EM, Weiner ML. A re-evaluation of risk of in utero exposure to lithium. *JAMA: the journal of the American Medical Association*. 1994;271(2):146-150.
566. Jacobson S, Ceolin L, Kaur P, et al. Prospective multicentre study of pregnancy outcome after lithium exposure during first trimester. *The Lancet*. 1992;339(8792):530-533.
567. Schou M, Goldfield M, Weinstein M, Villeneuve A. Lithium and pregnancy—I, report from the register of lithium babies. *Br Med J*. 1973;2(5859):135.
568. Kallen B, Tanberg A. Lithium and pregnancy. A cohort study on manic-depression. *Acta Psychiatr Scand*. 1983;68:134-139.
569. Nora J, Nora A, Toews W. Letter: Lithium, Ebstein's anomaly, and other congenital heart defects. *Lancet*. 1974;2(7880):594.
570. Schou M, Amdisen A. Lithium and pregnancy—III, lithium ingestion by children breast-fed by women on lithium treatment. *Br Med J*. 1973;2(5859):138-138.
571. McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. Lithium toxicity profile: A systematic review and meta-analysis. *The Lancet*. 2012;379(9817):721-728.
572. Yonkers KA, Wisner KL, Stowe Z, et al. Management of bipolar disorder during pregnancy and the postpartum period. *Am J Psychiatry*. 2004;161(4):608-620.
573. Zalstein E, Koren G, Einarson T, Freedom RM. A case-control study on the association between first trimester exposure to lithium and Ebstein's anomaly. *Am J Cardiol*. 1990;65(11):817-818.
574. Gentile S. Lithium in pregnancy: The need to treat, the duty to ensure safety. *Expert opinion on drug safety*. 2012;11(3):425-437.
575. Sykes P, Quarrie J, Alexander F. Lithium carbonate and breast-feeding. *Br Med J*. 1976;2(6047):1299.
576. Tunnessen Jr WW, Hertz CG. Toxic effects of lithium in newborn infants: A commentary. *J Pediatr*. 1972;81(4):804.
577. Newport DJ, Viguera AC, Beach AJ, Ritchie JC, Cohen LS, Stowe ZN. Lithium placental passage and obstetrical outcome: Implications for clinical management during late pregnancy. *Am J Psychiatry*. 2005;162(11):2162-2170.
578. Ryan D., MD, personal communication, May 2013.
579. Bogen DL, Sit D, Genovese A, Wisner KL. Three cases of lithium exposure and exclusive breastfeeding. *Archives of Women's Mental Health*. 2012;15(1):69-72.
580. Moretti ME, Koren G, Verjee Z, Ito S. Monitoring lithium in breast milk: An individualized approach for breast-feeding mothers. *Ther Drug Monit*. 2003;25(3):364-366.
581. Janssen Inc., ed. *Topiramate (Topamax) product monograph*; August 20, 2012.
582. Janssen Ortho LLC, ed. *Topiramate (Topamax) product monograph*; October 2012.
583. Hunt S, Russell A, Smithson W, et al. Topiramate in pregnancy preliminary experience from the UK epilepsy and pregnancy register. *Neurology*. 2008;71(4):272-276.
584. Ornoy A, Zvi N, Arnon J, Wajnberg R, Shechtman S, Diav-Citrin O. The outcome of pregnancy following topiramate treatment: A study on 52 pregnancies. *Reproductive Toxicology*. 2008;25(3):388-389.
585. Green MW, Seeger JD, Peterson C, Bhattacharyya A. Utilization of topiramate during pregnancy and risk of birth defects. *Headache: The Journal of Head and Face Pain*. 2012;52(7):1070-1084.
586. Vajda F, Graham J, Roten A, Lander C, O'Brien T, Eadie M. Teratogenicity of the newer antiepileptic drugs—the Australian experience. *Journal of Clinical Neuroscience*. 2012;19(1):57-59.

587. Margulis AV, Mitchell AA, Gilboa SM, et al. Use of topiramate in pregnancy and risk of oral clefts. *Obstet Gynecol.* 2012.
588. Rihtman T, Parush S, Ornoy A. Preliminary findings of the developmental effects of in utero exposure to topiramate. *Reproductive Toxicology.* 2012.
589. Gorman MP, Soul JS. Neonatal hypocalcemic seizures in siblings exposed to topiramate in utero. *Pediatr Neurol.* 2007;36(4):274-276.
590. Öhman I, Vitols S, Luef G, Söderfeldt B, Tomson T. Topiramate kinetics during delivery, lactation, and in the neonate: Preliminary observations. *Epilepsia.* 2002;43(10):1157-1160.
591. Abbott Laboratories Limited, ed. *Valproic acid (depakene) product monograph*; September 10, 2010.
592. Abbott Laboratories Limited, ed. *Valproic acid (depakene) US product monograph*; November 2009.
593. Vajda FJ, O'brien TJ, Hitchcock A, et al. Critical relationship between sodium valproate dose and human teratogenicity: Results of the Australian register of anti-epileptic drugs in pregnancy. *Journal of Clinical Neuroscience: Official Journal of the Neurosurgical Society of Australasia.* 2004;11(8):854.
594. Vajda F, Eadie M. Maternal valproate dosage and foetal malformations. *Acta Neurol Scand.* 2005;112(3):137-143.
595. CDC. Valproate: A new cause of birth defects -- report from Italy and follow-up from France. *MMWR Weekly.* 1983;32(33):438-439.
596. Winter R, Donnai D, Burn J, Tucker S. Fetal valproate syndrome: Is there a recognisable phenotype? *J Med Genet.* 1987;24(11):692-695.
597. Jentink J, Loane MA, Dolk H, et al. Valproic acid monotherapy in pregnancy and major congenital malformations. *N Engl J Med.* 2010;362(23):2185-2193.
598. Jäger-Roman E, Deichl A, Jakob S, et al. Fetal growth, major malformations, and minor anomalies in infants born to women receiving valproic acid. *J Pediatr.* 1986;108(6):997-1004.
599. Thisted E, Ebbesen F. Malformations, withdrawal manifestations, and hypoglycaemia after exposure to valproate in utero. *Arch Dis Child.* 1993;69(3 Spec No):288-291.
600. Ebbesen F, Joergensen A, Hoseth E, et al. Neonatal hypoglycaemia and withdrawal symptoms after exposure in utero to valproate. *Archives of Disease in Childhood-Fetal and Neonatal Edition.* 2000;83(2):F124-F129.
601. Moore S, Turnpenny P, Quinn A, et al. A clinical study of 57 children with fetal anticonvulsant syndromes. *J Med Genet.* 2000;37(7):489-497.
602. Williams G, King J, Cunningham M, Stephan M, Kerr B, Hersh JH. Fetal valproate syndrome and autism: Additional evidence of an association. *Developmental Medicine & Child Neurology.* 2001;43(3):202-206.
603. Von Unruh G, Froescher W, Hoffmann F, Niesen M. Valproic acid in breast milk: How much is really there? *Ther Drug Monit.* 1984;6(3):272-276.
604. Philbert A, Pedersen B, Dam M. Concentration of valproate during pregnancy, in the newborn and in breast milk. *Acta Neurol Scand.* 1985;72(5):460-463.
605. Piontek CM, Baab S, Peindl KS, Wisner KL. Serum valproate levels in 6 breastfeeding mother-infant pairs. *J Clin Psychiatry.* 2000;61(3):170.
606. Stahl M, Neiderud J, Vinge E. Thrombocytopenic purpura and anemia in a breast-fed infant whose mother was treated with valproic acid. *J Pediatr.* 1997;130(6):1001-1003.
607. Bristol-Myers Squibb Canada., ed. *Aripiprazole (abilify®) product monograph*; February 1, 2013.
608. Bristol-Myers Squibb., ed. *Aripiprazole (Abilify®) product monograph*; February 2012.
609. Boden R, Lundgren M, Brandt L, Reutfors J, Kieler H. Antipsychotics during pregnancy: Relation to fetal and maternal metabolic effects. *Arch Gen Psychiatry.* 2012;69(7):715-721. doi: 10.1001/archgenpsychiatry.2011.1870; 10.1001/archgenpsychiatry.2011.1870.
610. Mendhekar D, Sharma J, Srilakshmi P. Use of aripiprazole during late pregnancy in a woman with psychotic illness. *Ann Pharmacother.* 2006;40(3):575-575.
611. Mendhekar D, Sunder KR, Andrade C. Aripiprazole use in a pregnant schizoaffective woman. *Bipolar Disord.* 2006;8(3):299-300.

612. Watanabe N, Kasahara M, Sugibayashi R, et al. Perinatal use of aripiprazole: A case report. *J Clin Psychopharmacol*. 2011;31(3):377.
613. Lutz UC, Hiemke C, Wiatr G, Farger G, Arand J, Wildgruber D. Aripiprazole in pregnancy and lactation: A case report. *J Clin Psychopharmacol*. 2010;30(2):204-205.
614. Schlotterbeck P, Leube D, Kircher T, Hiemke C, Gründer G. Aripiprazole in human milk. *The International Journal of Neuropsychopharmacology*. 2007;10(03):433-433.
615. Merck Canada Inc., ed. *Asenapine (Saphris®) product monograph*; February 13, 2013.
616. Merck & Co Inc., ed. *Asenapine (Saphris®) product monograph*; October 2012.
617. Novartis Pharmaceuticals Canada Inc., ed. *Clozapine (clozaril®) product monograph*; February 14, 2013.
618. Trixler M, Tényi T. Antipsychotic use in pregnancy. *Drug safety*. 1997;16(6):403-410.
619. Dev V, Krupp P. The side effects and safety of clozapine. *Rev Contemp Pharmacother*. 1995;6:197-208.
620. Barnas C, Bergant A, Hummer M, Saria A, Fleischhacker WW. Clozapine concentrations in maternal and fetal plasma, amniotic fluid, and breast milk. *Am J Psychiatry*. 1994;151(6):945.
621. Iqbal MM, Aneja A, Rahman A, et al. The potential risks of commonly prescribed antipsychotics: During pregnancy and lactation. *Psychiatry (Edgmont)*. 2005;2(8):36.
622. Gupta N, Grover S. Safety of clozapine in 2 successive pregnancies. *Can J Psychiatry*. 2004;49:863.
623. Newham JJ, Thomas SH, MacRitchie K, McElhatton PR, McAllister-Williams RH. Birth weight of infants after maternal exposure to typical and atypical antipsychotics: Prospective comparison study. *The Br J Psychiatry*. 2008;192(5):333-337.
624. Makikyro T, Leinonen E, Koponen H. Early developmental differences between DSM-III-R schizophrenics treated with clozapine and typical neuroleptics. *J Psychiatr Res*. 1998;32(2):105-110.
625. Eli Lilly Canada Inc., ed. *Olanzapine (Zyprexa®) product monograph*; February 11, 2013.
626. Lilly USA., ed. *Olanzapine (Zyprexa®) product monograph*; June 2, 2011.
627. McKenna K, Koren G, Tetelbaum M, et al. Pregnancy outcome of women using atypical antipsychotic drugs: A prospective comparative study. *J Clin Psychiatry*. 2005;66(4):444-449.
628. Goldstein DJ, Corbin LA, Fung MC. Olanzapine-exposed pregnancies and lactation: Early experience. *J Clin Psychopharmacol*. 2000;20(4):399.
629. Gilad O, Merlob P, Stahl B, Klinger G. Outcome of infants exposed to olanzapine during breastfeeding. *Breastfeeding Medicine*. 2011;6(2):55-58.
630. Newport D, Calamaras M, DeVane C, et al. Atypical antipsychotic administration during late pregnancy: Placental passage and obstetrical outcomes. *Am J Psychiatry*. 2007;164(8):1214-1220.
631. Littrell KH, Johnson CG, Peabody CD, Hilligoss N. Antipsychotics during pregnancy. *Am J Psychiatry*. 2000;157(8):1342-1342.
632. Vemuri MP, Rasgon NL. A case of olanzapine-induced gestational diabetes mellitus in the absence of weight gain. *J Clin Psychiatry*. 2007;68(12):1989-1989.
633. Gentile S. Prophylactic treatment of bipolar disorder in pregnancy and breastfeeding: Focus on emerging mood stabilizers. *Bipolar Disord*. 2006;8(3):207-220.
634. Babu GN, Desai G, Tippeswamy H, Chandra PS. Birth weight and use of olanzapine in pregnancy: A prospective comparative study. *J Clin Psychopharmacol*. 2010;30(3):331.
635. Spyropoulou A, Zervas I, Soldatos C. Hip dysplasia following a case of olanzapine exposed pregnancy: A questionable association. *Archives of women's mental health*. 2006;9(4):219-222.
636. Gardiner SJ, Kristensen JH, Begg EJ, et al. Transfer of olanzapine into breast milk, calculation of infant drug dose, and effect on breast-fed infants. *Am J Psychiatry*. 2003;160(8):1428-1431.
637. Lutz UC, Wiatr G, Orlikowsky T, Gaertner H, Bartels M. Olanzapine treatment during breast feeding: A case report. *Ther Drug Monit*. 2008;30(3):399-401.
638. Janssen Inc., ed. *Paliperidone (Invega®) and Invega sustenna® product monographs*; November 16, 2012a.
639. Janssen Pharmaceuticals Inc., ed. *Paliperidone (invega®) product monographs*; 2011.

640. Hill RC, McIvor RJ, Wojnar-Horton RE, Hackett LP, Ilett KF. Risperidone distribution and excretion into human milk: Case report and estimated infant exposure during breast-feeding. *J Clin Psychopharmacol*. 2000;20(2):285-286.
641. Ilett KF, Hackett LP, Kristensen JH, Vaddadi KS, Gardiner SJ, Begg EJ. Transfer of risperidone and 9-hydroxyrisperidone into human milk. *Ann Pharmacother*. 2004;38(2):273-276.
642. Aichhorn W, Stuppaeck C, Whitworth A. Risperidone and breast-feeding. *Journal of Psychopharmacology*. 2005;19(2):211-213.
643. Weggelaar NM, Keijer WJ, Janssen PK. A case report of risperidone distribution and excretion into human milk: How to give good advice if you have not enough data available. *J Clin Psychopharmacol*. 2011;31(1):129-131.
644. AstraZeneca Canada Inc. Quetiapine (Seroquel®) and Seroquel XR® product monographs. March 26, 2012.
645. AstraZeneca Pharmaceuticals LP, ed. *Quetiapine (Seroquel®) product monograph*; December, 2011.
646. LEE A, GIESBRECHT E, DUNN E, ITO S. Excretion of quetiapine in breast milk. *Am J Psychiatry*. 2004;161(9):1715-a-1716.
647. Rampono J, Kristensen JH, Ilett KF, Hackett LP, Kohan R. Quetiapine and breast feeding. *Ann Pharmacother*. 2007;41(4):711-714.
648. Janssen Inc., ed. *Risperidone (Risperdal®) and risperdal consta® product monographs*; February 25, 2013b.
649. Janssen Pharmaceuticals Inc., ed. *Risperidone (Risperdal®) and risperdal consta® product monographs*; June/August 2012b.
650. Coppola D, Russo LJ, Kwarta Jr RF, Varughese R, Schmider J. Evaluating the postmarketing experience of risperidone use during pregnancy. *Drug Safety*. 2007;30(3):247-264.
651. Grover S, Avasthi A. Risperidone in pregnancy: A case of oligohydramnios. *German J Psychiatry*. 2004;7:56-57.
652. Kim S, Kim K, Kim J, et al. Use of long-acting injectable risperidone before and throughout pregnancy in schizophrenia. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 2007;31(2):543-545.
653. Mishra AC, Mohanty B. Lactational exposure to atypical antipsychotic drugs disrupts the pituitary-testicular axis in mice neonates during post-natal development. *Journal of Psychopharmacology*. 2010;24(7):1097-1104.
654. Pfizer Canada Inc., ed. *Ziprasidone (Zeldox®) product monograph*; October 24, 2011.
655. Pfizer Inc., ed. *Ziprasidone (Geodon®) product monograph*; October 2012.
656. Schlotterbeck P, Saur R, Hiemke C, et al. Low concentration of ziprasidone in human milk: A case report. *Int J Neuropsychopharmacol*. 2009;12(3):437-438. doi: 10.1017/S1461145709009936; 10.1017/S1461145709009936.
657. Bristol-Myers Squibb Canada., ed. *Fluphenazine (Modecate®) product monograph*; November 16, 2011.
658. Canadian Pharmacists Association., ed. *Fluphenazine monograph*. Available from: Compendium of Pharmaceuticals and Specialties, online version (e-CPS); October 2010.
659. Apotex Inc, ed. *Fluphenazine (apo-fluphenazine®) product monograph*; February 21, 2012.
660. Merlob P, Stahl B, Maltz E. Is fluphenazine a teratogen? *Am J Med Genet*. 1994;52(2):231-232.
661. Mazzotta P, Magee LA. A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. *Drugs*. 2000;59(4):781-800.
662. Koren G. Misrepresentation and miscommunication of teratogenic risk of drugs; analysis of three highly publicized international cases. *Reprod Toxicol*. 2001;15(1):1-3.
663. Cleary M. Fluphenazine decanoate during pregnancy. *Am J Psychiatry*. 1977;134(7):815-816.
664. Hill RM, Desmond MM, Kay JL. Extrapyrmidal dysfunction in an infant of a schizophrenic mother. *J Pediatr*. 1966;69(4):589-595.
665. O'Connor M, Johnson GH, James DI. Intrauterine effect of phenothiazines. *Med J Aust*. 1981;1(8):416-417.
666. Nath SP, Miller DA, Muraskas JK. Severe rhinorrhea and respiratory distress in a neonate exposed to fluphenazine hydrochloride prenatally. *Ann Pharmacother*. 1996;30(1):35-37.

667. Apotex Inc., ed. *Haloperidol (apo-haloperidol®) product monograph*; January 28, 2013.
668. Canadian Pharmacists Association., ed. *Haloperidol – haloperidol decanoate monograph*. Compendium of Pharmaceuticals and Specialties, online version (e-CPS). © Canadian Pharmacists Association; August 2012.
669. Pfizer Inc., ed. *Haloperidol product monograph*; April 2011.
670. Diav-Citrin O, Shechtman S, Ornoy S, et al. Safety of haloperidol and penfluridol in pregnancy: A multicenter, prospective, controlled study. *J Clin Psychiatry*. 2005;66(3):317-322.
671. Hanson JW, Oakley Jr GP. Haloperidol and limb deformity. *JAMA: the journal of the American Medical Association*. 1975;231(1):26-26.
672. Kopelman AE, McCullar FW, Heggeness L. Limb malformations following maternal use of haloperidol. *JAMA: the journal of the American Medical Association*. 1975;231(1):62-64.
673. Hansen LM, Megerian G, Donnenfeld AE. Haloperidol overdose during pregnancy. *Obstetrics & Gynecology*. 1997;90(4, Part 2):659-661.
674. Collins KO, Comer JB. Maternal haloperidol therapy associated with dyskinesia in a newborn. *American Journal of Health-system Pharmacy*. 2003;60(21):2253-2255.
675. Sexson WR, Barak Y. Withdrawal emergent syndrome in an infant associated with maternal haloperidol therapy. *J Perinatol*. 1989;9(2):170-172.
676. Kuniyoshi M, Inanaga K. Haloperidol and biperiden plasma levels in a pregnant atypical psychotic woman and a neonate--a case report. *Kurume Med J*. 1985;32(3):199-202.
677. Einer-Jensen N, Secher N. Diminished weight of rat foetuses after treatment of pregnant rats with haloperidol. *J Reprod Fertil*. 1970;22(3):591-594.
678. Yoshida K, Smith B, Kumar R. Psychotropic drugs in mothers' milk: A comprehensive review of assay methods, pharmacokinetics and of safety of breast-feeding. *Journal of Psychopharmacology*. 1999;13(1):64-80.
679. Yoshida K, Smith B, Craggs M, Kumar R. Neuroleptic drugs in breast-milk: A study of pharmacokinetics and of possible adverse effects in breast-fed infants. *Psychol Med*. 1998;28(1):81-91.
680. Whalley L, Blain P, Prime J. Haloperidol secreted in breast milk. *Br Med J (Clin Res Ed)*. 1981;282(6278):1746.
681. Stewart R, Karas B, Springer P. Haloperidol excretion in human milk. *Am J Psychiatry*. 1980;137(7):849-850.
682. Canadian Pharmacists Association., ed. *Loxapine monograph*. Compendium of Pharmaceuticals and Specialties, online version (e-CPS); October 2010.
683. Lannett Company Inc., ed. *Loxapine product monograph*; August 2011.
684. Pharmel Inc., ed. *Loxapine (Phl-loxapine®) product monograph*; June 17, 2004.
685. Pharmascience Inc., ed. *Loxapine (Xylax®) product monograph*; May 15, 2012.
686. Heel R, Brogden R, Speight T, Avery G. Loxapine: A review of its pharmacological properties and therapeutic efficacy as an antipsychotic agent. *Drugs*. 1978;15(3):198-217.
687. Perinatal Services BC. Obstetric guideline 19: Maternity care pathway. 2010;19. Accessed June 5, 2013.



**BC MENTAL HEALTH
& SUBSTANCE USE SERVICES**

An agency of the Provincial Health Services Authority

BC Reproductive Mental Health

Mental Health Building (Room p1-228)

4500 Oak Street

Vancouver, BC V6H 3N1

Tel: 604 875 2025.

www.reproductivementalhealth.ca



Perinatal Services BC

An agency of the Provincial Health Services Authority

Perinatal Services BC

West Tower, Suite 350

555 West 12th Avenue

Vancouver, BC Canada V5Z 3X7

Tel: 604-877-2121

www.perinatalservicesbc.ca

The purpose of these guidelines is to support healthcare providers in the detection and coordinated treatment of pregnant and postpartum women with mental health challenges and disorders. Every attempt has been made to ensure that the information contained herein is clinically accurate and current but some issues may be subject to practice interpretation. Decision-making in a specific context is the responsibility of attending healthcare providers. Nothing contained in these guidelines should in any way be construed as being either official or unofficial policy of British Columbia Mental Health Society Branch, Children's and Women's Health Centre of British Columbia Branch, Perinatal Services BC or Provincial Health Services Authority (together, the 'Societies'). The Societies assume no responsibility or liability arising from any error in or omission of information or from any use of any information, link, contact, opinion or advice provided in the Guide.