ACOG
The American College of Obstetricians and Gynecologists

CLINICAL PRACTICE GUIDELINE

NUMBER 5
JUNE 2023
REPLACES PRACTICE BULLETIN NUMBER 92, APRIL 2008

Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum

Committee on Clinical Practice Guidelines—Obstetrics. This Clinical Practice Guideline was developed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics in collaboration with Emily S. Miller, MD, MPH; Torri Metz, MD, MS; Tiffany A. Moore Simas, MD, MPH, MEd; and M. Camille Hoffman, MD, MSc; with consultation from Nancy Byatt, DO, MS, MBA; and Kay Roussos–Ross, MD.

The Society for Maternal-Fetal Medicine endorses this document.
The Committee on Women's Mental Health of the American Psychiatric Association reviewed and provided feedback on this document.

PURPOSE: To assess the evidence regarding safety and efficacy of psychiatric medications to treat mental health conditions during pregnancy and lactation. The conditions reviewed include depression, anxiety and anxiety-related disorders, bipolar disorder, and acute psychosis. For information on screening and diagnosis, refer to American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" (1).

TARGET POPULATION: Pregnant or postpartum individuals with mental health conditions with onset that may have predated the perinatal period or may have occurred for the first time in pregnancy or the first year postpartum or may have been exacerbated in that time.

METHODS: This guideline was developed using an a priori protocol in conjunction with a writing team consisting of one specialist in obstetrics and gynecology and one maternal–fetal medicine subspecialist appointed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics and two external subject matter experts. ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. Included studies underwent quality assessment, and a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into recommendation statements.

RECOMMENDATIONS: This Clinical Practice Guideline includes recommendations on treatment and management of perinatal mental health conditions including depression, anxiety, bipolar disorders, and acute postpartum psychosis, with a focus on psychopharmacotherapy. Recommendations are classified by strength and evidence quality. Ungraded

Good Practice Points are included to provide guidance when a formal recommendation could not be made because of inadequate or nonexistent evidence.

INTRODUCTION

Perinatal mental health conditions include a broad array of diagnoses, including but not limited to depressive, anxiety, bipolar, trauma-related, and psychotic disorders (2). These conditions can precede a pregnancy or can develop during the perinatal period. These conditions can affect pregnancy or the 12 months after delivery, regardless of whether onset occurred before pregnancy or during this full perinatal period. The 2021 prevalence of any mental illness in women in the United States was 27.2%, compared with 18.1% for men in the United States (3). During pregnancy or postpartum, approximately one in five women will develop an incident mental health condition (4). Thus, most obstetric care professionals can expect to encounter perinatal mental health conditions commonly throughout clinical care provision.

Despite their prevalence, perinatal mental health conditions are often not treated or are undertreated (5). Untreated and undertreated perinatal mental health conditions are associated with negative consequences for pregnant and postpartum people, including disrupted health behaviors, relationships, parenting, and physiology. These complications interact in complex ways to create risk for the fetus or offspring, the partner, and the family as a whole (including other children who may be affected). Understanding, discussing, and recommending treatment, including pharmacotherapy when indicated and needed (particularly for perinatal depression and anxiety), is within the scope of the obstetrician–gynecologist's (ob-gyn's) practice. Definitions and the epidemiology of each covered mental health condition are described in detail within American College of Obstetricians and Gynecologists (ACOG) Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" (1); a high-level overview of the conditions covered in this document is presented below.

For depression (6, 7) and anxiety disorders (8), psychotherapy and pharmacotherapy are efficacious treatments, and, when they are used in tandem, clinical benefits are enhanced (9, 10). Although this document includes brief information on the important role of psychotherapy in the treatment of perinatal mental health conditions, the focus of the guidance provided pertains to psychopharmacotherapy because direct delivery of psychotherapy is outside the scope of obstetric and gynecologic practice. It is important to acknowledge, particularly in the context of pregnancy or lactation, when exposures should be thoughtfully weighed, that psychotherapy is often a first-line treatment recommendation for mild-to-moderate depression or anxiety disorders (11). Nevertheless, psychotherapy is not always accessible or acceptable to individuals, and shared decision making is paramount to identify a treatment plan. For more severe mental health conditions, including but not limited to bipolar or psychotic disorders, or depression or anxiety that is refractory to first-line treatment, referral to or consultation with behavioral health resources is indicated.

As is true with many medications in pregnancy and lactation, psychopharmacology studies often rely on drug registries to support ongoing risk assessments. Obstetric care professionals and perinatal individuals can find information about psychopharmacology on the National Pregnancy Registry for Psychiatric Medications (12, 13).

Depressive Disorders

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) defines perinatal depression as a major depressive disorder with a time-onset specifier (2). Specifically, this includes an onset of depressive symptoms in pregnancy or up to 4 weeks postpartum, although most clinical experts recommend the application of this terminology until 12 months postpartum. The recognition of perinatal depression as a distinct entity carries importance for two reasons. First, it underscores the fact that pregnancy does not protect people from depression. Second, it serves to acknowledge how pregnancy and childbirth can be potent precipitants for psychiatric illness. The importance of treatment of perinatal depression should not be minimized; one quarter of women with perinatal depression will have symptoms for 3 years postpartum (14).

This document will focus primarily on the pharmacologic *management* of mental health conditions, including perinatal depression. However, more recent data support *prevention* of perinatal depression among those at high risk (15) through the use of counseling interventions, such as cognitive behavioral therapy (CBT) (eg, Mothers and Babies) (16–19), and interpersonal therapy (eg, the ROSE [Reach Out, Stay Strong, Essentials for mothers of newborns] program) (20–24), which has been shown to be cost effective (25). How clinicians can best identify and implement these psychotherapy-based interventions remains an area of active research (26).

Bipolar Disorder

The onset of bipolar disorder typically occurs in late adolescence or early adulthood (27). Thus, individuals with bipolar disorder often have the symptoms or diagnosis for the majority of their reproductive years. Moreover, recognition of incident bipolar disorders is important in obstetrics, because childbirth is one of the most potent precipitants of hypomania or mania (28). Additionally, for women with bipolar disorder, the risk of psychiatric

hospitalization in the postpartum period is significantly greater than at any other point in their lives (29).

Bipolar disorders include both bipolar I disorder and bipolar II disorder. Bipolar I disorder is defined by at least one episode of mania that may include psychotic features. Bipolar II disorder is characterized by hypomania, which is a less severe form of mania without any psychotic symptoms. In bipolar disorder, episodes of mania or hypomania occur in addition to episodes of depression. Importantly, sex differences in bipolar disorder have been documented, with females more often presenting with depressive polarity compared to manic/hypomanic polarity (30), and bipolar II disorder compared to bipolar I disorder (30, 31). Accordingly, women with bipolar disorder are often diagnosed later or misdiagnosed with a depressive disorder. It is important to note that almost a quarter (22.6%) of individuals with a positive perinatal depression screen will have bipolar disorder if further evaluated (4). Given that depressive symptomatology is more prominent than manic symptomatology in perinatal women, bipolar disorder is often mistaken for unipolar depression (32). Thus, before prescribing antidepressant monotherapy for presumed unipolar depression, a bipolar disorder screen is needed to avoid precipitating mania or psychosis, which has been associated with self-harm and infanticide (33).

The overall risk of bipolar disorder relapse postpartum is 35% (95% CI 29–41), with marked differences in those not treated with pharmacotherapy (66%, 95% CI 57–75) compared with those in whom pharmacotherapy is continued (23%, 95% CI 14–37) (34). Discontinuation of pharmacotherapy for bipolar disorder in pregnancy or postpartum is associated with a threefold higher risk of relapse compared with discontinuation of pharmacotherapy in nonperinatal women (35). Therefore, continuation of pharmacotherapy for pregnant individuals with bipolar disorder is highly recommended.

Anxiety Disorders

According to the DSM-5, the seven types of anxiety disorders are generalized anxiety disorder, panic disorder, agoraphobia, separation anxiety disorder, social phobia, selective mutism, and phobia-related disorders (2). Although each of these conditions holds distinct diagnostic criteria, they are often comorbid and share the common symptoms of fear and anticipatory anxiety and behaviors, often manifesting as avoidance. Notably, both obsessive-compulsive disorders (OCD) and trauma- and stressor-related disorders (including posttraumatic stress disorder [PTSD]) are now canonically separated from anxiety disorders into their own categories, reflecting the unique differences between them and anxiety disorders at large. However, although psychotherapy-based approaches to treatment of anxiety disorders, OCD, and PTSD are different, the pharmacologic approach is similar in that first-line treatment is an antidepressant.

Anxiety disorders are strikingly common, with contemporary data identifying that one in five women meet the diagnostic criteria for one or more disorders (36). Anxiety disorders can cause significant functional impairment, and, although not specific to pregnancy or postpartum, individuals with anxiety are more likely to have suicidal ideation and attempts compared with those without anxiety (37). Anxiety disorders are often comorbid with perinatal depression (38), and, even if not immediately comorbid, prenatal anxiety disorders are strong harbingers of postpartum depression (39, 40). Anxiety disorders during pregnancy have been associated with preterm birth and low birth weight (41), and perinatal anxiety disorders have been associated with behavioral challenges in offspring (42–45).

Postpartum Psychosis

Postpartum psychosis is rare, occurring in 1–2 per 1,000 pregnancies, and refers to the onset of psychosis in the postpartum period, which is often acute in onset. Postpartum psychosis often occurs in the context of bipolar disorder type I and can occur during an episode of mania, depression, or a mixed episode with psychotic features. Although the DSM-5 specifies that this diagnosis occurs "within the first 4 weeks post-birth," typical onset is 3–10 days after birth, and it can also occur after 4 weeks postpartum (2). Other symptoms of postpartum psychosis include agitation and delusions, disorganized thoughts, bizarre behavior, and auditory or visual hallucinations. Patients often have limited to no insight into their symptoms and may experience a dramatic shift from their usual level of function (46). Symptoms often fluctuate over time, making prompt recognition of the utmost importance.

Most women admitted to hospitals with postpartum psychosis as their ultimate diagnosis do not have a known psychiatric history (47, 48). If there is a psychiatric history, it is most likely bipolar disorder. Thus, early detection and ascertainment of a history of bipolar disorder specifically can help to identify individuals at risk for postpartum psychosis.

Individuals with bipolar I disorder and a history of postpartum psychosis have the highest recurrence risk, warrant specialty psychiatric care during pregnancy and postpartum, and should be seen by a psychiatrist (34). A prebirth planning meeting including the partner, family, friends, other support persons, mental health professionals, and obstetric care or primary care teams should be used to coordinate postpartum psychosis–prevention planning, including psychopharmacology, observation and support, and adequate sleep strategies (49).

Although long-term treatment of postpartum psychosis is beyond the scope of the ob-gyn, acute treatment by either an obstetrics team or emergency medicine team while awaiting psychiatric evaluation and treatment is warranted. Pharmacotherapy typically includes treatment with an antipsychotic and sometimes a benzodiazepine (such as lorazepam). Given that postpartum psychosis is associated with infanticide and suicide, psychiatric hospitalization is generally indicated; continuous observation can be used until this transfer can occur. An evaluation by a psychiatrist

that includes an assessment of risk of harm to self and the infant is critical. Longer-term treatment of this condition includes pharmacotherapy and sometimes requires electroconvulsive therapy; therefore, a psychiatrist must be involved in both acute and long-term care.

In studies evaluating prevention of postpartum psychosis, the initiation of high-dose lithium immediately after delivery has the strongest evidence (50). Foregoing breastfeeding overnight as part of sleep preservation and support can also be helpful in the early phase of treatment and stabilization. If treated quickly and appropriately, full remission can be achieved by 2 months postpartum (49, 50).

SUMMARY OF RECOMMENDATIONS

General Approach to Psychopharmacotherapy

ACOG recommends that obstetricians be prepared to counsel patients on the benefits and risks of psychopharmacotherapy for perinatal mental health conditions when clinically indicated. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends that obstetricians initiate psychopharmacotherapy for perinatal depression or anxiety disorders, refer patients to appropriate behavioral health resources when indicated, or both. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends that a validated screening tool be used to monitor for response to treatment or remission of depression or anxiety symptoms. If clinically indicated, the pharmacotherapy dosage should be up-titrated, with the goal of remission of depressive and anxiety symptoms. **(STRONG RECOMMENDATION, HIGH-QUALITY EVIDENCE)**

ACOG recommends that treatment for perinatal mood and anxiety disorders be equitably available and accessible to all pregnant and postpartum individuals. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends against withholding or discontinuing medications for mental health conditions due to pregnancy or lactation status alone. **(STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)**

Use Perinatal Psychiatry Access Programs as a resource for management and treatment guidance for individuals with mental health conditions. **(GOOD PRACTICE POINT)**

Safety and Efficacy of Pharmacologic Interventions for Perinatal Depressive Disorders

ACOG recommends that psychotherapy be considered a first-line treatment for mild-to-moderate perinatal depression. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends that selective serotonin reuptake inhibitors be used as first-line pharmacotherapy for perinatal depression. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications. **(STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)**

ACOG recommends consideration of brexanolone administration in the postpartum period for moderate-to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum. The decision to use brexanolone should balance the benefits (eg, rapid onset of action) with the risks and challenges (eg, limited access, high cost, lack of data supporting safety with breastfeeding, requirement for inpatient monitoring during the infusion, lack of efficacy data beyond 30 days). **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

Safety and Efficacy of Pharmacologic Interventions for Perinatal Anxiety Disorders

ACOG recommends that selective serotonin reuptake inhibitors be used as first-line psychopharmacotherapy for perinatal anxiety. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications. **(STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)**

ACOG recommends that benzodiazepines be avoided or prescribed sparingly as a treatment for perinatal anxiety. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

Safety and Efficacy of Pharmacologic Interventions for Bipolar Disorder during the Perinatal Period

ACOG recommends against discontinuing mood stabilizers, except for valproate, during pregnancy due to the risk of recurrence or exacerbation of mood symptoms. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends against valproate as a first-line treatment for bipolar disorder. Valproate should be avoided in pregnancy because reasonable alternatives usually can be identified. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends that pregnant individuals using antipsychotic medications undergo screening for gestational diabetes mellitus, consistent with standard prenatal care. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

ACOG recommends that pregnant patients taking lithium in the first trimester receive a detailed ultrasound

STRENGTH OF RECOMMENDATION

STRONG

ACOG recommends:

Benefits clearly outweigh harms and burdens. Most patients should receive the intervention.

ACOG recommends against:

Harms and burdens clearly outweigh the benefits. Most patients should not receive the intervention.

CONDITIONAL

ACOG suggests:

The balance of benefits and risks will vary depending on patient characteristics and their values and preferences. Individualized, shared decision making is recommended to help patients decide on the best course of action for them.

QUALITY OF EVIDENCE

HIGH

Randomized controlled trials, systematic reviews, and meta-analyses without serious methodologic flaws or limitations (eg, inconsistency, imprecision, confounding variables)
Very strong evidence from observational studies without serious methodologic flaws or limitations
There is high confidence in the accuracy of the findings and further research is unlikely to change this

MODERATE

Randomized controlled trials with some limitations
Strong evidence from observational studies without serious methodologic flaws or limitation

LOW

Randomized controlled trials with serious flaws
Some evidence from observational studies

VERY LOW

Unsystematic clinical observations
Very indirect evidence from observational studies

GOOD PRACTICE POINTS

Ungraded Good Practice Points are incorporated when clinical guidance is deemed necessary in the case of extremely limited or non-existent evidence. They are based on expert opinion as well as review of the available evidence.

examination in the second trimester. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

It is imperative that lithium dosing be monitored during pregnancy and postpartum. **(GOOD PRACTICE POINT)**

Safety and Efficacy of Pharmacologic Interventions for Postpartum Psychosis

Postpartum psychosis is a psychiatric emergency. Treatment options that are within the scope of obstetricians, while awaiting further assessment, recommendations, and a treatment plan by a psychiatrist, include sedating antipsychotic medications such as olanzapine or haloperidol that can be used with benzodiazepines such as lorazepam. If haloperidol is used, benztropine or diphenhydramine should be administered to prevent extrapyramidal symptoms and dystonia. **(GOOD PRACTICE POINT)**

METHODS

ACOG Clinical Practice Guidelines provide clinical management recommendations for a condition or procedure by assessing the benefits and harms of care options through a systematic review of the evidence. This guideline was developed using an a priori protocol in conjunction with a writing team consisting of one specialist in obstetrics and gynecology and one maternal–fetal medicine subspecialist appointed by the ACOG Committee on Clinical Practice Guidelines–Obstetrics and two external subject matter experts. A full description of the Clinical Practice Guideline methodology is published separately (51). The following description is specific to this Clinical Practice Guideline.

Literature Search

ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE. Parameters for the search included human-only studies published in English. The Agency for Healthcare Research and Quality's (AHRQ) "Maternal, Fetal, and Child Outcomes of Mental Health Treatments in Women: A Systematic Review of Perinatal Pharmacologic Interventions" systematic review served as an evidence base for this Clinical Practice Guideline (52). For topics in this guideline related to the AHRQ review, the literature search was limited to the end date of the AHRQ search until 2021. For all topics included in this guideline but not included in the AHRQ review, the literature search was restricted to studies from 2000 to 2021. The MeSH terms and keywords used to guide the literature search can be found in Appendix A. An updated literature search was completed in December 2022 and reviewed by two members of the writing team using the same systematic process as the original literature search. A final supplemental literature search was performed in February 2023 to ensure that any newly published high-level sources were addressed in the Clinical Practice Guideline.

Study Selection

A title and abstract screen of all studies was completed by ACOG research staff. Studies that moved forward to the full-text screening stage were assessed by two authors from the writing team based on standardized inclusion and exclusion criteria. To be considered for inclusion, studies had to be conducted in countries ranked very high on the United Nations Human Development Index (53), published in English, and include participants identified as female or women. Although systematic reviews, randomized controlled trials, and observational studies were prioritized, case reports, case series, and narrative reviews were considered for topics with limited evidence. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the included and excluded studies can be found in Appendix B. All studies that underwent quality assessment had key details extracted (study design, sample size, details of interventions, outcomes) and descriptions included in the summary evidence tables (Appendix C).

Recommendation and Manuscript Development

A modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-to-decision framework was applied to interpret and translate the evidence into draft recommendation statements, which were classified by strength and evidence quality (54, 55). Ungraded Good Practice Points were incorporated to provide clinical guidance in the case of extremely limited or nonexistent evidence. They are based on expert opinion as well as review of the available evidence (56). The recommendations and supporting evidence tables were then reviewed, revised as appropriate, and affirmed by the Committee on Clinical Practice Guidelines–Obstetrics at a meeting. The guideline manuscript was then written and subsequently reviewed and approved by the Committee on Clinical Practice Guidelines–Obstetrics and other internal review bodies before continuing to publication. Committee membership includes a physician triple-boarded in obstetrics and gynecology, psychiatry, and addiction medicine. Board-certified psychiatrists served as reviewers for this Clinical Practice Guideline

Use of Language

ACOG recognizes and supports the gender diversity of all patients who seek obstetric and gynecologic care. In original portions of this document, authors seek to use gender-inclusive language or gender-neutral language. When describing research findings, this document uses gender terminology reported by investigators. To review ACOG's policy on inclusive language, see https://www.acog.org/clinical-information/policy-and-position-statements/statements-of-policy/2022/inclusive-language.

CLINICAL OVERVIEW

Psychoeducation Regarding Self-Care

For all pregnant and postpartum individuals, education regarding self-care is an essential component of holistic well-being that accounts for both physical and emotional or mental health. This includes the role of adequate sleep, exercise, and balanced nutrition. In addition, building skills in creating time for oneself, minimizing stressors when possible, and asking for support are opportunities for wellness promotion in all individuals. Promoting dialogue regarding wellness may facilitate an open space to discuss mental health concerns. In addition to conversations about overall wellness, educating pregnant and postpartum patients about symptoms of depression and anxiety and the risks of untreated mental health conditions is a recommended clinical practice (33). The role of engaging partners or other support people in these conversations is also important and an area of active research.

Counseling Regarding Psychopharmacotherapy During Pregnancy

General Treatment Approach

Once the choice to initiate or continue pharmacotherapy has been made, and assuming that a conversation about psychotherapy options and other adjuncts to care has already been held, optimal dosing is critical to avoid undertreatment. Although it is important to consider the individual patient's illness severity and prior psychiatric history, general principles to psychopharmacotherapy during pregnancy include:

1. Use the lowest effective dose. The goal of any treatment plan is to use the lowest dose of any medication that achieves the clinical goal. After the initial care plan is enacted, the perinatal individual requires symptom monitoring and adjustment or titration as needed to ensure illness remission.
2. Avoid polypharmacy. If symptom remission is possible with a single agent, this is preferred because polypharmacy increases exposures and, thus, the risk of potential adverse outcomes.
3. Minimize switching medications. Transitioning to another psychopharmacologic agent often requires a cross-taper (ie, the dose of the initial medication is down-titrated while the newer agent is initiated and up-titrated). This results in increased exposure, which is best avoided if a therapeutic effect can be reached with a single agent. For this reason, a careful assessment of what (if any) medication has been effective in the past is of particular importance. Furthermore, assuming that side effects are not prohibitive, dose optimization should be considered before switching medications.

4. Consider untreated or inadequately treated mental health disorders an exposure. Although the perinatal risks associated with any psychopharmacologic agent should be considered in clinical decision making, obstetric care professionals should also recognize the risks associated with inadequate treatment of mental health conditions (Table 1).

Psychopharmacotherapy Titration and Discontinuation

For most medications, follow-up and dose adjustment are informed by symptom monitoring. This can be done through the use of validated instruments initially used for screening (1), clinical assessment, or both. If symptoms are not improving, the dose of the medication may need to be up-titrated. Up-titration in pregnancy may be required with advancing gestation secondary to expected physiologic changes, such as increased renal clearance and distribution volume, as well as changes in the activity of drug-metabolizing enzymes. Some psychiatric medications, including lithium and tricyclic antidepressants, have therapeutic drug ranges that require monitoring. Others, such as selective serotonin reuptake inhibitors (SSRIs), do not have an established therapeutic concentration, but their concentration-to-dose ratios are known to be dynamic across pregnancy and postpartum (57). Regardless of whether symptoms or drug levels are used, systems should be in place to follow these results to facilitate safe and efficacious treatment.

Up-titration of pharmacotherapy in pregnancy raises the question of whether down-titration is required in the third trimester to avoid neonatal withdrawal symptoms or postpartum, with the resolution of pregnancy physiology. Down-titration of psychopharmacotherapy in the third trimester is not recommended, because it is not associated with improved neonatal outcomes and is associated with increased risk of exacerbation of the mental health condition (58–60). Optimized dosing for psychopharmacotherapy across the postpartum transition is incompletely understood. The postpartum transition can be a particularly destabilizing period for depression or anxiety disorders, and SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) are well-tolerated medications. Thus, experts recommend against empiric down-titration postpartum for SSRIs or SNRIs. However, some medications, including lithium and lamotrigine, do need to be carefully but expeditiously down-titrated postpartum back to prepregnancy dosing schedules to avoid toxicity. Postpartum care plans, including any anticipated dose titrations, should be in place before delivery. Although it is generally not recommended to discontinue or avoid pharmacotherapy due to pregnancy, individuals may stop or not initiate recommended psychiatric medications in pregnancy. In such cases, treatment should be started or reinitiated postpartum. This is particularly salient for women with a history of postpartum psychosis, which has a 66% recurrence risk in the absence of pharmacotherapy (34).

In general, pregnant and postpartum individuals with severe mental health conditions, such as bipolar disorder or psychotic disorders, should continue medication management. For most individuals with depression or anxiety disorders diagnosed during pregnancy or postpartum, obstetric care professionals should recommend continued treatment of psychopharmacotherapy for at least 6–12 months of symptom remission before considering discontinuation. If 9–12 months after remission of symptoms occurs in pregnancy or in the early postpartum period, discontinuation carries higher risk. In general, discontinuing effective pharmacotherapy during pregnancy or the postpartum period increases risk of relapse and is not recommended. If discontinuation is being considered, it requires careful consideration of the risk of recurrence. For major depressive disorder, discontinuation of medications before remission (ie, complete resolution of symptoms) and an increasing number of lifetime depressive episodes are strong predictors of recurrence (61).

Abrupt discontinuation of SSRIs or SNRIs is associated with symptoms including gastrointestinal upset, dizziness, fatigue, headache, sleep disruption, agitation or anxiety, myalgias, tremors, headaches, and electric-like shocks (62). The timing of onset of discontinuation symptoms is predicated on the half-life of the medication being used, with longer half-life SSRIs such as fluoxetine having the lowest incidence and severity of symptoms (63). To avoid this complication, individuals who have been on an SSRI or SNRI should undergo a progressive taper over 2–4 weeks (64).

Psychopharmacotherapy During Lactation

In general, individuals with mental health conditions should not be discouraged from breastfeeding if that is their desired form of infant feeding. Furthermore, if a woman is stable on a particular medication throughout pregnancy, the psychopharmacotherapy should not be changed postpartum because fetal exposure supersedes exposure through lactation (65, 66). However, if pharmacotherapy is being initiated during lactation, passage through breast milk should be considered alongside the likelihood of drug efficacy. As is true during pregnancy, medications for which there are available safety data are preferred over medications recently introduced, although any personal history of effectiveness should drive clinical decision making. Measures such as the relative infant dose should be considered, which reflects the measure of the infant's exposure to the medication through breast milk relative to the mother's dose. This measurement is influenced by several factors, including lipid solubility, half-life, oral bioavailability, molecular weight, drug ionization, and protein binding. In general, a relative infant dose less than 10% is considered compatible with breastfeeding, although data specific to each medication should also be considered. In addition to the relative infant dose, preterm birth, and the infant's age should be considered, because immature metabolism can reduce medication clearance. Existing resources that can be useful

Table 1. General Approach to Risk Counseling for Depression Psychopharmacotherapy	
Risks of under-treatment or no treatment for depression during pregnancy include…	**Risks of antidepressant use during pregnancy include…***
Limited engagement in medical care and self-care	PPHN
Substance use	Transient neonatal adaptation syndrome
Preterm birth	Preeclampsia (SNRIs)
Low birth weight	Spontaneous abortion (SNRIs)
Preeclampsia	
Postpartum depression	
Impaired infant attachment (which carries long-term developmental effects)	
Disrupted relationship with partner	
Suicide†	

PPHN, persistent pulmonary hypertension of the newborn; SNRI, serotonin-norepinephrine reuptake inhibitor.

*Data derived from literature that accounts for the underlying indication for antidepressant use.

†Suicide is a leading preventable contributor to maternal mortality in the United States, exceeding hemorrhage and hypertensive disorders.

Data from Trost SL, Beauregard J, Nijie F. Pregnancy-related deaths: data from maternal mortality review committees in 36 US states, 2017–2019. Centers for Disease Control and Prevention; 2022. Accessed December 7, 2022. https://www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/data-mmrc.html *and* Viswanathan M, Middleton JC, Stuebe A, Berkman N, Goulding AN, McLaurin-Jiang S, et al. Maternal, fetal, and child outcomes of mental health treatments in women: a systematic review of perinatal pharmacologic interventions. Comparative Effectiveness Review, No. 236. Agency for Healthcare Research and Quality; 2021. Accessed February 8, 2023. https://www.ncbi.nlm.nih.gov/books/NBK570101/

in guiding these decisions include the Drugs and Lactation Database (13) and the MotherToBaby service from the Organization of Teratology Information Specialists (67).

Finally, although breastfeeding is recommended in general, the individual risks and benefits of infant feeding modalities should also balance destabilizing factors such as stress and sleep deprivation. These factors can be particularly destabilizing in the context of bipolar disorder.

Health Systems Approaches

The treatment of pregnant and postpartum individuals with mental health conditions requires a systems-based approach to support the care cascade from screening to remission of symptoms. One example of a health systems approach is the collaborative care model, a structured health services intervention that includes a care manager (typically a licensed clinical social worker) to coordinate patient-centered care delivery. The collaborative care model also includes a patient registry and weekly care meetings, both of which serve to track symptom response and support treatment to remission. Two randomized trials have shown the collaborative care model to improve mental health care within obstetrics and gynecology clinics (68, 69).

Another systems resource to support the care of pregnant and postpartum individuals with mental health conditions is Perinatal Psychiatric Access Programs (70). The majority of these programs are state-based; however, there exists support through Postpartum Support International's Perinatal Psychiatric Consult Line (71) for clinicians in states without a designated Perinatal Psychiatry Access Program and through the U.S. Department of Veterans Affairs (VA) Women's Mental Health Line for VA clinicians (72). The state-based and national Perinatal Psychiatry Access Programs connect clinicians with perinatal psychiatrists and resource and referral specialists who provide education and resources to support management of mental health conditions for pregnant and postpartum individuals. There also exists a Health Resources & Services Administration–funded 24/7, free, confidential national maternal mental health hotline (1-833-943-5746 [1-833-9-HELP4MOMS]) for pregnant and postpartum individuals, with services available by phone or text and in multiple languages (73).

CLINICAL RECOMMENDATIONS AND EVIDENCE SUMMARY

General Approach to Psychopharmacotherapy

ACOG recommends that obstetricians be prepared to counsel patients on the benefits and risks of psychopharmacotherapy for perinatal mental health conditions when clinically indicated. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

The high prevalence of perinatal mental health conditions alongside their association with significant negative

outcomes has resulted in a near universal recommendation from multiple colleges, societies, and governmental organizations to screen for various mental health conditions during pregnancy and postpartum (74–80). Yet screening alone does not improve health outcomes. Thus, the recommendation to screen should be partnered with preparedness to discuss and provide treatment options for individuals who screen positive.

ACOG recommends that obstetricians initiate psychopharmacotherapy for perinatal depression or anxiety disorders, refer patients to appropriate behavioral health resources when indicated, or both. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Discussing and initiating pharmacotherapy for depression or anxiety disorders is an important component of comprehensive reproductive health care and, as such, is within the clinical scope of ob-gyns. Many obstetric care professionals report discomfort with and insufficient training in the treatment of perinatal mental health conditions (81, 82). Additional clinical education in psychopharmacology is available through several training modules, including the National Curriculum in Reproductive Psychiatry, Postpartum Support International Frontline Provider Trainings, and Lifeline for Moms e-modules available through ACOG (83–85).

In general, SSRIs are considered first-line medications for the treatment of perinatal depression or anxiety disorders. For individuals who have been treated effectively with an antidepressant from any class (eg, SSRI, SNRI) in the past, that medication should be the pharmacotherapy of choice. For those who have not taken a medication in the past and for those for whom other medications were not effective, sertraline is often preferred due to its extensive and reassuring safety evaluation in the medical literature. Escitalopram is a reasonable alternative based on efficacy and acceptability data in the general population (86). Fluoxetine has a long half-life and active metabolites, which have been associated with an increased risk of neonatal adaptation syndrome and accumulation in breastfed infants (87). These data should not preclude the use of fluoxetine if it has been previously effective outside of pregnancy.

Unopposed SSRIs or SNRIs can precipitate mania in individuals with bipolar disorder. Before the use of any pharmacologic agent for the treatment of suspected depression, screening for bipolar disorder is recommended. Psychoeducation regarding symptoms of mania should be provided with any prescription of an antidepressant medication, and patients should be advised to stop the medication and return for a clinical assessment if these symptoms arise. See ACOG Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" for details of this assessment (1).

Other complementary, alternative, and integrative medicine approaches to the treatment of perinatal mental health conditions exist, including acupuncture, massage, yoga, exercise, bright-light therapy, mindfulness-based stress reduction, and dietary supplements. Because the delivery of these interventions is outside of the general practice of most ob-gyns, details are not included in this document. In addition, because psychotherapy is also outside of the clinical practice of most ob-gyns, details on the types and efficacy of psychotherapy used for perinatal mental health conditions are not included in this document. Nonetheless, psychotherapy is first-line treatment for mild-to-moderate depression and anxiety; thus, establishing timely referral pathways is recommended (33).

ACOG recommends that a validated screening tool be used to monitor for response to treatment or remission of depression or anxiety symptoms. If clinically indicated, the pharmacotherapy dosage should be up-titrated, with the goal of remission of depressive and anxiety symptoms. (STRONG RECOMMENDATION, HIGH-QUALITY EVIDENCE)

The goal of any treatment is remission, defined as resolution of the underlying symptoms; often, particularly in pregnancy, up-titration of medications is required. Undertreatment in obstetrics is common (88) and results in exposures to both the underlying illness as well as the pharmacologic agent.

For most medications that will be prescribed by obstetric care clinicians (eg, SSRIs or SNRIs), monitoring requires symptom assessment. Validated screening instruments should be used to track symptom response (defined as an improvement of 50% of more from baseline) and remission. To ensure comparability in symptom scores across time, obstetric care professionals should use the same screen to follow symptom trajectory after treatment. Existing algorithms have been published to support dose adjustments in the setting of perinatal depression, with an example of serial monitoring and medication adjustment using serial validated screens such as the PHQ-9 (Patient Health Questionnaire-9) or EPDS (Edinburgh Postnatal Depression Scale) to inform up-titration. An example of one of these algorithms is shown in Figures 1 and 2. Similar approaches can be used for anxiety by incorporating validated screens for anxiety (1).

Health Equity

ACOG recommends that treatment for perinatal mood and anxiety disorders be equitably available and accessible to all pregnant and postpartum individuals. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

The field of mental health also experiences the inequities that plague perinatal health in general. As an extreme example, there have been growing disparities in suicide rates in the United States across race, ethnicity, geography, sexual minority status, and socioeconomic status

(89). Systems-based approaches are required to achieve perinatal mental health equity. One example of an approach to mitigation of disparities in perinatal mental health care is a collaborative care model—an equity-focused health services intervention to integrate mental health into primary care settings. Implementation of the collaborative care model, adapted for perinatal care, was associated with reductions in racial disparities in screening for perinatal depression and in obstetric care professional recommendations for treatment (90).

ACOG recommends against withholding or discontinuing medications for mental health conditions due to pregnancy or lactation status alone. (STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)

With almost all psychiatric mediations (with the notable exception of valproic acid), withholding or discontinuing medications due to pregnancy or lactation alone is not typically indicated. Particularly if a therapeutic benefit has been achieved, discontinuation runs the risk of destabilization, which can result in adverse outcomes (91). Although no randomized clinical trials have been conducted that evaluate discontinuing pharmacotherapy in pregnant individuals, randomized trials in the general population suggest that continuation of medications reduces the risk of relapse (92). Observational data from pregnant women who discontinued treatment for affective disorders, including depression, demonstrate a higher rate of symptom relapse compared with those who continued psychopharmacotherapy (68% vs 26%, hazard ratio 5.0, 95% CI 2.8–9.1) (93, 94). This risk is particularly heightened for pregnant women with multiple episodes of psychiatric illness (95).

The decision to withhold or discontinue pharmacotherapy is often driven by perceived risks of the medication. Details on the safety profile of each medication are described within the relevant sections; however, the absolute risks of adverse obstetric, perinatal, or infant developmental outcomes for almost all psychiatric medications appear to be low and should be balanced against the high risk of illness recurrence. In general, for most pregnant individuals and for most medications, this balance favors continuation of psychopharmacotherapy. For individuals presenting to care prepregnancy, shared decision making should include discussion of the risks of the medication during pregnancy and lactation, alternative treatments (and their associated efficacy and risks), the potential for psychiatric destabilization during the treatment transition, and the risks of the mental health condition if it is untreated.

Use Perinatal Psychiatry Access Programs as a resource for management and treatment guidance for individuals with mental health conditions. (GOOD PRACTICE POINT)

Perinatal Psychiatry Access Programs were developed to increase the capacity of obstetric care clinicians to care for pregnant, postpartum, and lactating individuals and those planning pregnancy who have perinatal mental health and substance use disorders. Perinatal Psychiatry Access Programs include 1) training and toolkits for perinatal mental health treatment; 2) real-time psychiatric consultation; and (3) resource and referral linkages to community-based mental health resources (96, 97) (see the "Health Systems Approaches" section for additional information).

Safety and Efficacy of Pharmacologic Interventions for Perinatal Depressive Disorders

ACOG recommends that psychotherapy be considered a first-line treatment for mild-to-moderate perinatal depression. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Psychotherapy, including CBT or interpersonal therapy, is an effective treatment for perinatal depression (98). The use of psychotherapy as an initial treatment approach aligns with the recommendations of multiple professional societies, including the American Psychiatric Association (99) and the National Institute for Health and Care Excellence (76). Although psychotherapy is appropriate as a first-line treatment for some pregnant and postpartum people, shared decision making and individualized patient-centered care are prudent. For example, for individuals who previously did not respond to psychological interventions, those for whom culturally responsive psychotherapy is not accessible, or those for whom the resource commitment for psychotherapy precludes engagement, pharmacotherapy should be considered as a first-line treatment option. Access to psychotherapy remains limited for many pregnant and postpartum individuals, including but not limited to those who are non–English-speaking, uninsured, or geographically isolated. Future research on the role of psychotherapy embedded within digital mental health tools may show promise in improving access to evidence-based psychotherapy.

ACOG recommends that selective serotonin reuptake inhibitors be used as first-line pharmacotherapy for perinatal depression. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications. (STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)

No randomized trials have evaluated the efficacy or safety of pharmacotherapy for antenatal depression. The paucity of high-quality evidence is of particular importance

considering the number of pregnant women exposed to antidepressants (100). Clinical decision making regarding pharmacology relies on extrapolation of efficacy data from the general population. Meta-analytic data demonstrate antidepressant medications to be more effective than placebo (101). This conclusion holds true for the use of antidepressants in primary care settings, where SSRIs have a median number needed to treat of 7 and a number needed to harm of 20–90 (102). Although the efficacy of adequately dosed SSRIs or SNRIs is unlikely to differ due to pregnancy or lactation, the potential pregnancy-associated pharmacokinetic changes raise concerns about how to best achieve a therapeutic response (103).

For individuals with a prior history of pharmacologic treatment of depression, any previously effective medication should be considered first-line treatment for reinitiation during pregnancy and postpartum. For those without a history of effective treatment or with incident depression, SSRIs are preferred as first-line treatment. Although SSRIs and SNRIs are both effective treatments for major depressive disorder in adults, SSRIs are generally preferred because of their safety and tolerability. Specifically, when compared with unexposed women with depression, SNRIs were associated with an increased risk of preeclampsia in two studies (8.8% vs 5.4%, adjusted relative risk 1.52, 95% CI 1.25–1.83; 4.5% vs 2.4%, adjusted relative risk 1.95, 95% CI 1.25–3.03) (52). Similarly, one cohort study (N=9,014) identified an increased risk of spontaneous abortion in individuals exposed to SNRIs in the first trimester compared with those with a history of depression (15.0% vs 8.1%) and found a 1.7-fold increased risk (95% CI 1.2–2.6) of spontaneous abortion after adjusting for confounders and correcting for induced abortions (104). However, the quality of evidence for the risks of preeclampsia and spontaneous abortion is low; thus, if an individual is stable on an SNRI or has had therapeutic benefit in the past, the risk–benefit balance likely favors use of the previously effective medication. Although some data suggest a class effect for SSRIs (105), other data suggest that sertraline and escitalopram are favored first-line SSRIs because of their efficacy and tolerability profiles (86). However, other factors, such as comorbid illnesses, potential drug–drug interactions, cost, and side-effect profile, should be considered for each individual patient.

Although most SSRIs are generally well-tolerated, side effects can occur. These include nausea, dry mouth, insomnia, diarrhea, headache, dizziness, agitation or anxiety, drowsiness, and sexual dysfunction. Most of these side effects dissipate with time, with the notable exception of sexual dysfunction. Specifically, some patients, particularly those with comorbid anxiety symptoms, report an initial exacerbation of agitation or anxiety symptoms. This particular side effect is often mitigated by starting with half of the lowest dose and gradually up-titrating over 4–10 days. Insofar as most individuals with perinatal depression have concomitant anxiety symptoms (4), many experts consider dose titration to be a best practice for initiating treatment for perinatal depression. In addition, activating antidepressants such as fluoxetine, duloxetine, venlafaxine, and bupropion may exacerbate anxiety symptoms. Thus, in someone with moderate-to-severe comorbid anxiety, alternatives to these medications should be considered when appropriate.

Selective serotonin reuptake inhibitors are perhaps one of the best studied class of medications in pregnancy. Although randomized trials to assess safety have not been conducted, multiple observational studies support a favorable safety profile. Some of the safety risks that have been evaluated in the literature, referencing some of the highest quality data available, are described in Table 2. Importantly, much of the published literature uses a comparison framework of exposure to antidepressant medications for the treatment of depression compared with no exposures (ie, no history of depression and no use of antidepressant medications). These types of comparisons can lead to false or misleading conclusions because they do not account for the underlying medical illness.

The two neonatal risks consistently identified in the literature when the proper comparison groups were used include persistent pulmonary hypertension of the newborn (PPHN) and neonatal adaptation syndrome (with resultant neonatal intensive care unit [NICU] admission). Persistent pulmonary hypertension of the newborn is a rare but potentially fatal condition, characterized clinically by respiratory distress within the first hours of life and carrying a 10–20% risk of mortality. Biological plausibility for an association between SSRI exposure in utero and PPHN exists because serotonin exposure can cause vasoconstriction and smooth muscle cell proliferation in the fetal lung. In 2006, the U.S. Food and Drug Administration (FDA) issued a public health advisory regarding SSRIs based on a case–control study that identified increased odds of PPHN with exposure to SSRIs after 20 weeks of gestation (adjusted odds ratio [aOR] 6.1, 95% CI 2.2–16.8) (106). Multiple observational studies and meta-analyses have corroborated the association between antenatal exposure to SSRIs or SNRIs and PPHN (107–109). When ranked by individual drug-related risk, sertraline ranked as the least likely to be associated with PPHN, followed by escitalopram (108).

Notably, each of the aforementioned studies is limited by confounding by indication. Attempting to account for this residual bias, a cohort study nested within an administrative database of individuals with Medicaid insurance defined a relevant exposure to antidepressants as 90 days before delivery through delivery (110). Women were considered exposed if they filled at least one prescription for an antidepressant and International Classification of Diseases, Ninth Revision diagnostic

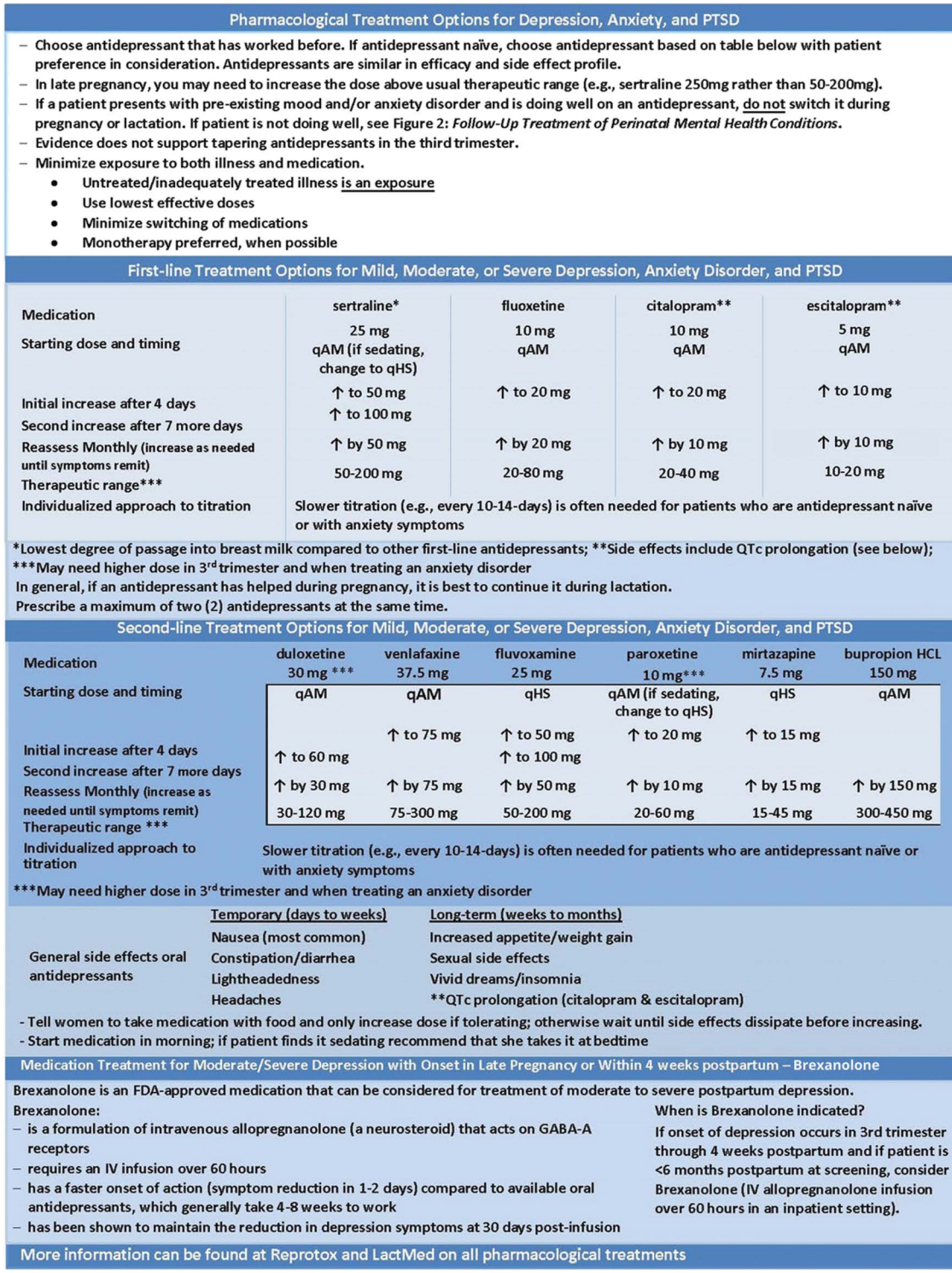

Fig. 1. Starting treatment for perinatal mental health conditions. FDA, U.S. Food and Drug Administration; GABA-A, gamma aminobutyric acid type A; IV, intravenous; mg, milligrams; PTSD, posttraumatic stress disorder; qAM, every morning; qHS, every bedtime.
Modified from Byatt N, Mittal LP, Brenckle L, Logan DG, Masters GA, Bergman A, et al. Lifeline for Moms Perinatal Mental Health Toolkit. University of Massachusetts Medical School; 2019. Accessed March 20, 2023. https://www.umassmed.edu/lifeline4moms/products-resources/toolkits-and-apps/2019/11/lifeline4moms-perinatal-mental-health-toolkit/

codes defined the outcome of PPHN. Analyses were restricted to women with a diagnosis of depression and used propensity score stratification to address additional confounding by disease severity. The primary analysis demonstrated no increased odds of PPHN for those exposed to SSRIs (aOR 1.12, 95% CI 0.95–1.31) or non-SSRI antidepressants (aOR 1.01, 95% CI 0.76–1.35). Secondary analyses, focused on primary PPHN, restricted the sample by excluding preterm infants and infants with congenital cardiac malformations or lung abnormalities. These analyses identified increased odds of PPHN for SSRIs (aOR 1.28, 95% CI 1.01–1.64) but not for non-SSRI antidepressants (aOR 1.14, 95% CI 0.74–1.74). This body of literature, in its totality, suggests that there may be an increased risk of PPHN associated with SSRI exposure. Importantly, the absolute risk of PPHN is low (approximately 1–2/1,000 additional cases of PPHN) and should be balanced against the significant risks associated with untreated depression. Accordingly, the FDA updated their guidance and advised clinicians to not alter their clinical practice of treating depression during pregnancy due to concerns for PPHN (106).

Neonatal adaptation syndrome includes a constellation of neonatal symptoms that have been associated with SSRI and SNRI exposure in utero, including irritability, restlessness, tremors, hyperreflexia, hypoglycemia, hypothermia, disruptions in sleep, poor feeding, and, rarely, seizures. Neonatal adaptation symptoms typically emerge within the first few days of life and resolve within 2 weeks (111). The estimated prevalence of neonatal adaptation syndrome varies widely due to heterogeneity in the case definition and ranges in the published literature from 5% to 85% (112), although most studies estimate the incidence to be 10% to 30%. Fluoxetine and paroxetine have been implicated more commonly in neonatal adaptation syndrome (113).

The phenomenology of neonatal adaptation syndrome is poorly understood. Some hypothesize that the symptoms are related to serotonergic withdrawal, whereas others suggest that they are related to serotonergic toxicity. As with much of the literature on antenatal SSRI exposure, many of the data compare newborns exposed to antidepressant medications with newborns not exposed to either perinatal depression (or with an unknown depression status) or antidepressant medications (112, 114). Importantly, although neonatal adaptation syndrome is self-limited without evidence of long-term risks, pregnant individuals taking an SSRI or SNRI should deliver in a hospital to facilitate pediatric assessment and monitoring if needed. Supportive measures, such as skin-to-skin contact and frequent feedings, can be used for neonatal symptom management.

To mitigate against the risk of neonatal adaptation syndrome, some have suggested discontinuing or decreasing the dose of the SSRI or SNRI in the third trimester, before delivery. Observational data suggest that these changes are not associated with neonatal adaptation syndrome risk mitigation (58, 59). Moreover, tapering antidepressant medication increases the risk of symptom relapse. Thus, discontinuing or decreasing the dose of the antidepressant before delivery to reduce the risk of neonatal adaptation syndrome is not recommended clinical practice.

Two randomized trials (N=162, N=38) have evaluated the efficacy of SSRIs (specifically sertraline) for the treatment of postpartum depression (115, 116). In these studies, sertraline improved response and remission rates relative to placebo, although the small sample size and loss to follow-up limit the quality of this evidence (52).

ACOG recommends consideration of brexanolone administration in the postpartum period for moderate-to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum. The decision to use brexanolone should balance the benefits (eg, rapid onset of action) with the risks and challenges (eg, limited access, high cost, lack of data supporting safety with breastfeeding, requirement for inpatient monitoring during the infusion, lack of efficacy data beyond 30 days).

(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Brexanolone is a neurosteroid that mimics the action of allopregnanolone, a progesterone metabolite that acts as a positive allosteric modulator of the GABA-A receptor. Three randomized trials (N=267 total) evaluated the efficacy of brexanolone for the treatment of depression with onset in the third trimester or within 4 weeks postpartum. Compared with placebo, brexanolone led to a greater response within 24 hours (risk ratio 1.34, 95% CI 1.03–1.73) (117). The integrated analyses demonstrated an effect size for only 7 days (risk ratio 1.32, 95% CI 1.01–1.73). A marked clinical improvement was seen in the placebo arm, which, given the observed duration, may reflect the benefits of self-care and sleep that were likely facilitated by hospitalization. Based on these results, in 2019, brexanolone became the first medication to be FDA-approved for the treatment of moderate-to-severe postpartum depression. Brexanolone is given intravenously over 60 hours. Because a risk of sedation or loss of consciousness was identified, brexanolone is currently approved only within supervised medical settings that can support continuous pulse oximetry (118). Registration in a Risk Evaluation and Mitigation Strategy (REMS) registry is required, and brexanolone is administered only in certified health care facilities.

No comparative effectiveness trials have been conducted to assess the relative efficacy of brexanolone compared with SSRIs or SNRIs. The perceived advantages of brexanolone are the large effect size and quick time to response and remission. Disadvantages include the

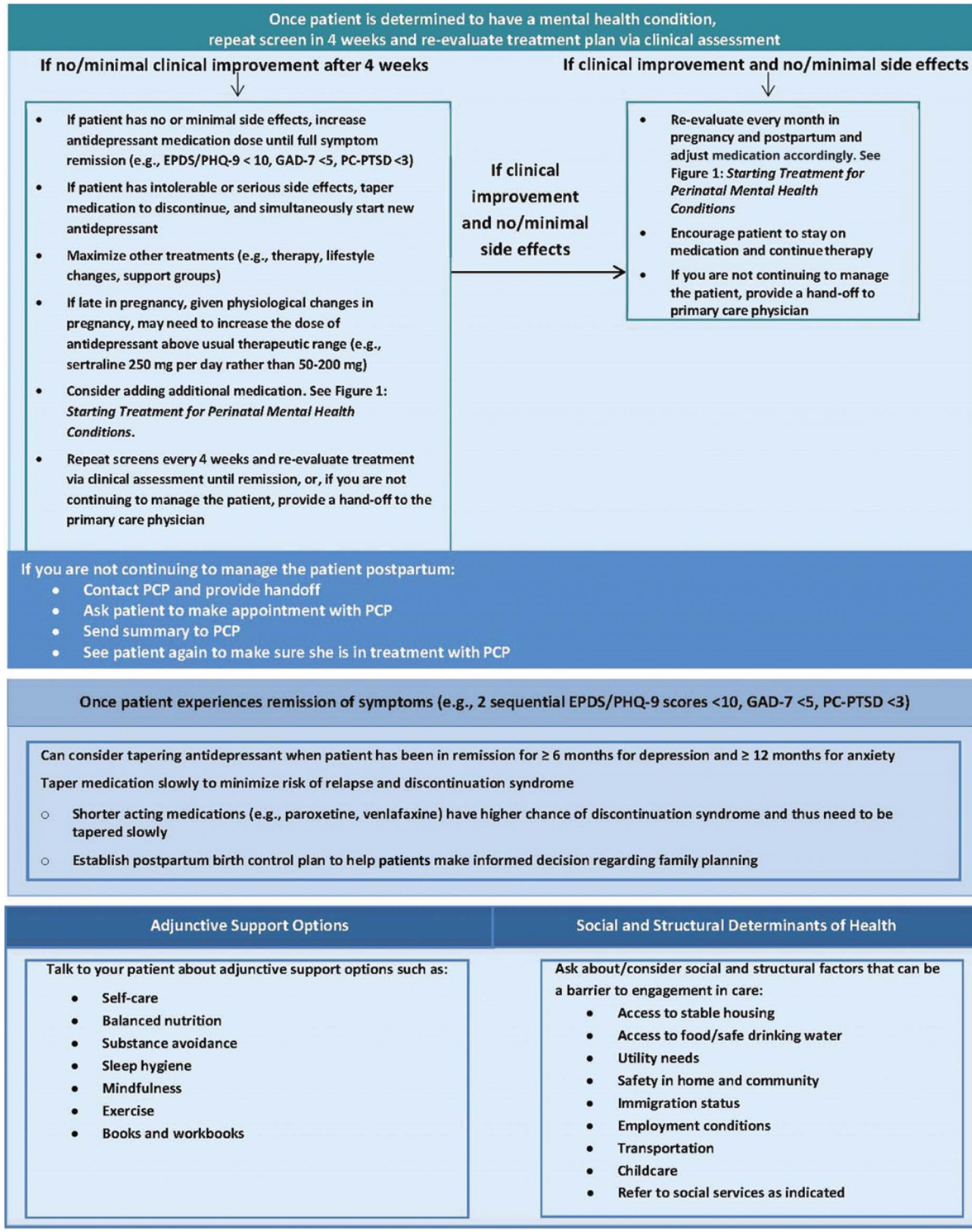

Fig. 2. Follow-up treatment of perinatal mental health. EPDS, Edinburgh Postnatal Depression Scale; GAD-7, Generalized Anxiety Scale 7; mg, milligrams; PC-PTSD, Primary Care Post Traumatic Stress Disorder; PCP, primary care physician; PHQ-9, Patient Health Questionnaire-9.
Modified from Byatt N, Mittal LP, Brenckle L, Logan DG, Masters GA, Bergman A, et al. Lifeline for Moms Perinatal Mental Health Toolkit. University of Massachusetts Medical School; 2019. Accessed March 20, 2023. https://www.umassmed.edu/lifeline4moms/products-resources/toolkits-and-apps/2019/11/lifeline4moms-perinatal-mental-health-toolkit/

requirement for hospitalization for administration and monitoring, which adds substantively to the already significant cost of treatment. Furthermore, data on outcomes beyond 30 days have yet to be published, which raises questions regarding long-term efficacy. Finally, although expected to rapidly clear from breast milk, cessation of breastfeeding is recommended during and for 4 days after treatment with brexanolone, whereas breastfeeding can continue uninterrupted with SSRI or SNRIs. Although the treatment of refractory postpartum depression is a logical role for brexanolone in treatment algorithms, efficacy for this specific indication has not been evaluated.

Safety and Efficacy of Pharmacologic Interventions for Perinatal Anxiety Disorders

ACOG recommends that selective serotonin reuptake inhibitors be used as first-line psychopharmacotherapy for perinatal anxiety. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications. **(STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)**

Perinatal anxiety disorders may be more common than perinatal depression and are associated with adverse perinatal outcomes (1). Yet a recent systematic review identified no effectiveness or comparative effectiveness evidence to inform the treatment of perinatal anxiety disorders (52). Rather, as with antenatal depression, extrapolation of treatment from the general population is required. As with depression, comparative effectiveness studies of psychotherapy (specifically CBT) compared with pharmacotherapy in the general adult population are limited but demonstrate similar efficacy (8, 119).

Both SSRIs and SNRIs are effective for the treatment of generalized anxiety disorder in the general adult population (120). Comparisons between specific medications are limited, but the side-effect and safety profile of SSRIs renders them a first-line recommendation. As with perinatal depression, sertraline and escitalopram are favored first-line SSRIs in treatment-naïve individuals because of their efficacy and tolerability profiles (86). However, other factors, such as comorbid illnesses, potential drug–drug interactions, cost, and side-effect profile, should be considered for each individual patient. Most experts recommend initiation of SSRIs or SNRIs for anxiety at half of the lowest recommended dose range to avoid early side effects such as agitation or insomnia (121). Additionally, the treatment of anxiety and anxiety-related conditions often requires uptitration to doses that are higher than those for depression. Finally, experts recommend that individuals with anxiety and anxiety-related conditions be in remission longer than those with an indication of depression before considering tapering or discontinuing psychopharmacotherapy.

The DSM-5 separates PTSD and OCD into discrete sections from anxiety disorders (2). Although they are clinically important in pregnant and postpartum people, their treatment often requires additional support by psychiatric professionals, including more specialized psychotherapy. Thus, although the pharmacotherapy approach for these anxiety-related disorders is identical to that for anxiety disorders, more specific management details are not included in this Clinical Practice Guideline.

ACOG recommends that benzodiazepines be avoided or prescribed sparingly as a treatment for perinatal anxiety. **(STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)**

If benzodiazepines are prescribed, they should preferably be prescribed transiently as a bridge until SSRIs, SNRIs, or psychotherapy achieve their expected response. Benzodiazepines are an effective and rapid-onset treatment for generalized anxiety disorder in the general adult population (120, 122). However, due to their side-effect profile and addictive potential, they are not recommended as first-line treatment for the treatment of anxiety disorders. Avoidance is particularly prudent in the setting of a history of substance use disorder. Other agents, such as hydroxyzine, can be used as an adjuvant treatment, particularly for the acute management of associated insomnia.

However, benzodiazepines do have a clinical role in the pharmacologic management of anxiety disorders in specific clinical contexts. Specifically, they are often used to manage acute symptoms until the benefits of SSRIs or SNRIs are achieved in the setting of moderate-to-severe anxiety symptoms. Other settings in which benzodiazepines may be beneficial include when first-line treatment options have not been effective. In these settings, obstetric care professionals should consult with or refer to a perinatal mental health subspecialist, because psychotherapy has a stronger evidence base for anxiety treatment than benzodiazepines do.

Although their use as primary treatment for anxiety is not recommended due to their side effects and addictive potential, benzodiazepines have a limited but overall relatively reassuring perinatal safety profile. Although earlier observational data suggested an association between first-trimester benzodiazepine exposure and cleft lip or palate (123), more recent studies have not demonstrated this association (124). Meta-analytic data demonstrate associations between prepregnancy benzodiazepine exposure and ectopic pregnancy, as well as early-pregnancy benzodiazepine exposure and spontaneous abortion, although the strength of evidence was low. Benzodiazepine exposure during pregnancy has been associated with an increased risk of neonatal sedation, decreased muscle tone, respiratory compromise, and NICU admission. For this reason,

Table 2. Perinatal Safety Outcomes Associated With Psychopharmacotherapy Exposure in Pregnancy

Exposure Group	Comparison Group	Outcome	Results
Pregnant women exposed to antidepressants in the 1st trimester*	Pregnant women with depression (propensity score adjustment for depression severity)	Congenital cardiac malformations	aOR 1.02 95% CI 0.90–1.15
Pregnant women exposed to SSRIs or SNRIs in the 1st trimester†	Pregnant women with a diagnosis of depression (no adjustment for depression severity)	Pregnancy loss	SSRI: aRR 1.2 95% CI 0.94–1.5 SNRI: aRR 1.7 95% CI 1.2–2.6
Pregnant women exposed to SSRIs or SNRIs‡	Pregnant women with a diagnosis of depression (no adjustment for depression severity)	Preeclampsia	SSRI: RR 1.0 95% CI 0.93–1.07 SNRI: RR 1.5 95% CI 1.26–1.83
Pregnant women exposed to SSRIs§	Women exposed to SSRIs before pregnancy but not during pregnancy (propensity score adjustment for probability of treatment)	Gestational diabetes	RR 1.1 95% CI 0.84–1.44
Pregnant women exposed to SSRIs‖	Pregnant women with a psychiatric diagnosis not exposed to SSRIs	Preterm birth	aOR 0.84 95% CI 0.74–0.96
Pregnant women exposed to SSRIs‖	Pregnant women with a psychiatric diagnosis not exposed to SSRIs	FGR, SGA	aOR 0.92 95% CI 0.77–1.10
Pregnant women exposed to SSRIs in proximity to delivery¶	Pregnant women with mood or anxiety disorder	Postpartum hemorrhage	aRR 1.47 95% CI 1.33–1.62
Pregnant women exposed to SSRIs#	Pregnant women with depression (propensity score adjustment for depression severity)	PPHN	aOR 1.28 95% CI 1.01–1.64**
Pregnant women exposed to SSRIs††	Pregnant women with depression	NICU admission	OR 2.64 95% CI 1.58–4.40

(*continued*)

Perinatal Safety Outcomes Associated With Psychopharmacotherapy Exposure in Pregnancy (continued)

Exposure Group	Comparison Group	Outcome	Results
Pregnant women exposed to SSRIs[‡‡]	Pregnant women with a depression-related psychiatric disorder	Neurodevelopmental delays	Speech–language disorder: aHR 1.20 95% CI 0.97–1.49 Scholastic disorder: aHR 1.00 95% CI 0.63–1.59 Motor disorder: aHR 1.18 95% CI 0.81–1.72

aHR, adjusted hazard ratio; aOR, adjusted odds ratio; aRR, adjusted relative risk; FGR, fetal growth restriction; NICU, neonatal intensive care unit; OR, odds ratio; PPHN, persistent pulmonary hypertension of the newborn; SGA, small for gestational age; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

*Huybrechts KF, Palmsten K, Avorn J, Cohen LS, Holmes LB, Franklin JM, et al. Antidepressant use in pregnancy and the risk of cardiac defects. N Engl J Med 2014;370:2397–407. doi: 10.1056/NEJMoa1312828

†Almeida ND, Basso O, Abrahamowicz M, Gagnon R, Tamblyn R. Risk of miscarriage in women receiving antidepressants in early pregnancy, correcting for induced abortions. Epidemiology 2016;27:538–46. doi: 10.1097/EDE.0000000000000484

‡Palmsten K, Huybrechts KF, Michels KB, Williams PL, Mogun H, Setoguchi S, et al. Antidepressant use and risk for preeclampsia. Epidemiology 2013;24:682–91. doi: 10.1097/EDE.0b013e31829e0aaa

§Wartko PD, Weiss NS, Enquobahrie DA, Chan KC, Stephenson-Famy A, Mueller BA, et al. Antidepressant continuation in pregnancy and risk of gestational diabetes. Pharmacoepidemiol Drug Saf 2019;28:1194–203. doi: 10.1002/pds.4799

‖Malm H, Sourander A, Gissler M, Gyllenberg D, Hinkka-Yli-Salomäki S, McKeague IW, et al. Pregnancy complications following prenatal exposure to SSRIS or maternal psychiatric disorders: results from population-based national register data. Am J Psychiatry 2015;172:1224–32. doi: 10.1176/appi.ajp.2015.14121575

¶Palmsten K, Hern ndez-Díaz S, Huybrechts KF, Williams PL, Michels KB, Achtyes ED, et al. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States. BMJ 2013;347:f4877. doi: 10.1136/bmj.f4877

#Huybrechts KF, Bateman BT, Palmsten K, Desai RJ, Patorno E, Gopalakrishnan C, et al. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. JAMA 2015;313:2142–51. doi: 10.1001/jama.2015.5605

**Restricted to term deliveries in the absence of congenital cardiac malformations and lung hypoplasia.

††Kautzky A, Slamanig R, Unger A, Höflich A. Neonatal outcome and adaption after in utero exposure to antidepressants: a systematic review and meta-analysis. Acta Psychiatr Scand 2022;145:6–28. doi: 10.1111/acps.13367

‡‡Brown AS, Gyllenberg D, Malm H, McKeague IW, Hinkka-Yli-Salomäki S, Artama M, et al. Association of selective serotonin reuptake inhibitor exposure during pregnancy with speech, scholastic, and motor disorders in offspring. JAMA Psychiatry 2016; 73:1163–70. doi: 10.1001/jamapsychiatry.2016.2594

tapering off of or avoiding use in the third trimester is often recommended, although the absolute risk for NICU admission is low (133/1,000, 95% CI 17–274) and residual confounding and existing hospital protocols may explain some of the observed risk (52). Case reports exist of neonatal benzodiazepine withdrawal after in utero exposure, including the risk of neonatal seizure, although this is also uncommon. Although tapering in the third trimester has been recommended, it is also critical to consider the risks of a taper for the pregnant individual and the fetus. For example, if attempts to taper the benzodiazepine precipitate re-emergence of anxiety, the benefits of continuation may outweigh the risks.

Clinically significant risks of benzodiazepine use include dependence, withdrawal, and misuse; for these reasons, their use as a first-line treatment for anxiety disorders is not recommended. If benzodiazepines are prescribed, the lowest effective dose should be used. For those with hepatic disease or preeclampsia, benzodiazepines that bypass first-pass metabolism (eg, lorazepam, oxazepam, temazepam) should be preferentially selected. Alprazolam should be avoided due to its high addictive potential and heightened risk of acute withdrawal symptoms after cessation. If started, experts recommend continuing the benzodiazepine as needed for 2–4 weeks, until a response to the SSRI has been achieved. The benzodiazepine can then be tapered by 25–50% per week. Abrupt cessation is not recommended due to the risk of withdrawal.

Safety and Efficacy of Pharmacologic Interventions for Bipolar Disorder During the Perinatal Period

ACOG recommends against discontinuing mood stabilizers, except for valproate, during pregnancy due to the risk of recurrence or exacerbation of mood symptoms. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Bipolar disorders include both bipolar type I and bipolar type II; the epidemiology and clinical perinatal risks are discussed in detail in ACOG Clinical Practice Guideline Number 4, "Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum" (1). Untreated bipolar disorder carries a 25–50% increased risk of postpartum psychosis, representing a 100-fold increased risk compared with the general population (125). Postpartum psychosis, in turn, increases the risk of suicide and homicide (126). Outside of the risk of postpartum psychosis, untreated bipolar disorder carries a profound risk of mood worsening postpartum, including sevenfold increased odds of hospitalization (127). In addition to the risks to the pregnant woman, untreated bipolar disorder is associated with negative birth outcomes, including fetal growth restriction, preterm birth, and adverse neurodevelopmental outcomes (128). Thus, the goals of treatment for bipolar disorder are both remission of symptoms and prevention of relapse.

Bipolar disorder in pregnancy and postpartum ideally is treated by psychiatrists or other mental health specialists in collaboration with obstetric care professionals. Typical treatments include mood-stabilizing agents such as lithium, anticonvulsants (eg, lamotrigine), antipsychotic medications (eg, haloperidol, aripiprazole, lurasidone, olanzapine, quetiapine, risperidone), or combination therapy. A prepregnancy consultation provides an ideal setting to engage in shared decision making regarding medication exposures in pregnancy. However, in general, for individuals who are taking medications at the time of pregnancy and are clinically stable, it is preferable to continue the same regimen rather than switch medications. Switching requires a cross-taper to optimize maternal stability, exposes the fetus to additional medications, and may increase the risk of recurrent mood episodes. One notable exception is valproate. Due to the risk of teratogenicity (129) with exposure in the first trimester, most experts recommend a transition away from carbamazepine and oxcarbazepine before pregnancy or, at least, increased folate supplementation at 4 mg daily. If an individual is already pregnant and taking carbamazepine or oxcarbazepine, the decision to switch medications should balance whether the individual is already outside of the teratogenic window alongside the risk of destabilization with any medication transition.

For individuals who have not previously received pharmacotherapy, the decision regarding which medication to initiate can be guided by the presence or absence of mania as well as whether the individual is prepregnancy compared with already pregnant. For those with bipolar I disorder experiencing mania, lithium is often used as first-line treatment because of its efficacy in mania treatment, although consultation with a psychiatric care professional is prudent when initiating lithium.

Many perinatal individuals with bipolar disorder will present with a depressive phenotype (4). Commonly used medications include lamotrigine, quetiapine, and lurasidone. Lamotrigine is a preferred option for the treatment of bipolar II disorder for reproductive-aged females due to the low risk of teratogenicity. Lamotrigine is metabolized by UGT1A4, which is upregulated in pregnancy, increasing the clearance of the drug by up to 330% (130, 131). Pragmatically, this results in the need for a twofold to threefold dose increase in pregnancy, although there is high interindividual variability (132). Up-titration of lamotrigine needs to occur slowly because of the risk of agranulocytosis and rare Stevens–Johnson syndrome. This can pose a challenge in achieving a therapeutic dose during gestation if lamotrigine is started during pregnancy, given the prolonged time window to achieve efficacy (133). However, if an individual is stable on lamotrigine before pregnancy, obtaining a trough drug level can allow for monitoring of trough levels throughout pregnancy to support therapeutic dosing. The dose needs to be carefully down-titrated again postpartum to avoid toxicity, with close monitoring of the patient clinically.

Second-generation antipsychotics (eg, quetiapine, olanzapine, risperidone, aripiprazole) are more often prescribed compared with first-generation antipsychotics (eg, haloperidol, chlorpromazine) due to fewer extrapyramidal side effects and improved tolerability (134). However, this benefit should be balanced with the knowledge that there are fewer published data regarding the use of second-generation antipsychotics in pregnancy. Quetiapine has the lowest placental passage and thus is often a preferred first-line antipsychotic (135). Additionally, quetiapine has established efficacy for the treatment of bipolar disorder in randomized trials in the general adult population compared with placebo (136, 137), lithium (138), and paroxetine (138). However, quetiapine is associated with metabolic risks, including increased weight gain and risk of gestational diabetes.

Alongside quetiapine, lurasidone is one of three FDA-approved medications for the treatment of depression symptoms in the setting of bipolar disorder. The efficacy, tolerability, and lower propensity for metabolic complications make lurasidone a compelling clinical option for the treatment of bipolar disorder with depressive symptoms (139). However, as a newer agent, limited data exist on the safety and appropriate dosing of lurasidone during

pregnancy (140). Reporting outcomes with lurasidone and other agents in the National Pregnancy Registry for Psychiatric Medications is recommended to enhance this knowledge (12, 141).

As with pharmacotherapy for depression and anxiety during pregnancy, general principles of treatment, regardless of agent used, include using the minimal effective dose and avoiding polypharmacy if clinically possible. Notably, polypharmacy is often clinically required in the setting of bipolar disorder (142). For anticonvulsants, supplementing with 4 mg of folic acid daily before pregnancy and during early pregnancy is recommended to reduce the risk of fetal neural tube defects (143). Some experts also recommend 4 mg of folic acid in the setting of lithium use to reduce congenital cardiac defects (144).

Compared with continued use of mood-stabilizing medication for bipolar disorder, two cohort studies found that discontinuing use of medications during pregnancy is associated with an increased risk of recurrence (adjusted hazard ratio 2.2, 95% CI 1.2–4.2) and reduced time to recurrence of mood disorders (2 weeks vs 28 weeks; adjusted hazard ratio 12.1, 95% CI 1.6–91) (52). Although pharmacotherapy represents an exposure, for most individuals and most medications, the risk of this exposure is lower than the risks associated with symptom exacerbation or relapse.

ACOG recommends against valproate as a first-line treatment for bipolar disorder. Valproate should be avoided in pregnancy because reasonable alternatives usually can be identified. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Valproate is not recommended during pregnancy during any trimester due to the risks of teratogenicity as well as adverse effects on neurodevelopment. The majority of relevant data are derived from valproate use in the setting of epilepsy. Nonetheless, reasonable alternatives exist for the treatment of bipolar disorder; thus, valproate should be avoided.

Prenatal exposure to valproate is associated with a 1–3.8% risk of neural tube defects, with a corresponding dose–response relationship (145–152). Other congenital malformations associated with valproate use include craniofacial anomalies (153), limb abnormalities (154), and cardiovascular anomalies (155–157). A "fetal valproate syndrome" has been described, with features of fetal growth restriction, facial dysmorphology, and limb and heart defects (158–160). Varying degrees of cognitive impairment, including mental development delay (161), autism (162–165), and Asperger syndrome (163), have been reported with fetal valproate syndrome (163, 166, 167). Acute neonatal risks include hepatotoxicity (168), coagulopathies (169), neonatal hypoglycemia (170), and withdrawal symptoms (171).

ACOG recommends that pregnant individuals using antipsychotic medications undergo screening for gestational diabetes mellitus, consistent with standard prenatal care. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Many of the existing antipsychotic medications are associated with metabolic side effects, including weight gain (172) and metabolic syndrome (173), including insulin resistance. Evidence regarding the association between exposure to antipsychotic medications and gestational diabetes is conflicting (174–176); thus, this concern should not inform clinical decision making regarding discontinuation of an antipsychotic agent. These medications can be continued in individuals with a diagnosis of diabetes or gestational diabetes. Additionally, no evidence exists to support the practice of early screening for gestational diabetes based on exposure to psychiatric medications.

ACOG recommends that pregnant patients taking lithium in the first trimester receive a detailed ultrasound examination in the second trimester. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Early literature on lithium exposure in pregnancy identified a markedly increased risk of teratogenicity, with 400-fold increased odds of Ebstein anomaly associated with first-trimester lithium exposure. More contemporary data affirm increased odds of congenital anomalies, but with an odds ratio of 1.81 (95% CI 1.35–2.41) for congenital anomalies overall and an odds ratio of 1.86 (95% CI 1.16–2.96) for cardiac anomalies (177). These more contemporary data shift the risk/benefit ratio and render lithium a reasonable treatment option, particularly for individuals with a history of mania or for whom lithium has been effective in the past. Although the absolute risk and absolute risk increase are relatively low, a detailed ultrasound examination to evaluate the fetal anatomy with a particular focus on cardiac anatomy is recommended. In centers where fetal echocardiography is available, this can be considered (178).

It is imperative that lithium dosing be monitored during pregnancy and postpartum. (GOOD PRACTICE POINT)

The same tenets of psychopharmacology apply for lithium, including using the lowest clinically effective dose. Because lithium has a narrow therapeutic window, ideally the therapeutic goal level would be established before pregnancy in an individual who is symptomatically stabilized. For individuals who enter pregnancy without these data, a serum lithium concentration (taken 12 hours after dosing) of 0.6–1.0 mEq/L can be used as an appropriate therapeutic level (with symptom assessment to corroborate that therapeutic efficacy has been achieved). However, lithium is renally metabolized and dose

increasing during pregnancy is required to maintain a therapeutic response. To minimize fetal exposure, avoidance of high peak concentrations can be achieved by changing the dose to twice daily.

Lithium toxicity often presents at serum lithium concentrations of 1.5 mEq/L or greater and includes symptoms such as nausea, vomiting, lethargy, tremor, and fatigue. This can progress to symptoms such as confusion, agitation, seizures, hypothermia, and loss of consciousness at higher concentrations. Due to the potential to alter the glomerular filtration rate, careful attention to lithium dosing is required in the setting of preeclampsia, with concomitant nonsteroidal anti-inflammatory medications postpartum, or in the setting of renal impairment. After delivery, as the glomerular filtration rate rapidly returns to baseline, careful but rapid down-titration is required to prevent toxicity. Similarly, obstetric conditions that alter plasma volume, such as hyperemesis or acute blood loss, can affect lithium concentrations; these conditions necessitate closer lithium dose monitoring.

Lithium crosses the placenta, with umbilical cord drug levels mirroring serum levels within the pregnant woman (179). Higher neonatal lithium drug levels are associated with hypotonia, lethargy, and respiratory difficulties in the newborn. To mitigate this risk, some experts recommend holding the lithium dose at the onset of labor or 24–48 hours before a scheduled induction or cesarean delivery. Lithium is then reinitiated postpartum at the prepregnancy dose (if applicable), or dosing can be guided by drug trough levels for the first 2 weeks postpartum (180).

Recommendations regarding breastfeeding or lactation in the setting of lithium exposure are controversial. Serum infant levels in infants fed with breast milk ranged from 10% to 60% of maternal serum concentrations (181). Because of immature kidney function and the risk of relative dehydration, lithium toxicity in newborns is a clinical risk. Thus, if lactation is being considered, close coordination of care among the obstetrician, pediatrician, and psychiatrist is required.

Safety and Efficacy of Pharmacologic Interventions for Postpartum Psychosis

Postpartum psychosis is a psychiatric emergency. Treatment options that are within the scope of obstetricians, while awaiting further assessment, recommendations, and a treatment plan by a psychiatrist, include sedating antipsychotic medications such as olanzapine or haloperidol that can be used with benzodiazepines such as lorazepam. If haloperidol is used, benztropine or diphenhydramine should be administered to prevent extrapyramidal symptoms and dystonia. **(GOOD PRACTICE POINT)**

Postpartum psychosis is a psychiatric emergency. Given that postpartum psychosis is associated with infanticide and suicide, psychiatric hospitalization is generally indicated. Therefore, an assessment by a psychiatrist that includes an assessment of risk of harm to self and the infant is critical. This should include one-on-one continuous observation to ensure the safety of the patient and their infant. Many hospitals have policies regarding newborn separation. Given that postpartum psychosis can present with symptoms that can appear like delirium, it is important to assess for delirium, which is caused by another medical condition. It is also important to evaluate for medical illnesses that can either cause or exacerbate psychiatric illness.

Health care professionals are encouraged to administer pharmacotherapy to stabilize the patient while awaiting further assessment and recommendations by a psychiatrist. Initiation of a sedative antipsychotic medication such as olanzapine or haloperidol with short-term benzodiazepines such as lorazepam is the first-line treatment for postpartum psychosis. If intramuscular haloperidol is used in a dose greater than 5 mg, benztropine or diphenhydramine should be administered to prevent extrapyramidal symptoms and dystonia. Once maternal and infant safety are secured, an extensive interview of the partner or family members present is also included as part of the psychiatric evaluation, diagnosis, and risk assessment (49).

REFERENCES

1. Screening and diagnosis of mental health conditions during pregnancy and postpartum. Clinical Practice Guideline No. 4. American College of Obstetricians and Gynecologists. Obstet Gynecol 2023;141:1232–61. doi: 10.1097/AOG.0000000000005200
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, text revision (DSM-5-TR™). 5th ed. American Psychiatric Association Publishing; 2022
3. Substance Abuse and Mental Health Services Administration. 2021 National Survey of Drug Use and Health. Accessed March 20, 2023. https://www.samhsa.gov/data/release/2021-national-survey-drug-use-and-health-nsduh-releases
4. Wisner KL, Sit DK, McShea MC, Rizzo DM, Zoretich RA, Hughes CL, et al. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. JAMA Psychiatry 2013;70:490–8. doi: 10.1001/jamapsychiatry.2013.87
5. Vigod SN, Wilson CA, Howard LM. Depression in pregnancy. BMJ 2016;352:i1547. doi: 10.1136/bmj.i1547
6. Gartlehner G, Gaynes BN, Amick HR, Asher GN, Morgan LC, Coker-Schwimmer E, et al. Comparative benefits and harms of antidepressant, psychological, complementary, and exercise treatments for major depression: an evidence report for a clinical practice guideline from the American College of Physicians. Ann Intern Med 2016;164:331–41. doi: 10.7326/M15-1813
7. Cuijpers P, van Straten A, van Oppen P, Andersson G. Are psychological and pharmacologic interventions equally effective in the treatment of adult depressive disorders? A meta-

analysis of comparative studies. J Clin Psychiatry 2008;69:1675–41. doi: 10.4088/jcp.v69n1102

8. Mitte K. Meta-analysis of cognitive-behavioral treatments for generalized anxiety disorder: a comparison with pharmacotherapy. Psychol Bull 2005;131:785–95. doi: 10.1037/0033-2909.131.5.785
9. Cuijpers P, Dekker J, Hollon SD, Andersson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. J Clin Psychiatry 2009;70:1219–29. doi: 10.4088/JCP.09r05021
10. Cuijpers P, van Straten A, Warmerdam L, Andersson G. Psychotherapy versus the combination of psychotherapy and pharmacotherapy in the treatment of depression: a meta-analysis. Depress Anxiety 2009;26:279–88. doi: 10.1002/da.20519
11. Zhang A, Franklin C, Jing S, Bornheimer LA, Hai AH, Himle JA, et al. The effectiveness of four empirically supported psychotherapies for primary care depression and anxiety: a systematic review and meta-analysis. J Affect Disord 2019;245:1168–86. doi: 10.1016/j.jad.2018.12.008
12. MGH Center for Women's Mental Health. National Pregnancy Registry for Psychiatric Medications©. Accessed February 8, 2023. https://womensmentalhealth.org/research/pregnancyregistry/
13. National Library of Medicine. Drugs and lactation database (LactMed®). NLM; 2006. Accessed May 1, 2023. https://www.ncbi.nlm.nih.gov/books/NBK501922
14. Putnick DL, Sundaram R, Bell EM, Ghassabian A, Goldstein RB, Robinson SL, et al. Trajectories of maternal postpartum depressive symptoms. Pediatrics 2020;146:e20200857. doi: 10.1542/peds.2020-0857
15. Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Interventions to prevent perinatal depression: US preventive services task force recommendation statement. US preventive services task force. JAMA 2019;321:580–7. doi: 10.1001/jama.2019.0007
16. Tandon SD, Leis JA, Mendelson T, Perry DF, Kemp K. Six-month outcomes from a randomized controlled trial to prevent perinatal depression in low-income home visiting clients. Matern Child Health J 2014;18:873–81. doi: 10.1007/s10995-013-1313-y
17. Tandon SD, Perry DF, Mendelson T, Kemp K, Leis JA. Preventing perinatal depression in low-income home visiting clients: a randomized controlled trial. J Consulting Clin Psychol 2011;79:707–12. doi: 10.1037/a0024895
18. Mu oz RF, Le HN, Ippen CG, Diaz MA, Urizar GG, Soto J, et al. Prevention of postpartum depression in low-income women: development of the mam s y beb s/mothers and babies course. Cogn Behav Pract 2007;14:70–83. doi: 10.1016/j.cbpra.2006.04.021
19. Le HN, Perry DF, Stuart EA. Randomized controlled trial of a preventive intervention for perinatal depression in high-risk Latinas. J Consulting Clin Psychol 2011;79:135–41. doi: 10.1037/a0022492
20. Phipps MG, Raker CA, Ware CF, Zlotnick C. Randomized controlled trial to prevent postpartum depression in adolescent mothers. Am J Obstet Gynecol 2013;208:192.e1–6. doi: 10.1016/j.ajog.2012.12.036
21. Zlotnick C, Tzilos G, Miller I, Seifer R, Stout R. Randomized controlled trial to prevent postpartum depression in mothers on public assistance. J Affective Disord 2016;189:263–8. doi: 10.1016/j.jad.2015.09.059
22. Zlotnick C, Johnson SL, Miller IW, Pearlstein T, Howard M. Postpartum depression in women receiving public assistance: pilot study of an interpersonal-therapy-oriented group intervention. Am J Psychiatry 2001;158:638–40. doi: 10.1176/appi.ajp.158.4.638
23. Zlotnick C, Miller IW, Pearlstein T, Howard M, Sweeney P. A preventive intervention for pregnant women on public assistance at risk for postpartum depression. Am J Psychiatry 2006;163:1443–5. doi: 10.1176/ajp.2006.163.8.1443
24. Zlotnick C, Capezza NM, Parker D. An interpersonally based intervention for low-income pregnant women with intimate partner violence: a pilot study. Arch Womens Ment Health 2011;14:55–65. doi: 10.1007/s00737-010-0195-x
25. Franta G, Hersh AR, Cirino NH, Caughey AB. Prevention of perinatal depression with counseling in adolescents: a cost-effectiveness analysis. J Maternal-Fetal Neonatal Med 2022;35:9593–9. doi: 10.1080/14767058.2022.2049746
26. Johnson JE, Wiltsey-Stirman S, Sikorskii A, Miller T, King A, Blume JL, et al. Protocol for the ROSE sustainment (ROSES) study, a sequential multiple assignment randomized trial to determine the minimum necessary intervention to maintain a postpartum depression prevention program in prenatal clinics serving low-income women. Implementation Sci 2018;13:115–9. doi: 10.1186/s13012-018-0807-9
27. Yonkers KA, Wisner KL, Stowe Z, Leibenluft E, Cohen L, Miller L, et al. Management of bipolar disorder during pregnancy and the postpartum period. Am J Psychiatry 2004;161:608–20. doi: 10.1176/appi.ajp.161.4.608
28. Jones I, Craddock N. Bipolar disorder and childbirth: the importance of recognising risk. Br J Psychiatry 2005;186:453–4. doi: 10.1192/bjp.186.6.453
29. Munk-Olsen T, Laursen TM, Mendelson T, Pedersen CB, Mors O, Mortensen PB. Risks and predictors of readmission for a mental disorder during the postpartum period. Arch Gen Psychiatry 2009;66:189–95. doi: 10.1001/archgenpsychiatry.2008.528
30. Arnold LM. Gender differences in bipolar disorder. Psychiatr Clin North Am 2003;26:595–620. doi: 10.1016/s0193-953x(03)00036-4
31. Diflorio A, Jones I. Is sex important? Gender differences in bipolar disorder. Int Rev Psychiatry 2010;22:437–52. doi: 10.3109/09540261.2010.514601
32. Gordon-Smith K, Perry A, Di Florio A, Forty L, Fraser C, Casanova Dias M, et al. Symptom profile of postpartum and non-postpartum manic episodes in bipolar I disorder: a within-subjects study. Psychiatry Res 2020;284:112748. doi: 10.1016/j.psychres.2020.112748
33. Alliance for Innovation on Maternal Health. Perinatal mental health conditions. Accessed March 20, 2023. https://saferbirth.org/psbs/perinatal-mental-health-conditions/
34. Wesseloo R, Kamperman AM, Munk-Olsen T, Pop VJ, Kushner SA, Bergink V. Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis. Am J Psychiatry 2016;173:117–27. doi: 10.1176/appi.ajp.2015.15010124
35. Viguera AC, Nonacs R, Cohen LS, Tondo L, Murray A, Baldessarini RJ. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. Am J Psychiatry 2000;157:179–84. doi: 10.1176/appi.ajp.157.2.179
36. Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The prevalence of anxiety disorders during pregnancy and the postpartum period: a multivariate Bayesian meta-analysis. J Clin Psychiatry 2019;80:18r12527. doi: 10.4088/JCP.18r12527

37. Kanwar A, Malik S, Prokop LJ, Sim LA, Feldstein D, Wang Z, Murad MH. The association between anxiety disorders and suicidal behaviors: a systematic review and meta-analysis. Depress Anxiety 2013;30:917–29. doi: 10.1002/da.22074

38. Falah-Hassani K, Shiri R, Dennis CL. The prevalence of antenatal and postnatal co-morbid anxiety and depression: a meta-analysis. Psychol Med 2017;47:2041–53. doi: 10.1017/S0033291717000617

39. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry 2004;26:289–95. doi: 10.1016/j.genhosppsych.2004.02.006

40. Sutter-Dallay AL, Giaconne-Marcesche V, Glatigny-Dallay E, Verdoux H. Women with anxiety disorders during pregnancy are at increased risk of intense postnatal depressive symptoms: a prospective survey of the MATQUID cohort. Eur Psychiatry 2004;19:459–63. doi: 10.1016/j.eurpsy.2004.09.025

41. Ding XX, Wu YL, Xu SJ, Zhu RP, Jia XM, Zhang SF, et al. Maternal anxiety during pregnancy and adverse birth outcomes: a systematic review and meta-analysis of prospective cohort studies. J Affective Disord 2014;159:103–10. doi: 10.1016/j.jad.2014.02.027

42. Schreier A, Wittchen HU, Höfler M, Lieb R. Anxiety disorders in mothers and their children: prospective longitudinal community study. Br J Psychiatry 2008;192:308–9. doi: 10.1192/bjp.bp.106.033589

43. O'Connor TG, Heron J, Glover V. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. J Am Acad Child Adolesc Psychiatry 2002;41:1470–7. doi: 10.1097/00004583-200212000-00019

44. O'Connor TG, Heron J, Golding J, Glover V. Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis. J Child Psychol Psychiatry 2003;44:1025–36. doi: 10.1111/1469-7610.00187

45. Mennes M, Stiers P, Lagae L, Van den Bergh B. Long-term cognitive sequelae of antenatal maternal anxiety: involvement of the orbitofrontal cortex. Neurosci Biobehavioral Rev 2006;30:1078–86. doi: 10.1016/j.neubiorev.2006.04.003

46. Rodriguez-Cabezas L, Clark C. Psychiatric emergencies in pregnancy and postpartum. Clin Obstet Gynecol 2018;61:615–27. doi: 10.1097/GRF.0000000000000377

47. Laursen TM, Laursen TM, Meltzer-Brody S, Mortensen PB, Jones I. Psychiatric disorders with postpartum onset: possible early manifestations of bipolar affective disorders. Arch Gen Psychiatry 2012;69:428–34. doi: 10.1001/archgenpsychiatry.2011.157

48. Blackmore ER, Rubinow DR, O'Connor TG, Liu X, Tang W, Craddock N, et al. Reproductive outcomes and risk of subsequent illness in women diagnosed with postpartum psychosis. Bipolar Disord 2013;15:394–404. doi: 10.1111/bdi.12071

49. Bergink V, Rasgon N, Wisner KL. Postpartum psychosis: madness, mania, and melancholia in motherhood. Am J Psychiatry 2016;173:1179–88. doi: 10.1176/appi.ajp.2016.16040454

50. Luykx JJ, Di Florio A, Bergink V. Prevention of infanticide and suicide in the postpartum period-the importance of emergency care. JAMA Psychiatry 2019;76:1221–2. doi: 10.1001/jamapsychiatry.2019.1929

51. American College of Obstetricians and Gynecologists' Evidence-Based Medicine Expert Work Group. Clinical practice guideline methodology: methodology. Obstet Gynecol 2021;138:518–22. doi: 10.1097/AOG.0000000000004519

52. Viswanathan M, Middleton JC, Stuebe A, Berkman N, Goulding AN, McLaurin-Jiang S, et al. Maternal, fetal, and child outcomes of mental health treatments in women: a systematic review of perinatal pharmacologic interventions. Comparative Effectiveness Review No. 236. AHRQ Publication No. 21-EHC001. Agency for Healthcare Research and Quality; 2021. Accessed May 1, 2023. https://effectivehealthcare.ahrq.gov/products/mental-health-pregnancy/research

53. United Nations Development Programme. Human Development Index (HDI). Accessed March 15, 2023. https://hdr.undp.org/data-center/human-development-index#/indicies/HDI

54. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schunemann HJ. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. GRADE Working Group BMJ 2008;336:924–6. doi: 10.1136/bmj.39489.470347.ad

55. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383–94. doi: 10.1016/j.jclinepi.2010.04.026

56. Guyatt GH, Schünemann HJ, Djulbegovic B, Akl EA. Guideline panels should not GRADE good practice statements. J Clin Epidemiol 2015;68:597–600. doi: 10.1016/j.jclinepi.2014.12.011

57. Sit DK, Perel JM, Helsel JC, Wisner KL. Changes in antidepressant metabolism and dosing across pregnancy and early postpartum. J Clin Psychiatry 2008;69:652–8. doi: 10.4088/jcp.v69n0419

58. Warburton W, Hertzman C, Oberlander TF. A register study of the impact of stopping third trimester selective serotonin reuptake inhibitor exposure on neonatal health. Acta Psychiatr Scand 2009;121:471–9. doi: 10.1111/j.1600-0447.2009.01490.x

59. Kieviet N, Hoppenbrouwers C, Dolman KM, Berkhof J, Wennink H, Honig A. Risk factors for poor neonatal adaptation after exposure to antidepressants in utero. Acta Paediatr 2015;104:384–91. doi: 10.1111/apa.12921

60. Trinh NTH, Munk-Olsen T, Wray NR, Bergink V, Nordeng HME, Lupattelli A, et al. Timing of antidepressant discontinuation during pregnancy and postpartum psychiatric outcomes in Denmark and Norway. JAMA Psychiatry 2023:e230041. doi: 10.1001/jamapsychiatry.2023.0041

61. Solomon DA, Keller MB, Leon AC, Mueller TI, Lavori PW, Shea MT, et al. Multiple recurrences of major depressive disorder. Am J Psychiatry 2000;157:229–33. doi: 10.1176/appi.ajp.157.2.229

62. Fava GA, Gatti A, Belaise C, Guidi J, Offidani E. Withdrawal symptoms after selective serotonin reuptake inhibitor discontinuation: a systematic review. Psychother Psychosom 2015;84:72–81. doi: 10.1159/000370338

63. Zajecka J, Fawcett J, Amsterdam J, Quitkin F, Reimherr F, Rosenbaum J, et al. Safety of abrupt discontinuation of fluoxetine: a randomized, placebo-controlled study. J Clin Psychopharmacol 1998;18:193–7. doi: 10.1097/00004714-199806000-00003

64. American Psychiatric Association. American Psychiatric Association practice guidelines. Accessed February 8, 2023. https://psychiatryonline.org/guidelines

65. Eberhard-Gran M, Eskild A, Opjordsmoen S. Use of psychotropic medications in treating mood disorders during lactation: practical recommendations. CNS Drugs 2006;20:187–98. doi: 10.2165/00023210-200620030-00002

66. Gentile S. Infant safety with antipsychotic therapy in breastfeeding: a systematic review. J Clin Psychiatry 2008;69:666–73. doi: 10.4088/jcp.v69n0421

67. MotherToBaby. Information about medications in pregnancy & lactation. Accessed February 8, 2023. https://mothertobaby.org/

68. Melville JL, Reed SD, Russo J, Croicu CA, Ludman E, LaRocco-Cockburn A, et al. Improving care for depression in obstetrics and gynecology: a randomized controlled trial. Obstet Gynecol 2014;123:1237–46. doi: 10.1097/AOG.0000000000000231

69. Grote NK, Katon WJ, Russo JE, Lohr MJ, Curran M, Galvin E, et al. Collaborative care for perinatal depression in socioeconomically disadvantaged women: a randomized trial. Depress Anxiety 2015;32:821–34. doi: 10.1002/da.22405

70. UMass Chan Medical School. Our national network of Perinatal Psychiatry Access Programs. Accessed March 15, 2023. https://www.umassmed.edu/lifeline4moms/Access-Programs

71. Postpartum Support International. Perinatal psychiatric consult line. Accessed February 8, 2023. https://www.postpartum.net/professionals/perinatal-psychiatric-consult-line/

72. U.S. Department of Veterans Affairs. Women veterans health care: mental health. Accessed March 14, 2023. https://www.womenshealth.va.gov/WOMENSHEALTH/topics/mental-health.asp

73. Health Resources & Services Administration. National maternal mental health hotline. Accessed February 8, 2023. https://mchb.hrsa.gov/national-maternal-mental-health-hotline

74. Siu AL, Bibbins-Domingo K, Grossman DC, Baumann LC, Davidson KW, Ebell M, et al. Screening for depression in adults: US preventive services task force recommendation statement. JAMA 2016;315:380–7. doi: 10.1001/jama.2015.18392

75. Joffres M, Jaramillo A, Dickinson J, Lewin G, Pottie K, Shaw E, et al. Recommendations on screening for depression in adults. CMAJ 2013;185:775–82. doi: 10.1503/cmaj.130403

76. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline [CG 192]. Accessed March 20, 2023. https://www.nice.org.uk/guidance/cg192

77. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Mental health care in the perinatal period. Best practice statement. Accessed March 20, 2023. https://ranzcog.edu.au/wp-content/uploads/2022/05/Mental-Health-Care-in-the-Perinatal-Period-C-Obs-48.pdf

78. Earls MF, Yogman MW, Mattson G, Rafferty J, Baum R, Gambon T, et al. Incorporating recognition and management of perinatal depression into pediatric practice. Pediatrics 2019;143:e20183259. doi: 10.1542/peds.2018-3259

79. American College of Nurse Midwives. Mental health during childbirth and across the lifespan. Position statement. Accessed March 20, 2023. https://www.midwife.org/acnm/files/acnmlibrarydata/uploadfilename/000000000324/PS-Mental%20Health%20During%20Childbirth%20and%20Across%20Lifespan.pdf

80. Registered Nurses' Association of Ontario. Assessment and interventions for perinatal depression. Best practice guideline. Accessed December 7, 2022 https://rnao.ca/bpg/guidelines/assessment-and-interventions-perinatal-depression

81. LaRocco-Cockburn A, Melville J, Bell M, Katon W. Depression screening attitudes and practices among obstetrician-gynecologists. Obstet Gynecol 2003;101:892–8. doi: 10.1016/s0029-7844(03)00171-6

82. Byatt N, Biebel K, Lundquist RS, Moore Simas TA, Debordes-Jackson G, Allison J, et al. Patient, provider, and system-level barriers and facilitators to addressing perinatal depression. J Reprod Infant Psychol 2012;30:436–49. doi: 10.1080/02646838.2012.743000

83. National Curriculum in Reproductive Psychiatry. NCRP. Accessed February 8, 2023. https://ncrptraining.org/

84. UMass Chan Medical School. Addressing perinatal mental health conditions in obstetric settings. Accessed March 16, 2023. https://www.pathlms.com/acogwebinars/courses/49949

85. Postpartum Support International. Frontline provider trainings. Accessed February 8, 2023. https://www.postpartum.net/professionals/frontline-provider-trainings%20

86. Cipriani A, Furukawa TA, Salanti G, Geddes JR, Higgins JP, Churchill R, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet 2009;373:746–58. doi: 10.1016/S0140-6736(09)60046-5

87. Weissman AM, Levy BT, Hartz AJ, Bentler S, Donohue M, Ellingrod VL, et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. Am J Psychiatry 2004;161:1066–78. doi: 10.1176/appi.ajp.161.6.1066

88. Taouk LH, Matteson KA, Stark LM, Schulkin J. Prenatal depression screening and antidepressant prescription: obstetrician-gynecologists' practices, opinions, and interpretation of evidence. Arch Womens Ment Health 2018;21:85–91. doi: 10.1007/s00737-017-0760-7

89. Perry SW, Rainey JC, Allison S, Bastiampillai T, Wong ML, Licinio J, et al. Achieving health equity in US suicides: a narrative review and commentary. BMC Public Health 2022;22:1360. doi: 10.1186/s12889-022-13596-w

90. Snowber K, Ciolino JD, Clark CT, Grobman WA, Miller ES. Associations between implementation of the collaborative care model and disparities in perinatal depression care. Obstet Gynecol 2022;140:204–11. doi: 10.1097/AOG.0000000000004859

91. Metz TD, Rovner P, Hoffman MC, Allshouse AA, Beckwith KM, Binswanger IA. Maternal deaths from suicide and overdose in Colorado, 2004-2012. Obstet Gynecol 2016;128:1233–40. doi: 10.1097/AOG.0000000000001695

92. Glue P, Donovan MR, Kolluri S, Emir B. Meta-analysis of relapse prevention antidepressant trials in depressive disorders. Aust N Z J Psychiatry 2010;44:697–705. doi: 10.3109/00048671003705441

93. Roca A, Imaz ML, Torres A, Plaza A, Subirà S, Vald s M, et al. Unplanned pregnancy and discontinuation of SSRIs in pregnant women with previously treated affective disorder. J Affective Disord 2013;150:807–13. doi: 10.1016/j.jad.2013.02.040

94. Cohen LS, Altshuler LL, Harlow BL, Nonacs R, Newport DJ, Viguera AC, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment 2006;295:499–507. doi: 10.1001/jama.295.5.499

95. Yonkers KA, Gotman N, Smith MV, Forray A, Belanger K, Brunetto WL, et al. Does antidepressant use attenuate the risk of a major depressive episode in pregnancy? Epidemiology 2011;22:848–54. doi: 10.1097/EDE.0b013e3182306847

96. Byatt N, Biebel K, Moore Simas TA, Sarvet B, Ravech M, Allison J, et al. Improving perinatal depression care: the Massachusetts

child psychiatry access project for moms. Gen Hosp Psychiatry 2016;40:12–7. doi: 10.1016/j.genhosppsych.2016.03.002

97. Byatt N, Straus J, Stopa A, Biebel K, Mittal L, Moore Simas TA. Massachusetts child psychiatry access program for moms: utilization and quality assessment. Obstet Gynecol 2018;132: 345–53. doi: 10.1097/AOG.0000000000002688

98. Li C, Sun X, Li Q, Sun Q, Wu B, Duan D. Role of psychotherapy on antenatal depression, anxiety, and maternal quality of life: a meta-analysis. Medicine (Baltimore) 2020;99:e20947. doi: 10.1097/MD.0000000000020947

99. Yonkers KA, Wisner KL, Stewart DE, Oberlander TF, Dell DL, Stotland N, et al. The management of depression during pregnancy: a report from the American psychiatric association and the American college of obstetricians and gynecologists. Obstet Gynecol 2009;114:703–13. doi: 10.1097/AOG.0b013e3181ba0632

100. Ko JY, Farr SL, Dietz PM, Robbins CL. Depression and treatment among U.S. pregnant and nonpregnant women of reproductive age, 2005-2009. J Women's Health 2012;21:830–6. doi: 10.1089/jwh.2011.3466

101. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet 2018;391:1357–66. doi: 10.1016/S0140-6736(17)32802-7

102. Arroll B, Elley CR, Fishman T, Goodyear-Smith FA, Kenealy T, Blashki G, et al. Antidepressants versus placebo for depression in primary care. The Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD007954. doi: 10.1002/14651858.CD007954

103. Avram MJ, Stika CS, Rasmussen-Torvik LJ, Ciolino JD, Pinheiro E, George AL Jr, et al. Rationale and design for an investigation to optimize selective serotonin reuptake inhibitor treatment for pregnant women with depression. Clin Pharmacol Ther 2016;100:31–3. doi: 10.1002/cpt.375

104. Almeida ND, Basso O, Abrahamowicz M, Gagnon R, Tamblyn R. Risk of miscarriage in women receiving antidepressants in early pregnancy, correcting for induced abortions. Epidemiology 2016;27:538–46. doi: 10.1097/EDE.0000000000000484

105. Gartlehner G, Hansen RA, Morgan LC, Thaler K, Lux L, Van Noord M, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. Ann Intern Med 2011;155: 772–85. doi: 10.7326/0003-4819-155-11-201112060-00009

106. U.S. Food and Drug Administration. Selective serotonin reuptake inhibitor (SSRI) antidepressant use during pregnancy and reports of a rare heart and lung condition in newborn babies. FDA drug safety communication. Accessed March 20, 2023. https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-selective-serotonin-reuptake-inhibitor-ssri-antidepressant-use-during

107. Grigoriadis S, Vonderporten EH, Mamisashvili L, Tomlinson G, Dennis CL, Koren G, et al. Prenatal exposure to antidepressants and persistent pulmonary hypertension of the newborn: systematic review and meta-analysis. BMJ 2014;348:f6932. doi: 10.1136/bmj.f6932

108. Masarwa R, Bar-Oz B, Gorelik E, Reif S, Perlman A, Matok I. Prenatal exposure to selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors and risk for persistent pulmonary hypertension of the newborn: a systematic review, meta-analysis, and network meta-analysis. Am J Obstet Gynecol 2019;220:57.e1–13. doi: 10.1016/j.ajog.2018.08.030

109. Ng QX, Venkatanarayanan N, Ho CYX, Sim WS, Lim DY, Yeo WS. Selective serotonin reuptake inhibitors and persistent pulmonary hypertension of the newborn: an updated meta-analysis. J Women's Health 2019;28:331–8. doi: 10.1089/jwh.2018.7319

110. Huybrechts KF, Bateman BT, Palmsten K, Desai RJ, Patorno E, Gopalakrishnan C, et al. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn. JAMA 2015;313:2142–51. doi: 10.1001/jama.2015.5605

111. Yang A, Ciolino JD, Pinheiro E, Rasmussen-Torvik LJ, Sit DKY, Wisner KL. Neonatal discontinuation syndrome in serotonergic antidepressant-exposed neonates. J Clin Psychiatry 2017;78: 605–11. doi: 10.4088/JCP.16m11044

112. Grigoriadis S, VonderPorten EH, Mamisashvili L, Eady A, Tomlinson G, Dennis CL, et al. The effect of prenatal antidepressant exposure on neonatal adaptation: a systematic review and meta-analysis. J Clin Psychiatry 2013;74:e309–20. doi: 10.4088/JCP.12r07967

113. Moses-Kolko EL, Bogen D, Perel J, Bregar A, Uhl K, Levin B, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications. JAMA 2005;293:2372–83. doi: 10.1001/jama.293.19.2372

114. McDonagh MS, Matthews A, Phillipi C, Romm J, Peterson K, Thakurta S, et al. Depression drug treatment outcomes in pregnancy and the postpartum period: a systematic review and meta-analysis. Obstet Gynecol 2014;124:526–34. doi: 10.1097/AOG.0000000000000410

115. O'Hara MW, Pearlstein T, Stuart S, Long JD, Mills JA, Zlotnick C. A placebo controlled treatment trial of sertraline and interpersonal psychotherapy for postpartum depression. J Affective Disord 2019;245:524–32. doi: 10.1016/j.jad.2018.10.361

116. Hantsoo L, Ward-O'Brien D, Czarkowski KA, Gueorguieva R, Price LH, Epperson CN. A randomized, placebo-controlled, double-blind trial of sertraline for postpartum depression. Psychopharmacology (Berl) 2014;231:939–48. doi: 10.1007/s00213-013-3316-1

117. Zheng W, Cai DB, Zheng W, Sim K, Ungvari GS, Peng XJ, et al. Brexanolone for postpartum depression: a meta-analysis of randomized controlled studies. Psychiatry Res 2019;279:83–9. doi: 10.1016/j.psychres.2019.07.006

118. U.S. Food and Drug Administration. Zulresso (brexanolone). Approved risk evaluation and mitigation strategies (REMS). Accessed March 20, 2023. https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=387

119. Carl E, Witcraft SM, Kauffman BY, Gillespie EM, Becker ES, Cuijpers P, et al. Psychological and pharmacological treatments for generalized anxiety disorder (GAD): a meta-analysis of randomized controlled trials. Cogn Behav Ther 2020;49:1–21. doi: 10.1080/16506073.2018.1560358

120. Slee A, Nazareth I, Bondaronek P, Liu Y, Cheng Z, Freemantle N. Pharmacological treatments for generalised anxiety disorder: a systematic review and network meta-analysis. Lancet 2019;393:768–77. doi: 10.1016/S0140-6736(18)31793-8

121. Thorsness KR, Watson C, LaRusso EM. Perinatal anxiety: approach to diagnosis and management in the obstetric setting. Am J Obstet Gynecol 2018;219:326–45. doi: 10.1016/j.ajog.2018.05.017

122. Gomez AF, Barthel AL, Hofmann SG. Comparing the efficacy of benzodiazepines and serotonergic anti-depressants for adults with generalized anxiety disorder: a meta-analytic review. Expert Opin Pharmacother 2018;19:883–94. doi: 10.1080/14656566.2018.1472767

123. Dolovich LR, Addis A, Vaillancourt JMR, Power JDB, Koren G, Einarson TR. Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case-control studies. BMJ 1998;317:839–43. doi: 10.1136/bmj.317.7162.839

124. Wikner BN, Stiller CO, Bergman U, Asker C, Käll n B. Use of benzodiazepines and benzodiazepine receptor agonists during pregnancy: neonatal outcome and congenital malformations. Pharmacoepidemiol Drug Saf 2007;16:1203–10. doi: 10.1002/pds.1457

125. Clark CT, Wisner KL. Treatment of peripartum bipolar disorder. Obstet Gynecol Clin North America 2018;45:403–17. doi: 10.1016/j.ogc.2018.05.002

126. Gilden J, Kamperman AM, Munk-Olsen T, Hoogendijk WJG, Kushner SA, Bergink V. Long-term outcomes of postpartum psychosis: a systematic review and meta-analysis. J Clin Psychiatry 2020;81:19r12906. doi: 10.4088/JCP.19r12906

127. Terp IM, Mortensen PB. Post-partum psychoses. Clinical diagnoses and relative risk of admission after parturition. Br J Psychiatry 1998;172:521–6. doi: 10.1192/bjp.172.6.521

128. Jablensky AV, Morgan V, Zubrick SR, Bower C, Yellachich LA. Pregnancy, delivery, and neonatal complications in a population cohort of women with schizophrenia and major affective disorders. Am J Psychiatry 2005;162:79–91. doi: 10.1176/appi.ajp.162.1.79

129. Jentink J, Dolk H, Loane MA, Morris JK, Wellesley D, Garne E, et al. Intrauterine exposure to carbamazepine and specific congenital malformations: systematic review and case-control study. BMJ 2010;341:c6581. doi: 10.1136/bmj.c6581

130. Karanam A, Pennell PB, French JA, Harden CL, Allien S, Lau C, et al. Lamotrigine clearance increases by 5 weeks gestational age: relationship to estradiol concentrations and gestational age. Ann Neurol 2018;84:556–63. doi: 10.1002/ana.25321

131. Pennell PB, Newport DJ, Stowe ZN, Helmers SL, Montgomery JQ, Henry TR. The impact of pregnancy and childbirth on the metabolism of lamotrigine [published erratum appears in Neurology 2010;74:2028]. Neurology 2004;62:292–5. doi: 10.1212/01.wnl.0000103286.47129.f8

132. Polepally AR, Pennell PB, Brundage RC, Stowe ZN, Newport DJ, Viguera AC, et al. Model-based lamotrigine clearance changes during pregnancy: clinical implication. Ann Clin Transl Neurol 2014;1:99–106. doi: 10.1002/acn3.29

133. Tran TA, Leppik IE, Blesi K, Sathanandan ST, Remmel R. Lamotrigine clearance during pregnancy. Neurology 2002;59:251–5. doi: 10.1212/wnl.59.2.251

134. Toh S, Li Q, Cheetham TC, Cooper WO, Davis RL, Dublin S, et al. Prevalence and trends in the use of antipsychotic medications during pregnancy in the U.S., 2001-2007: a population-based study of 585,615 deliveries. Arch Womens Ment Health 2013;16:149–57. doi: 10.1007/s00737-013-0330-6

135. Newport DJ, Calamaras MR, DeVane CL, Donovan J, Beach AJ, Winn S, et al. Atypical antipsychotic administration during late pregnancy: placental passage and obstetrical outcomes. Am J Psychiatry 2007;164:1214–20. doi: 10.1176/appi.ajp.2007.06111886

136. Calabrese JR, Keck PE Jr, Macfadden W, Minkwitz M, Ketter TA, Weisler RH, et al. A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 2005;162:1351–60. doi: 10.1176/appi.ajp.162.7.1351

137. Thase ME, Macfadden W, Weisler RH, Chang W, Paulsson B, Khan A, et al. Efficacy of quetiapine monotherapy in bipolar I and II depression: a double-blind, placebo-controlled study (the BOLDER II study) [published erratum appears in J Clin Psychopharmacol 2007;27:51]. J Clin Psychopharmacol 2006;26:600–9. doi: 10.1097/01.jcp.0000248603.76231.b7

138. Young AH, McElroy SL, Bauer M, Philips N, Chang W, Olausson B, et al. A double-blind, placebo-controlled study of quetiapine and lithium monotherapy in adults in the acute phase of bipolar depression (EMBOLDEN I). J Clin Psychiatry 2010;71:150–62. doi: 10.4088/JCP.08m04995gre

139. Fornaro M, De Berardis D, Perna G, Solmi M, Veronese N, Orsolini L, et al. Lurasidone in the treatment of bipolar depression: systematic review of systematic reviews. Biomed Res Int 2017;2017:1–17. doi: 10.1155/2017/3084859

140. Montiel C, Newmark RL, Clark CT. Perinatal use of lurasidone for the treatment of bipolar disorder. Exp Clin Psychopharmacol 2022;30:249–52. doi: 10.1037/pha0000509

141. Cohen LS, Viguera AC, McInerney KA, Freeman MP, Sosinsky AZ, Moustafa D, et al. Reproductive safety of second-generation antipsychotics: current data from the Massachusetts general hospital national pregnancy registry for atypical antipsychotics. Am J Psychiatry 2016;173:263–70. doi: 10.1176/appi.ajp.2015.15040506

142. Santucci AK, Singer LT, Wisniewski SR, Luther JF, Eng HF, Sit DK, et al. One-year developmental outcomes for infants of mothers with bipolar disorder. J Clin Psychiatry 2017;78:1083–90. doi: 10.4088/JCP.15m10535

143. Neural tube defects. Practice Bulletin No. 187. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e279–90. doi: 10.1097/AOG.0000000000002412

144. Huhta JC, Linask K. When should we prescribe high-dose folic acid to prevent congenital heart defects?. Curr Opin Cardiol 2015;30:125–31. doi: 10.1097/HCO.0000000000000124

145. Jäger-Roman E, Deichl A, Jakob S, Hartmann AM, Koch S, Rating D, et al. Fetal growth, major malformations, and minor anomalies in infants born to women receiving valproic acid. J Pediatr 1986;108:997–1004. doi: 10.1016/s0022-3476(86)80949-0

146. Lindhout D, Schmidt D. In-utero exposure to valproate and neural tube defects. Lancet 1986;327:1392–3. doi: 10.1016/s0140-6736(86)91711-3

147. Centers for Disease Control and Prevention. Spina bifida incidence at birth—United States, 1983-1990. MMWR Morb Mortal Wkly Rep 1992;41:497–500.

148. Samr n EB, Duijn CM, Koch S, Hiilesmaa VK, Klepel H, Bardy AH, et al. Maternal use of antiepileptic drugs and the risk of major congenital malformations: a joint European prospective study of human teratogenesis associated with maternal epilepsy. Epilepsia 1997;38:981–90. doi: 10.1111/j.1528-1157.1997.tb01480.x

149. Omtzigt JGC, Los FJ, Meijer JWA, Lindhout D. The 10,11-epoxide-10,11-diol pathway of carbamazepine in early pregnancy in maternal serum, urine, and amniotic fluid: effect of dose, comedication, and relation to outcome of pregnancy. Ther Drug Monit 1993;15:1–10. doi: 10.1097/00007691-199302000-00001

150. Samr n EB, van Duijn CM, Lieve Christiaens GCM, Hofman A, Lindhout D. Antiepileptic drug regimens and major congenital abnormalities in the offspring. Ann Neurol 1999;46:739–46.

doi: 10.1002/1531-8249(199911)46:5<739::aid-ana9>3.0.co;2-2

151. Canger R, Battino D, Canevini MP, Fumarola C, Guidolin L, Vignoli A, et al. Malformations in offspring of women with epilepsy: a prospective study. Epilepsia 1999;40:1231–6. doi: 10.1111/j.1528-1157.1999.tb00851.x

152. Kaneko S, Battino D, Andermann E, Wada K, Kan R, Takeda A, et al. Congenital malformations due to antiepileptic drugs. Epilepsy Res 1999;33:145–58. doi: 10.1016/s0920-1211(98)00084-9

153. Paulson GW, Paulson RB. Teratogenic effects of anticonvulsants. Arch Neurol 1981;38:140–3. doi: 10.1001/archneur.1981.00510030034003

154. Rodríguez-Pinilla E, Arroyo I, Fondevilla J, Garca MJ, Martnez-Fras ML. Prenatal exposure to valproic acid during pregnancy and limb deficiencies: a case-control study. Am J Med Genet 2000;90:376–81. doi: 10.1002/(sici)1096-8628(20000228)90:5<376::aid-ajmg6>3.0.co;2-v

155. Dalens B, Raynaud EJ, Gaulme J. Teratogenicity of valproic acid. J Pediatr 1980;97:332–3. doi: 10.1016/s0022-3476(80)80517-8

156. Koch S, Jäger-Roman E, Rating D, Helge H. Possible teratogenic effect of valproate during pregnancy. J Pediatr 1983;103:1007–8. doi: 10.1016/s0022-3476(83)80750-1

157. Sodhi P, Poddar B, Parmar V. Fatal cardiac malformation in fetal valproate syndrome. Indian J Pediatr 2001;68:989–90. doi: 10.1007/BF02722604

158. Winter RM, Donnai D, Burn J, Tucker SM. Fetal valproate syndrome: is there a recognisable phenotype? J Med Genet 1987;24:692–5. doi: 10.1136/jmg.24.11.692

159. Ardinger HH, Atkin JF, Blackston RD, Elsas LJ, Clarren SK, Livingstone S, et al. Verification of the fetal valproate syndrome phenotype. Am J Med Genet 1988;29:171–85. doi: 10.1002/ajmg.1320290123

160. Martínez-Frías ML. Clinical manifestation of prenatal exposure to valproic acid using case reports and epidemiologic information. Am J Med Genet 1990;37:277–82. doi: 10.1002/ajmg.1320370224

161. Kozma C. Valproic acid embryopathy: report of two siblings with further expansion of the phenotypic abnormalities and a review of the literature. Am J Med Genet 2001;98:168–75. doi: 10.1002/1096-8628(20010115)98:2<168::aid-ajmg1026>3.0.co;2-o

162. Williams PG, Hersh JH. A male with fetal valproate syndrome and autism. Dev Med Child Neurol 2008;39:632–4. doi: 10.1111/j.1469-8749.1997.tb07500.x

163. Moore SJ, Turnpenny P, Quinn A, Glover S, Lloyd DJ, Montgomery T, et al. A clinical study of 57 children with fetal anticonvulsant syndromes. J Med Genet 2000;37:489–97. doi: 10.1136/jmg.37.7.489

164. Bescoby-Chambers N, Forster P, Bates G. Foetal valproate syndrome and autism: additional evidence of an association. Dev Med Child Neurol 2001;43:847. doi. 10.1017/s0012162201211542

165. Williams G, King J, Cunningham M, Stephan M, Kerr B, Hersh JH. Fetal valproate syndrome and autism: additional evidence of an association. Dev Med Child Neurol 2001;43:202–6. doi: 10.1111/j.1469-8749.2001.tb00188.x

166. Gaily E, Kantola-Sorsa E, Granström ML. Specific cognitive dysfunction in children with epileptic mothers. Dev Med Child Neurol 2010;32:403–14. doi: 10.1111/j.1469-8749.1990.tb16959.x

167. Adab N, Jacoby A, Smith D, Chadwick D. Additional educational needs in children born to mothers with epilepsy. J Neurol Neurosurg Psychiatry 2001;70:15–21. doi: 10.1136/jnnp.70.1.15

168. Kennedy D, Koren G. Valproic acid use in psychiatry: issues in treating women of reproductive age. J Psychiatry Neurosci 1998;23:223–8. doi: 10.1016/s0140-6736(70)90636-7

169. Mountain KR, Hirsh J, Gallus AS. Neonatal coagulation defect due to anticonvulsant drug treatment in pregnancy. Lancet 1970;295:265–8. doi: 10.1016/s0140-6736(70)90636-7

170. Thisted E, Ebbesen F. Malformations, withdrawal manifestations, and hypoglycaemia after exposure to valproate in utero. Arch Dis Child 1993;69:288–91. doi: 10.1136/adc.69.3_spec_no.288

171. Ebbesen F, Joergensen A, Hoseth E, Kaad PH, Moeller M, Holsteen V, et al. Neonatal hypoglycaemia and withdrawal symptoms after exposure in utero to valproate. Arch Dis Child Fetal Neonatal Edition 2000;83:F124–9. doi: 10.1136/fn.83.2.f124

172. Bak M, Fransen A, Janssen J, van Os J, Drukker M. Almost all antipsychotics result in weight gain: a meta-analysis. PLoS One 2014;9:e94112. doi: 10.1371/journal.pone.0094112

173. Vancampfort D, Stubbs B, Mitchell AJ, De Hert M, Wampers M, Ward PB, et al. Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. World Psychiatry 2015;14:339–47. doi: 10.1002/wps.20252

174. Gentile S. Pregnancy exposure to second-generation antipsychotics and the risk of gestational diabetes. Expert Opin Drug Saf 2014;13:1583–90. doi: 10.1517/14740338.2014.931368

175. Wang Z, Man KK, Ma T, Howard LM, Wei L, Wong IC, et al. Association between antipsychotic use in pregnancy and the risk of gestational diabetes: population-based cohort studies from the United Kingdom and Hong Kong and an updated meta-analysis. Schizophrenia Res 2021;229:55–62. doi: 10.1016/j.schres.2020.11.021

176. Wilson CA, Newham J, Rankin J, Ismail K, Simonoff E, Reynolds RM, et al. Systematic review and meta-analysis of risk of gestational diabetes in women with preconception mental disorders. J Psychiatr Res 2022;149:293–306. doi: 10.1016/j.jpsychires.2022.03.013

177. Fornaro M, Maritan E, Ferranti R, Zaninotto L, Miola A, Anastasia A, et al. Lithium exposure during pregnancy and the postpartum period: a systematic review and meta-analysis of safety and efficacy outcomes. Am J Psychiatry 2020;177:76–92. doi: 10.1176/appi.ajp.2019.19030228

178. AIUM practice parameter for the performance of fetal echocardiography. J Ultrasound Med 2020;39:E5–16. doi: 10.1002/jum.15188

179. Newport DJ, Viguera AC, Beach AJ, Ritchie JC, Cohen LS, Stowe ZN. Lithium placental passage and obstetrical outcome: implications for clinical management during late pregnancy. Am J Psychiatry 2005;162:2162–70. doi: 10.1176/appi.ajp.162.11.2162

180. Clark CT, Newmark RL, Wisner KL, Stika C, Avram MJ. Lithium pharmacokinetics in the perinatal patient with bipolar disorder. J Clin Pharmacol 2022;62:1385–92. doi: 10.1002/jcph.2089

181. Uguz F, Sharma V. Mood stabilizers during breastfeeding: a systematic review of the recent literature. Bipolar Disord 2016;18:325–33. doi: 10.1111/bdi.12398

APPENDICES

Supplemental Digital Content

A. Literature search strategy: http://links.lww.com/AOG/D142.

B. PRISMA diagram: http://links.lww.com/AOG/D143.

C. Evidence tables: http://links.lww.com/AOG/D144.

CONFLICT OF INTEREST STATEMENT

All ACOG committee members and authors have submitted a conflict of interest disclosure statement related to this published product. Any potential conflicts have been considered and managed in accordance with ACOG's Conflict of Interest Disclosure Policy. The ACOG policies can be found on acog.org. For products jointly developed with other organizations, conflict of interest disclosures by representatives of the other organizations are addressed by those organizations. The American College of Obstetricians and Gynecologists has neither solicited nor accepted any commercial involvement in the development of the content of this published product.

American College of Obstetricians and Gynecologists
409 12th Street SW, Washington, DC 20024-2188

Treatment and management of mental health conditions during pregnancy and postpartum. Clinical Practice Guideline No. 5. American College of Obstetricians and Gynecologists. Obstet Gynecol 2023;141:1262-88.