SOGC CLINICAL PRACTICE GUIDELINE

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No. 454, October 2024

Guideline No. 454: Identification and Treatment of Perinatal Mood and Anxiety Disorders

(En français : Identification et traitement des troubles périnataux de l'humeur et de l'anxiété)

The English document is the original version; translation may introduce small differences in the French version.

This clinical practice guideline was prepared by the authors, reviewed by the SOGC Clinical Obstetrics Committee (2023), and approved by the SOGC Guideline Management and Oversight Committee (2024).

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Informed consent: Everyone has the right and responsibility to make informed decisions about their care together with their health care providers. To facilitate this, the SOGC recommends that health care providers provide patients with information and support that is evidence-based, culturally appropriate, and personalized.

Language and inclusivity: The SOGC recognizes the importance to be fully inclusive and when context is appropriate, gender-neutral language will be used. In other circumstances, we continue to use gendered language because of our mission to advance women's health. The SOGC recognizes and respects the rights of all people for whom the information in this document may apply, including but not limited to transgender, non-binary, and intersex people. The SOGC encourages health care providers to engage in respectful conversation with their patients about their gender identity and preferred gender pronouns and to apply these guidelines in a way that is sensitive to each person's needs

Weeks Gestation Notation: The authors follow the World Health Organization's notation on gestational age: the first day of the last menstrual period is day 0 (of week 0); therefore, days 0 to 6 correspond to completed week 0, days 7 to 13 correspond to completed week 1, etc.

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KEY MESSAGES

- Perinatal mental illness (mental health issues and psychiatric disorders during and after pregnancy, up to the first year following delivery) is a major public health issue; it is a common complication during pregnancy and the first year after delivery.
- Perinatal mood and anxiety disorders are the most common forms of perinatal mental illness.
- Untreated perinatal mood and anxiety disorders have shortand long-term consequences on maternal health, fetal development, and longer-term physical and mental health.
- Health care providers can play an essential role in identifying perinatal mood and anxiety disorders and facilitating timely access to pharmacotherapy and/or psychosocial support and treatment.
- Risk factors for perinatal mood and anxiety disorders include perinatal loss, experience of intimate partner violence, and history of mental health issues.
- 6. Certain groups are more likely to experience perinatal mental illness, including perinatal mood and anxiety disorders, as well as barriers to care. These groups include, but are not limited to, individuals who are racialized minorities, immigrants and refugees, adolescents, and 2SLGBTQ+ individuals, as well as those living in poverty, experiencing unstable housing and food insecurity, and actively using substances and/or experiencing addiction.
- Patient-centred care, using a culturally, gender- and traumainformed care approach is important when caring for patients with perinatal mood and anxiety disorders.

DEFINITIONS

Assessment: The process of defining the nature of a problem. It can start with questions about medical history and risk factors. If risk factors are identified, the use of a validated screening tool is warranted (screening).

Screening: A medical test (including validated questionnaires) or procedure that is performed to assess the likelihood of having a particular disease or health condition. Screening is not diagnostic, but rather identifies the need for further evaluation. Perinatal period: From conception up to the first year after delivery.

Postpartum period: Inclusive of the 12 months following delivery.

ABSTRACT

Objective: To help perinatal health care providers identify and assist pregnant and postpartum patients with perinatal mental illness, specifically perinatal mood and anxiety disorders. Areas of focus include risk factors and identification, screening, treatment, and referral

Target Population: All individuals who are pregnant or in the first year postpartum.

Outcomes: Open dialogue and evidence-informed care for perinatal mood and anxiety disorders, including competency for identification, screening, treatment, and referral, which will lead to improvements in patient care.

Benefits, Harms, and Costs: Pregnant and postpartum individuals with untreated perinatal mental illness, including mood and anxiety disorders, may suffer devastating effects and their family may experience short- and long-term adverse outcomes.

Evidence: A literature search was conducted using Medline (Ovid), PubMed, Embase and the Cochrane library from inception to June 2024. Additional articles were identified from article bibliographies and grey literature published by reputable societies and organizations (see online Appendix A).

Validation Methods: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See online Appendix B (Tables B1 for definitions and B2 for interpretations of strong and weak recommendations).

Intended Audience: All heath care providers who provide preconception counselling and/or care during pregnancy and the postpartum period. The term "perinatal" will be used throughout this guideline to refer to these health care providers.

Social Media Abstract: New SOGC Guideline! Identify, support, and treat perinatal mood and anxiety disorders. Focused on risk factors, screening, treatment and referrals during pregnancy and the postpartum period. Let's open dialogue and provide evidenceinformed care for improved patient outcomes.

SUMMARY STATEMENTS:

 Perinatal mood and anxiety disorders are common (high); postpartum depression and anxiety are the most common maternal complications of pregnancy (high).

- 2. The psychological aspects of the transition to parenthood are important factors that affect perinatal mental health (*moderate*).
- 3. Suicide in the perinatal period is emerging as one of the most common causes of maternal mortality in Canada (*moderate*).
- Symptoms of anxiety or depression during pregnancy are highly predictive of postpartum mental illness (high).
- 5. Untreated depression or anxiety during pregnancy is associated with adverse perinatal outcomes, including persistent depression in pregnant patients and their partners, maternal self-harm, low birth weight, preterm birth, and poor infant development (high).
- Experiencing a perinatal loss, having a history of previous mental illness, and intimate partner violence are important risk factors for perinatal mood and anxiety disorders (high).
- Race, culture, language, ability, age, and sexual identity may contribute to an individual's risk for perinatal mental illness (high).
- 8. Perinatal care providers may be the patients's first point of contact with the health care system as well as the first health care provider to establish a positive and trusting relationship with them. They play an important role in identification, screening, and referral for perinatal mood and anxiety disorders (moderate).
- 9. Different treatment approaches/intensities may be required, depending on the severity of illness and individual preferences (high).
- Most of the common pharmacologic agents to treat perinatal mood and anxiety disorders are not teratogenic (high).
- Tapering or stopping antidepressant medication during pregnancy can lead to relapse in patients with history of severe disease (moderate).
- 12. Pregnant and postpartum individuals will benefit from counselling focused on shared decision-making (*moderate*).

RECOMMENDATIONS

IDENTIFICATION AND RISK

- 1. Perinatal death or losing custody of the infant both increase a patient's vulnerability for mental illness, and additional monitoring and support may be needed in these circumstances (*strong*, *high*).
- 2. For patients who have experienced trauma, education to help reduce fears related to childbirth should be provided (*strong, moderate*).
- A review of health history should be included in mental health assessments, and risk factors should be discussed during preconception counselling and/or during pregnancy (strong, high).
- Perinatal care providers should inquire about mental health status at each visit throughout pregnancy and in the year following the pregnancy, especially in circumstances of perinatal loss (strong, high).

SCREENING

5. Screening should be complemented with a clearly defined and locally tailored referral process (*strong*, *high*).

- Patients with risk factors for mood and anxiety disorders should be screened at least once during pregnancy and once during the postpartum period using a validated screening tool (e.g., Edinburgh Postnatal Depression Scale, Personalized Health Questionnaire-9, Generalized Anxiety Disorder-7) (strong, moderate).
- 7. When a concern about mental health is identified by the patient or provider, the patient should be screened at that visit using a validated screening tool (e.g., Edinburgh Postnatal Depression Scale, Personalized Health Questionnaire-9, Generalized Anxiety Disorder-7) (strong, moderate).
- 8. Perinatal care providers should provide information about psychosocial and community-based supports (in person, virtual, or hybrid models) with patients presenting with perinatal mental health concerns (*strong, moderate*).

TREATMENT

- For pregnant and postpartum patients with moderate perinatal depression or anxiety, health care providers should recommend psychoeducation, psychotherapy, pharmacological therapy, or a combination of these approaches as first-line treatment (*strong*, *high*).
- 10. Perinatal care providers should recommend that patients with perinatal mood or anxiety disorders receive routine counselling about the psychological aspects of the transition to parenthood and other important factors that can affect perinatal mental health (strong, moderate).
- 11. The health care provider should have a comprehensive discussion about possible maternal, fetal, and neonatal risks and side effects to initiating, continuing, or changing medication as well as its benefits (strong, high).
- 12. Patients with pre-existing mental health diagnoses who are well maintained on pharmacological agents should not abruptly discontinue medication during pregnancy. Patients should speak to their mental health clinician and obstetrical care provider prior to considering discontinuation or tapering medications during pregnancy (strong, moderate).
- 13. Patients taking certain pharmacologic agents (see online Appendix C) should be referred for preconception counselling by their health care provider; if the patient is already pregnant, consultation with a psychiatrist is warranted, particularly for individuals with mental disorders such as bipolar disorder and schizophrenia (strong, high).
- 14. Pregnant individuals with a severe perinatal mood or anxiety disorder should be urgently referred by their care provider to specialized psychiatric services with immediate action (strong, high).
- Shared decision-making regarding treatment options should consider the patient's values, beliefs, and preferences (strong, moderate).

INTRODUCTION

What is Perinatal Mental Illness?

Perinatal mental illness (PMI) encompasses mental health issues and psychiatric disorders during and after pregnancy, up to one year following delivery. PMI can include both pre-existing and new onset mental health problems, and some data suggest that almost half of pregnant patients may experience PMI.² Studies show that mood (i.e., depression) and anxiety disorders are the most common presentations in pregnancy and are frequently encountered in clinical care.³ Although this guideline will briefly discuss other perinatal mental health conditions, mood and anxiety disorders will be the primary focus.

Summary Statement 1

Why is Perinatal Mental Illness Important?

The transition to parenthood may be difficult,⁴ and the perinatal period, from conception up to one year after delivery, is a time of increased vulnerability for individuals with pre-existing mental illness or risk factors specific to PMI. Untreated or poorly managed PMI can adversely affect maternal, partner, fetal, and infant health, and the consequences can be significant and persistent.^{5,6} For example, prenatal depression and anxiety have been associated with poor prenatal nutrition, preterm birth, low birth weight, and decreased initiation of breast feeding⁷⁻⁹; when untreated, these conditions have been linked to persistent depression in pregnant patients and their partners, 10,11 maternal selfharm, and maternal suicide. 12,13 In fact, PMI is emerging as a key contributing factor to maternal mortality in the United Kingdom, 14 the United States, 15 and Canada. 16 Symptoms of anxiety or depression during pregnancy also predict postpartum mental illness symptoms.¹

ABBREVIATIONS

ADHD attention-deficit/hyperactivity disorder DSM-5-TR Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision GAD generalized anxiety disorder OCD obsessive-compulsive disorder PMI perinatal mental illness PPD postpartum depression **PTSD** posttraumatic stress disorder SSRI selective serotonin reuptake inhibitor

Data show that untreated PMI can have acute and long-term effects on infants and children in terms of impaired parental-infant interactions, 18 impaired cognitive or psychosocial development, 19 and poor infant developmental outcomes at 12 months of age.²⁰ Parental mental illness increases vulnerability to adverse childhood experiences, 21 and studies show that the mother's mental health during pregnancy and the first year postpartum plays a defining role in the cognitive, social, and emotional development of the child.²²

Some of the effects on maternal and child outcomes result from biological impacts of PMI, while others result from living in an environment where a parent has untreated PMI. For example, maternal mental health has epigenetic impacts that can affect long-term health, including cardiovascular and metabolic risk, 23 altered behaviour, and neuropsychiatric disorders. Age-related brain diseases are also influenced by the epigenome. 24-26 Mechanisms have been shown to include disruption of the fetal adaptation process²³ and DNA methylation of the developing fetus's genes, which appear to be particularly vulnerable later in gestation.²⁷ Given the impact of fetal development and programming on later postnatal health trajectories, 28 ensuring the physical and mental well-being of pregnant individuals is an important step toward healthiest outcomes.

In addition to the impacts of PMI on fetal development through biological mechanisms, children living with a parent with a mental health disorder may be at higher risk of developing psychiatric²⁹ and neurodevelopmental problems later in life, 30-33 experiencing poor physical health, and premature death. 34,35 Blair et al. reported that children whose mothers were depressed when the child was 1 year of age were at higher risk of behavioural problems and poor social functioning at age 9, signalling the need for early and repeated maternal depression screening. 36

Although few systematic investigations have been conducted to examine whether maternal mental health interventions can reduce potential negative impacts on children's outcomes, emerging data suggest that interventions for perinatal depression were effective at reducing maternal depressive symptoms and also led to improved infant growth and vaccine uptake as well as improved stress reactivity in infants.^{37,38} Larger randomized controlled trials (RCTs) are required to detect clinically meaningful effects from other interventions and on broader outcomes.

Summary Statements 2, 3, 4, and 5

PREVALENCE AND TYPES OF PERINATAL MENTAL ILLNESS

Prevalence of Perinatal Mental Illness

The estimated prevalence of PMI varies based on the diagnostic criteria (e.g., self-report vs. clinical interview) and timing of assessment (e.g., antenatal vs. postpartum). The 2019 report Maternal Mental Health in Canada noted that almost one-quarter (23%) of mothers who recently gave birth reported symptoms consistent with postpartum depression (PPD) or postpartum anxiety. ³⁹ Limited data in Canada about prevalence of different types of PMIs are shown in Table 1.

Types of Perinatal Mental Illness

Mood Disorders

Mood disorders are characterized by marked disruptions in emotions; marked lows in mood are referred to as depression, while elevated mood is referred to as hypomania or mania. The *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, Text Revision (DSM-5-TR) has broadly categorized mood disorders as bipolar disorders and depressive disorders.

Depressive Disorders

Depressive disorders are characterized by severe lows in mood or sadness that is severe or sufficiently persistent as to interfere with functioning.⁴⁰ Depressive disorders include major depressive disorder, persistent depressive

Table 1	Prevalence	of Parinatal	Mental Illness
Table 1.	Frevalence	oi Permatai	wentai iiiiess

	Prevalence, %		
Mental Illness	During pregnancy	After delivery	
Depressive and anxiety disorders			
Mood disorders 131,132	6-19	23*	
Anxiety disorders 131,133	2-29	23*	
Tokophobia ¹³⁴	14	N/A	
Sleep-wake disorders ¹³⁵	16-19	5-11	
Trauma-related disorders ¹³⁶	3-18	4-15	
Obsessive-compulsive and related disorders 137	2.9	7	
Bipolar disorder ¹³⁸	2-8	2-8	
Postpartum psychosis ¹³⁹	N/A	0.008-0.02	
Eating disorders 140,141	5	2-12	

^{*}Denotes prevalence in Canada.

N/A: not applicable

disorder (dysthymia), and premenstrual dysphoric disorder, as well as those that occur in relation to substance use.

Postpartum Depression

PPD is defined as a major depressive disorder episode that has an onset within the first 4-6 weeks following delivery, but many experts identify PPD as occurring within the first 12 months after delivery. For a major depressive disorder episode, postpartum or otherwise, the DSM-5-TR states that symptoms must be present for at least 2 weeks and should include at least 5 of the symptoms presented in Box 1. Households and the symptoms are sented in Box 1.

PPD should not be confused with the "baby blues" which can occur in up to 76% of individuals during the first 2 weeks postpartum and includes mood swings, crying episodes, increased anxiety, and difficulty sleeping. When these symptoms persist *beyond* 2 weeks and impair functioning, the clinician should consider a diagnosis of PPD. It is crucial to provide psychoeducation to all patients and their partners as individuals without any prior history of depression may also experience PPD. For women at higher risk for PMI, an earlier follow-up visit in the postpartum period may be considered to provide an opportunity for a mental health check-in.

Bipolar Disorders

Bipolar disorders represent a group of brain disorders that may cause extreme fluctuations in a person's mood, energy, and ability to function, and are further categorized as bipolar 1 disorder, bipolar 2 disorder, and cyclothymia. Bipolar 1 disorder can exist both with or without psychotic symptoms, while bipolar 2 disorder is typically less severe and does not significantly impair function. Cyclothymia is a cyclic disorder that causes brief episodes of hypomania and depression. A history of a bipolar disorder is a risk factor for postpartum psychosis, which should be discussed with the patient during pregnancy.

Postpartum Psychosis

Postpartum psychosis is a medical emergency that can present in the first 4 weeks following childbirth, but more

Box 1. Symptoms of postpartum depression

- Low mood, sleep (increased or decreased)
- · Interest (decreased)
- Guilt or hopelessness
- Energy (decreased)
- Concentration (decreased)
- Appetite (increased or decreased)
- Psychomotor changes (agitation or retardation)

often within hours to a few days. This rare disorder often has an acute and rapid onset and is characterized by lability of mood, paranoia, grandiosity or bizarre delusions, confused thinking, and grossly disorganized behaviour. The associated impaired insight and psychotic symptoms can put both the mother and infant at risk.

Many patients who develop postpartum psychosis have a history of bipolar disorder or schizoaffective disorder, further supporting the need for the perinatal care provider to elicit information on past mental health. However, an episode that occurs following delivery may also be the first presentation for bipolar disorder. Other risk factors include postpartum hormonal changes, obstetrical complications, and lack of sleep. Some Canadian hospitals have adopted policies for sleep protection and support involving a prolonged postpartum admission (3–5 days) for those with a history of bipolar disorder, to decrease the risk for postpartum psychosis.

Anxiety Disorders

Anxiety is a common emotion and reaction to stress. Anxiety disorders represent a group of mental illnesses associated with anxiety symptoms that interfere with daily functioning and may worsen over time if left untreated. The most recent version of the DSM (DSM-5-TR) has categorized anxiety-related disorders into 3 categories (Box 2). 40

Perinatal Generalized Anxiety Disorder

Perinatal anxiety occurs during pregnancy or during the first year postpartum; the most common is generalized anxiety disorder. Perinatal generalized anxiety disorder often goes undiagnosed and untreated. Symptoms include excessive worry, insomnia, decreased appetite, muscle tension, irritability, 44 which may be misinterpreted as typical symptoms of pregnancy or being a new parent. Common themes among those suffering from perinatal anxiety include worst-case scenarios about the delivery or the baby, worry about the ability to parent, or fears about germs or harm to the baby. This type of anxiety has also been recently recognized as

Box 2. Categorization of anxiety-related disorders

Anxiety disorders	Obsessive- compulsive disorders	Trauma and stressor- related disorders		
 Generalized anxiety disorder Social anxiety disorder Panic disorder Specific phobia Separation anxiety disorder Agoraphobia 	 Obsessive- compulsive disorder Body dysmorphic disorder Hoarding disorder Trichotillomania Excoriation disorder 	 Posttraumatic stress disorder Acute stress disorder Attachment disorder 		

pregnancy-specific anxiety, in which cognitions are focused on pregnancy, labour, and parenting.⁴⁵

Perinatal Obsessive-Compulsive Disorder

In perinatal obsessive-compulsive disorder (OCD), some patients experience intrusive, repetitive thoughts (i.e., obsessions) about the baby that cause significant distress. New mothers may experience these obsessions, presenting as intense images of injury, death, or thoughts of physical or sexual harm. 46 However, this differs from those who harm their infants, in that women with OCD do not have psychosis and do not experience delusions or hallucinations. Rather, those with OCD are extremely distressed by such obsessions and thoughts. Although not all new mothers with OCD have associated compulsions, those that do may display excessive checking behaviours (e.g., frequent checking on a healthy, sleeping infant), overattachment to the infant, excessive cleaning and washing behaviours, avoidance of the infant, or seeking repeated reassurance regarding the infant's health. 46

Phobias

Specific phobias can also be a concern for perinatal care providers; phobias of needles (trypanophobia) and of childbirth (tokophobia) can cause significant distress for some individuals. Acknowledging the patient's fear and discussing what to expect may be helpful for some. However, for others, treatment in the form of cognitive behavioural therapy may be warranted (see Treatment section). For patients with severe tokophobia, the health care provider may receive requests for elective cesarean delivery in lieu of vaginal delivery, and a discussion of risks and benefits of these modes of delivery is important.

Trauma-Related Disorders

Trauma-related disorders are important for health care providers to be aware of in the perinatal period, as these conditions may influence how the patient experiences care or stressful events related to the pregnancy and/or childbirth itself. Posttraumatic stress disorder (PTSD) is diagnosed after a traumatic event, where the patient experiences persistent, bothersome symptoms, including feelings of re-experiencing the event (i.e., flashbacks); avoidance of feelings, people, or places; and increased levels of arousal or anxiety. 40 Symptoms should be present for more than 1 month to classify the diagnosis as PTSD; a shorter duration of symptoms is referred to as acute stress disorder. Pregnant patients with a history of PTSD may have a relapse in their symptoms during pregnancy if their trauma was related to childhood maltreatment or sexual abuse.⁴⁷ If a patient reports a history of trauma or PTSD, it is prudent to ask them if they have any

preferences about their care and to create a safe space for them to receive care. It is important to be aware that for some individuals the childbirth process itself may also lead to PTSD.

Other Common Mental Illnesses Relevant for Obstetrical Care

Although a discussion of all mental illnesses that may affect pregnant and postpartum patients is beyond the scope of this guideline, it is important to note that attention-deficit/hyperactivity disorder (ADHD), eating disorders, and personality disorders can also significantly impact the experience and outcomes of pregnancy.

ADHD is a chronic disorder that is characterized by inattention, hyperactivity, and impulsivity. The prevalence of ADHD has increased over the last several years in all adults, 48,49 including pregnant individuals, along with the use of stimulant medication. 50–52 Safety of stimulants in pregnancy is not well established. Some reports suggest an association between the use of stimulants and adverse maternal and fetal outcomes, but more research is warranted, and continued use should be considered on a case-by-case basis using a shared decision-making process. 53,54

The term *eating disorders* refers to a group of mental health disorders ranging from restricted eating (anorexia nervosa) to binge eating that may include purging behaviours. Although it can occur during pregnancy, an eating disorder often pre-dates pregnancy. All eating disorders are characterized by significant disturbances in eating patterns that can impact physical and psychosocial health. ⁵⁵ While management remains a challenge for patients and health care providers, ⁵⁶ ideal strategies employ a multidisciplinary approach. ⁵⁷

The term *personality disorders* encompasses a wide range of mental health conditions, including borderline personality disorder and obsessive-compulsive personality disorder. Personality disorders are defined as an enduring pattern of inner experience and behaviour that deviate markedly from expectations of the individual's culture, are pervasive and inflexible, and cause distress or negatively impact one's functioning. Treatment typically involves various forms of psychotherapy.

Compounding the impact of the conditions noted above, personality disorders, eating disorders, and ADHD may co-exist with each other and/or with anxiety or depression. Individuals affected by mental illness are also at increased risk of substance use, alcohol use disorder,

substance use disorder, and their associated harms in pregnancy and on the developing fetus.^{58,59}

Risk Factors for Perinatal Mental Illness

Certain groups and individuals may be at increased risk of PMI, and social, cultural, and environmental factors all contribute to the psychosocial factors of risk. More specifically, when social factors, such as the quality and quantity of social support, are considered on a multidimensional level, they can impact environmental factors, which influence the prevalence and severity of perinatal

Box 3. Risk factors for perinatal mental illness

Generalized anxiety disorder:

- · Personal or family history of anxiety
- Life changes / stress
- · Lack of social support
- · Health challenges for pregnant person or baby
- Poor sleep
- · Depressed mood
- Intolerance of uncertainty
- · Adverse childhood experiences

Major depressive disorder:

- Personal* or family history of depression (including PPD)
- Fetal/newborn loss
- Substance use and/or dependence
- Pregnancy/birth complications
- · Baby health challenges
- Unplanned pregnancy
- Intimate partner violence
- Adverse childhood experiences*

Obsessive-compulsive disorders:

- Pre-existing beliefs about uncertainty
- Symptoms of depression
- Poor sleep
- Family history of OCD
- Obstetric complications
- Obsessive-compulsive personality disorder
- · Avoidant personality disorder
- History of pregnancy loss
- Preterm delivery
- · Cesarean delivery

Postpartum posttraumatic disorder:

- Depression or trauma during pregnancy
- · Obstetrical emergency
- Fetal or newborn loss
- Infant complication
- History of trauma / sexual abuse
- Fear of childbirth (tokophobia)
- · Inadequate social support

Postpartum psychosis:

- · Bipolar disorder
- History of psychosis (postpartum or other)
- Family history of psychotic illness
- Sleep deprivation
- Medication discontinuation

Reference for Trauma-Associated disorders, Grekin et al. (2021)⁶⁹

PPD: postpartum depression; OCD: obsessive-compulsive disorder.

*The 2 strongest predictors of PPD according to results from Hutchens and Kearney. 68

anxiety and depression. Similarly, different cultures and subcultures develop strategies to adapt to the environment, and, in this way, environment is influenced by culture.⁶⁰

Pregnancy and postpartum experiences uniquely impact the mental health and well-being of 2SLGBTQ+ individuals, largely due to systems-level inequities and exclusion from perinatal care. Preliminary evidence shows racial and ethnic differences possibly due to health care delivery failures, including inadequate risk assessment, care coordination, and communication. Other critical factors include losing custody of the infant, having experienced a perinatal loss, history of abuse or intimate partner violence, and having a prior history of mental illness.

Box 3 outlines psychological, social, emotional, and physical risk factors for PMI. Typically, a single risk factor alone does not cause PMI, unless the person has a strong biological predisposition for a mental health condition.⁶⁷ Additionally, some PMIs have unique risk factors.

It is also important to emphasize that often only a small number of factors can be controlled by the perinatal health care provider, and it is critical for them to recognize the nature of their role is, including the care they can provide and the care they can provide well. PMI is complex and there are additional challenges in providing respectful and responsive care, such as circumstances where the patient may be either unwilling to access or receive care or non-adherent with care recommendations for a multitude of reason.

Summary Statement 6 and Recommendation 1

Racialized Minorities

In any discussion of PMI, it is important to acknowledge the impact that race, culture, language, ability, age, and sexual identity may contribute to an individual's risk for PMI, comfort with disclosing signs/symptoms of PMI, and access to perinatal mental health services.

Racialized minorities have higher incidences of perinatal depression and anxiety compared with pregnant individuals who are White. Racialized pregnant women often fear the compounded stigma associated with a diagnosis of PMI along with being a member of a minority group. Multiple factors contribute to the fear of stigmatization, including historic mistrust of the health care system and personal negative experiences with accessing health care. Differences in the timing of treatment

initiation have also been observed among racialized pregnant patients, who are less likely to initiate treatment for a new diagnosis of PMI during pregnancy but more likely to initiate treatment postpartum when compared with White women. ⁷³

Immigrants and Refugees

Immigrants and refugees represent a diverse group of different ethnic, individuals with linguistic, geographical backgrounds as well as differences in education and socioeconomic status. Despite the heterogeneity of this group is, for immigrants and refugees from low- and middle-income countries, rates are as high as 1 in 3 and 1 in 5 for perinatal depression and major depressive disorder, respectively.^{74,75} An identified barrier to disclosing and accessing perinatal mental health care among immigrant and refugee pregnant individuals is an understanding of perinatal depression and anxiety symptoms and sequelae, thereby leading to less treatment seeking.

Adolescents

Teenage pregnant individuals are also at increased risk of PMI. Significantly higher rates of depression and anxiety in pregnancy were reported in adolescents as compared with adult pregnant individuals in a recent Canadian sample. Compounding this risk is increased use of substances known to negatively impact mental health (e.g., cannabis and alcohol) in pregnancy among this population compared with adult pregnant individuals.

Gender-Diverse Patients

The gender-diverse community faces stressors like stigma and discrimination that impact their health and the health of their families. Adverse perinatal health outcomes are higher for 2SLGBTQ+ individuals, and they experience an increased prevalence of mental distress, anxiety, and depression.⁷⁷

Summary Statement 7

TRAUMA-INFORMED CARE

Perinatal care, given its somewhat invasive nature, has the potential to traumatize or cause retraumatization. Trauma-related disorders are common and can present or worsen in the perinatal period. In the perinatal period, a trauma history can negatively impact treatment engagement and adversely affect the experience of pregnancy, childbirth, and parenting. A trauma-informed care approach can mitigate these effects.

Trauma has been defined as "an event, series of events, or set of circumstances that is experienced by an individual as physically or emotionally harmful or life threatening and that has lasting adverse effects on the individual's functioning and mental, physical, social, emotional, or spiritual well-being." Trauma can take many forms that can be grouped into discrete events, the experience of the events, and the effects of those events. Events may include experiencing or observing physical, sexual, or emotional abuse; enduring severe life-threatening childhood neglect; experiencing natural disasters; having a family member with mental health or substance use disorder, including having a loved one who had committed suicide; experiencing poverty; and experiencing systemic discrimination.

How a person experiences such stressful events is highly variable and individually determined. An individual's cultural beliefs, social supports, age, and stage of development all influence the interpretation of the stressful event. The adverse effects of an event may be evident immediately or may be delayed and short- or long-term in duration. A trauma-informed care approach is essential to caring for individuals at risk for mood or anxiety disorders in the perinatal period. This approach acknowledges the need to understand a patient's life experiences to deliver effective care, while improving patient engagement, treatment adherence, health outcomes, and provider wellness.⁸⁰

An important precursor to providing trauma-informed care is ensuring that the organizational culture is conducive to this approach, which is reflected in policies, procedures, and practices. A full discussion of this topic is

Box 4. Principles of trauma-informed care

- 1. Safety (e.g., a physically safe setting and psychologically safe interpersonal interactions)
- Trustworthiness and transparency (maintain trust with individuals, such as disclosing if/when mandatory reporting is required and in what circumstances)
- Peer support (e.g., providing linkages to trauma survivors and specialized programs)
- Collaboration and mutuality (everyone in the health care setting has a role in trauma-informed approaches, including receptionists, health care providers, cleaning staff, etc.)
- Empowerment, voice, and choice (i.e., recognizing the individual's strengths and past/present resiliency; ensuring values and beliefs are integrated through shared decision-making for treatments and care planning)
- Cultural, historical, and gender issues (e.g., abolition of systemic discrimination based on race, ethnicity, sexual orientation, age, religion, gender identity, and/or geography; incorporating genderresponsive care and encouraging traditional cultural healing connections/practices)

Source: Centers for Disease Control and Prevention (U.S.). Office of Public Health Preparedness and Response. 6 guiding principles to a trauma-informed approach. 2018 Available at: https://stacks.cdc.gov/view/cdc/56843

beyond the scope of this guideline; however, some key points are summarized here. A trauma-informed approach includes a realization about how trauma can affect individuals and an understanding of coping strategies being used to manage the effects of the traumatic experience(s) (e.g., substance use). Recognizing the signs of trauma is important as is responding appropriately when trauma has been identified. Asking open-ended questions may help provide the space for patients to feel safe. Health care providers can facilitate referrals to trauma counselling and/or support groups.

The six principles of a trauma-informed approach are listed in Box 4.

To reduce future trauma, health care providers can focus on education to help reduce fears related to childbirth (tokophobia). Discussion may include options to increase support in labour, methods to increase locus of control in labour, and options for reducing pain.⁶⁹

Recommendation 2

SCREENING AND ASSESSMENT FOR PERINATAL MENTAL ILLNESS

The terms *screening* and *assessment* are often used interchangeably, but they are different.

Assessment refers to the process of defining the nature of a problem. It can start with questions about medical history and risk factors. If risk factors are identified, the use of a validated screening tool is warranted (screening).

Screening involves a medical test (includes validated screening tools) or procedure that is performed on individuals in a population to assess the likelihood of having a particular disease or health condition. Screening tests are not diagnostic but rather identify the need for further evaluation. The objective of a screening test is to reduce morbidity and mortality, by identifying those who need

Box 5. Prompting questions

- · How are you feeling?
- How are you doing?
- How are you coping?
- · How are you sleeping?
- How are you enjoying being pregnant and/or a new parent?
- Do you have any concerns or questions about how you are feeling?

further testing.⁸¹ In the perinatal context, the benefits of screening and early intervention apply to both the pregnant/parenting individual, as well as the fetus/newborn.

How to Assess

A preliminary mental health *assessment* should begin with questions about medical history and risk factors, and questions about mental health should be asked at every encounter up to 1 year following the pregnancy. Box 5 provides suggestions for prompting questions that can be used to begin the conversation about mental health.

All pregnant patients should be assessed for a history of mental illness to identify risk factors. This is typically captured on the provincial antenatal records, and some records include suggested screening questions, but there is no standardization across Canada. Using a "two casefinding question" approach is also an acceptable first step. This involves asking perinatal individuals the following questions: 1) During the past month, have you been bothered by feeling down, depressed or hopeless? and 2) During the past month, have you been bothered by little interest or pleasure in doing things? This approach has been validated in prenatal and postnatal settings with a reported 100% negative predictive value (ruling out women who do not have depression).

How to Screen

There is no universally accepted recommendation on whom should be screened, or when, using validated tools during the perinatal period. The US Preventive Services Task Force (2016)⁸⁶ the American College of Obstetricians and Gynecologists (2018)⁸⁷ and Australian Centre of Perinatal Excellence (2017)⁸⁸ have recommended universal screening, at least once during the perinatal period, using a validated tool. This contrasts with a recently updated statement from the Canadian Preventive Taskforce on Primary Health Care, which recommended against instrumental-based universal screening for PPD specifically; this conditional recommendation was based on the very-low-certainty evidence regarding the effect of screening on health outcomes and limited evidence of harms.⁸⁹ These mixed messages are confusing, and although the evidence is not strong, the risk of not capturing individuals with PMI because of lack of screening can have devastating consequences. Data from the United States and the United Kingdom clearly illustrate that the postpartum period up to 365 days following pregnancy, including situations of perinatal loss, is a time where maternal health concerns and suicide are rising. 14,15

Analysis of available data does support the use of screening tools for PMI. A recent meta-analysis (10 RCTs)

suggested that PPD rates at follow-up (3–8 months postpartum) were reduced using standardized psychometric scales to screen perinatal patients (ranging from the second trimester to 8 weeks postpartum) (OR 0.55; 95% CI: 0.45-0.66). 90,91

Screening for PMI typically involves the use of self-report questionnaires with established cut-off scores to indicate clinically significant symptomology. These tools are most often used to assess symptoms of depression and anxiety, but other tools can be used to assess general levels of distress, including partner distress, and other types of mental illness that can occur during the perinatal period, such as sleep-wake disorders (e.g., insomnia disorder). Table 2 summarizes the specific screening tools for PMIs. Additionally, screening for psychosocial concerns should be considered, such as with the Antenatal Risk Questionnaire, which is effective at predicting cases of depression (moderate quality evidence). 88,92–94

Screening should be complemented with a clearly defined and locally tailored referral process that is part of a comprehensive care pathway. A number of models have been developed based on steps that include inquiry, standardized rating scales (tools) to estimate severity, (see Table 2 for screening tools) referral and intervention approaches, and education and resources for patients. Some provincial and local care pathways have been developed in Canada, but they differ depending on the system in place, the capacity of that system, and the services that are available and accessible within that system. See Figure 1 for an adapted version of the Ontario Provincial Council for Maternal Child Health pathway for national use.

Recommendations 3, 4, and 5

Whom to Screen

If risk factors are identified, the health care provider should screen for PMI with a validated, standardized tool or scale (Table 2). If any concerns are identified and/or the patient reports active symptoms of mental illness, a validated standardized tool should be used to aid in assessment.

When a pregnant patient presents with worry or anxiety, the health care provider can assess OCD-related beliefs (e.g., concern about harm to the child) during pregnancy, as these can predict postpartum OCD symptoms. The use

Tool	Use	Format	Scoring
Depression			
EPDS ¹⁴²	 Detects clinically significant depressive symptoms Assesses depressive symptom severity during pregnancy and the postpartum period 	 5-point scale (10 items) scores on each item combined to yield a total scale score 	 <8: depression not likely 9-11: depression possible 12-13: fairly high possibility of depression ≥14: positive screen (probable depression) Score of 1, 2, or 3 on Q10 indicates suicidality risk and prompts immediate discussion and referra
CES-D scale ¹⁴³	Measures depressive symptoms and behaviours over the previous week	20-item, self-report scale	Items are rated on a scale from 0 to 3, with a total score that can range from 0 to 60, with higher scores indicating the presence of more symptomatology
Anxiety			
State Trait Anxiety Inventory ¹⁴⁴	Measures anxiety (apprehension, tension, nervousness, and worry)	20 items rated on a 4-point scale and yields a total score	Scale scores are calculated as the sum of respective items
GAD-7 ¹⁴⁵	Screens for generalized anxiety disorder	 7 items rated on a 4-point scale total score for the seven items ranges from 0 to 21 	 0-4: minimal anxiety 5-9: mild anxiety 10-14: moderate anxiety 15-21: severe anxiety >8 is cut-point for identifying probable cases of generalized anxiety disorder
PSAT ¹⁴⁶	Measures pregnancy-specific anxiety and its severity (validated for use during pregnancy)	33-item, self-report scale	 PSAT total score ranges from 6 to 24 Score >10 should be further assessed.
Mood Disorder Questionnaire ¹⁴⁷	Screens for bipolar disorder symptoms	3 items about manic and hypomanic symptoms	Yes to 7 or more items is a positive screen
Insomnia Severity Index ¹⁴⁸	Screens for insomnia	Scores range from 0 to 28, with higher scores indicating greater severity	Cut-off values of ISI ≥10 for a diagnosis of insomnia
Y-BOCS ¹⁴⁹	Rates severity of symptoms of obsessive- compulsive disorder that is not influenced by the type of obsessions or compulsions present	54 common obsessions and compulsive behaviors over the past week, grouped according to thematic content and rated on a 5-point scale	 0-13: mild symptoms 14-25: moderate symptoms 26-34: moderate—severe 40: severe symptoms

CES-D: Center of Epidemiological Studies - Depression; EPDS: Edinburgh Postnatal Depression Scale; GAD-7: Generalized Anxiety Disorder 7-item; PSAT: Pregnancy-Specific Anxiety Tool; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale.

Ask - Patient reports distress/depres sion/anxiety to obstetrical care provider or risk factors identified **Screen** with a validated self-report tool for pregnant individual Edinburgh Postnatal Depression Scale (EPDS) Generalized Anxiety Disorder-7 Question (GAD-7) **Urgent** Moderate scores: Mild scores: Severe scores: Psychosis, mania or FPDS: 10-12 FPDS: 13-18 FPDS: 19+ risk of harm to self or GAD-7:5-9 GAD-7: 10-14 GAD-7:15+ others Step 1 Step 4 Step 3 Step 2 (mild distress): (urgent, risk to self or (moderate distress): (severe distress): others) Psychosocial and Psychological Additional support community interventions and needed or incomplete interventions medication response to Step 2 Self-help books Cognitive Refer to psychiatry Consider calling (e.g., When Baby 911 behavioural either locally or Brings the Blues; therapy (CBT) or through e-consult Escort patient to The Pregnancy interpersonal available online emergency and Postpartum psychotherapy department Anxiety Medications within Workbook) Consider form for the scope of a involuntary Guided self-help primary care admission for (internet- or provider (e.g., assessment; close paper-based sertraline. follow up after for interventions) citalopram) ongoing risk Peer support assessment Supportive counselling (e.g., Postpartum Support International, Anxiety Canada). See Table 3 for comprehensive list.

Figure 1. National pathway for perinatal depression and anxiety symptoms in obstetrical care.

Adapted from the Care Pathway for the Management of Perinatal Mental Health created by the Provincial Council for Maternal and Child Health (2021). Available at: PCMCH-Care-Pathway-for-the-Management-of-Perinatal-Mental-Health_23July2021.pdf

of perinatal-specific measures for OCD symptoms (e.g., Post-Partum Intrusions Interview) are warranted in these cases. However, it is prudent to be supportive in discussions, as many patients are afraid to share their obsessions (i.e., intrusive thoughts) due to judgment and fear of infant/child apprehension.

When to Screen

Screening should be timed to make use of the routine contacts that individuals have throughout the perinatal period (e.g., completed during the first antenatal visit, as part of the medical history). If a concern is raised, or a risk factor is identified during a conversation between the

provider and patient, the health care provider would give the patient additional information and assess them further as required, including screening, referral, and/or recommending supports. Repeat screening is necessary at the postpartum visit. Pregnant and parenting individuals can also be directed to online screening tools for self-screening, which has been positively rated as acceptable, credible, and appealing for patients. More research is needed regarding the timing of the screening and to determine the efficacy of repeated screening at designated time points.

Summary Statement 8 and Recommendations 6, 7 and 8

TREATMENT AND MANAGEMENT OF PERINATAL MENTAL ILLNESS

Treatment and referral pathway recommendations for PMI depend on the severity of the illness, the patient's willingness to engage, and the resources available. There may also be cultural barriers to accepting a mental health diagnosis and the need for intervention. A common help-seeking barrier is a person's inability to disclose their feelings, which may be reinforced by family members. Despite the high prevalence of PMI and its significant consequences for the pregnant individual, fetus, partner, including its potential impact on infant and child development, current estimates suggest that only 54% of Canadians experiencing symptoms consistent with either PPD or an anxiety disorder consult their health care provider about it. 39

It is important to explain to the patient that many safe treatment options exist and that by seeking treatment, they will improve both their health and the health of their infant. Supportive dialogue is imperative for patients to seek help and move toward the pathway to recovery and wellness. Treatment options include psychoeducation, self-help books and worksheets, social support (including peer support), support groups, psychotherapy, and medication. Additionally, physical activity during pregnancy significantly reduces depressive symptoms. 98,99

Recent advances have made many of these options available online or virtually (through telephone or video), which significantly increases access for those who live in remote areas and/or do not have access to transportation or childcare.

Psychoeducation and Self-help

Psychoeducation simply means providing the patient with information regarding their symptoms or diagnosis. This includes discussion around a condition's causes, symptoms, prognosis, and treatment options, which can reduce fear and confusion. Providers can help engage individuals by providing them with links to helpful websites and/or having handouts. Information given to those with a mental health concern can also include a list of books and smart phone applications that can both educate and provide self-guided therapy, which represent low-barrier treatment options. See Table 3 for examples of resources.

Mild to Moderate Depression, Anxiety or Tokophobia In addition to psychoeducation and self-help books, there are several accessible options for online peer and group support, including some that are free of charge. 100,101

There is good evidence for psychotherapy for PMI, particularly cognitive behavioural therapy and interpersonal psychotherapy for mild to moderate depression and anxiety

Table 3. Suggested self-help books and online tools for perinatal depression and anxiety

Concern

Books, workbooks, and online tools

Depression •

- When Baby Brings the Blues: Solutions for Postpartum Depression
- This Isn't What I Expected: Overcoming Postpartum Depression
- The Postpartum Depression Workbook: Strategies to Overcome Negative Thoughts, Calm Stress, and Improve Your Mood
- Postpartum Support International: https://www.postpartum.net/
- "Managing depression" from best start: https://resources.beststart.org/product/m14e-managing-depression-workbook/
- "Coping with depression during pregnancy and following the birth" from the BC Reproductive Mental Health Program (free PDF online): http://www.bcwomens.ca/Specialized-Services-Site/Documents/Reproductive%20mental%20health/coping_with_depression.pdf

Anxiety

- The Pregnancy and Postpartum Anxiety Workbook: Practical Skills to Help You Overcome Anxiety, Worry, Panic Attacks, Obsessions, and Compulsions
- "Coping with anxiety during pregnancy and following the birth" from the BC Reproductive Mental Health Program (free PDF online): http://www.bcwomens.ca/Specialized-Services-Site/Documents/Reproductive%20mental%20health/bcrmh_anxietyguide_final_whole_document.pdf
- "Perinatal Anxiety: Anxiety During Pregnancy and Baby's First Year" from Anxiety Canada: https://www.anxietycanada.com/articles/perinatal-anxiety-anxiety-during-pregnancy-and-babys-first-year/

either as individual or group sessions. 102,103 Some health care providers do have local resources, including social work or perinatal psychiatry programs, but this is not widely available across Canada. Wait times for referrals can be long which is problematic when the concern is acute. If a patient has access to private health benefits or the financial means to pay out of pocket, they may be able to access psychotherapy privately in the community or via a virtual platform which are increasingly available. Patients in the perinatal period tend to prefer supportive talk therapy and psychotherapy, which should be considered when discussing treatment options. 97,104 Pregnant and postpartum individuals also report a strong preference for evidence-based individual psychotherapy over pharmacotherapy or group-based interventions to address mental health concerns. 105-112 Routine counselling about the psychological aspects of the transition to parenthood and other important factors that can affect perinatal mental health is important for those experiencing moderate PMI. However, for more severe cases, pharmacotherapy may be warranted and needed.

Pharmacotherapy

Pharmacotherapy may be prescribed to manage mood and anxiety symptoms, either as a first-line treatment, in conjunction with counselling or psychotherapy, or when other treatment options have not provided sufficient relief of symptoms. In a survey of individuals living with PMI, the main reasons for starting medication were to achieve normalcy in daily life, to help sustain the family, to deal with loss, to reduce symptoms, to reduce relapse, and to reduce the risk of suicide. ¹¹³

As with the initiation of any medication, the health care provider needs to have a conversation about the anticipated benefits as well as possible risks and side effects. In the perinatal period this includes potential risks to the fetus and breastfed neonates, although most of the common pharmacologic agents used to treat perinatal mood and anxiety disorders are not teratogenic.

Box 6. Treatment plan		
Treatment plan	Date:	
Track symptoms: • Worsening symptoms • Suicide ideation or planning • Insomnia • Euphoria (mood overly elevated) • Adverse effects	Who to contact if these occur:	
Community-based support available		
Crisis lines		

Expectations regarding timing should be discussed, as it typically takes several weeks (up to 6 weeks) to see a significant change with these medications. If no improvement in symptoms has been noted by this time, the health care provider may recommend switching to a different medication in the same class or in another class. Expert advice or referral may be warranted. A key component of pharmacotherapy for mood and anxiety disorders is the development of a safety treatment plan for the individual living with PMI (see Box 6 for an example).

Patients with pre-existing mental health diagnoses who are well maintained on pharmacological agents should not abruptly discontinue medication during pregnancy. Patients who are taking pharmacologic agents (see online Appendix C) should be referred for preconception counselling by their health care provider, or to psychiatrist for consultation if they are already pregnant. Pregnant individuals with a PMI should be urgently referred to specialized psychiatric services with immediate action.

The most studied class of medications used in the management of perinatal mood disorders is selective serotonin reuptake inhibitors (SSRIs). SSRIs are effective for the management of both anxiety and depression, and they have a more tolerable side effect profile compared with other classes of medications. The most common side effects are drowsiness, nausea, decreased libido, headache, agitation, insomnia, and diarrhea. These side effects often improve as treatment progresses. Caution must be used when initiating SSRIs in adolescents and young adults, as they may increase suicidality.¹¹⁴ There is an increased risk of relapse or recurrence of depressive symptoms when an antidepressant is discontinued.¹¹⁵

Summary Statements 9, 10, 11 and Recommendation 9, 10, 11, 12, 13 and 14

Shared Decision-Making

Shared decision-making about treatment for PMI is a collaborative process between the pregnant individual, their supports, and the health care provider. The hallmarks of shared decision-making are the sharing of information and perspectives, respect for autonomy, and shared responsibility for decisions around treatment. 116

Decisions about treatment for PMI have an added layer of complexity, given personal and societal stigma around mental health and the use of medication in pregnancy. Factors that have been associated with a positive

experience of shared decision-making for pregnant individuals living with PMI include feeling that they were being heard, understood, and respected by the health care provider and having the opportunity to ask questions. 113 Those reporting a negative experience included feeling the conversation was rushed, not feeling like they had a choice in their care, feeling ashamed, and feeling unsure what to say in the moment.

In addition to the conversation between the pregnant individual and the health care provider, decision aids (e.g., information pamphlets, questionnaires) may be provided to support the decision-making process. A meta-analysis in patients with pre-existing morbidity in pregnancy showed that decision aids increase knowledge about the preexisting condition and modestly reduce internal conflict around the decision. 117,118

Summary Statement 12 and Recommendation 15

Barriers to Treatment and Referral

Perinatal mental health issues are substantially underdiagnosed and under-treated. A systematic review of 32 articles showed that adequate treatment (i.e., daily use of antidepressants or psychotherapy for at least 6 weeks) was offered to only 9% of those with antenatal depression and 6% of those with PPD. 119,120 Barriers to addressing perinatal mental health issues may be related to individual, provider, organizational, political, and societal factors. 121 Individuals may refrain from communicating mental health challenges or seeking support for various reasons, such as lack of emotional literacy; perceptions about maternity care providers' role; not wanting to be seen as vulnerable; stigma; uncertainty about the outcomes of disclosure or whether an immediate support would be available; and perceptions about recommended treatments or medications. 120 Lack of referrals, long waitlists for initial assessment, lack of basic information about availability of services and cost, or inability to attend treatment sessions due to logistics obstacles or limited support (e.g., cost, lack of childcare, transportation) can also reduce the access to mental health services. 120 At the provider level, insufficient or lack of training and knowledge, unclear or limited scope of practice, time constraints, beliefs and perceptions about treatment and medications, and lack of clinical support and collaborative care can all impact the identification, treatment, and referral of patients with PMI. 120,121 Organizational and political barriers may include a lack of clear pathways and integrated health care services; complex administrative processes within a system; unavailability of policies, funding, or local and contextual guidelines; and limited available referral resources.

Facilitators to Identification, Treatment and Referral

How barriers influence provider behaviour is important, especially since providers are making several complex diagnostic and treatment decisions every day with imperfect information and time pressures. They may be unknowingly influenced by environmental cues and heuristics to guide their decision-making processes and behaviours, such as habits, choosing the default treatment, or conducting examinations that confirm prior beliefs. In other words, providers may intend to screen but fail to act. Providers may knowingly refrain from screening, because of the perception that they lack expertise on depression, feel it is out of scope to diagnose depression, or have concerns about whether patients have access to the recommended services.

Collaborative and Multidisciplinary Care

Collaborative care models with a team-based approach have been effective in enhancing detection and treatment of perinatal mental health issues. 119 A randomized controlled trial in the United States found that, compared with usual care, a collaborative care model improved the likelihood of receiving adequate treatment and adherence to treatment plans for perinatal mental health; collaborative care was also associated with higher remission rates, improved functioning in work, and greater satisfaction with social and family life. 122 It is possible that a collaborative care model embedded directly in maternity care clinics can make mental health services more accessible to patients by reducing stigma associated with mental health support seeking, and reducing the need for multiple separate appointments that require additional time off and possible childcare challenges. This model would also clarify pathways of care and available treatment as well as referral resources for both patients and providers. Ongoing communication and the presence of dual-certified practitioners (e.g., nurses/midwives with dual specialty in reproductive health and psychiatric care) can facilitate the integration of collaborative care. 123 Training providers can also improve the providers' dedication and attitude toward addressing mental health concerns and increase their confidence in identifying and managing mental health conditions. 120

Community-based Resources

Two Canadian RCTs have shown telephone-based peersupport interventions offered by volunteers who have recovered from PPD to be effective in both preventing and improving the symptoms of PPD. 124 Others have

shown that cognitive behavioural therapy delivered by peers significantly reduced symptoms of depression and anxiety in the postpartum period among mothers living in Canada. ¹²⁵ Innovative approaches such as these will help to further provide resources and can often happen remotely to reduce barriers to care.

ACCESS TO PERINATAL MENTAL HEALTH CARE

Language and Literacy

Health care providers should consider social and cultural factors that will influence how an individual understands and interprets the language of a screening questionnaire; engages in conversations about their well-being and social, economic, or family circumstances; and how they choose accept referral and treatment recommendations. Whenever possible, strategies to assess the mental wellbeing of non-English speaking individuals should be used, including translations of validated screening questionnaires and the use of professional translation services. Screening for and information about PMI should be provided in the patient's preferred language, with the assistance of an interpreter or through written translations of the screening tool. Whenever possible, the health care provider should ask patients about their understanding of PMI and provide additional information as needed. 126

Social Determinants of Health

The role of the social determinants of health in accessing perinatal mental health care cannot be overstated. Recurring barriers to accessing perinatal mental health care include marginal housing, lack of childcare, lack of social support, lack of transportation, lack of money, and food insecurity.⁷¹

Protective Factors

Social and community support has been identified as a protective factor for pregnant people living with PMI who are immigrants and refugees, ¹²⁷ reside in rural locations, ¹²⁸ identify as 2SLGBTQ+¹²⁹ and are Indigenous. ¹³⁰ In addition, health care providers who advocacate on behalf of pregnant individuals living with PMI and create an environment where the pregnant individual feels heard and understood foster psychological safety and trust for ongoing discussion about PMI. ⁷²

Decolonizing and Destigmatizing Perinatal Mental Health Care

Black scholars' recommendations for the provision of perinatal mental health care services⁷¹ align with those set out by Indigenous scholars¹³⁰ as well as the specific calls to

action of the Truth and Reconciliation Commission of Canada¹. Restated, the recommendations include to:

- Provide education and training to health care providers on cultural safety
- Develop a perinatal mental health workforce that reflects the population it serves
- Support community-led initiatives around perinatal mental health
- Provide care that affirms dignity and addresses social and medical needs
- Integrate perinatal mental health care and shared decision-making into routine perinatal care

This aligns with the approaches to meet the needs of gender-diverse patients, where solutions must be integrated into systems and health care providers must receive training and education in order foster trust and to be responsive and inclusive to the voices of the community. At the same time, environments and policies must be respectful and affirming in order to serve the many marginalized populations in Canada including the 2SLGBTQ+ community.⁷⁷

CONCLUSION

PMI is a major public concern that can adversely affect pregnant and postpartum patients as well as their infants and families. Innovative strategies and approaches to delivering care are urgently needed to meet the demand posed by these conditions and provide support to individuals experiencing them. Additional research is needed to provide evidence for strong recommendations in the delivery of PMI care. This guideline is intended to facilitate the recognition, diagnosis, and care of pregnant and postpartum individuals with PMI. It will help guide health care provider in caring for these patients using a harm-reduction and trauma-informed approach that ultimately improves health outcomes.

SUPPLEMENTARY MATERIAL

Supplementary material related to this article can be found at https://doi.org/10.1016/j.jogc.2024.102696.

REFERENCES

 O'Hara MW, Wisner KL. Perinatal mental illness: definition, description and aetiology. Best Pract Res Clin Obstet Gynaecol 2014;28:3–12. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24140480.

¹ https://ehprnh2mwo3.exactdn.com/wp-content/uploads/2021/01/Calls_to_Action_English2.pdf

- Zikic O, Stojanov J, Kostic J, et al. Depression in the Perinatal Period: Course and Outcome of Depression in the Period from the Last Trimester of Pregnancy to One Year after Delivery in Primiparous Mothers. Medicina (Kaunas, Lithuania) 2024;60:970.
- Shklarski L, Kalogridis L. Promotion and Prevention of Perinatal Mood and Anxiety Disorders: Doulas' Roles and Challenges. J Perinat Educ 2022;31:82—93. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/35386494.
- Holopainen A, Hakulinen T. Easing the transition to parenthood: the importance of perinatal and postnatal mental health for mothers and fathers. JBI database of systematic reviews and implementation reports 2019;17:1727–8.
- 5. Slomian J, Honvo G, Emonts P, et al. Consequences of maternal postpartum depression: A systematic review of maternal and infant outcomes. Women's health 2019;15:1745506519844044. Available at: https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med16 &AN=31035856 http://sfx.scholarsportal.info/mcmaster?sid=OVID: medline&id=pmid:31035856&id=doi:10.1177%2F1745506519844044 &issn=1745-5057&isbn=&volume=15&issue=&spage=1745506519844044 044&pages=1745506519844044&date=2019&title=Women%27 s+health&atitle=Consequences+of+maternal+postpartum+depression%3A+A+systematic+review+of+maternal+and+infant+outcomes. &aulast=Slomian&pid=%3Cauthor%3ESlomian+J%3BHonvo+G%3BEmonts+P%3BReginster+JY%3BBruyere+O%3C%2Fauthor%3E%3CAN%3E31035856%3C%2FAN%3E%3CDT%3EJournal+Article%3C%2FDT%3E.
- 6. Thiel F, Eberhard-Gran M, Garthus-Niegel S. The Impact of Perinatal Life Stress on Infant Temperament and Child Development: A 2-Year Follow-Up Cohort Study. Journal of Developmental & Behavioral Pediatrics 2021;42:299-306. Available at: https://libaccess.mcmaster.ca/login? url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS= N&PAGE=fulltext&D=med18&AN=33229970 http://sfx scholarsportal.info/mcmaster?sid=OVID:medline&id=pmid:3322997 0&id=doi:10.1097%2FDBP.000000000000887&issn=0196-206 X&isbn=&volume=42&issue=4&spage=299&pages=299-306&date=2 021&title=Journal+of+Developmental+%26+Behavioral+Pediatrics& atitle=The+Impact+of+Perinatal+Life+Stress+on+Infant+ Temperament+and+Child+Development%3A+A+2-Year+Follow-Up+Cohort+Study.&aulast=Thiel&pid=%3Cauthor%3EThiel+F% 3BEberhard-Gran+M%3BGarthus-Niegel+S%3C%2Fauthor%3E% 3CAN%3E33229970%3C%2FAN%3E%3CDT%3EJournal+Article%3C %2FDT%3E.
- Rose MS, Pana G, Premji S. Prenatal Maternal Anxiety as a Risk Factor for Preterm Birth and the Effects of Heterogeneity on This Relationship: A Systematic Review and Meta-Analysis. Biomed Res Int 2016;2016:8312158.
- Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. J Clin Psychiatry 2013;74:e321—41. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23656857.
- Grigoriadis S, Graves L, Peer M, et al. Maternal Anxiety During Pregnancy and the Association With Adverse Perinatal Outcomes: Systematic Review and Meta-Analysis. J Clin Psychiatry 2018;79. Available at: https://www. ncbi.nlm.nih.gov/pubmed/30192449.
- Da Costa D, Danieli C, Abrahamowicz M, et al. A prospective study of postnatal depressive symptoms and associated risk factors in first-time fathers. Journal of Affective Disorders2019. p. 371-377.
- Vismara L, Rolle L, Agostini F, et al. Perinatal Parenting Stress, Anxiety, and Depression Outcomes in First-Time Mothers and Fathers: A 3- to 6-Months Postpartum Follow-Up Study. Front Psychol 2016;7:938. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27445906.
- Mangla K, Hoffman MC, Trumpff C, et al. Maternal self-harm deaths: an unrecognized and preventable outcome. Am J Obstet Gynecol 2019;221:295—303. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/30849358.
- Grigoriadis S, Wilton AS, Kurdyak PA, et al. Perinatal suicide in Ontario, Canada: a 15-year population-based study. Cmaj 2017;189:E1085. e92.

- MacGregor B, Shakespeare J, Kotnis R, et al. MBRRACE 2021: preventing maternal deaths - we are all part of the solution. Br J Gen Pract 2022;72:148–9. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/35361581.
- Chin K, Wendt A, Bennett IM, et al. Suicide and Maternal Mortality. Curr Psychiatry Rep 2022;24:239

 75. Available at: https://www.ncbi.nlm.nih. gov/pubmed/35366195.
- Jago CA, Crawford SG, Gill SJ, et al. Mental Health and Maternal Mortality-When New Life Doesn't Bring Joy. J Obstet Gynaecol Can 2021;43:67—73. e1. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/32978085.
- Cheng C-Y, Chou Y-H, Chang C-H, et al. Trends of Perinatal Stress, Anxiety, and Depression and Their Prediction on Postpartum Depression. International journal of environmental research and public health 2021;18:9307.
- Hall RAS, Hoffenkamp HN, Braeken J, et al. Maternal psychological distress after preterm birth: Disruptive or adaptive? Infant Behavior and Development. Elsevier Ltd; 2017. p. 272–80.
- 19. Gentile S. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. Neuroscience 2017;342:154–66. Available at: https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.egi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med14&AN=26343292 http://sk.scholarsportal.info/mcmaster?sid=OVID:medline&id=pmid:26343292&id=doi:10.1016%2Fj.neuroscience.2015.09.001&issn=0306-4522&isbn=&volume=342&issue=&spage=154&pages=154-166&date=2017&title=Neuroscience&atitle=Untreated+depression+during+pregnancy%3A+Short+and+long-term+effects+in+offspring+A+systematic+review.&aulast=Gentile&pid=%3Cauthor%3EGentile+S%3C%2Fauthor%3E%3CAN%3E26343292%3C%2FAN%3E%3CDT%3EJournal+Article%3C%2FDT%3E.
- Racine N, Plamondon A, Madigan S, et al. Maternal Adverse Childhood Experiences and Infant Development. Pediatrics 2018;141. Available at: https://doi.org/10.1542/peds.2017-2495.
- Wang X, Chen W, Wen L, et al. Adverse childhood experiences in offspring living with parental mental illness: a controlled study from China. J Ment Health 2023;32:541-50. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/35775503.
- Goodman JH. Perinatal depression and infant mental health. Arch Psychiatr Nurs 2019;33:217—24. Available at: https://www.ncbi.nlm.nih. gov/pubmed/31227073.
- Arima Y, Fukuoka H. Developmental origins of health and disease theory in cardiology. J Cardiol 2020;76:14

 –7.
- Barter JD, Foster TC. Aging in the Brain: New Roles of Epigenetics in Cognitive Decline. Neuroscientist 2018;24:516—25. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29877135.
- Daskalakis NP, Yehuda R. Site-specific methylation changes in the glucocorticoid receptor exon 1F promoter in relation to life adversity: systematic review of contributing factors. Front Neurosci 2014;8:369. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25484853.
- Lardenoije R, Iatrou A, Kenis G, et al. The epigenetics of aging and neurodegeneration. Prog Neurobiol 2015;131:21—64. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26072273.
- Cao-Lei L, van den Heuvel MI, Huse K, et al. Epigenetic Modifications Associated with Maternal Anxiety during Pregnancy and Children's Behavioral Measures. Cells 2021;10. Available at: https://www.ncbi.nlm. nih.gov/pubmed/34572069.
- Gluckman PD, Hanson MA, Buklijas T. A conceptual framework for the developmental origins of health and disease. J Dev Orig Health Dis 2010;1:6–18
- Rasic D, Hajek T, Alda M, et al. Risk of mental illness in offspring of parents with schizophrenia, bipolar disorder, and major depressive disorder: a meta-analysis of family high-risk studies. Schizophr Bull 2014;40:28—38. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23 960245.

- Berg L, Back K, Vinnerljung B, et al. Parental alcohol-related disorders and school performance in 16-year-olds-a Swedish national cohort study. Addiction 2016;111:1795

 –803. Available at: https://www.ncbi.nlm.nih. gov/pubmed/27178010.
- Fairthorne J, De Klerk N, Leonard H. The relationship between maternal psychiatric disorder, autism spectrum disorder and intellectual disability in the child: a composite picture. Journal of Autism 2015;2:1—5.
- Shen H, Magnusson C, Rai D, et al. Associations of Parental Depression With Child School Performance at Age 16 Years in Sweden. JAMA Psychiatry 2016;73:239

 –46. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/26842307.
- 33. Webb RT, Pickles AR, King-Hele SA, et al. Parental mental illness and fatal birth defects in a national birth cohort. Psychol Med 2008;38:1495—503. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18076770.
- Webb R, Abel K, Pickles A, et al. Mortality in offspring of parents with psychotic disorders: a critical review and meta-analysis. Am J Psychiatry 2005;162:1045—56. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/15930050.
- 35. Webb RT, Abel KM, Pickles AR, et al. Mortality risk among offspring of psychiatric inpatients: a population-based follow-up to early adulthood. Am J Psychiatry 2006;163:2170—7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17151170.
- Blair LM, Wheeler E, Hutti MH. Social and Behavioral Problems in School-Aged Children After Maternal Postpartum Depression: A Secondary Analysis of Future of Families and Child Wellbeing Study. Matern Child Health J 2023;27:1081

 –8. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36988793.
- Rahman A, Fisher J, Bower P, et al. Interventions for common perinatal mental disorders in women in low- and middle-income countries: a systematic review and meta-analysis. Bull World Health Organ 2013;91:593

 –601i.
- 38. Milgrom J, Holt C, Holt CJ, et al. Feasibility study and pilot randomised trial of an antenatal depression treatment with infant follow-up. Arch Womens Ment Health 2015;18:717—30.
- Maternal Mental Health in Canada, 2018/2019. Retrieved March 14, 2023. Statistics Canada; 2019.
- Association AP. Diagnostic and Statistical Manual of Mental Disoders, Fifth Edition, Text Revision (DSM-5-TR). Available at: https://doi.org/1 0.1176/appi.books.9780890425787. Accessed on March 6, 2023.
- MacQueen GM, Frey BN, Ismail Z, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 6. Special Populations: Youth, Women, and the Elderly. Can J Psychiatry 2016;61:588–603.
- Rezaie-Keikhaie K, Arbabshastan ME, Rafiemanesh H, et al. Systematic Review and Meta-Analysis of the Prevalence of the Maternity Blues in the Postpartum Period. J Obstet Gynecol Neonatal Nurs 2020;49:127–36. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32035973.
- Masters GA, Hugunin J, Xu L, et al. Prevalence of Bipolar Disorder in Perinatal Women: A Systematic Review and Meta-Analysis. J Clin Psychiatry 2022;83.
- Misri S, Abizadeh J, Sanders S, et al. Perinatal Generalized Anxiety Disorder: Assessment and Treatment. J Womens Health (Larchmt) 2015;24:762—70. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/26125602.
- Huizink AC, Mulder EJ, Robles de Medina PG, et al. Is pregnancy anxiety a distinctive syndrome? Early Hum Dev 2004;79:81–91. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15324989.
- Hudepohl N, MacLean JV, Osborne LM. Perinatal Obsessive-Compulsive Disorder: Epidemiology, Phenomenology, Etiology, and Treatment. Curr Psychiatry Rep 2022;24:229—37.
- 47. Choi KR, Seng JS. Predisposing and Precipitating Factors for Dissociation During Labor in a Cohort Study of Posttraumatic Stress Disorder and Childbearing Outcomes, 61. J Midwifery Womens Health; 2016. p. 68–76. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26774007.

- American Psychiatric Association. What is ADHD?. Available at: https://www.psychiatry.org/patients-families/adhd/what-is-adhd. Accessed on March 6, 2023.
- Centers for Disease control and Prevention. What is ADHD? Available at: https://www.cdc.gov/ncbddd/adhd/facts.html#: ~:text=ADHD%20is% 20one%20of%20the,)%2C%20or%20be%20overly%20active. Accessed on March 6, 2023.
- Louik C, Kerr S, Kelley KE, et al. Increasing use of ADHD medications in pregnancy. Pharmacoepidemiol Drug Saf 2015;24:218–20. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25630904.
- Anderson KN, Dutton AC, Broussard CS, et al. ADHD Medication Use During Pregnancy and Risk for Selected Birth Defects: National Birth Defects Prevention Study, 1998-2011. J Atten Disord 2020;24: 479–89. Available at: https://www.ncbi.nlm.nih.gov/pubmed/295 19207.
- Smid MC, Metz TD, Gordon AJ. Stimulant Use in Pregnancy: An Underrecognized Epidemic Among Pregnant Women. Clin Obstet Gynecol 2019;62:168

 –84. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3 0601144.
- 53. Camacho X, Zoega H, Gomes T, et al. The association between psychostimulant use in pregnancy and adverse maternal and neonatal outcomes: results from a distributed analysis in two similar jurisdictions. International Journal of Epidemiology 2022;52:190—202. Available at: https://doi.org/10.1093/ije/dyac180.
- 54. Centers for Disease control and Prevention. Use of ADHD Medicine in Increasing among Pregnant Women. Available at: https://www.cdc.gov/ pregnancy/meds/treatingfortwo/features/keyfinding-ADHD-medincrease.html. Accessed on March 6, 2023.
- Charbonneau KD, Seabrook JA. Adverse Birth Outcomes Associated with Types of Eating Disorders: A Review. Canadian Journal of Dietetic Practice and Research 2019;80:131—6. Available at: https://dcjournal.ca/doi/abs/1 0.3148/cjdpr-2018-044.
- Bye A, Shawe J, Bick D, et al. Barriers to identifying eating disorders in pregnancy and in the postnatal period: a qualitative approach. BMC Pregnancy Childbirth 2018;18:114.
- Janas-Kozik M, Žmijowska A, Zasada I, et al. Systematic Review of Literature on Eating Disorders During Pregnancy-Risk and Consequences for Mother and Child. Front Psychiatry 2021;12:777529.
- 58. Marshall CA, Jomeen J, Huang C, et al. The Relationship between Maternal Personality Disorder and Early Birth Outcomes: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health 2020;17.
- Mental Health Commission of Canada. Mental Health and Substance Use. Available at: https://mentalhealthcommission.ca/what-we-do/mental-health-and-substance-use/. Accessed on March 6, 2023.
- Ojeleye OA, Beckie TM, Oruche UM. Psychosocial Factors Associated With Perinatal Anxiety and Perinatal Depression Among Adolescents: A Rapid Review. J Psychosoc Nurs Ment Health Serv 2024;62:13—22.
- Kirubarajan A, Barker LC, Leung S, et al. LGBTQ2S+ childbearing individuals and perinatal mental health: A systematic review. BJOG 2022;129:1630–43. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/35048502.
- Dagher RK, Bruckheim HE, Colpe LJ, et al. Perinatal Depression: Challenges and Opportunities. J Womens Health (Larchmt) 2021;30:154—9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33156730.
- 63. Shorter JM, Koelper N, Sonalkar S, et al. Racial Disparities in Mental Health Outcomes Among Women With Early Pregnancy Loss. Obstet Gynecol 2021;137:156—63. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33278280.
- 64. Glazer KB, Howell EA. A way forward in the maternal mortality crisis: addressing maternal health disparities and mental health. Arch Womens Ment Health 2021;24:823—30. Available at: https://www.ncbi.nlm.nih. gov/pubmed/34427773.
- Davoudian T, Gibbins K, Cirino NH. Perinatal Loss: The Impact on Maternal Mental Health. Obstet Gynecol Surv 2021;76:223. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33908614.

- Biaggi A, Conroy S, Pawlby S, et al. Identifying the women at risk of antenatal anxiety and depression: A systematic review. J Affect Disord 2016;191:62—77. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/26650969.
- Psychiatry in primary care: A concise Canadian pocket guide. 2nd Edition. Toronto, ON: CAMH Publications; 2019.
- Hutchens BF, Kearney J. Risk Factors for Postpartum Depression: An Umbrella Review. J Midwifery Womens Health 2020;65:96—108. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31970924.
- Grekin R, O'Hara MW, Brock RL. A model of risk for perinatal posttraumatic stress symptoms. Archives of Women's Mental Health 2021;24:259—70. Available at: https://doi.org/10.1007/s00737-020-01068-2.
- Lyndsay A, Avalos, Ph.D., M.P.H., Nerissa Nance, M.P.H., Esti Iturralde, Ph.D., et al. Racial-Ethnic Differences in Treatment Initiation for New Diagnoses of Perinatal Depression. Psychiatric Services.0:appi.ps. 20220173. Available at: https://ps.psychiatryonline.org/doi/abs/10.1176/appi.ps.20220173.
- Estriplet T, Morgan I, Davis K, et al. Black Perinatal Mental Health: Prioritizing Maternal Mental Health to Optimize Infant Health and Wellness. Frontiers in Psychiatry 2022;13. Available at: https://www.frontiersin.org/articles/10.3389/fpsyt.2022.807235.
- Kemet S, Yang Y, Nseyo O, et al. "When I think of mental healthcare, I think of no care." Mental Health Services as a Vital Component of Prenatal Care for Black Women. Matern Child Health J 2022;26:778

 –87.
- Avalos LA, Nance N, Iturralde E, et al. Racial-Ethnic Differences in Treatment Initiation for New Diagnoses of Perinatal Depression. Psychiatr Serv 2022:appips20220173.
- Daoud N, O'Brien K, O'Campo P, et al. Postpartum depression prevalence and risk factors among Indigenous, non-Indigenous and immigrant women in Canada. Can J Public Health 2019;110:440—52.
- Fellmeth G, Fazel M, Plugge E. Migration and perinatal mental health in women from low- and middle-income countries: a systematic review and meta-analysis. Bjog 2017;124:742—52.
- Wong SPW, Twynstra J, Gilliland JA, et al. Risk Factors and Birth Outcomes Associated with Teenage Pregnancy: A Canadian Sample. Journal of Pediatric and Adolescent Gynecology 2020;33:153–9. Available at: https://www.sciencedirect.com/science/article/pii/S10833188193 03237.
- 77. Wingo E, Ingraham N, Roberts SCM. Reproductive Health Care Priorities and Barriers to Effective Care for LGBTQ People Assigned Female at Birth: A Qualitative Study. Womens Health Issues 2018;28:350–7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29661698.
- 78. Sachdeva J, Nagle Yang S, Gopalan P, et al. Trauma Informed Care in the Obstetric Setting and Role of the Perinatal Psychiatrist: A Comprehensive Review of the Literature. J Acad Consult Liaison Psychiatry 2022;63:485—96. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35513261.
- Substance Abuse and Mental Health Services Administration. SAMHSA's Concept of Trauma and Guidance for a Trauma-Informed Approach. HHS Publication No. (SMA) 14-4884. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.
- 80. Menschner C MA. Issue Brief: Key ingredients for successful traumainformed care implementation The Center for Health Care Strategies; 2016.
- 81. Maxim LD, Niebo R, Utell MJ. Screening tests: a review with examples. Inhalation Toxicology 2014;26:811–28. Available at: https://doi.org/10.3109/08958378.2014.955932.
- 82. Whooley MA ea. Case-finding instruments for depression: two questions are as good as many. J Gen Intern Med 1997;12:439-45.
- Kroenke K, Spitzer R, Williams J. The patient health questionnaire-2: Validity of a two item depression screener. Medical Care 2003;41:1284—94.
- Mann R, Adamson J, Gilbody SM. Diagnostic accuracy of case-finding questions to identify perinatal depression. CMAJ 2012;184:E424–30.
 Available at: https://www.ncbi.nlm.nih.gov/pubmed/22451686.
- 85. Mann R, Gilbody S. Validity of two case finding questions to detect postnatal depression: a review of diagnostic test accuracy. J Affect Disord

- 2011;133:388-97. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21146230.
- Force USPST, Curry SJ, Krist AH, et al. Interventions to Prevent Perinatal Depression: US Preventive Services Task Force Recommendation Statement. JAMA 2019;321:580—7. Available at: https://www.ncbi.nlm. nih.gov/pubmed/30747971.
- ACOG Committee Opinion No. 757: Screening for Perinatal Depression. Obstet Gynecol 2018;132:e208–12. Available at: https://www.ncbi.nlm. nih.gov/pubmed/30629567.
- 88. Austin M-P, Highet N. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne: Centre of Perinatal Excellence; 2017.
- Lang E, Colquhoun H, LeBlanc JC, et al. Recommendation on instrumentbased screening for depression during pregnancy and the postpartum period. Canadian Medical Association Journal 2022;194:E981. Available at: http://www.cmaj.ca/content/194/28/E981.abstract.
- Waqas A, Koukab A, Meraj H, et al. Screening programs for common maternal mental health disorders among perinatal women: report of the systematic review of evidence. BMC Psychiatry 2022;22:54. Available at: https://doi.org/10.1186/s12888-022-03694-9.
- Myers ER, Aubuchon-Endsley N, Bastian LA, et al. Efficacy and Safety of Screening for Postpartum Depression. AHRQ Comparative Effectiveness Reviews. AHRQ Comparative Effectiveness Reviews. Rockville (MD)2013.
- Austin MP, Colton J, Priest S, et al. The antenatal risk questionnaire (ANRQ): acceptability and use for psychosocial risk assessment in the maternity setting. Women Birth 2013;26:17—25. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21764399.
- 93. Austin MP, Hadzi-Pavlovic D, Saint K, et al. Antenatal screening for the prediction of postnatal depression: validation of a psychosocial Pregnancy Risk Questionnaire. Acta Psychiatr Scand 2005;112:310—7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16156839.
- 94. Carroll JC, Reid AJ, Biringer A, et al. Effectiveness of the Antenatal Psychosocial Health Assessment (ALPHA) form in detecting psychosocial concerns: a randomized controlled trial. CMAJ 2005;173:253—9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16076821.
- Kendig S, Keats JP, Hoffman MC, et al. Consensus Bundle on Maternal Mental Health: Perinatal Depression and Anxiety. Obstet Gynecol 2017;129:422—30. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/28178041.
- Reilly N, Austin MP. Attitudes and Engagement of Pregnant and Postnatal Women With a Web-Based Emotional Health Tool (Mummatters): Crosssectional Study. J Med Internet Res 2021;23:e18517. Available at: https:// www.ncbi.nlm.nih.gov/pubmed/33769302.
- Dennis C-L, Chung-Lee L. Postpartum Depression Help-Seeking Barriers and Maternal Treatment Preferences: A Qualitative Systematic Review. Birth 2006;33:323—31. Available at: https://doi.org/10.1111/j.1523-536 X.2006.00130.x.
- Kolomanska D, Zarawski M, Mazur-Bialy A. Physical Activity and Depressive Disorders in Pregnant Women-A Systematic Review. Medicina (Kaunas) 2019;55. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/31130705.
- Davenport MH, McCurdy AP, Mottola MF, et al. Impact of prenatal exercise on both prenatal and postnatal anxiety and depressive symptoms: a systematic review and meta-analysis. Br J Sports Med 2018;52:1376—85. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30337464.
- Perinatal Wellbeing Ontario. Group peer support program. Available at: https://www.perinatalwellbeing.ca/group-peer-support. Accessed on February 13, 2023.
- Postpartum Support International. PSI online support meetings. Available at: https://www.postpartum.net/get-help/psi-online-support-meetings/. Accessed on February 13, 2023.
- 102. Green SM, Haber E, Frey BN, et al. Cognitive-behavioral group treatment for perinatal anxiety: a pilot study. Archives of Women's Mental Health 2015;18:631—8. Available at: https://doi.org/10.1007/s00737-015-0498-z.

- 103. Loughnan SA, Wallace M, Joubert AE, et al. A systematic review of psychological treatments for clinical anxiety during the perinatal period. Archives of Women's Mental Health 2018;21:481—90. Available at: https://doi.org/10.1007/s00737-018-0812-7.
- 104. Simhi M, Sarid O, Cwikel J. Preferences for mental health treatment for post-partum depression among new mothers. Israel Journal of Health Policy Research 2019;8:84. Available at: https://doi.org/10.1186/s13584-019-0354-0.
- 105. Goodman JH. Women's Attitudes, Preferences, and Perceived Barriers to Treatment for Perinatal Depression. Birth 2009;36:60-9.
- Gibson K, Cartwright C, Read J. Patient-Centered Perspectives on Antidepressant Use. International Journal of Mental Health 2014;43:81—99.
- Sedov ID, Goodman SH, Tomfohr-Madsen LM. Insomnia Treatment Preferences During Pregnancy. JOGNN - Journal of Obstetric, Gynecologic, and Neonatal Nursing2017.
- 108. Dimidjian S, Goodman SH. Preferences and attitudes toward approaches to depression relapse/recurrence prevention among pregnant women. Behaviour Research and Therapy 2014;54:7—11.
- Lemon E, Vanderkruik R, Arch JJ, et al. Treating Anxiety During Pregnancy: Patient Concerns About Pharmaceutical Treatment. Maternal and Child Health Journal 2020;24:439

 –46.
- 110. Hinton L, Locock L, Knight M. Support for mothers and their families after life-threatening illness in pregnancy and childbirth:a qualitative study in primary care. British Journal of General Practice 2015:e563—9. Royal College of General Practitioners.
- 111. Hinton L, Locock L, Knight M. Partner experiences of "near-miss" events in pregnancy and childbirth in the UK: A qualitative study. PLoS ONE: Public Library of Science 2014.
- 112. Hinton L, Locock L, Knight M. Maternal critical care: what can we learn from patient experience? A qualitative study. BMJ open: BMJ Open 2015:e006676.
- 113. Price SK, Bentley KJ. Psychopharmacology decision-making among pregnant and postpartum women and health providers: informing compassionate and collaborative care women's health. Women Health 2013;53:154—72.
- 114. Hetrick SE, McKenzie JE, Bailey AP, et al. New generation antidepressants for depression in children and adolescents: a network meta-analysis. Cochrane Database Syst Rev 2021;5:CD013674. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34029378.
- 115. Kovich H, Kim W, Quaste AM. Pharmacologic Treatment of Depression, 107. American family physician; 2023. p. 173—81.
- Mistler LA, Drake RE. Shared decision making in antipsychotic management. J Psychiatr Pract 2008;14:333

 –44.
- 117. Whybrow R, Webster LM, Seed PT, et al. The effectiveness of decision aids for pregnancy related decision-making in women with pre-pregnancy morbidity; systematic review and meta-analysis. BMC Pregnancy and Childbirth 2022;22:81. Available at: https://doi.org/10.1186/s12884-022-04402-x.
- Vigod SN, Hussain-Shamsy N, Stewart DE, et al. A patient decision aid for antidepressant use in pregnancy: Pilot randomized controlled trial. J Affect Disord 2019;251:91—9. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/30913472.
- Cox EQ, Sowa NA, Meltzer-Brody SE, et al. The Perinatal Depression Treatment Cascade: Baby Steps Toward Improving Outcomes. J Clin Psychiatry 2016;77:1189–200.
- 120. Webb R, Uddin N, Ford E, et al. Barriers and facilitators to implementing perinatal mental health care in health and social care settings: a systematic review. Lancet Psychiatry 2021;8:521–34.
- Bayrampour H, Hapsari AP, Pavlovic J. Barriers to addressing perinatal mental health issues in midwifery settings. Midwifery 2018;59:47—58.
- Melville JL, Reed SD, Russo J, et al. Improving care for depression in obstetrics and gynecology: a randomized controlled trial. Obstet Gynecol

- 2014;123:1237—46. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24807320.
- 123. Cox EQ, Raines C, Kimmel M, et al. Comprehensive Integrated Care Model to Improve Maternal Mental Health. J Obstet Gynecol Neonatal Nurs 2017;46:923—30. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/28888920.
- 124. Dennis CL, Hodnett E, Kenton L, et al. Effect of peer support on prevention of postnatal depression among high risk women: multisite randomised controlled trial. Bmj 2009;338:a3064.
- Amani B, Merza D, Savoy C, et al. Peer-Delivered Cognitive-Behavioral Therapy for Postpartum Depression: A Randomized Controlled Trial. J Clin Psychiatry 2021;83.
- Iliadou M, Papadakaki M, Sioti E, et al. Addressing mental health issues among migrant and refugee pregnant women: A call for action. European Journal of Midwifery 2019;3. Available at: https://doi.org/10.18332/ ejm/108626.
- Foster VA, Harrison JM, Williams CR, et al. Reimagining Perinatal Mental Health: An Expansive Vision For Structural Change. Health Aff (Millwood) 2021;40:1592—6. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/34606355.
- Ross LE, Villegas L, Dennis CL, et al. Rural residence and risk for perinatal depression: a Canadian pilot study. Arch Womens Ment Health 2011;14:175—85. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/21311926.
- 129. Ross LE, Steele L, Goldfinger C, et al. Perinatal depressive symptomatology among lesbian and bisexual women. Arch Womens Ment Health 2007;10:53—9. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17262172.
- 130. Roy A, Thurston WE, the Voices and PHACES Study Team. Depression and mental health in pregnant Aboriginal women: Key results and recommendations from the Voices and PHACES study (Final report). Calgary, AB: University of Calgary; 2015. Available at: https://novascotia. cmha.ca/wp-content/uploads/2020/01/voices-phaces-study-finalreport. pdf. Accessed on March 27, 2023.
- 131. Canada S, editor Survey on Maternal Health2019.
- 132. Yonkers KA, Vigod S, Ross LE. Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. Focus 2012;10:51—66.
- 133. K V, GD E, V S. Prevalence, onset and course of anxiety disorders during pregnancy: A systematic review and meta analysis. J Affect Disord 2019;1:27–40.
- 134. O'Connell MA, Leahy-Warren P, Khashan AS, et al. Worldwide prevalence of tocophobia in pregnant women: systematic review and meta-analysis. Acta Obstet Gynecol Scand 2017;96:907—20.
- 135. Quin N, Lee JJ, Pinnington DM, et al. Differentiating perinatal Insomnia Disorder and sleep disruption: a longitudinal study from pregnancy to 2 years postpartum. Sleep 2022;45:14. Available at: https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?

 T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=34989808 http://sfx.scholarsportal.info/mcmaster?sid=OVID:medline&id=pmid: 34989808&id=doi:10.1093%2Fsleep%2Fzsab293&issn=0161-8105 &isbn=&volume=45&issue=2&spage=&pages=&date=2022&title= Sleep&atitle=Differentiating+perinatal+Insomnia+Disorder+and+ sleep+disruption%3A+a+longitudinal+study+from+pregnancy+to+2 +years+postpartum.&aulast=Quin&pid=%3Cauthor%3EQuin+N% 3BLee+JJ%3BPinnington+DM%3BNewman+L%3BManber+R% 3BBei+B%3C%2Fauthor%3F%3CAN%3E34989808%3C%2FAN%3E %3CDT%3EJournal+Article%3C%2FDT%3E.
- Khoramroudi R. The prevalence of posttraumatic stress disorder during pregnancy and postpartum period. J Family Med Prim Care 2018;7:220—3. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29915763.
- 137. Fairbrother N, Collardeau F, Albert AYK, et al. High Prevalence and Incidence of Obsessive-Compulsive Disorder Among Women Across Pregnancy and the Postpartum. J Clin Psychiatry 2021;82. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34033273.

- 138. Masters GA, Brenckle L, Sankaran P, et al. Positive screening rates for bipolar disorder in pregnant and postpartum women and associated risk factors. Gen Hosp Psychiatry 2019;61:53—9. Available at: https://www. ncbi.nlm.nih.gov/pubmed/31710859.
- 139. VanderKruik R, Barreix M, Chou D, et al. The global prevalence of postpartum psychosis: a systematic review. BMC Psychiatry 2017;17:272. Available at: https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med14&AN=28754094 http://sfx.scholarsportal.info/mcmaster?sid=OVID:medline&id=pmid:28754094&id=doi:10.1186%2Fs12888-017-1427-7&issn=1471-244X&cisbn=&volume=17&cissue=18&cspage=272&pages=272&date=2017&title=BMC+Psychiatry&atitle=The+global+prevalence+of+postpartum+psychosis%3A+a+systematic+review.&aulast=VanderKruik&pid=%3Cauthor%3EVanderKruik+R%3BBarreix+M%3BChou+D%3BAllen+T%3BSay+L%3BCohen+LS%3BMaternal+Morbidity+Working+Group%3C%2Fauthor%3E%3CAN%3E28754094%3C%2FAN%3E%3CDT%3EJournal+Article%3C%2FDT%3E.
- 140. Bye A, Martini MG, Micali N. Eating disorders, pregnancy and the postnatal period: a review of the recent literature. Current Opinion in Psychiatry 2021;34:563—8. Available at: https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=med19&AN=34475353 http://sfx.scholarsportal.info/mcmaster?sid=OVID:medline&id=pmid:34475353 &id=doi:10.1097%2FYCO.000000000000748&issn=0951-7367&isbn=&volume=34&issue=6&spage=563&pages=563-568&date=2021&title=Current+Opinion+in+Psychiatry&atitle=Eating+disorders%2C+pregnancy+and+the+postnatal+period%3A+a+review+of+the+recent+literature.&aulast=Bye&pid=%3Cauthor%3EBye+A%3BMartini+MG%3BMicali+N%3C%2Fauthor%3E%3CAN%3E34475353%3C%2FAN%3E%3CDT%3EJournal+Article%3C%2FDT%3E.
- 141. CB P, M Z, D C. Eating disorder symptoms pre- and postpartum. Arch Womens Ment Health 2016;19:675—80.

- 142. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150:782—6. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/3651732.
- Radloff L. The CES-D scale: A self-report depression scale for research in the general population. Applied psychological measurement 1977;1:385–401.
- 144. Spielberger CD, Sydeman SJ. State-Trait Anxiety Inventory and State-Trait Anger Expression Inventory. In: Maruish ME, editor. The use of psychological tests for treatment planning and outcome assessment. Hillsdale, NJ: LEA; 1994. p. 292–321.
- Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166: 1092—7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/16717171.
- 146. Bayrampour H, Hohn RE, Tamana SK, et al. Pregnancy-Specific Anxiety Tool (PSAT): Instrument Development and Psychometric Evaluation. J Clin Psychiatry 2023;84. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37074299.
- 147. Hirschfeld RM, Williams JB, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. Am J Psychiatry 2000;157:1873—5. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11058490.
- 148. Morin CM, Belleville G, Belanger L, et al. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep 2011;34:601–8. Available at: https://www.ncbi.nlm.nih. gov/pubmed/21532953.
- 149. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry 1989;46:1006—11. Available at: https://www.ncbi.nlm.nih.gov/ pubmed/2684084.