

PERINATAL MENTAL AND SUBSTANCE USE DISORDERS



AMERICAN
PSYCHIATRIC
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FUNDING

The project described is partially supported by funding from the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services grant #NU38OT000288. The contents provided are solely the responsibility of the authors and do not necessarily represent the official views of, nor an endorsement of HHS/CDC or the CDC Foundation.

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Recommended Citation

Clarke DE, De Faria L, Alpert JE, The Perinatal Mental Health Advisory Panel, The Perinatal Mental Health Research Team. Perinatal Mental and Substance Use Disorder: White Paper. Washington, DC: American Psychiatric Association; 2023 [Available from: <https://www.psychiatry.org/maternal>].



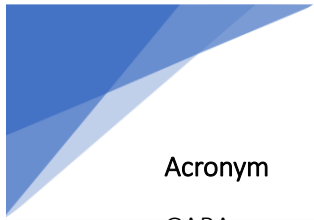
GLOSSARY OF TERMS

Term	Definition
Antenatal	Before birth
Antepartum	Before birth
Prenatal	Before birth
Peripartum	The period shortly before, during, and immediately after giving birth
Postnatal	After birth
Postpartum	Refers to the postnatal period up to 1 year following giving birth
Perinatal	Covers pregnancy and the postpartum period
Parental	The inclusive term used instead of maternal
Pregnant person(s)	The inclusive term instead of pregnant woman or women
Sexual and gender minorities	The inclusive term for sexual and gender minorities (e.g., lesbian, gay, bisexual, transgender, etc.)

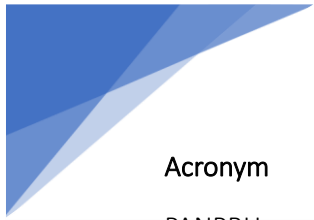


LIST OF ACRONYMS USED AND THEIR MEANINGS

Acronym	Meaning
AACN	American Association of Colleges of Nursing
ACGME	Accreditation Council for Graduate Medical Education
ACOG	American College of Obstetricians and Gynecologists
ACT	Acceptance and Commitment Therapy
ADHD	Attention-Deficit/Hyperactivity Disorder
AFAB	Assigned Female At Birth
AMAB	Assigned Male At Birth
APA	American Psychiatric Association
APRN	Advanced Practice Nurse
ART	Assisted Reproductive Technology
BMI	Body Mass Index
BP	Bipolar Disorder
CBT	Cognitive-Behavioral Therapy
CBT-I	Cognitive Behavioral Therapy for Insomnia
CCNE	Commission on Collegiate Nursing Education
CI	Confidence Interval
DBS	Deep Brain Stimulation
DOVE	Domestic Violence Enhanced Home Visitation Program
ECT	Electroconvulsive Therapy
ED	Eating Disorder
EDNOS	Eating Disorder Not Otherwise Specified
EPDS	Edinburgh Postnatal Depression Scale
ERP	Exposure and Response Prevention
FASD	Fetal Alcohol Spectrum Disorder
FDA	Food and Drug Administration



Acronym	Meaning
GABA	Gamma-Aminobutyric Acid
GDM	Gestational Diabetes Mellitus
GWG	Gestational Weight Gain
HCUP	Healthcare Cost and Utilization Project
HIV	Human Immunodeficiency Virus
HPA	Hypothalamic-Pituitary-Adrenal Axis
IPT	Interpersonal Therapy
IPT	Interpersonal Psychotherapy
IPV	Intimate Partner Violence
IUGR	Intrauterine Growth Restriction
IVF	In Vitro Fertilization
LBW	Low Birth Weight
MCAP	Massachusetts Child Psychiatry Access Program
MDD	Major Depressive Disorder
MOUD	Medication for Opioid Use Disorder
NAS	Neonatal Abstinence
NAS	Neonatal Adaptation Syndrome
NCRP	National Curriculum for Reproductive Psychiatry
NICU	Neonatal Intensive Care Unit
NIS	National Inpatient Sample
NONPF	National Organization of Nurse Practitioner Faculties
NRT	Nicotine Replacement Therapy
NSDUH	National Survey on Drug Use and Health
nuMoM2b	Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be
OB/GYN	Obstetrics and Gynecology
OCD	Obsessive-Compulsive Disorder
OR	Odds Ratio



Acronym	Meaning
PANPBH	Psychiatrist and Non-Physician Behavioral Health
PMAD	Perinatal Mood and Anxiety Disorders
POCS	Perinatal Obsessive-Compulsive Scale
PPD	Postpartum Depression
PPHN	Persistent Pulmonary Hypertension
PRAMS	Pregnancy Risk Assessment Monitoring System
PSI	Postpartum Support International
PTSD	Posttraumatic Stress Disorder
REMS	Risk Evaluation and Mitigation Strategy
ROSE	Reach Out, Stand Strong Essentials for New Mothers
RR	Relative Risk
SDOH	Social Determinants of Health
SGA	Small for Gestational Age
SGM	Sexual and Gender Minority
SNRI	Serotonin-Norepinephrine Reuptake Inhibitors
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressants
tDCS	transcranial Direct Current Stimulation
TMS	Transcranial Magnetic Stimulation
TSH	Thyroid-Stimulating Syndrome
USPSTF	U.S. Preventive Services Task Force
WOS	Web of Science
Y-BOCS	Yale-Brown Obsessive-Compulsive Scale




EXECUTIVE SUMMARY

Annually, an estimated 500,000 pregnant women in the United States will experience a mental disorder either prior to or during pregnancy (Doering et al. 1978, Gavin et al. 2005, Fawcett et al. 2019). Anxiety and major depressive disorders are the most commonly diagnosed perinatal mental disorders (Doering et al. 1978, Gavin et al. 2005, Fairbrother et al. 2015, Fawcett et al. 2019, Van Niel et al. 2020). Although bipolar disorders, substance use disorders, obsessive-compulsive disorder, psychotic disorders, and eating disorders are less common, they can incur serious health and psychosocial consequences (Godwin et al. 2020, Howard et al. 2020). Also, suicide is a major cause of mortality for women in the perinatal period, accounting for 5%–20% of maternal deaths (Kendig et al. 2017a, Rodriguez-Cabezas et al. 2018, Davis et al. 2019a). Untreated perinatal mental disorders may lead to harmful outcomes such as high-risk pregnancies, in which the birthing person, her fetus, or both are at higher risk for problems during the pregnancy and delivery periods (James et al. 2011, Betcher et al. 2020, Howard et al. 2020, Dagher et al. 2021). Pregnant persons with psychiatric illness are also at a higher risk of engaging in unhealthy behaviors, such as risky sexual behavior, substance use, poor sleep, and poor nutritional intake during pregnancy, as well as inadequate maternal–infant bonding prenatally and post-delivery (Rossen et al. 2016, Betcher et al. 2020, Dagher et al. 2021). In addition, psychosis, suicidal ideation, and suicide attempt that occur during pregnancy are considered psychiatric emergencies that require immediate interventions and, if untreated, may lead to hospitalization and maternal death (Rodriguez-Cabezas et al. 2018). Also, pregnant persons with psychiatric illness are at a greater vulnerability for substance misuse, poor self-care, and suicidal thoughts and behaviors (Betcher et al. 2020, Dagher et al. 2021). Combined, suicide and overdose are the leading cause of death for childbearing persons in the year after delivery (Rodriguez-Cabezas et al. 2018, Davis et al. 2019b).

Despite these health risks, pregnant persons are often termed “therapeutic orphans” due to the low rates of receiving treatment (Wisner 2012, Wisner et al. 2020). Upwards of 75% of pregnant persons affected by mental health symptoms remain untreated (Byatt et al. 2015, Cox et al. 2016, Sanmartin et al. 2019, Griffen et al. 2021a). Substance misuse and dependence are also often undertreated (Forray et al. 2015). For instance, only one-third of pregnant persons with opioid use disorders receive methadone and buprenorphine (Martin et al. 2015). Even when treatment is obtained, it is more likely to be offered during the postpartum period than prior or during pregnancy (Munk-Olsen et al. 2016). Furthermore, known disparities in the screening and treatment of perinatal mental health conditions exist by race and socioeconomic status (Byatt et al. 2013, Sidebottom et al. 2021). These trends are especially concerning given that effective pharmacologic (Betcher et al. 2020) and nonpharmacologic (van Ravesteyn et al. 2017, Dominguez-Solis et al. 2021) treatments exist that can be used safely during the perinatal period despite some inconclusive evidence

Research suggests behavioral health practitioners’ lack of knowledge, training, or comfort in how to treat perinatal persons safely and effectively as important barriers to perinatal mental health and substance use disorder identification and management (CHCF 2019, Jackson 2020). In addition, reservations among physicians about liability issues surrounding antidepressant or other medication use in pregnancy; financial barriers; stigma surrounding mental disorders; lack of access to health care; lack of coordinated care between obstetricians, primary care providers, and behavioral health specialists; and lack of specialized training and educational resources for providers who treat this population have been



identified as other obstacles to quality care (Weinreb et al. 2014, Sanmartin et al. 2019, Jackson 2020, Dagher et al. 2021).

Objective

Gaining a comprehensive picture and understanding of the barriers to screening and treatment of perinatal mental and substance use disorders and symptoms is a vital public health endeavor. This white paper is one component of a CDC Foundation-funded needs assessment to identify standard practices and barriers to perinatal persons with mental and substance use disorders or symptoms receiving quality care. This white paper was informed by an advisory panel of 21 clinicians and researchers from across the United States with expertise in perinatal mental health. The advisory panel included representatives from the American Psychiatric Association, the American Psychological Association, the American Association of Nurse Practitioners, the American Counseling Association, and the National Association of Social Workers.


Methods

Four broad areas of interest were identified by the advisory panel for literature review: (1) epidemiology, etiology, and maternal/infant outcomes; (2) clinical management; (3) perinatal mental health and substance use disorders in vulnerable and underserved populations; and (4) training and education in behavioral health. Four workgroups were convened consisting of 3-7 advisory panel members plus 1-2 staff facilitators, who identified specific subtopics per area of interest and high priority terms for the literature search. APA staff performed the literature search using Web of Science (Mongeon et al. 2015), which covers over 30,000 journals, including citations from PUBMED/Medline. A top-down approach was employed given the wide variety of synonymous terminologies for perinatal mental health conditions uncovered during exploratory search. Search results were filtered to excluded manuscripts with abstracts containing terms that would indicate preclinical research (e.g., guinea pig). Filters were additionally used to limit results to 2011-2022, English language manuscripts, and original research or review articles (e.g., excluding conference papers and other gray literature). A total of 46,453 manuscripts were identified.

Named entity recognition (spacy) and topic modeling (SciBERT) were used on the abstracts of the extracted literature to remove manuscripts that were either missed by the WOS filters (e.g., gray literature, countries other than the US, non-English language) or about an unrelated topic (Beltagy et al. 2019, Schmitt et al. 2019). Generated keyword and topic embeddings were used to organize the citations into a hierarchy of relevant subtopics for each main section. All procedures were performed using Python (3.11.0). The number of citations per subtopic was limited to ≤ 500 with priority placed on number of citations to enrich for the highest priority literature. Automated text summarization via Scholarcy was performed (Rysavy et al. 2022). The summarization included a subset of highlights for each manuscript as well as select details on background, materials and methods, results, and discussion.

Sections:

- a. **Epidemiology, Etiology, and Adverse Outcomes.** This section focuses on risk factors for perinatal depression, anxiety, psychosis, and substance use. Genetic, biological, environmental, psychological, reproductive, and social determinants of health–related risk factors are described in detail. To help improve existing care and guide future research, data on the impact of perinatal mental and substance use disorders on maternal outcomes are reviewed. Obstetric, gynecologic,




medical, psychosocial, and economic outcomes, as well as psychiatric outcomes of severe maternal morbidity, are discussed. Although there is a paucity of relevant well-designed studies, the available data show that perinatal mental and substance use disorders negatively impact maternal health, relationships, and economic outcomes. The effects of perinatal mental and substance use disorders on fetal and neonatal outcomes are also discussed, such as congenital malformations, preterm birth, poor fetal growth, fetal distress, and neonatal abstinence syndrome, as well as infant outcomes and later childhood outcomes.

- b. **Clinical Management of Perinatal Mental Health and/or Substance Use Disorders.** The benefits and risks of psychotropic medications such as antidepressants, antipsychotics, mood stabilizers, benzodiazepines, sedatives, antihistamines, and medications for substance use disorders (primarily opioid use disorder) during pregnancy and breastfeeding are comprehensively addressed in this section. The importance of nonpharmacologic treatment, such as psychotherapy, support groups, and alternative treatment approaches, is also highlighted. Growing evidence supports the use of neuromodulation interventions, such as deep brain stimulation, electroconvulsive therapy, transcranial magnetic stimulation, and transcranial direct current stimulation, which can be highly effective and are a nonpharmacologic options for perinatal persons wanting to avoid psychotropics.
- c. **Vulnerable and Underserved Populations with Perinatal Mental Health and/or Use Disorders.** This section describes current gaps in training across the continuum of behavioral healthcare practitioner training programs, including psychiatry, advanced practice nursing, psychology, mental health counseling, and social work, and addresses graduate, postgraduate, and continuing professional education. This section also discusses the adverse consequences of limited education and training to address perinatal mental health needs. Current challenges to improve training and continuing education across the behavioral health disciplines are included, and available educational resources and training opportunities in each domain are listed to aid readers in obtaining additional training as needed or desired. Lastly, the section provides recommendations to improve education and training of behavioral healthcare practitioners to be better equipped to treat perinatal persons.
- d. **Behavioral Health Education and Training in Perinatal Mental Health and/or Substance Use Disorders.** Vulnerable and often underserved groups often have additional unique mental healthcare needs, including adolescents; individuals who identify as lesbian, gay, bisexual, transgender, queer, or intersex; incarcerated individuals; refugees and immigrants; persons experiencing infertility; persons who experience pregnancy loss; and patients experiencing intimate partner violence. With a focus on these populations, this section discusses perinatal mental health prevalence rates, screening requirements, specific and tailored treatment approaches, and disparities in mental health care access.

Conclusions

Mental and substance use disorders are common in perinatal persons, yet they remain largely undiagnosed, untreated, or undertreated. The results of the literature review for this white paper show an association between unmanaged perinatal mental health problems and adverse outcomes for the birthing parent and fetus/child, including increased morbidity and mortality. This underscores the need for more widespread and standardized screening practices and a greater commitment by the field to developing and implementing perinatal-specific prevention and treatment initiatives. This white paper articulates the



need for behavioral healthcare practitioners to be more vigilant about screening and treating perinatal patients and to seek training to address gaps in knowledge about safe and effective practices for this population. Given the gaps in training in the area of perinatal mental and substance use disorders across behavioral health, proportions of the behavioral health workforce is likely ill-equipped to meet the growing psychiatric needs of this population. As such, significant reforms in education credentialing and in academic and continuous education curricula are required to develop a workforce that is both competent and confident in working with perinatal patients.


Perinatal mental and substance use disorders, which refer to these conditions that occur before, during, and up to one year after giving birth, represent a vastly overlooked and undertreated public health problem. Poor mental health status during the perinatal period is linked to a wide variety of negative health outcomes for the mother as well as the fetus/infant. An accurate understanding of the epidemiology of perinatal mental and substance use disorders is critical to informing local and national efforts related to their prevention and treatment. For instance, screening and detection, risk reduction and prevention strategies, development and implementation of formal treatments and informal support as well as resource-based interventions and shaping public health practices and policymaking can be informed by accurate understanding of the epidemiology of perinatal mental and substance use disorders.

EPIDEMIOLOGY

The epidemiology of perinatal mental and substance use disorders should be interpreted in the context of some important limitations. First, literature to date primarily has reported prevalence rates rather than incidence rates, making it harder to assess the onset of new cases. Efforts are also needed to further scrutinize prevalence data to ensure its accuracy with respect to representativeness for many underserved and vulnerable populations who are more likely to lack access to treatment and included in data used to determine these statistics (Allen et al. 2023). The literature on perinatal substance use disorders is also limited by the fact that studies of perinatal addiction typically report on patterns of use and misuse rather than full-blown disorders, except for opioid use disorder.

Mental disorders reported in the literature typically include affective disorders, major depressive disorder (MDD) and postpartum depression, bipolar disorders, borderline personality disorder, anxiety disorders, posttraumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD). Substances reported on during the perinatal period generally include nicotine/e-cigarette use, tobacco/cigarettes, cannabis, co-use of cannabis and other substances, opioids, cocaine, and methamphetamine. Of note is the paucity of studies that examined the bidirectional relationship between perinatal mental and substance use disorders and symptoms (Pentecost et al. 2021). Additionally, many studies report on mental disorder symptoms rather than clinical syndromes, including symptoms of psychosis, depression, obsessive and/or compulsive tendencies, insomnia, self-harm, and suicidal ideation. Data on subclinical conditions is still useful, as these symptoms are often impairing and the target of prevention strategies and/or therapeutic intervention.

This section is limited in scope and focused predominantly on discussing the incidence and prevalence of perinatal mental and substance use disorders in the United States rather than that of subsyndromal conditions or symptoms, dual diagnoses (i.e., co-occurring mental and substance use disorders), or global rates. This section also largely omits the incidence and prevalence of mental- or substance use disorder-related phenomena that are of public health importance but are beyond the focus here, such as maternal mortality, comorbid health conditions seen with perinatal mental and substance use disorders, infanticide/neonaticide, and maternal homicide. However, a summary of the incidence, prevalence, and trends in attempted and completed suicide is included given their strong correlation with several mental and substance use disorders and relevance to treatment and prevention planning. Finally, this section does not discuss variations in incidence and prevalence among perinatal populations with an increased



vulnerability to mental and substance use disorders, such as people of color, low-income populations, and rural dwellers. However, clinicians should be mindful that the rates reported here are largely based on studies of White, heterosexual, cisgender females from middle- or upper-income backgrounds and thus are underestimates for many other populations.

Importance of Capturing the Epidemiology of Perinatal Mental and Substance Use Disorders

Epidemiology plays a critical role in highlighting the extent to which mental and substance use disorders are present in the perinatal population, which informs prevention and intervention efforts. This information is critical to public health because untreated perinatal mental and substance use disorders are associated with a wide range of adverse outcomes for the birthing person, fetus and child and can affect individuals, families, communities, the healthcare system, and society. For instance, a systematic review of 43 studies of untreated depression in pregnant women reported a variety of negative biological consequences to the developing fetus and newborn infants (Gentile 2017). These included an increased rate of irregular fetal heart rate; dysregulations in cortisol, dopamine, and norepinephrine; alterations in electroencephalogram activity; reduced vagal tone; and a higher risk of premature death and neonatal intensive care unit admission (Gentile 2017). Other studies of fetal and maternal health outcomes linked to untreated perinatal mental and substance use disorders similarly report increased rates of intrauterine growth restriction, low birth weight, infant behavioral difficulties, preterm delivery, infant malnutrition, frequent infant illness, infant developmental delay, impaired mother-infant attachment, poor growth, social interaction difficulties, gestational hypertension, and antepartum hemorrhage (Jablensky et al. 2005, Fishell 2010, Davalos et al. 2012).

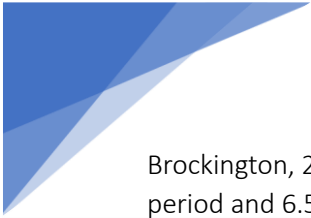
The danger in ignoring perinatal mental and substance use disorders is reflected in its association with harm to self or others, particularly maternal suicide; neonaticide, infanticide, or filicide; and other infant harm.

The danger in ignoring perinatal mental and substance use disorders is reflected in its association with harm to self or others, particularly maternal suicide; neonaticide, infanticide, or filicide; and other infant harm. Suicide in the antenatal period has been linked to multiple psychiatric correlates, including any preexisting and/or comorbid psychiatric disorder such as MDD, bipolar disorders, anxiety disorders, sleep-wake disorders, and substance use disorders (Orsolini et al. 2016). Maternal neonaticide, infanticide, and filicide have been documented in women who are acutely psychotic, including with psychotic depression, as well as women with other forms of severe mental illness, such as severe substance use disorders, schizophrenia, and delusional disorders (West 2007, Flynn et al. 2013, Milia et al. 2022).

Incidence of Perinatal Mental and Substance Use Disorders

Perinatal Mental Disorders

Studies on the incidence of perinatal mental and substance use disorders and symptoms are limited. The few available studies showed that the incidence of perinatal mental and disorders were lower than symptoms of the conditions. For instance, the incidence of psychiatric hospitalizations for postpartum psychosis among women without previous psychiatric hospitalizations was 0.04%, while those with any psychiatric hospitalization before delivery for first births had an incidence of 9.24% (Terp et al., 1998;



Brockington, 2004). Conversely, the incidence of major depressive episode was 7.5% in the prenatal period and 6.5% in the postnatal period (Gavin et al., 2005). Another study reported the incidence of depression symptoms to be 25.4% in the postpartum period (Howard et al., 2023). Anxiety symptoms and anxiety related disorders had incidence rates of 23% (Howard et al., 2023) and 3-11% (Ross et al., 2006) respectively. Additionally, 7.6% of postpartum women met full criteria for PTSD and 16.6% met partial criteria (Verreault et al., 2012).

One study reported an incidence of 12.5% for OCD symptoms at 1 month postpartum, however the sample consisted of only 44 pregnant women observed prospectively through to the postpartum period (Chaudron et al. 2010). Data from Canada showed an incidence rate of 4.7% (95% CI 3.2%–6.1%) for OCD (Fairbrother et al. 2021). At 1 month postpartum, the cumulative incidence of new onset OCD was reported to be 5%, increasing to 6% at 2 months postpartum, and 9% by 6 months postpartum (Fairbrother et al. 2021).

Perinatal substance use disorders

There is a lack of studies reporting the incidence of substance use and substance use disorders during pregnancy and postpartum. This is likely due to the stigma associated with use of substances during pregnancy and postpartum (Weber et al. 2021).


Prevalence of Perinatal Mental and Substance Use Disorders

Perinatal Mental Disorders

In the 2007–2012 National Inpatient Sample (N=23,507,597), the prevalence of psychosis at delivery was 698.76 per 100,000 hospitalizations (Zhong et al. 2018a). Specifically, the prevalence of schizophrenia was 60.09 per 100,000 hospitalizations, affective psychosis was 649.69 per 100,000 hospitalizations, and other psychoses was 10.15 per 100,000 hospitalizations (Zhong et al. 2018a).

Numerous studies have documented the prevalence of perinatal mood disorders, including depressive and bipolar disorders. In the United States, antenatal depression has been estimated to affect 17% of women and postnatal depression approximately 13% of women (Underwood et al. 2016). Data from a nationally representative sample of pregnant women from the 2006 Behavioral Risk Factor Surveillance System (N=68,620) showed a 6.1% prevalence rate for MDD and 16.6% for minor depression (Ashley et al. 2016). Analyses of the 2000 – 2015 National Inpatient Sample revealed a 7-fold increase in recorded diagnoses of depressive disorders, from 4.1 per 1,000 delivery hospitalizations in 2000 to 28.7 per 1,000 delivery hospitalizations in 2015 (Haight et al. 2019). Bipolar disorder appears to be much rarer. In a 2022 review and meta-analysis of 22 studies, the pooled prevalence of bipolar disorder among perinatal women (pregnant or within 12 months postpartum) was 2.6% (Masters et al. 2022).

Regarding anxiety and related disorders, a systematic review and meta-analysis (N= 102 studies of 221,974 women from 34 countries) reported a prevalence of 15.2% for any anxiety disorder and 4.1% for generalized anxiety disorder during pregnancy (Dennis et al. 2017). Another systematic review found very wide variability in reported rates of any perinatal anxiety disorder, from 2.6% to 39% (Leach et al. 2020). The pooled prevalence of PTSD has been reported at 4.7% and 1.2% among new mothers and fathers, respectively (Heyne et al. 2022). In contrast, the pooled prevalence of posttraumatic stress among new mothers and fathers were 12.3% and 1.3%, respectively (Heyne et al. 2022). A U.S. national survey reported a prevalence range of 1.7%–9% for PTSD following childbirth (Beck et al. 2011). Other studies have reported similar rates ranging from 3.1% to 15.7% (Grekin et al. 2014, Yildiz et al. 2017).



Analysis of data from Illinois and Maryland reported that approximately 6% of pregnant women and 11%–14% of postpartum women exhibited clinical levels of OCD symptoms (Farr et al. 2014, Miller et al. 2022). A meta-analysis of 34 studies from around the world including the United States found a 3% prevalence of OCD during pregnancy and nearly 17% during postpartum (Viswasam et al. 2019).

Perinatal Substance Use Disorders

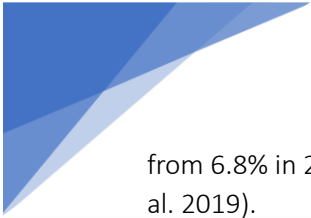
Most prevalence data on substance use disorders during the perinatal period concerns alcohol, opioids, cannabis, and tobacco. Perinatal substance use disorders, in general, have been estimated to occur in 5.5% of deliveries (Kotelchuck et al. 2017). Among currently pregnant women (N=2,215) in the 2016–2018 National Survey of Drug Use and Health (NSDUH), about 22% reported using at least one substance in the previous month (Kim 2022). Of those, 35% said they used alcohol only, 10% used marijuana/cannabis, and 46% used tobacco only (Kim 2022). Among those who reported using more than one substance, 5% indicated using tobacco and opioids both, and 5% engaged in polysubstance use (Kim 2022).

Perinatal substance use disorders, in general, have been estimated to occur in 5.5% of deliveries.

Among a sample of 363,240 U.S. women screened for substance use at their first prenatal visit, self-reported weekly alcohol use during pregnancy was 1.7%, whereas self-reported daily alcohol use during pregnancy was 0.2% (Young-Wolff et al. 2020). A smaller sample (N=365) of women screened for substance use disorders in a prenatal care program found 24.1% engaged in binge drinking during early pregnancy (Bakhireva et al. 2018). In the Behavioral Risk Factor Surveillance System (2011–2020; N=49,098), the prevalence of binge drinking among pregnant women was 6.1% in 2020 and the prevalence of heavy alcohol use among pregnant women was 3.2% (Howard et al. 2022a). Data from the 2001–2008 Maryland Pregnancy Risk Assessment Monitoring System (N=12,611) observed that nearly 8% of women consumed alcohol during their last trimester of pregnancy (Cheng et al. 2011).

Rates of OUD among perinatal persons are typically less than 1%. For instance, in a retrospective claims analysis of commercially insured U.S. women who recently delivered (N=110,285), 0.25% had a diagnosis of OUD (Gressler et al. 2019). Data from the 2000–2014 North Carolina State Inpatient Database of pregnancy-related hospitalizations (N=1,937,455) report a prevalence rate of 3.14 cases per 1,000 hospital discharges associated with opioid use (Alemu et al. 2020). In a New York claims database analysis, the prevalence of OUD during pregnancy or at the time of delivery was 0.57% (Shen et al. 2020). Finally, analysis of the 2005–2014 National Survey on Drug Use and Health (NSDUH; N=154,179) showed that approximately 1% of pregnant women engaged in nonmedical use of prescription opioid medication in the previous month (Kozhimannil et al. 2017).

Few data have addressed rates of cannabis use disorder and instead primarily describe cannabis use. Findings from the 2002–2019 NSDUH indicated a prevalence rate of 4.7% for cannabis use among pregnant women in 2018–2019 (N=15,109) (Mallinson et al. 2021). In a population-based survey of California women (N=18,638), 4.9% of pregnant women and 5.7% of postpartum women reported using cannabis (Azenkot et al. 2023). A 2017 study reported rates of cannabis use before pregnancy ranging



from 6.8% in 2009 to 12.5% in 2017 and 1.9% in 2009 to 3.4% in 2017 during pregnancy (Young-Wolff et al. 2019).

In terms of tobacco use, the 2005–2014 NSDUH (N=80,498 adolescent and 152,043 adult women) revealed 23% of pregnant adolescents and nearly 15% of pregnant adult women endorsed past-month tobacco use (Oh et al. 2017a). Rates of use tended to be smaller when looking at cigarette use, specifically, versus tobacco use, in general. In the California Maternal and Infant Health Assessment of more than 18,000 women, 2.1% of pregnant women reported smoking cigarettes (Azenkot et al. 2023). Similarly, the U.S. Centers for Disease Control and Prevention (2023) found that in 2021 4.6% of women smoked cigarettes at any time during pregnancy.

Trends in Perinatal Substance Use Disorders

The number of mothers using or dependent on opiates increased from 1.19 to 5.63 per 1000 hospital births per year between 2000 and 2009 (Patrick et al. 2012). Two Danish studies found that the proportion of women reporting several binge episodes of opiate use peaked in week 3 of pregnancy (17.8%) and then declined to 1.7% in week 7 (Kesmodel 2001, Kesmodel et al. 2004). Marijuana use in pregnant women increased from 3.4 % to 7.7% between 2015 and 2021 (SAMHSA 2016a, SAMHSA 2021). However, there was a trend of decline in marijuana use with advancing gestation from 37% of first-, 26% of second-, and 18% of third trimester (Klebanoff et al. 2021).


Alcohol use increased slightly in pregnant women from 9.3% to 9.8% between 2015 and 2021, while heavy alcohol use increased from 0.8% to 1.2% in the same period (SAMHSA 2016b, SAMHSA 2021). On the contrary, tobacco use decreased from 13.9% to 10.8% between 2015 and 2021 in pregnant women. However, use of smokeless tobacco increased from 0.2% to 1.1% in the same time period (SAMHSA 2016b, SAMHSA 2021).

Prevalence of Perinatal Suicide

A 2016 review of 57 studies found suicidal ideation in perinatal populations ranged from 7%–12% during pregnancy and 4%–9% during the postpartum, depending on assessment measure used (Gelaye et al. 2016). Another recent review found from 2006–2017 the prevalence of suicidality (i.e., completed suicide, suicidal ideation, and suicide attempts) in pregnant or postpartum women rose from 0.2% to 0.6% (Chin et al. 2022). The prevalence of suicide attempt during pregnancy was 680 per 100,000 women and during the first year postpartum was 210 per 100,000 (Chin et al. 2022). Finally, in an analysis of U.S. death certificates from 33 states and the District of Columbia from 2010-2019 (N=11,782), 5.4% of pregnancy-related deaths were due to suicide, with a pregnancy-associated death ratio of 2.2 per 100,000 live births (Margerison et al. 2022).

Conclusion

Mental and substance use disorders are not uncommon in pregnant and postpartum persons. Certain disorders such as MDD, postpartum depression, anxiety disorders, and alcohol, cannabis, and tobacco use disorders demonstrate higher incidence and/or prevalence rates than others including psychosis, bipolar disorder, OCD, and OUD. Although fully exploring the epidemiology of mental and substance use disorders among all subpopulations of perinatal patients was beyond the scope of this section, the estimates discussed here reflect an urgent need for more emphasis on research and standard practice related



mental and substance use disorders in perinatal populations. The documented association of perinatal mental and substance use disorders with adverse outcomes for the mother and fetus/child, including increased mortality and morbidity, may help drive screening behaviors and increase the uptake of prevention and treatment programs. More epidemiologic research is needed to further refine reported incidence and prevalence rates for improved representativeness and to better understand variations in the occurrence of mental and substance use disorders among subgroups of perinatal persons, especially vulnerable populations (e.g., people of color, individuals with low incomes).

The documented association of perinatal mental and substance use disorders with adverse outcomes for the mother and fetus/child, including increased mortality and morbidity, may help drive screening behaviors and increase the uptake of prevention and treatment programs.


ETIOLOGY

Understanding disease etiology is imperative to developing effective prevention and risk reduction strategies. Despite their prevalence and high potential to cause disability, the causes behind most perinatal mental and substance use disorders are not well-studied. Although existing literature has aimed to identify the relationship between various risk factors—whether genetic, biological, environmental, reproductive, or social—there is a paucity of research reporting strong associations between these factors and mental health- and substance use-related outcomes. This section reviews recent evidence on risk factors for perinatal mental and substance use disorders. Risk factors discussed below are categorized as genetic, biological, environmental, psychological, reproductive, and those related to social determinants of health (SDOH).

Genetic Risk Factors

Few studies have examined the association of various genes or epigenetic alterations and mental and substance use disorder risks in perinatal populations. In one review, several prenatal epigenetic haplotypes and markers, including brain-derived neurotrophic factor Val66-Met, FKBP5 polymorphism, and an altered messenger ribonucleic acid methylation marker in NR3C1, demonstrated an impact on the risk for developing PTSD across the life course (Pierce et al. 2022).

A larger number of studies have investigated the effects of genetic risk on the development of peripartum depression specifically. A 2015 systematic literature review reported that the influence of genetic factors on the onset of depressive symptoms differed based on trimester, highlighting potential hormonal and environmental influences (Figueiredo et al. 2015). These results are supported by another systematic literature review showing a positive association between postnatal depression and polymorphisms in several genes, including HMNC1, COMT, MAOT, PRKCB, ESR1, and SLC6A4, in the presence of stressful life events and environmental influences (Elwood et al. 2019). In another literature review, epigenetic biomarkers on genes responsive to estrogen also were found to predict peripartum depression (McEvoy et al. 2017). Similarly, the genes identified in the Pregnancy, Race, Environment, Genes study— a prospective longitudinal cohort study—corroborated with previous allelic, transcriptomic, and DNA methylation related to depressive phenotypes (Lapato et al. 2021). Additionally, a meta-analysis identified a potential protective effect of polymorphisms in the allelic and dominant models of 5-HTTLPR against postpartum



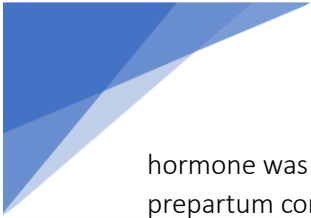
depression (Li et al. 2020). Finally, the associations between several candidate genes and postpartum depression, smoking, alcohol use, prepregnancy body weight, and weight gain during pregnancy are inconclusive and require further study to shed light on potential associations (Couto et al. 2015, Wehby et al. 2015).

Biological Risk Factors

Biological factors of interest in the risk of perinatal mental and substance use disorders include those pertaining to physical contributors (e.g., hormones, medical conditions) as well as nutritional contributors (e.g., nutritional deficiencies, poor nutrition in general). For instance, a secondary data analysis based on pregnant Kaiser Permanente Northern California enrollees observed a non-statistically significant association between lower pregnancy folate levels and prenatal depression (Avalos et al. 2023). Similarly, one systematic literature review found 14 studies that reported associations of perinatal depression with lower levels of folate as well as reductions in vitamin D, iron, selenium, zinc, and fatty acids. Trace mineral deficiency (e.g., zinc, selenium) is associated with an increased risk for postpartum depression (Ellsworth-Bowers et al. 2012), as is low plasma level of omega-3 (or n-3) polyunsaturated fatty acids and prenatal depression (Lin et al. 2017). Of note, some studies are inconclusive on the effects of nutritional intake on risk of depression (Sparling et al. 2017), including levels of plasma fatty acids (Jensen 2006) and vitamin B intake (Ellsworth-Bowers et al. 2012).

Some research shows an association between low circulating levels of vitamin D and an increased risk of peripartum depression (Cassidy-Bushrow et al. 2012a, Accortt et al. 2016, Williams et al. 2016, Aghajafari et al. 2018, Lamb et al. 2018, Amini et al. 2019, Tiderencel et al. 2019, Accortt et al. 2021, Lin et al. 2021, Tan et al. 2021). These results are however not confirmed in review by Gould and colleagues (Gould et al. 2022) or a meta-analysis of 9 longitudinal studies by (Wang et al. 2018). Other research has shown that vitamin D supplementation may help reduce postpartum depressive symptoms (Tiderencel et al. 2019). The association between low vitamin D and peripartum depressive symptoms may be modified by physical activity (Huang et al. 2014a).

Multiple hormonal factors have been investigated as contributors to mental health during the perinatal period, including progesterone metabolites, oxytocin, cortisol, and thyroid-stimulating hormone (TSH). Effects of the progesterone metabolites allopregnanolone and pregnanolone show a potential dynamic relationship with postpartum depression based on trimester (Wenzel et al. 2021, Standeven et al. 2022). Further, lower allopregnanolone during pregnancy may predict signs of postpartum depression (Osborne et al. 2017). In contrast, a literature review suggested the effects of prolactin are unclear among women with major depressive disorder (MDD) in the perinatal period (Szpunar et al. 2018). Oxytocin levels may be persistently higher in women with depression or anxiety at 6 weeks postpartum (Lara-Cinisomo et al. 2019a); however, this observation was not duplicated in a systematic literature review where only measures the endogenous oxytocin level through urine concentration, while the remaining 11 studies measured plasma oxytocin concentration and found no association overall with depressive symptomatology (Thul et al. 2020). Defects in gamma-aminobutyric acid (GABA) signaling may be a potential factor in the development of MDD and perinatal depression (Maguire 2019), possibly through interaction with allopregnanolone, which can augment GABA receptor inhibition (Burke et al. 2019). Regarding cortisol, placental corticotrophin-releasing hormone has been investigated in relationship to perinatal depression; depressive symptoms at 3 months postpartum were associated with elevated midgestational placental corticotrophin-releasing hormone. However, placental corticotrophin-releasing



hormone was not predictive of postpartum depressive symptoms at 6 months postpartum. Additionally, prepartum cortisol and corticotrophin profiles were not associated with postpartum depressive symptoms (Glynn et al. 2014), whereas reduced morning cortisol in pregnant and postpartum women with MDD has been more reliably observed (Szpunar et al. 2018). Maternal child abuse could moderate the relationship between diurnal cortisol patterns and peripartum mood symptoms (Bublitz et al. 2013).

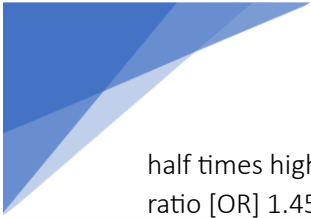
Changes in TSH have been investigated in several studies but appear to be largely unrelated to the development of MDD during the perinatal period (Szpunar et al. 2018, Schmidt et al. 2022). On the other hand, one study reported a positive association between low–normal thyroid function and anxiety scoring during pregnancy and postpartum (Konstantakou et al. 2021). Further, in a meta-analysis, thyroid autoimmunity during pregnancy and in the weeks after childbirth was associated with an increased risk of developing postpartum depression (Minaldi et al. 2020).

Higher levels of inflammatory markers may increase susceptibility to depressive and anxiety symptoms, although earlier results in different ethn racial groups are inconclusive (Blackmore et al. 2011, Cassidy-Bushrow et al. 2012b, Haeri et al. 2013, Buglione-Corbett et al. 2018, Osborne et al. 2019). Further, one study evaluating the relationship between serum C-reactive protein and postpartum depression found no association (Miller et al. 2019). Alternately, evidence supports an association between perinatal stress and dysregulation of the hypothalamic-pituitary-adrenal axis and immune system, as well as links between neuroendocrine or immune functioning and substance use disorder risk (Horn et al. 2018).

Howard and colleagues (2022) found a positive correlation at 12 months postpartum between higher scores of depression and poor sleep scores and fatigue (Howard et al. 2022b). This is consistent with other studies of poor maternal sleep showing an elevated risk of postpartum depression, obsessive-compulsive disorder (OCD), and anxiety (Park et al. 2013, Bhati et al. 2015, Okun 2015, Okun et al. 2018, Sharma 2019, Armstrong et al. 2022). In some research, the use of childcare reduced the link between maternal sleep and depressive symptoms (Armstrong et al. 2022). Poor sleep quality also may be a risk factor for recurrence of postpartum depression in women with a history of MDD or postpartum depression (Okun et al. 2011). Additionally, in a U.S. sample of Black women, ethn racial discrimination was associated with poorer sleep quality during pregnancy, especially during the early stages, which could increase their vulnerability for later mood or anxiety symptoms (Gillespie et al. 2021, Cohen et al. 2022).

Overweight or obese pregnant women are more likely to experience elevated antenatal and postpartum depression symptoms, whereas those with lower body mass index have no increased risk.

Other medical conditions are thought to have an impact on perinatal mental health. Two meta-analyses found anemia during or after pregnancy was significantly associated with an increased risk of postpartum depression (Azami et al. 2019a, Kang et al. 2020a). In addition, pregnant women with sickle cell disease demonstrate a four-fold increased risk of experiencing opioid-related disorders compared with pregnant women without sickle cell disease (Darlington et al. 2020). Polycystic ovary syndrome was associated with an increased prevalence of postpartum depressed mood and symptoms in a population-based study of more than 3,900 postpartum (2–6 months) women (Koric et al. 2021). Additionally, data from a systematic literature review and meta-analysis indicate women with polycystic ovary syndrome have nearly one and a



half times higher risk for postpartum depression than women without polycystic ovary syndrome (odds ratio [OR] 1.45, $P < 0.001$) (Schoretsantis et al. 2022).

Chronic conditions, such as obesity and diabetes, seem to play a role in perinatal mental health. Overweight or obese pregnant women are more likely to experience elevated antenatal and postpartum depression symptoms, whereas those with lower body mass index have no increased risk (Molyneaux et al. 2014a, Steinig et al. 2017, Schuette et al. 2018, Pavlik et al. 2020, Zhao et al. 2020a, de Los Reyes et al. 2023). However, a meta-analysis suggests that neither women who gain weight nor those who lose weight during pregnancy have a higher risk for depressive syndromes (Dachew et al. 2020). Depressive symptoms during pregnancy also may strongly predict excessive gestational weight gain (Hecht et al. 2021). Other conditions such as preeclampsia, diabetes, or snoring during pregnancy have been linked with prenatal depressive symptoms (O'Brien et al. 2013, Zhao et al. 2020a). In a systematic literature review and meta-analysis, having a diagnosis of chronic medical conditions such as diabetes, heart disease, hypertension, migraine, or other neurologic disorders increased the risk of perinatal mental illness overall, with an adjusted pooled OR of 1.43 (95% confidence interval [CI] 1.25–1.63) (Brown et al. 2018).

Several studies have reported higher rates of perinatal depressive symptoms among human immunodeficiency virus (HIV)-infected and at-risk HIV-uninfected women (Rubin et al. 2011, Kapetanovic et al. 2014, Angrand et al. 2018, Momplaisir et al. 2018). This association could be due to stress and fear over the child's health. A small retrospective cohort study of 215 women found maternal disclosure of HIV serostatus to family members was associated with a reduction in postpartum depression (Miller et al. 2016a). Tuberculosis and HIV co-infection may further exacerbate the risk of obstetric complications related to mental health, including risk of substance use and depression (Fernandez et al. 2018).

The effects of medical conditions on perinatal mental and substance use disorders also extends to the role of disability and functioning as risk factors. Data from the 2012–2017 Massachusetts Pregnancy Risk Assessment Monitoring System ($N = 8,453$) found 37.4% of women with disabilities (any mental or physical impairment that limits one's functionality or activity) had postpartum depressive symptoms, versus 8.79% of women without disabilities ($P < 0.001$) (Booth et al. 2021). Women with disabilities also may be more likely to smoke before, during, and after their pregnancy; less likely to quit smoking during pregnancy (Mitra et al. 2012, Iezzoni et al. 2015); and more likely to report having any mental health problems (Iezzoni et al. 2015).

Environmental factors associated with perinatal mental and substance use outcomes include poor air quality and secondhand smoking.

Finally, physical activity has been associated with a reduced risk of perinatal depression in few studies (Davis et al. 2012, Loprinzi et al. 2012). In a systematic literature review and two meta-analyses, regular physical activity prior to and during pregnancy and in the postnatal period was linked to a reduced risk of developing peripartum depression (Kolomanska-Bogucka et al. 2019, Nakamura et al. 2019). However, no protective effect of physical activity against depressive symptoms was observed in a cohort of Latina pregnant women (Szegda et al. 2018).



Environmental Risk Factors

Environmental factors associated with perinatal mental and substance use outcomes include poor air quality and secondhand smoking. Higher levels of air pollutants have been associated with an increased risk of postpartum depression or unspecified mental disorders (Ahlers et al. 2021, Kanner et al. 2021, Pourhoseini et al. 2022). These results were replicated in a low-income cohort consisting of primarily Hispanic/Latina women, which found that exposure to ambient air pollution, especially during mid-pregnancy, increased the risk of depression at 12 months after childbirth (Bastain et al. 2021).

Exposure to secondhand smoking was associated with a significant increase in the odds of depressive symptoms (OR 1.77, 95% CI 1.12–2.79, $P=0.01$) in a meta-analysis of 7 studies (Suzuki et al. 2019). Exposure to certain metals and chemicals in the environment can influence mental health. In an analysis of the Programming of Intergenerational Stress Mechanisms pregnancy cohort ($N=380$) found exposure to metals (i.e., barium, cadmium, chromium, cesium, lead, or antimony) in the environment was associated with an increased odds of elevated anxiety symptoms during pregnancy (Levin-Schwartz et al. 2022). Endocrine-disrupting chemicals, such as bisphenols and phthalates, also may influence hormonal shifts during pregnancy and thus contribute to postpartum depression (Jacobson et al. 2021).


Additionally, the season in which a pregnant woman delivers is potentially related to postpartum depression. Specifically, a meta-analysis of cohort studies ($N=103,986$) found women who gave birth in the winter were more likely to have postpartum depression (Tung et al. 2022).

Psychological Risk Factors

Personality traits identified as increasing the risk for postpartum depression and anxiety include neuroticism, anxiety, obsessive-compulsive personality traits, and vulnerable personality style (Bayrampour et al. 2018, van Broekhoven et al. 2019, Puyane et al. 2022). Perfectionistic concerns may be associated with peripartum depression and anxiety, with its effects on depression potentially mitigated by increased social support (Sweeney et al. 2013, Arnold et al. 2021, Bull et al. 2022, Evans et al. 2022). Body dissatisfaction during the third trimester of pregnancy also appears to be associated with a higher risk of postpartum depression (Sweeney et al. 2013, Silveira et al. 2015).

Mental health history has emerged as a highly relevant risk factor in perinatal mental and substance use disorders.

Mental health history has emerged as a highly relevant risk factor in perinatal mental and substance use disorders. In a meta-analysis of 26 studies, there was two-fold increase in the risk of developing postpartum depression among mothers with a family history of any psychiatric disorder compared with those without such a family history (Zacher Kjeldsen et al. 2022). Relatedly, in a national commercial insurance claims study, having a prior diagnosis for depression as well as a history of other psychiatric conditions, including anxiety, panic disorders, bipolar disorder, OCD, PTSD, or eating disorders, were associated with an increased risk for developing postpartum depression (Johansen et al. 2020). Another study of a large general population cohort of women with prior pregnancy ($N=10,877$) showed an increased vulnerability to depression and anxiety disorders perinatally in women with prior eating




disorder symptoms or past depression (Micali et al. 2011). Additionally, women with an established eating disorder diagnosis are at an increased risk for eating disorder relapse during or after pregnancy (Makino et al. 2020). History of premenstrual dysphoric disorder also may be significantly associated with the development of perinatal depression (Buttner et al. 2013, Pereira et al. 2022). For instance, in a meta-analysis of 19 studies, women with a prepregnancy history of premenstrual syndrome had more than twice the odds of postpartum depression compared with those without premenstrual syndrome (OR 2.20, 95% CI 1.81–2.68) (Cao et al. 2020).

Family or personal history of psychiatric disorders are associated with an increased risk for new onset peripartum anxiety or worsening anxiety (Cheadle et al. 2018, Furtado et al. 2018). In a prospective study of pregnant women with a history of mood disorders, over half (53.3%) of women who developed postpartum depression had a family history of mental disorders, whereas a family history of mental disorders was present in only 11.8% of women who did not develop postpartum depression (P=0.02) (Kimmel et al. 2015). Prenatal obsessive-compulsive-related beliefs predicted postpartum obsessive-compulsive symptoms as well as characteristics of and behavioral responses to postpartum intrusive thoughts of harm, including harm to the infant, in a relatively small prospective cohort of women pregnant with their first child (N=100) (Fairbrother et al. 2018).

History of substance use may be associated with an increased risk of mental and substance use disorders during the perinatal period. Women who engaged in analgesic opioid use in a prospective cohort study (N=2,748) were more likely to report using illicit drugs during the second or third trimester of pregnancy (OR 3.10, P<0.05) and were nearly three times as likely to report smoking cigarettes in the second or third trimester of pregnancy (OR 2.87, P<0.001) than women not using opioids (Smith et al. 2015). Additionally, women who report depression or anxiety appear to be more likely to smoke before and during pregnancy and less likely to quit smoking during the prenatal period (Tong et al. 2016, Goodwin et al. 2017). In a retrospective population-based analysis of Ohio vital birth records, women who reduced their smoking during their first pregnancy rather than quitting were more than five times as likely to smoke during their subsequent pregnancy compared with those who quit smoking altogether (Hall et al. 2016). Exposure to stressful life events prior to conception was associated with tobacco use before pregnancy and alcohol and tobacco use during pregnancy in an analysis of the Early Childhood Longitudinal Study-Birth Cohort (N=9,350) (Witt et al. 2015). Additionally, high perinatal stress levels, smoking, drinking, and substance use are associated with a higher rate of postpartum depression and anxiety in multiple studies (Chapman et al. 2013a, Banker et al. 2014, Katon et al. 2014, Reid et al. 2015, Biaggi et al. 2016, Shmulewitz et al. 2019, Mark et al. 2021, Pentecost et al. 2021, Yang et al. 2022).

History of substance use may be associated with an increased risk of mental and substance use disorders during the perinatal period.

Data from the National Survey on Drug Use and Health (NSDUH) show an increase in the prevalence of cannabis use among unmarried pregnant women, from 5.4% to 10.0%, between 2005–2014, whereas the prevalence of cannabis use among married pregnant women remained stable at 1.5% (Oh et al. 2017b). The same analysis also found that past-year anxiety and depression diagnoses were linked with cannabis use among unmarried pregnant women (Oh et al. 2017b). In another analysis of NSDUH data, from 2005–2018, women with depression were three-times more likely to use cannabis during pregnancy versus



women without depression (Goodwin et al. 2020). Recreational cannabis legalization in some states has been associated with a significant increase in pre-conception and postpartum cannabis use, compared with states without recreational legalization (Skelton et al. 2021).


Psychological functioning appears to play a role in perinatal suicide risk. Among a cohort of perinatal women screened for depression, 3.8% reported suicidal ideation; 1.1% of this subgroup were at an elevated risk for suicide, with about half reporting an attempted suicide (Kim et al. 2015a). Among a sample of 267 women in their second or third trimester of pregnancy, high rumination and insomnia in mid-to-late pregnancy were associated with increased odds of both depression and suicidal ideation (Kalmbach et al. 2020). Additionally, in a sample of women with mild-to-moderate depression (N=70), nocturnal cognitive arousal predicted the development of suicidal ideation (OR 11.47, P=0.025), and perinatal-focused rumination predicted an increased suicidal ideation risk (OR 8.98, P=0.024) in late pregnancy and early parenting (Kalmbach et al. 2021). Other psychiatric factors associated with suicidality during and following pregnancy include the presence of somatic symptoms; past psychiatric diagnoses, such as depression or anxiety; current substance use; previous infanticide; intimate partner violence; a positive family history of psychiatric illness; and complications during pregnancy (Gold et al. 2012, Tabb et al. 2013, Sit et al. 2015).

Reproductive Risk Factors

A woman's reproductive health and pregnancy—including pregnancy intention and parity—also have been the subject of study. For instance, women with unintended or mistimed pregnancies are more likely to report severe or moderate prenatal depression symptoms compared with women with intended pregnancies, with an overall prevalence of depression of 21% among women reporting unintended pregnancies (Fellenzer et al. 2014, Abajobir et al. 2016). In a study investigating pregnancy intention and alcohol use behavior, no relationship between pregnancy intention and cessation or reduction in alcohol use was observed; however, women with unwanted pregnancies were significantly more likely to report binge drinking during pregnancy than women with intended or mistimed pregnancies (Terplan et al. 2014). Additionally, women with intended pregnancies were 31% less likely to consume any alcohol in early pregnancy, although most women stopped or decreased alcohol consumption in early pregnancy regardless of intention (Pryor et al. 2017). In addition, women with unwanted pregnancies demonstrate lower odds of quitting or reducing smoking compared with women with intended or mistimed pregnancies (Chisolm et al. 2014). Some research suggests women with unintended pregnancies are twice as likely to experience postpartum depression at 12 months than women with intended pregnancies, even after adjusting for confounding factors of age, poverty, and education level (Mercier et al. 2013). However, these results are not supported by other studies of first-time pregnancy, after controlling for confounders (Abbasi et al. 2013).

Maternal age and parity may predict future mental and substance use disorder outcomes.

Maternal age and parity may predict future mental and substance use disorder outcomes. Multiple studies have identified reproductive risk factors for maternal smoking during pregnancy or return to smoking in the postpartum period, including younger maternal age and multiparity (Masho et al. 2013, Orton et al. 2018, Hyer et al. 2020, Jones et al. 2020). Older maternal age is a reported risk factor for



postpartum drinking (Chapman et al. 2013a, Meschke et al. 2013, Hyer et al. 2020). On the other end of the age spectrum, adolescent pregnancy (13–17 years old) was associated with an increase in later suicide attempts (Alimi et al. 2022, Cioffi et al. 2022). In a sample of low-income mothers, giving birth as a teenager increased the odds of having a lifetime behavior disorder (OR 2.66), having current PTSD (OR 2.54), and having at least 1 anxiety disorder (OR 1.78) compared with older women at first birth (Tabet et al. 2016). Regarding parity, in a large international study of over 1 million women in 138 countries, first-time mothers reported higher rates of postpartum depression symptoms and symptom burden than multiparous women ($P < 0.0001$), and mothers of twins—especially older mothers—reported higher rates of depression than mothers of singletons ($P < 0.05$) (Bradshaw et al. 2022).

Experiencing obstetric interventions (e.g., cesarean delivery, emergency delivery), obstetric violence, trauma, or previous mental illness are all associated with an increased risk of PTSD or depression after birth (Andersen et al. 2012, Kim et al. 2018, Chen et al. 2020, Khsim et al. 2022, Smithson et al. 2022). In the 2009–2011 national Pregnancy Risk Assessment Monitoring System, the risk of postpartum depressive symptoms was 55% and 74% higher in women with preterm birth in both deliveries and index delivery only respectively, as compared with women with term deliveries (Ihongbe et al. 2017). Pregnant women experiencing a medically complicated pregnancy have demonstrated higher levels of anxiety symptoms versus uncomplicated pregnancy in multiple studies (Fischbein et al. 2019, Abrar et al. 2020). Infant complications, such as low support during labor and delivery, as well as psychological difficulties in pregnancy are documented risk factors for developing PTSD after labor (Andersen et al. 2012). In addition, in a systematic review and meta-analysis of 56 studies, the prevalence of anxiety and posttraumatic stress was markedly high among parents of babies admitted to neonatal units, with a pooled prevalence of anxiety of 41.9% and posttraumatic stress of 39.9% among parents up to 1 month after the birth (Malouf et al. 2022). Admission to the neonatal intensive care unit also is linked with an increased risk of maternal postnatal depressive symptomatology (Wyatt et al. 2019).

Experiencing obstetric interventions (e.g., cesarean delivery, emergency delivery), obstetric violence, trauma, or previous mental illness are all associated with an increased risk of PTSD or depression after birth.

Experiencing pregnancy pain during the third trimester or pain that does not subside after childbirth is associated with greater postpartum depressive symptoms (Mathur et al. 2021, Vignato et al. 2021). Treating perinatal pain may improve health-related quality of life, especially mental health, as well as reduce the risk of postpartum depression development (Kapulsky et al. 2021, Vignato et al. 2021).

Breastfeeding might represent a protective factor for maternal mental health struggles. In a meta-analysis, overall breastfeeding was associated with a 14% lower risk of postpartum depression, whereas exclusive breastfeeding was associated with a 53% lower risk for postpartum depression versus never breastfeeding (Alimi et al. 2022, Xia et al. 2022). Nonexclusive breastfeeding, however, did not demonstrate as protective an effect as did exclusive breastfeeding (Alimi et al. 2022, Xia et al. 2022).




Social Determinant of Health (SDOH) Risk Factors

SDOH during the perinatal period is a critical factor related to maternal and neonatal outcomes, including those related to psychiatric illness. Such factors include but are not limited to experiencing adverse childhood experiences, being a victim of abuse of any type, experiencing food or housing insecurity, having unstable employment or being unemployed, having low income, and lacking social support. Work-to-family conflict and higher total hours of workload are significantly related to worse mental health among employed pregnant women (Selix et al. 2015, Kornfeind et al. 2018, Newkirk et al. 2020, McCardel et al. 2022). Further, women who return to work by 6 weeks postpartum report worse mental health scores than women still on maternity leave at that time (Selix et al. 2015, Kornfeind et al. 2018, Newkirk et al. 2020, McCardel et al. 2022). In a cohort study of women hospitalized for childbirth, investigators found an increase in leave duration during the first postpartum year was associated with a decrease in depressive symptoms, that decrease lasted until 6 months postpartum (Dagher et al. 2014). Another study similarly reported that women with supportive coworkers and supervisors during pregnancy had the lowest levels of prenatal stress, anxiety, and postpartum depression (Schwab-Reese et al. 2017, Jones et al. 2021). However, a post hoc analyses of a previously conducted randomized controlled trial found being employed at 7 months postpartum was associated with lower depression symptomatology than being unemployed (Lewis et al. 2017a), suggesting a possible protective effect of employment on long-term postpartum depression.

SDOH during the perinatal period is a critical factor related to maternal and neonatal outcomes, including those related to psychiatric illness.

Ample research suggests adverse childhood experiences increase the risk for symptoms of prenatal depression, especially in low-income women (Alvarez-Segura et al. 2014, Ayers et al. 2016, Choi et al. 2016, Hutchens et al. 2017, Mersky et al. 2018, Shamblaw et al. 2019, Nidey et al. 2020, Racine et al. 2021, Shin et al. 2021, Fields et al. 2023). Childhood adversity also appears to increase the risk of perinatal PTSD and tobacco and alcohol use during pregnancy (Blalock et al. 2011, Frankenberger et al. 2015, Choi et al. 2016). Childhood sexual abuse is a significant precipitator of mental and substance use disorders in pregnancy, including opioid use, PTSD, depression, and anxiety, particularly in Black women (Wosu et al. 2015, Akinbode et al. 2021, Kors et al. 2022). A literature review showed inconsistent results on childhood sexual abuse and later development of perinatal PTSD (Wosu et al. 2015); however, a later systematic literature review and meta-analysis indicate a lifetime history of sexual victimization carries a 51% higher risk of experiencing perinatal depression (Lombardi et al. 2023).

Other types of violence, such as intimate partner violence and physical or sexual violence, also are associated with an increased risk for perinatal PTSD, depression, and suicidal ideation, attempt, and completion (Wu et al. 2012, Biaggi et al. 2016, Vignato et al. 2018, Zhang et al. 2019, Reid et al. 2022). In a systematic literature review of 14 studies, exposure to abuse or intimate partner violence and alcohol consumption behaviors of partners and family members were strong predictors of risky alcohol consumption during pregnancy (Ward et al. 2021). Intimate partner violence itself is linked with higher levels of symptoms of perinatal depression, anxiety, and PTSD (Sumner et al. 2012, Howard et al. 2013, Grekin et al. 2017, Yang et al. 2022), as well as an increased risk of antenatal suicidal ideation (Alhusen et




al. 2015a) and cannabis use during pregnancy (Miller-Graff et al. 2021). More severe abuse and multivictimization may increase the risk of developing postpartum psychosis (Kennedy et al. 2014). Experiencing a greater number of stressors, whether in childhood or in adulthood, is associated with elevated risk of postpartum depression (Liu et al. 2013, Heldreth et al. 2016) as well as with smoking (Allen et al. 2019). Stressors include but are not limited to events such as family illness, divorce or separation, intimate partner conflict, difficulty paying bills, spouse job loss, and death of a family member or loved one (Liu et al. 2013).

Racism, racial bias, and discrimination are key drivers of health inequities in perinatal women. In a cross-sectional study of Black women (N=428), gendered racial stress was associated with increased depressive symptoms in early pregnancy (Clarke et al. 2022). Another study reported that experiencing emotional upset due to racism was associated with higher prevalence of symptoms in postpartum people of color (Bossick et al. 2022). Similar results were reported in an Asian and Pacific Islander cohort of pregnant women (N=3,319), where experiencing racial discrimination was associated with a higher risk of postpartum depressive symptoms ($P<0.0005$) (Du et al. 2023). The association of discrimination with postpartum depressive symptoms has been upheld across multiple studies, and feeling distress due to racial discrimination is associated with about 3 times higher odds of postpartum depressive symptoms and over 2 and a half times the odds of smoking tobacco (Ertel et al. 2012, Nguyen et al. 2012, Segre et al. 2021, Norona-Zhou et al. 2022, Weeks et al. 2022). According to data from the National Center for Health Statistics, living in a less racially segregated area is related to a lower probability of smoking during pregnancy for Black women; however, living in a less racially segregated area could increase the probability of smoking for Asian and Hispanic women by two- and three-fold, respectively (Mendez et al. 2013, Yang et al. 2014).

Racism, racial bias, and discrimination are key drivers of health inequities in perinatal women.

Financial and housing stability appear to play a role in mental health risk among perinatal populations. Almost one-third of low income LatinX women who participated in a cross-sectional study had prenatal depressive symptoms, and those with food insecurity reported higher levels than those without food insecurity (Hromi-Fiedler et al. 2011). In addition, a lower perceived socioeconomic status is associated with an elevated risk for postpartum depression (Dolbier et al. 2013). Other research suggests socioeconomic status is linked with postpartum smoking relapse through increased stress, a reduced sense of agency, and increased craving for cigarettes (Businelle et al. 2013). In a meta-analysis and meta-regression of over 290 articles, nations with significantly higher rates of income inequality, maternal or infant mortality, or women of childbearing age working over 40 hours a week had higher rates of postpartum depression (Hahn-Holbrook et al. 2017). A multisite randomized trial of women screened for postpartum depression (N=2,343) found 61.1% of women who lost insurance in the first year postpartum reported a need for mental health care, compared to 27.1% of the women who maintained their insurance (Bobo et al. 2014). In a study exploring pregnancy and motherhood in unaccompanied young women experiencing homelessness, only 10% of mothers reported seeing their children every day, whereas 75% reported seeing their children weekly or monthly and 15% reported almost never seeing their children (Crawford et al. 2011). Of the participants with children in their care, about one-third had



either a major depressive episode (32.5%), over half had PTSD (51.8%), and about one-third reported drug abuse in their lifetime (34.9%) (Crawford et al. 2011).

Finally, in a systematic literature review, low social support was associated with antenatal depression and anxiety, and with self-harm during pregnancy (Sidebottom et al. 2017, Bedaso et al. 2021, Collins et al. 2021). Supportive co-parenting is associated with lower stress and depression, as are high rates of emotional and instrumental support and relationship satisfaction (Pilkington et al. 2015, Burke et al. 2022). Father involvement in childcare could help reduce maternal parenting stress and promoting maternal psychological adjustment in White, LatinX, and Black women (Zhang et al. 2022).

Conclusion

Clearly, a wide range of precipitating and predisposing factors are salient to the risk reduction of perinatal mental and substance use disorders, including those pertaining to genetic, biologic, psychological, environmental, reproductive, and SDOH factors. Mental and substance use disorders are complex entities that often co-occur and have multiple etiologies; thus, identifying and mitigating their risk factors is an equally complicated undertaking. Better understanding of personal susceptibility to perinatal psychiatric illness can help inform a more individualized approach to prevention, treatment, and supportive intervention for perinatal populations, thereby giving patients—and their offspring—the best chance possible at achieving health and wellness.


ADVERSE EFFECTS ON PREGNANT PERSON AND OFFSPRING

The perinatal period is marked by significant psychological and physiological changes that impact the pregnant patient, their relationships, and their infant (ACOG 2018). The necessary physiological changes required to sustain pregnancy, facilitate childbirth, and support postpartum recovery can also lead to hormonal imbalances and shifts in lifestyle. These changes raise the vulnerability to the onset or worsening of mental health disorders (Dowse et al. 2020). In turn, mental and substance use disorders can significantly affect pregnant persons' health, self-efficacy, and ability to engage in prenatal self-care, resulting in poor maternal outcomes, as outlined in the remainder of this section. Despite recent increase in the numbers of studies on maternal outcomes, current data on the impact of mental illness and substance use on maternal outcomes is limited by a paucity of studies, especially prospective ones; heterogeneity among studies; poor data on prepregnancy history of mental illness (especially on diagnosis other than depression); and a predominance of studies in Western countries. Further, most research data do not systematically and effectively report on preconception diagnosis of a specific mood and anxiety disorder when looking at maternal outcomes. This section briefly summarizes existing data on perinatal mental and substance use disorders and maternal outcomes and can be used to both improve existing care and guide future research.

Obstetric and Gynecologic Outcomes

Stress/Mental Health Affecting Maternal Prenatal Health Behaviors

Starting in the prenatal period, mental illness and substance use can shape obstetric outcomes by influencing prenatal health behaviors and consequently pregnancy and birth outcomes. Stress response, diet, and exercise impact gestational weight gain (GWG) and pregnancy outcomes, including postpartum depression (Qiu et al. 2022). According to Freeman et al. (2019), this is particularly important for women



diagnosed with a psychiatric disorder, and peripartum complications associated with obesity—including gestational diabetes and higher rates of cesarean section—are common among women with psychiatric illness (Freeman et al. 2019). However, modifying diet, exercise, and mental health reduces the risk of abnormal blood glucose levels by 73%, targeting just one of those factors independently leads to improved outcomes (Sauder et al. 2016). Among 164 postnatal women interviewed about lifetime stress exposure and prenatal health behaviors, investigators found that greater and more severe lifetime stress exposure was associated with engaging in more negative prenatal health behaviors, such as smoking and overeating, as well as negatively associated with engaging in positive prenatal health behaviors, such as exercising regularly and eating a balanced diet (Smith et al. 2020).

Starting in the prenatal period, mental illness and substance use can shape obstetric outcomes by influencing prenatal health behaviors and, consequently, pregnancy and birth outcomes.

Maternal stress exposure and stress coping styles can affect pregnancy outcomes (Oni et al. 2015). Use of denial as a coping style is associated with negative outcomes in pregnancy, including higher rates for gestational diabetes mellitus (GDM), whereas other coping styles (i.e., planning, acceptance, humor, instrumental support, and venting) mitigate the effects and reduce the occurrence of pregnancy complications (Oni et al. 2015). Trait anxiety and perceived stress are a significant predictor of symptoms of depression, gestation weight gain, and postpartum weight retention, all of which can result in worse outcomes, including GDM, hypertension, fetal loss, miscarriage, and stillbirth (Byrn et al. 2015, Leonard et al. 2021). Prenatal maternal stress can also affect maternal–fetal hemodynamics (Levine et al. 2016). A reverse association between diet quality and mental health during perinatal period has also been shown, with both unhealthy diet and decreased healthy diet independently and significantly associated with increased antenatal depressive symptoms (Baskin et al. 2015).

Sleep—which is often disrupted in many mental disorders—also impacts pregnancy outcomes (Facco 2021). Short sleep duration, altered sleep timing, and sleep disordered breathing are common comorbidities in overweight and obese pregnant individuals, and there is compelling evidence that they increase the risk of developing GDM and affect glycemic control in women diagnosed with GDM.

Lastly, it is important to discuss family planning in women with psychiatric vulnerabilities (i.e., those diagnosed with mood, anxiety, psychotic, substance use, conduct, or eating disorders [ED]). Poor planning capacities, lack of compliance with contraceptives, and risky sexual behavior may lead to unintended pregnancies, which can contribute to poor maternal and offspring outcomes (Schonewille et al. 2022). Preconception substance use is significantly and positively associated with unintended pregnancy, especially in the presence of other risk factors such as history of depressive symptoms prior to conception, young age (<17 years), living in urban areas, low education level, being unmarried, and annual income below the federal poverty level (Cunningham et al. 2016, Shafique et al. 2022). This underscores the need for universal screening of mental and substance use disorders in all women of childbearing age and for addressing effective contraceptive use to prevent unintended pregnancy and related adverse effects on maternal and child health.



Obstetric and Gynecologic Outcomes Associated With Mental Disorders

Perinatal Mood and Anxiety Disorders


Perinatal mood and anxiety disorders (PMAD) is an umbrella term used to describe feelings of distress and sadness during the perinatal period up to 1 year after delivery and covers the continuum between “baby blues” and postpartum depression. Most research data do not systematically and effectively report on preconception diagnosis of a specific mood and anxiety disorder when looking at maternal outcomes. Rather, most available data refers to the presence of depression and anxiety symptoms in pregnant and postpartum patients, without teasing out prior history and/or timeline of symptoms. For that reason, data on unspecified perinatal depression and anxiety will be found under this section. Nevertheless, PMAD is a serious condition that can reduce a woman’s ability to care for herself and her child and increase the odds of having an adverse perinatal outcome (Accortt et al. 2022). About 20% of women experience PMAD, with 10% meeting criteria for postpartum depression —although 50% of cases are never identified. Depression and/or anxiety during pregnancy increase negative health behaviors—including tobacco use and poor maternal weight gain, rates of preterm labor and preterm delivery, risk of postpartum depression and suicide, probability of primary cesarean section, and perception of obstetric pain (Byatt et al. 2014, Xiong et al. 2021, Zochowski et al. 2021, Accortt et al. 2022, Dunkel Schetter et al. 2022). Thus, PMAD should be universally screened for, just like other well-established risk factors for perinatal complications.

One perinatal complication strongly associated with PMAD is GDM and other glucose dysregulation during pregnancy. Given that there is only limited evidence of an increased risk in women with bipolar disorder and not enough evidence for association with mental disorders other than depression, this section will focus on the relationship between GDM and other glucose dysregulation and depression (Wilson et al. 2022).

Pregnancy and the postpartum period increase susceptibility for the interplay between depression and glucose intolerance phenotypes.

There is a well-established bidirectional association between GDM and perinatal maternal depression (Fischer et al. 2023), with the prevalence of depression among women with GDM ranging anywhere from 4.1% to 80% (Byrn et al. 2015, Ross et al. 2016, Lee et al. 2020, Wilson et al. 2020, Miller et al. 2021, Shuffrey et al. 2022, Wilson et al. 2022). Many studies have examined whether diabetes in pregnancy is a risk factor for depression or if depression is a risk factor for diabetes in pregnancy, even suggesting that depression symptoms may be a useful clinical indicator of increased GDM risk (Morrison et al. 2016).

Pregnancy and the postpartum period increase susceptibility for the interplay between depression and glucose intolerance phenotypes. Pregnancy hyperglycemia (including isolated hyperglycemia, impaired glucose tolerance, and GDM) has been cross-sectionally associated with higher risk of prenatal depressive symptoms, and women with prenatal depressive symptoms are more likely to have a higher glucose tolerance test glucose level (mean: 120 mg/dL vs 114 mg/dL) and an abnormal gestational glucose tolerance (25% vs 17%) (Huang et al. 2015). Glucose level directly correlates to depressive symptoms, with each standard deviation (SD) increase in the glucose level (SD = 27 mg/dL) resulting in 25% higher odds of prenatal depressive symptoms (odds ratio [OR] 1.25, 95% CI 1.07–1.48) (Huang et al. 2015).




The association between GDM and prenatal depression is thought to result from different mechanisms: 1) increased activity of the hypothalamic-pituitary-adrenal axis resulting in elevated adrenocorticotropic hormone and cortisol levels activated by stress; 2) hyperglycemia-induced increased oxidative stress, inflammation, or leptin resistance; and 3) increased psychological and physical stress caused by behavioral changes influenced by the presence of depression that makes management of diabetes harder (Hinkle et al. 2016, Clevesy et al. 2018, Kampmann et al. 2019, Lara-Cinisomo et al. 2022, Shuffrey et al. 2022). In addition, elevated cortisol levels contribute to insulin resistance, as do placental hormones (Kampmann et al. 2019). More recent and well-designed studies confirm that GDM increases risk for postpartum depression (Ross et al. 2016, Arafa et al. 2019, Azami et al. 2019b). Regardless of directionality of the association, it appears that cooccurrence of both GDM and depression results in higher perinatal complications (Miller et al. 2021, Packer et al. 2021). In a retrospective cohort analysis of more than 170,000 women, the combined burden of GDM and depression resulted in significantly higher rates of preeclampsia (adjusted OR 1.28, 95% CI 1.11–1.49), gestational hypertension (adjusted OR 1.23, 95% CI 1.05–1.44), and preterm delivery at <37 weeks and <34 weeks gestational age (adjusted ORs 1.33, 95% CI 1.18–1.50 and 1.36, 95% CI 1.15–1.61, respectively) (Packer et al. 2021). Other studies that specifically looked at ethnically diverse women found similar association between depression and GDM in those populations (Barakat et al. 2014, Ross et al. 2016, Shuffrey et al. 2022).

Depressive symptoms during pregnancy are significantly associated with longer predelivery stays (at or above the 95th percentile) at the end of pregnancy, mediated in part by antepartum complications.

Depressive symptoms during pregnancy are significantly associated with longer predelivery stays (at or above the 95th percentile) at the end of pregnancy, mediated in part by antepartum complications (Palladino et al. 2011). In turn, the course of depression may be complicated by isolation due to predelivery hospitalization, especially in Black, Asian, and other minority ethnic women. There is an association between antenatal depression and preterm birth, stillbirth/neonatal death, and hypertensive disorders of pregnancy, even when controlling for maternal sociodemographic factors, smoking, and prepregnancy body mass index (Straub et al. 2012, Thombre et al. 2015, Delanerolle et al. 2022, Price et al. 2022). In addition, prepregnancy history of depression and anxiety symptoms may be considered part of a risk profile for preterm preeclampsia (Thombre et al. 2015). There are a variety of biological mechanisms that may underlie these associations, including alterations to sleep quality, hypothalamic-pituitary-adrenal axis activity, and inflammatory processes. Mitigating factors include prior history and antidepressant use, which may be a protective factor for preterm birth, and prenatal care (Venkatesh et al. 2017, Price et al. 2022). Women who received antidepressants during pregnancy had no difference in preterm and early-term deliveries, Apgar scores, and small for gestational age (SGA). Other studies emphasize bidirectionality, with high-risk obstetric inpatients commonly experiencing depression and anxiety symptoms, yet less than 5% receive mental health assessment and/or treatment (Byatt et al. 2014, Zemtsov et al. 2022).

The association between preexisting depression and anxiety with cesarean delivery needs more research (Zochowski et al. 2021, Ayala et al. 2023). Women with preexisting depression and anxiety request more elective cesarean deliveries, and access to insurance may play an important factor in this (Olieman et al.



2017). A large study using national data from the Multistate Pregnancy Risk Assessment Monitoring System (N=61,605) found no association (Ayala et al. 2023).

After controlling for confounders, women from the 2007–12 National Inpatient Sample (N=23,507,597) who had bipolar disorder were at higher risk for antepartum hemorrhage, whereas women with unipolar depression had an increased risk of fetal distress and excessive fetal growth in women with affective psychosis (Zhong et al. 2018a).

Suicide

Women with preexisting a mental health diagnosis and perinatal complications are at a higher risk for suicide, with women with suicidal behavior being more likely to have nonpsychotic depression, psychosis, and substance—especially alcohol—abuse (Zhong et al. 2018b, Calthorpe et al. 2021). Furthermore, women with suicidal behavior are at risk for antepartum hemorrhage, placental abruption, postpartum hemorrhage, premature delivery, and poor fetal outcomes. Women of color may be at higher risk for suicide, although this finding has not been reported consistently (Zhong et al. 2018b, Delanerolle et al. 2022).

Anxiety Disorders

Anxiety disorders are often overlooked during pregnancy and the postpartum period even though they are relatively common, occurring in almost one-quarter of women who have never given birth (Gimbel et al. 2022a). Untreated anxiety is associated with preterm birth, SGA, placental abruption, and hypertensive disorders of pregnancy (Gimbel et al. 2022a). Anxiety can heighten the risk for postpartum hemorrhage and elevated maternal symptoms of depression and anxiety during the postpartum, including postpartum depression, although experiencing positive emotions may decrease the risk (Grigoriadis et al. 2019, Wouk et al. 2019). Emerging evidence suggests that posttraumatic stress disorder (PTSD) can increase the risk for cardiovascular morbidity in pregnancy, with an estimated 30% increased risk of preeclampsia among women with PTSD and an increased risk of hypertensive disorders of pregnancy among pregnant women with a history of PTSD (Bublitz et al. 2023). This seems to result in part via autonomic imbalance and has been positively associated with decreased nighttime blood pressure and blood pressure variability and negatively associated with awakening cortisol.


Untreated anxiety is associated with preterm birth, SGA, placental abruption, and hypertensive disorders of pregnancy.

Obsessive-Compulsive Disorders

Obsessive-compulsive disorder (OCD) is linked to obstetric and psychiatric complications (Abdulkadir et al. 2016, House et al. 2016, Hologue et al. 2021). Panic disorder and social anxiety disorder may be comorbid with OCD (House et al. 2016). Delivery complications related to co-occurring OCD and tic disorder include premature birth and morning sickness requiring medical attention (Abdulkadir et al. 2016). The hormonal changes in pregnancy, GDM, younger maternal age at delivery, and delivery by cesarean are significantly associated with exacerbation of OCD symptoms (House et al. 2016, Hologue et al. 2021).

Psychotic Disorders

Most previous studies on psychosis in pregnancy have focused on schizophrenia, and little is known about



the effects of affective psychosis in this population (Zhong et al. 2018a). In general, pregnant women with schizophrenia have elevated risk of several adverse obstetric outcomes, including gestational hypertension, preeclampsia/eclampsia, cesarean delivery, induced labor, antepartum and postpartum hemorrhage, placental abruption, preterm and very preterm birth, stillbirth, and premature rupture of membranes (Zhong et al. 2018a, Etchecopar-Etchart et al. 2022a). In the 2007–12 National Inpatient Sample, a diagnosis of schizophrenia was associated with cesarean delivery, hospital stays of more than 6 days, placental abruption, premature delivery, and premature rupture of membranes (Zhong et al. 2018a). In a literature review and meta-analysis, schizophrenia was also associated with a 2.44 increased risk of GDM (Wilson et al. 2022). Pregnant women with a diagnosis of schizophrenia tend to be older, single, and from a lower socioeconomic background; they also tend to have higher rates of obesity, hypertension before pregnancy, diabetes before pregnancy, and higher nicotine and illicit drug use (Etchecopar-Etchart et al. 2022b). A population-based cohort study in France (N=3,667, 461) found that women with schizophrenia had more pregnancy complications, such as GDM, gestational hypertension, and urinary tract infection, than women without a diagnosis of a severe mental disorder (Fabre et al. 2021). All of these are known to increase morbidity and mortality of patients with a diagnosis of schizophrenia.

Even though the enactment of the Affordable Care Act in 2010 has been associated with great improvements in women’s perinatal mental health care in the United States, access alone may not be enough to address the complex needs of women with schizophrenia. Pregnant people with a diagnosis of schizophrenia need a patient-centered, intensive care program with integrated, multidisciplinary interventions. Efforts to identify and manage pregnancies complicated by psychosis and the establishment of mother–baby units may contribute to improved outcomes.

Eating Disorders


Despite the myth that people with active anorexia nervosa are less likely to become pregnant, EDs are common in pregnancy. It is important to remember that EDs include a variety of presentations. Naturally, having an ED during pregnancy leads to significant obstetric complications, including inadequate gestational weight gain, higher rates of cesarean delivery, SGA, and anemia (Eik-Nes et al. 2018, Pan et al. 2022). On the other hand, patients with ED are less likely to experience pregnancy-related diabetes and postpartum hemorrhage (Pan et al. 2022, Wilson et al. 2022).

Attention-Deficit/Hyperactivity Disorder

About 3% of reproductive age women have attention-deficit/hyperactivity disorder, and in cases of moderate-to-severe impairment, the benefits of prescription stimulant use may outweigh risks. In a population-based cohort study of Medicaid enrollees, there was a small but elevated risk of preeclampsia and preterm birth among women with psychostimulant use during pregnancy (Cohen et al. 2017). Similarly, a literature review on stimulant use in pregnancy found women who filled at least 2 prescriptions for stimulants between 8 and 18 weeks had a higher risk of placental abruption, and those continuing to the third trimester had an increased risk of preterm delivery (Smid et al. 2019).

Obstetric and Gynecologic Outcomes Associated With Substance Use Disorders

Exposure to substances during the perinatal period has a well-documented association with adverse maternal health outcomes. Data from the 2016–19 U.S. National Survey on Drug Use and Health (NSDUH) determined that approximately 5%–9% of pregnant women 15–44 years of age reported past-month illicit drug use (SAMHSA 2020). Preconception substance use or substance use disorders (SUDs) increases the



risk of unintended pregnancy (Shafique et al. 2022). Women who report any substance use also report delayed or inadequate prenatal care and low rates of postpartum visit, which increases their risk of obstetric complications (Simmons et al. 2022). The stigma associated with substance use and fear of legal repercussions may prevent patients with substance use or substance use disorders from seeking care early in pregnancy. Thus, advocating for policies that do not criminalize drug use in the perinatal period is critically important.

Pregnant and postpartum women with substance use disproportionately experience co-occurring psychosocial issues that can negatively affect maternal and neonate outcomes, including comorbid mental disorders, lack of transportation and childcare, and limited availability and quality of care (Simmons et al. 2022). In addition, women with substance use during pregnancy, such as opioid use disorder (OUD), have a higher risk of dying by suicide (Prasad et al. 2019). Because substance use disorders is a systemic issue, implementing systemic strategies that address unconscious bias and antidiscrimination practices for pregnant patients with mental and substance use disorders and incorporating family-focused policies and practices into agencies and organizations may yield better results (Kroelinger et al. 2019).

Women with substance use during pregnancy, such as opioid use disorder (OUD), have a higher risk of dying by suicide.


Alcohol Use Disorder

In vitro studies have demonstrated that maternal uterine vasculature during pregnancy may be vulnerable to chronic binge-like alcohol use (Ramadoss et al. 2011). This has been corroborated in vivo, with prenatal alcohol exposure being associated with higher likelihood of placental abruption, decreased placental weight, altered placental vasculature, deoxyribonucleic acid methylation, and molecular pathways (Steane et al. 2021). A prospective study of women attending university hospital-affiliated obstetric clinics showed that alcohol use during the year prior to pregnancy was associated with premature rupture of membranes and fetal complications (Flynn et al. 2009). The study also highlighted the importance of universal screening for alcohol use in all women of childbearing age, given that many people do not report or deny actual alcohol use during pregnancy.

Cannabis Use Disorder

Cannabis is commonly used, in part due to widespread legalization, increasing social acceptability and accessibility and perceptions of low harm (Lo et al. 2022). Cannabinoid receptors are present in the male and female reproductive tract, sperm, and placenta and seem to be involved in regulating reproduction (Lo et al. 2022).

Unfortunately, the literature on cannabis use in pregnancy is limited, and available literature highlights fetal outcomes (Layoun et al. 2022). Existing literature indicates the use of cannabis prior to pregnancy is associated with infertility and during pregnancy with preterm births and pregnancy loss (Lo et al. 2022). As with other substance use disorders, people who use cannabis enter prenatal care later and have a higher likelihood of using other substances, including tobacco, cocaine, and methamphetamines (Sasso et al. 2021). Pregnant women who use cannabis have a higher rate of cesarean delivery (Sasso et al. 2021). Unfortunately, up to 70% of women believe using cannabis during pregnancy is safe, and 50% of healthcare providers do not specifically counsel against use (Lo et al. 2022). Surveillance data from California, Colorado, and Washington—where medical and recreational cannabis use has been legalized—



demonstrate an increase in cannabis use or detection in pregnant women associated with cannabis legalization (Wang et al. 2022a). In Colorado, where the sale of recreational cannabis started in 2014, there was more than a 2-fold increase in cannabis-involved pregnancy hospitalizations between 2011 and 2018 (Wang et al. 2022a). Data from the NSDUH show reported past-month cannabis use has doubled in pregnant women from 2002 to 2017, most evident among those in their first trimester (Volkow et al. 2019).

Tobacco Use Disorder

Cigarette smoking in pregnancy has been extensively studied and remains one of the few modifiable risk factors that can significantly improve maternal and child health (Layoun et al. 2022). Cigarette use in pregnancy is slowly decreasing, but electronic nicotine delivery systems and other forms of smokeless tobacco products are increasing in popularity (Layoun et al. 2022). Smoking tobacco increases the risk of miscarriage and spontaneous abortion, preterm birth, premature rupture of membranes, placenta abruption, premature descent of placenta, premature birth, and placenta accreta spectrum and is associated with a 150% increase in overall perinatal mortality (Aliyu et al. 2011, Kitsantas et al. 2013, Rogers et al. 2013, Shobeiri et al. 2017a, Shobeiri et al. 2017b, Pintican et al. 2019, Jenabi et al. 2022, Layoun et al. 2022). The effects on the placenta are due to the abnormal development of placental vascularization and vasoconstriction effect on the uterus circulation and are dose dependent (Aliyu et al. 2011, Shobeiri et al. 2017a, Pintican et al. 2019). Interestingly, smoking tobacco is strongly associated with a reduced risk of hyperemesis gravidum, excessive gestational weight gain, and preeclampsia, although the mechanisms of association are not fully understood and the other risks associated with it far outweigh any potential benefit (Levine et al. 2015, Wei et al. 2015, Jenabi et al. 2017, Sorrentino et al. 2022). Furthermore, the reduced risk of hypertensive disorders of pregnancy (i.e., gestational hypertension and preeclampsia) has been observed in Europe and North America but not Asia (Wang et al. 2022b). There are little data on the effects of electronic cigarettes and smokeless tobacco in pregnancy, and future studies should focus on this area. Finally, maternal smoking is also a risk factor for depressive symptoms during pregnancy and the postpartum period (Rogers et al. 2013).

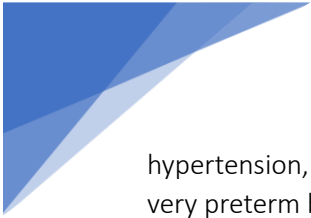
Opioid Use Disorder (OUD)

Since 1999, the rate of OUD has more than quadrupled, from 1.5 per 1,000 delivery hospitalizations to 6.5 (Kroelinger et al. 2019). OUD in pregnancy is associated with an increased odds of maternal death during hospitalization, cardiac arrest, intrauterine growth restriction, placental abruption, length of stay of more than 7 days, preterm labor, oligohydramnios, transfusion, stillbirth, premature rupture of membranes, and cesarean delivery (Maeda et al. 2014). Prenatal exposure to opioids can lead to placental epigenetic modifications and placental dysfunction (Borrelli et al. 2022).

Identifying preventive strategies and therapeutic interventions in pregnant persons who use substances is an important priority. Pregnant and postpartum women with OUD might experience stigma, including discrimination and criminalization (Kroelinger et al. 2019) and healthcare providers may have ethical concerns about screening, reporting, or treating OUD during pregnancy because some states require reporting to child welfare or protection agencies (Kroelinger et al. 2019).

Stimulant Use Disorder

Pregnant persons with a history of stimulant use disorder, which includes cocaine, amphetamines, and prescription stimulants, have a greater frequency of obstetric complications (Gorman et al. 2014). Pregnant women who use methamphetamines experience higher rates of pregnancy-associated



hypertension, gestational hypertension, preeclampsia, severe preeclampsia, eclampsia preterm birth and very preterm birth, intrauterine fetal demise, and abruption (Gorman et al. 2014). Methamphetamines are also associated with unplanned pregnancy in adolescents due to an increase in risky sexual behavior (Smid et al. 2019). In a case-control study of mothers who used cocaine (N=5,026 cases; N=5,026 controls), a similar increased association was observed with placenta-associated syndromes and cocaine use during pregnancy (OR 1.48, 95% CI 1.33–1.66), including elevated odds for placental abruption, placenta infarction, and preeclampsia, with the most pronounced odds noted for placental abruption (OR 2.79, 95% CI 2.19–3.55) (Mbah et al. 2012). Despite a decline in use nationally, cocaine use remains the leading cause of antepartum hospitalizations for substance use among pregnant women (Smid et al. 2019). Misuse or abuse of prescribed stimulants (i.e., nonprescription use, taking medications not prescribed to the individual or not taking them as prescribed) among pregnant persons has not been fully assessed. However, use of prescribed stimulants has been associated with elevated risk of preterm birth and placenta abruption (Smid et al. 2019).


[Stress/Mental Health Affecting Breastfeeding](#)

There is a complex relationship between breastfeeding and maternal mental health, and breastfeeding is often associated with fewer maternal mental health symptoms unless there are breastfeeding difficulties or a discordance between maternal role expectations and actual experience were present. (Yuen et al. 2022). The presence of elevated cortisol in postpartum women in response to postpartum stress is negatively correlated with the biological components responsible for the physiological functioning of breast milk production and secretion (Fernandez-Vaz et al. 2022). Further, in a sample of Hispanic women in Massachusetts (N=424), stress decreased the likelihood of breastfeeding (Insaf et al. 2011).

Breastfeeding is often associated with fewer maternal mental health symptoms unless there are breastfeeding difficulties or a discordance between maternal role expectations and actual experience were present.

In several studies, exclusive breastfeeding rates at hospital discharge appear to be influenced by mothers' perceived stress, anxiety, and depression without a direct relationship to cortisol levels (Watkins et al. 2011, Venkatesh et al. 2017, Fernandez-Vaz et al. 2022, Kim et al. 2022). Relatedly, antepartum depression is negatively correlated with continuing exclusive breastfeeding for longer than 3 months (Kim et al. 2022). Women with negative early breastfeeding experiences are more likely to have depressive symptoms at 2 months postpartum (Watkins et al. 2011). Venkatesh et al.'s (2017) observational cohort study looked at over 2,800 pregnant women who had been treated with antidepressants prior to pregnancy and found that women treated with an antidepressant throughout all 3 trimesters were less likely to breastfeed than women unexposed to antidepressants during pregnancy (adjusted OR 0.63, 95% CI 0.42–0.94) (Venkatesh et al. 2017). Women who took antidepressants during the third trimester only demonstrated even lower odds of breastfeeding versus unexposed women (adjusted OR 0.25, 95% CI 0.11–0.56).

The odds of breastfeeding initiation and continuation are significantly lower among individuals with both prenatal tobacco and illicit substance use (Nidey et al. 2022a). In one study, women who reported opioid use had significantly shorter duration of breastfeeding (compared to women without opioid use) and opioid exposure correlated with lower odds of having breastfed for 6 weeks or more, of the infant being



breastfed in the first hour after birth, of having skin-to-skin contact, feeding on demand, and receiving only breastmilk in the hospital (Bremer et al. 2023).

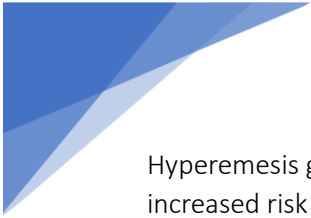
Medical Outcomes

Perinatal patients with mental and substance use disorders are at risk for numerous medical conditions, including chronic, costly, and potentially disabling conditions. Although more research is needed to confirm results, women with underlying mental disorders appear to use the emergency department during the postpartum period for psychiatric and obstetric reasons more frequently than women without mental health problems (Pluym et al. 2021). Women with underlying anxiety and depression—especially those with public insurance and who identify as Black or Asian—are more likely to visit the emergency department for hypertension and psychiatric symptoms (Pluym et al. 2021). For women with diabetes, achieving and maintaining glycemic control requires significant commitment and behavioral changes on the part of the patient, which the presence of depression can influence (Lara-Cinisomo et al. 2022). Patients with schizophrenia and schizoaffective disorders have significantly higher rates of chronic diseases, such as hypertension, diabetes, and urinary tract infection (M et al. 2011, Jayatilleke et al. 2018). Women with schizophrenia also tend to be older; are more likely to have substance use disorders, including tobacco and alcohol use disorder; are more likely to experience obesity, diabetes, and chronic obstructive pulmonary disease; and often are hospitalized in tertiary maternity hospitals (Fabre et al. 2021).

Psychiatric Outcomes of Severe Maternal Morbidity

Severe maternal and obstetric morbidity has been linked to psychiatric illnesses. For example, childbirth trauma (e.g., cesarean delivery, blood loss in vaginal delivery, preterm birth) increases the risk for postpartum depression and PTSD, even after controlling for race, ethnicity, age, parity, marital status, socioeconomic position, breastfeeding status, and anxiety and depression at time of delivery (Carter et al. 2022, Waller et al. 2022). People of color may be particularly vulnerable to these effects. Black and American Indian/Alaska Native women report more childbirth trauma, including mortality, than White women (Hill et al. 2022). Further, a systematic review and meta-analysis found preterm birth and delivery experiences increases the risk of PTSD and depressive symptoms among Black, Asian, and other minority ethnic women compared with full-term mothers (Delanerolle et al. 2022).

Many studies report morbidity risks associated with perinatal psychiatric illness. In a retrospective study of births in California from 2011–2017, women giving birth to preterm infants had 1.5 times and 1.3 times increased risk of being hospitalized with a mental health diagnosis within 3 months and 1 year after delivery, respectively (Calthorpe et al. 2021). In a systematic literature review of 17 studies, hyperemesis gravidarum, preterm birth, GDM, and cesarean section were associated with increased risk for postpartum psychosis (Nguyen et al. 2022). Hyperemesis gravidarum, gestational hypertension, preeclampsia, preterm birth, vaginal bleeding, preterm pre-labor rupture of membranes, kidney/bladder infection, being on bed rest, and cesarean section are associated with increased risk for postpartum depression in numerous studies (Sundaram et al. 2014, Caropreso et al. 2020, Truong et al. 2021, Delanerolle et al. 2022, Lantigua-Martinez et al. 2022, Nguyen et al. 2022, Zemtsov et al. 2022). Gestational weight gain and obesity prior to pregnancy and diabetes before pregnancy also appear to increase the risk of postpartum depression (Sundaram et al. 2014, Qiu et al. 2022, Rajabaliev et al. 2023).



Hyperemesis gravidarum, preterm birth, GDM, and cesarean delivery are also associated with an increased risk for postpartum acute stress (Nguyen et al. 2022).


Experiencing severe maternal morbidity was associated with an elevated risk of postpartum psychiatric morbidity, including elevated risk of hospitalization with a new psychiatric diagnosis following severe maternal morbidity, in a prospective study of childbirths in Georgia from 2013–2021 (Feng et al. 2022). Further, these effects persisted after controlling for a wide range of potential confounders using propensity scores and across several sensitivity analyses. Although 5.6% of delivering individuals received a psychiatric diagnosis at an outpatient obstetric visit in the postpartum year, only 1.2% attended an outpatient psychiatric visit (Feng et al. 2022).

There is some evidence that perinatal pain alone is a risk factor for postpartum depression, and that epidural analgesia could reduce the risk of postpartum depression, although perinatal pain is not the only factor contributing to the development of postpartum depression (Lim et al. 2020, Xiong et al. 2021). Independent predictors of postpartum depression include anxiety during pregnancy, perceived stress, number of previous stressful life events, lack of social support, and history of depression (Biaggi et al. 2016). Furthermore, depressive symptoms that do not meet criteria for postpartum depression are more likely in women with higher postpartum pain, potentially reflecting poorer birth recovery (Rajabaliev et al. 2023). A meta-analysis of 19 studies found neuraxial labor analgesia (i.e., an epidural) had a protective effect against postpartum depression when administered to pregnant women in regions with a high prevalence of postpartum depression but was a risk factor when administered to pregnant women in regions with a low prevalence of postpartum depression (Wang et al. 2022c).

It is important for obstetrician gynecologists to address their patients' physical, social, and mental well-being at the comprehensive postpartum visit and throughout the extended postpartum period, especially among medically underserved populations, and to refer them for specialized care if needed (Nelson et al. 2023). Screening for and providing mental health resources to birthing people after delivery are crucial, particularly among individuals giving birth to preterm infants, regardless of mental health history. Undetected psychiatric illness is a serious concern given that poor prepregnancy and antepartum mental health each independently increase the odds of having postpartum mental health problems, especially among women with other risk factors (e.g., women who identify as non-Hispanic, Asian/Pacific Islander race; women without a high school diploma; women with publicly funded insurance) (Witt et al. 2011, Truong et al. 2021).

Screening for and providing mental health resources to birthing people after delivery are crucial, particularly among individuals giving birth to preterm infants, regardless of mental health history.

Of note, the true prevalence rates of psychiatric outcomes of maternal morbidities are difficult to assess because not all women with perinatal mental disorders, such as postpartum depression, receive a diagnosis (Sundaram et al. 2014). Healthcare providers may either overlook symptoms, fail to discuss symptoms with patients, fail to screen for mental disorders, or misdiagnose patients after considering the symptoms and risk factors presented. In addition, many pregnant women seek care from the emergency department for mental health–related reasons (Tyson et al. 2022). It is unclear whether this happens



because pregnant individuals may be more vulnerable to mental health crises that require urgent care, needed services are absent, or patients may be hesitant to seek care due to stigma. Destigmatizing mental and substance use disorders and related struggles during pregnancy is crucial so that patients are comfortable seeking care as early as possible, giving them the greatest chance for timely diagnosis and, if needed, intervention.

Psychosocial and Economic Outcomes

Concerning economic outcomes, a recent large cohort analysis from the Fragile Families and Child Wellbeing Study examined the extent to which maternal depression affects individuals' economic welfare and financial stability years after delivery (Rokicki et al. 2022). Investigators found large and persistent impacts of maternal depression on material hardship and unemployment. Maternal depression was strongly and sustainably associated with not working for pay in Years 3, 5, 9, and 15 after delivery. Maternal depression also had a significant positive association with household poverty across Years 3–9 and with unemployment in Year 3.

Regarding psychosocial effects, maternal prenatal depression and PTSD are associated with problematic parenting (Romero et al. 2021). Additionally, postpartum depression symptoms may negatively influence maternal health practices in women after childbirth (Saxton et al. 2022). This underscores again the need for healthcare professionals to screen and address depression and anxiety in women of childbearing age and to provide early interventions for women at risk of depression, even before pregnancy. Physicians and behavioral health professionals should make it a priority to encourage positive maternal health practices and discuss the importance of regular healthcare visits before, during, and after pregnancy.


Conclusion

Despite the paucity of statistically relevant studies in this area, the available data suggest that mental and substance use disorders have a significant impact on maternal health, psychosocial, and economic outcomes. Most studies seem to support the use of universal screening for depression, anxiety, and substance use disorders; early interventions (especially in the form of education and counseling), and referral to appropriate care. Furthermore, healthcare providers—both behavioral and nonbehavioral—need to receive appropriate training on screening and early intervention.

Special populations need tailor-made programs to address specific concerns. For example, pregnant persons with schizophrenia benefit from a multidisciplinary approach that offers maximum support. Racial/ethnic minority patients benefit from culturally informed care that addresses barriers of racism and discrimination, help reduce stigma, and allow patients to better navigate systemic inequalities. Individualized care allows healthcare providers to better target symptoms and increases the chances of pregnant patients benefitting optimally from interventions.

Adverse Effects of Perinatal Mental and Substance Use Disorders on Offspring

A growing body of literature supports an association between perinatal mental and substance use disorders during pregnancy (antenatal) or in the year following delivery (postnatal) and adverse impacts on offspring. With a few exceptions, the potential mechanisms underlying this association remain to be defined. Moreover, as most studies are associational, further research is needed to better evaluate the impact of adequate treatment and/or response or remission of perinatal mental and substance use



disorders on offspring. This section focuses upon the evidence base concerning the impact of perinatal mental and substance use disorders upon fetal, neonatal (i.e., first 4 weeks), infant (first year), and later childhood outcomes.

Fetal and Neonatal Outcomes

Congenital malformations, preterm birth (< 37 weeks), small for gestational age (SGA), intrauterine growth restriction (IUGR), fetal distress and low birthweight (LBW) are the most well-studied fetal outcomes related to pregnancies of individuals with mental illness or addiction.

Congenital Malformations

Mental disorders, including mood disorders, anxiety disorders, and schizophrenia, have not been associated with any unique congenital malformations, particularly when controlling for confounding factors such as socioeconomic status, medications, and substance use. However, mental disorders may be associated with greater risk of malformations broadly. In a cross-sectional study using 2008–2014 data from the National Inpatient Sample (NIS), the largest nationally representative sample of hospital deliveries in United States, which has been assembled through the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP), the risk of fetal malformations among offspring born to women with serious mental illness—defined in that study as a diagnosis of major depressive disorder (MDD), bipolar disorder (BD), or schizophrenia—was significantly elevated, even when adjusted for demographic factors, insurance, substance use, and medical comorbidity (adjusted relative risk [RR] 1.33; 95% CI 1.23–1.44) (Heun-Johnson et al. 2019). As psychotropic medication use was not analyzed, it is not possible to exclude the potential contribution of medications with known teratogenic effects, such as valproate or lithium.


Fetal malformations associated with antenatal alcohol use disorder are widely documented; indeed, no safe amount of alcohol ingestion during pregnancy has been established.

A population-based cohort study among 7542 women with eating disorders in Sweden showed an increased risk of microcephaly among neonates born to women with any diagnosed eating disorder compared with those without (anorexia nervosa: RR 1.9, 95% confidence interval [CI] 1.5–2.4; bulimia nervosa: RR 1.6, 95% CI 1.1–2.4; eating disorder not otherwise specified [EDNOS] RR 1.4, 95% CI 1.2–1.9) (Mantel et al. 2020).

Fetal malformations associated with antenatal alcohol use disorder are widely documented; indeed, no safe amount of alcohol ingestion during pregnancy has been established. In utero exposure to alcohol is associated with a range of craniofacial, cardiovascular, and musculoskeletal defects which, along with subsequent learning and behavioral problems, characterize fetal alcohol spectrum disorder (FASD) (Mattson et al. 2019, Popova et al. 2019). Tobacco smoking has also been associated with congenital malformations, including urogenital defects such as cryptorchidism, hypospadias, and kidney malformations (Heun-Johnson et al. 2019).

Preterm Birth

Most major mental health conditions have been associated with an elevated risk of preterm birth. In the NIS, the incidence of preterm delivery between 2006–2015 was significantly higher among women with perinatal mood and anxiety disorders ([n= 219,294] 9.7 per 100, 95% CI 9.4–10.0) and serious mental



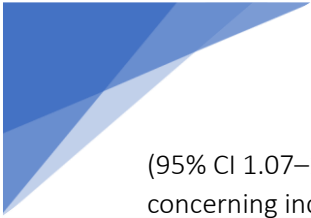
illness (BD and psychotic disorders [n = 50,178] 10.8, 95% CI 10.4–11.1) than among women without either condition ([n = 7,637,348] 6.7, 95% CI 6.7–7.0) (McKee et al. 2020). Using the HCUP data from 1999–2015, women with obsessive-compulsive disorder ([OCD] N = 3365) also had a higher risk of preterm births compared with women without OCD (adjusted odds ratio [OR] 1.31, 95% CI 1.17–1.46), even when controlling for other relevant variables such as age, comorbid psychiatric conditions, and substance use. A meta-analysis of 11 studies of birth outcomes among pregnant women with posttraumatic stress disorder ([PTSD] N= 49,115) also demonstrated increased risk of preterm birth (OR 1.42, 95% CI 1.16–1.73) (Sanjuan et al. 2021). The Swedish study referenced earlier that reported an association between eating disorders and microcephaly risk also found increased risk of preterm birth among individuals with all subtypes of eating disorders (anorexia nervosa: RR 1.6, 95% CI, 1.4–1.8; bulimia nervosa: RR 1.3, 95% CI 1.0–1.6; and EDNOS: RR 1.4, 95% CI 1.2–1.6) (Mantel et al. 2020).

Poor Fetal Growth and Fetal Distress

Gestational and birth outcomes that are often interrelated with, but not synonymous with, preterm birth are LBW (defined as < 2500 g), SGA (defined as < 10th percentile weight for gestational age), and IUGR (typically defined as < 10th percentile for estimated in utero fetal weight and/or abdominal circumference and often associated with other features such as fetal distress or asymmetric development). Not all infants who are SGA meet criteria for LBW; similarly, not all infants who are LBW, SGA, IUGR, and/or experience fetal distress are born at 37 weeks. However, each of these conditions is associated with higher risks of medical and behavioral problems during the neonatal period, infancy, and childhood (Heun-Johnson et al. 2019). Most studies on mental and substance use disorders and birth outcomes do not report all of these outcomes within the same study populations but rather focus on 1 or 2. Nevertheless, from the data available, it appears that just as major psychiatric disorders—including depression, OCD, PTSD, and eating disorders, as well as antenatal suicidal behavior—are associated with elevated risk of preterm births, they appear also to be risk factors for LBW, SGA, IUGR, and fetal distress (Lewis et al. 2016a, Venkatesh et al. 2019, Zhong et al. 2019, Mantel et al. 2020, Ghimire et al. 2021, Nasiri et al. 2021, Sanjuan et al. 2021). Further work is needed to characterize the full range of these outcomes within the same cohorts as well as to delineate the potential mechanisms underlying their relationship with mental disorders.

Similar associations of fetal/neonatal growth impairment and distress have been found with antenatal substance use during pregnancy. Although there is considerable heterogeneity in the literature, cannabis use may be an independent risk factor for preterm birth as well as LBW, SGA, IUGR, and fetal distress, even when controlling for tobacco and other substance use (Baia et al. 2022, Jones et al. 2022a, Marchand et al. 2022, Duko et al. 2023). Similar and generally more consistent elevated risk for LBW, SGA, IUGR, and fetal distress has been found for antenatal exposure to tobacco, opioids, and methamphetamine (Abdelwahab et al. 2022, Yen et al. 2022, Cohn et al. 2023).


Some but not all studies have shown an association between perinatal mental health problems and increased risk of admission to the neonatal intensive care unit (NICU), perhaps not surprising in view of the other associations including preterm birth and low birth weight. In one secondary analysis of outcomes from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMoM2b), of 8,293 women, 24% had anxiety, of which 3.8% received treatment and 20% were untreated. Newborns of women with untreated anxiety were significantly more likely to require NICU admission (17.3% vs 13.2%, $P < 0.001$) and NICU admission lasting more than 48 hours (11.9% vs 8.4%, $P < 0.001$) than those born to mothers without anxiety. In analyses adjusted for race, age, body mass index (BMI), depression, and alcohol and tobacco use, this equated to an OR of 1.24 (95% CI 1.05–1.46) for NICU admission and 1.30



(95% CI 1.07–1.58) for NICU admission lasting more than 48 hours (Gimbel et al. 2022b) Similar findings concerning increased risk of NICU admission have been reported in some but not all studies of children born to mothers with antenatal depression (Jacques et al. 2019).

Whether adequate treatment of underlying perinatal mental and substance use disorders mitigates risk of adverse fetal outcomes is a profoundly important question that has been insufficiently studied. In the nuMoM2b study, infants born to the small proportion of mothers with antenatal anxiety who received treatment, compared with those born to mothers with untreated anxiety, did not have higher rates of NICU admission than the comparison group born to individuals without anxiety, although the small number of treated mothers limits a definitive conclusion about whether treatment protected against risk of adverse neonatal outcomes (Gimbel et al. 2022b). An observational study of a longitudinal cohort (N=7,267) at the Massachusetts General Hospital found that 831 (11%) of the total pregnant sample screened positive for depression (Venkatesh et al. 2016a). In multivariable analyses adjusting for multiple factors, including lifetime diagnosis of MDD or anxiety as well as diabetes and preeclampsia, women who screened positive for depression during pregnancy experienced an increased risk of preterm birth (less than 37 weeks of gestation) (adjusted OR 1.27, 95% CI 1.04–1.55) and very preterm birth (less than 32 weeks of gestation) (adjusted OR 1.82, 95% CI 1.09–3.02) as well as of having an SGA neonate (adjusted OR 1.28, 95% CI 1.04–1.58), consistent with previous literature. In secondary analyses, among those women treated with an antidepressant during pregnancy (19% of those who screened positive and 5% of those who screened negative), depressive symptoms were not associated with a significantly increased risk of preterm and very preterm birth or an SGA neonate, suggesting the possibility that treatment exerted a protective effect against these adverse outcomes (Venkatesh et al. 2016a). Nevertheless, as the authors acknowledge, the study was not adequately powered for the secondary analysis. In addition, individuals treated with antidepressants in this sample may have differed from those not on antidepressants in ways that were not studied. Other treatments, such as psychotherapy, were also not evaluated nor was the relationship between depression response to treatment and preterm birth or SGA (Venkatesh et al. 2016a).

Another study suggesting a positive impact of mental disorder treatment on offspring outcomes was conducted at the University of Illinois at Chicago between 2006–16 using a retrospective case-control study design (Whelan et al. 2021). Among 20,000 individuals who delivered at the University of Illinois Hospital and Health Sciences System during that time, 148 women were identified who received antepartum inpatient psychiatric treatment. They were compared with a sample of pregnant individuals who had a documented psychiatric history without antepartum inpatient psychiatric treatment (n=301) as well as with those with no documented psychiatric history (n=301). As expected, individuals with antenatal psychiatric histories collectively had generally greater rates of adverse obstetrical and birth outcomes, including lower gestational age at birth, birthweight and 5-minute Apgar scores. However, compared to those individuals with documented psychiatric histories without antepartum inpatient treatment, those who had inpatient psychiatric treatment, though with generally more severe illness, had infants with longer gestational ages at delivery (38.01 + 2.15 weeks vs 37.19 + 4.23; $P < 0.01$) and a higher mean birthweight (3047.84 + 591.99 g vs. 2906.48 + 851.85 g; $P < 0.01$); findings which were significant even when controlling for maternal psychotropic medication use, BMI, and tobacco use. The investigators did not detect a significant difference in preterm birth, LBW, or Apgar scores related to inpatient psychiatric treatment. Clearly, additional work is needed. However, to the extent that inpatient psychiatric treatment was associated not with poorer but with modestly improved outcomes despite the greater



severity or acuity of the psychiatric illness, the investigators hypothesize that inpatient treatment may have helped advance greater multidisciplinary attention across mental health and obstetrical providers thereby contributing to better care.

Finally, another indirect line of evidence suggesting that access to mental disorder treatment may mitigate against adverse fetal/neonatal outcomes is derived from analysis of the impact of mental health parity laws enacted in 25 states between 1995 and 2002 on birth outcomes using the National Vital Statistics Systems birth data (Carney 2021). Among individuals believed to be among the most likely to benefit from the parity laws—namely those with private insurance, married, and with more than 12 years of education—implementation of the mental health parity laws decreased the probability of a baby being born with very low birth weight by 3%, increased length of gestation by 0.28 days (0.1%), and decreased the probability of a low Apgar score by about 6%. Although the inference is that mental health parity laws allowed for better access to mental health treatment during pregnancy, which contributed to more favorable birth outcomes, the study was not designed to assess this essential question directly.

Neonatal Abstinence Syndromes


Antenatal substance use including opioids, nicotine, and benzodiazepines has been associated with a syndrome of neonatal abstinence (NAS). Although not uncommonly occurring in the setting of polysubstance use, when NAS is related specifically to opioids, the term neonatal opioid withdrawal syndrome is sometimes used. The symptoms of NAS can include sleep and wake cycle disturbances, tachypnea, hypertonicity, jitteriness, hyperarousal, tremors, sweating, sneezing, nasal stuffiness, mottling, fever, yawning, vomiting, loose stools, disrupted feeding behaviors failure to thrive, and disrupted attachment behaviors. Not surprisingly, neonates with NAS are often admitted to the NICU, at least briefly.

Fetal malformations associated with antenatal alcohol use disorder are widely documented; indeed, no safe amount of alcohol ingestion during pregnancy has been established.

Between 1999 and 2014, the number of pregnant women with opioid use disorder, alone or in combination with other substances, increased from an estimated 1.5 to 6.5 cases per 1,000 hospital births (Yen et al. 2022). This was associated with a steep increase in the number of neonates with NAS from 1.2 to 8.0 per 1,000 hospital births, with some areas reaching 20.0 per 1,000 hospital births (Yen et al. 2022).

Infant Outcomes

Studies of infants born to mothers with mental and substance use disorders suggest that the risk of adverse consequences described during gestation and at birth continues into early life. For instance, a meta-analysis of 27 studies evaluated the association between mental illness and stillbirth/infant mortality (Adane et al. 2021). Of these, 13 studies focused on the association between maternal depression and anxiety and stillbirth/infant mortality (20 weeks gestation through 1 year of infant age) and yielded a pooled OR of 1.42 (95% CI 1.16–1.73). Another 13 studies evaluated the association between severe maternal mental illness and stillbirth/infant mortality with pooled OR of 1.47 (95% CI 1.28–1.68). The meta-analysis also found similar increased risk of stillbirth/infant mortality with any maternal mental disorder (OR 1.59; 95% CI 1.43–1.77); the association between mortality and any



maternal mental illness was at least as strong for infants (OR 1.72; 95% CI 1.40–2.11) as it was for fetuses (OR 1.47; 95% CI 1.28–1.68) or neonates (OR 1.54; 95% CI, 1.38–1.73) (Adane et al. 2021).

Another meta-analysis of 6 articles (N = 170,371) showed that children of mothers with prenatal and/or postnatal depressive symptoms or depression had 1.44 (95% CI 1.10–1.89) greater risk of hospitalization than children born to mothers without depression, whereas children of mothers with postpartum depressive symptoms or depression had 1.93 (95% CI 1.02–3.64) greater risk of death before 1 year than children born to mothers without depression (Jacques et al. 2019).


A systematic review of 122 studies on postpartum depression between 2005–2016 showed an association, similar to the meta-analysis above, with increased risk of infant mortality, as well as greater likelihood of disrupted or discontinued breastfeeding and poorer sleep patterns, with some but not all studies also suggesting delays in cognitive, language and motor development, and impairment on some measures of mother-infant attachment (Sloman et al. 2019). In low-income but not high-income countries, postpartum depression was also associated with reduced weight and length of infants in another systematic review (Farias-Antunez et al. 2018). As association between postpartum depression and less optimal feeding practices was also observed in a sample in the Women, Infants, and Children program (Weinfeld et al. 2022). These studies used variable definitions of postpartum depression and did not consistently control for salient potential confounding factors such as socioeconomic factors or tobacco or alcohol use. Postpartum depressive symptoms may also have an impact on cognitive development of infants. One analysis of 14 studies assessing the relationship between postpartum depression and cognitive development showed that the mean cognitive score on the Mental Development Index of the Bayley Scales for Infant and Toddler Development were about 4.2 units lower for infants ages 6–8 weeks whose mothers had high depressive symptoms during the first few weeks postpartum than infants born to mothers without depressive symptoms ($\hat{\beta} = -4.17$, 95% CI -8.01 to -0.32) (Liu et al. 2017).

A rare but profoundly tragic and preventable occurrence in the context of postpartum mental illness is infanticide.

A rare but profoundly tragic and preventable occurrence in the context of postpartum mental illness is infanticide (Luykx et al. 2019). Although early-life trauma, intimate partner violence, and substance use have all been linked to greater risk of infanticide, infanticide is most closely associated with postpartum psychosis, including depressive, manic, or mixed episodes with psychotic features or psychosis not otherwise specified, not infrequently with concurrent maternal suicidal thoughts or acts. In contrast, unwanted, ego-dystonic intrusive thoughts of harm to an infant, sometimes in the setting of OCD, without hallucinations or impairment in reality testing, do not appear to increase risk of harm to the infant (Fairbrother et al. 2022). Nevertheless, ruminations about harming an infant should prompt urgent evaluation for psychosis, postpartum mood disorder, and suicidality as well as intimate partner violence or other forms of extreme stress.

Childhood Outcomes

With respect to childhood outcomes, the long-term consequences of perinatal mental and substance use disorders are most well-documented with respect to antenatal alcohol use. Beyond facial dysmorphism



and other congenital abnormalities and growth retardation, which may persist throughout adolescence, FASD is associated with intellectual deficits, problems with social skills, adaptive function and executive function, and psychiatric comorbidity such as depression, anxiety, conduct disorder, and substance use disorders (Chu et al. 2022). Evidence for adverse childhood neurodevelopment outcomes related to other forms of prenatal substance use, including cannabis, are much less well-established (Thompson et al. 2023). In the Boston Birth Cohort followed from ages 6 months to 21 years (N = 3,138) between 1998–2019, self-reported prenatal opioid use was associated with an elevated risk of attention-deficit/hyperactivity disorder (ADHD) among offspring, as was the combination of opioids and cannabis or opioids and tobacco smoking (Garrison-Desany et al. 2022). A meta-analysis of 14 studies on the childhood impact of in utero methamphetamine exposure showed associations with poorer intellectual functioning (Cohen’s $d = 0.89$, 95 % CI 0.47–1.30), problem solving skills ($d = 0.82$, 95 % CI 0.07 –1.56), short-term memory ($d = 0.91$, 95 % CI 0.38–1.43), and language development ($d = 0.74$, 95 % CI 0.30–1.18), although samples were relatively small and there was considerable heterogeneity across studies (Kunkler et al. 2022).

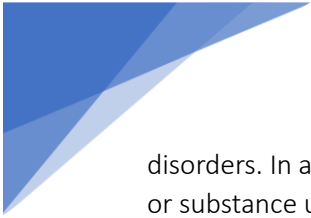
Some systematic reviews and meta-analyses have shown a possible association between antenatal or postnatal depression with childhood executive function problems or ADHD, although some studies were limited by reliance on parental report of offspring ADHD symptoms as well as lack of assessment of parental ADHD, which is known to have high heritability (Nidey et al. 2021, Christaki et al. 2022, Tucker et al. 2022). Studies of variable quality have suggested an association between antenatal and postpartum depressive symptoms with later internalizing and externalizing behavioral problems in toddlers and older children (Harris et al. 2020, Martucci et al. 2021). In many studies, it is difficult to disentangle the possible contributions of depression from other health conditions as well as the specific impact of depression during the perinatal period versus more enduring maternal mental health problems. More studies are needed which involve more specific ascertainment of antenatal and postpartum health, including comorbid psychiatric and medical conditions and their duration beyond the perinatal period, as well as data on social determinants relevant to childhood development.

In addition to their apparent impact on risk for neuropsychiatric conditions during childhood, antenatal mental health conditions may have an impact on other health problems. In particular, several meta-analyses have suggested a link between prenatal maternal depression or anxiety and elevated risk of childhood asthma (Chen et al. 2021).

Except for the teratogenic impact of substances such as alcohol on the developing fetus, the mechanisms through which mental and substance use disorders influence offspring outcomes are largely unknown and almost certainly multifactorial.

Potential Mechanisms

Except for the teratogenic impact of substances such as alcohol on the developing fetus, the mechanisms through which mental and substance use disorders influence offspring outcomes are largely unknown and almost certainly multifactorial. Biological factors likely to be relevant include genetic heritability, particularly with respect to behavioral, cognitive, and emotional problems such as depression, anxiety, ADHD, and substance use disorders, among offspring born to mothers with mental or substance use



disorders. In addition, the impact of stress, likely to be elevated among individuals with perinatal mental or substance use disorders, on hypothalamic-pituitary-adrenal axis (HPA) and inflammatory function may have direct effects on the in utero environment influencing programming of fetal HPA and neuroimmune function as well as brain connectivity in ways that may be relevant to the short and longer term general health and cognitive, behavioral, and emotional development of offspring (Gentile 2017, Bleker et al. 2020, Ruffaner-Hanson et al. 2022).

Compared with other pregnant individuals, those with mental and substance use disorders during pregnancy also are likely to receive less adequate prenatal care, to engage less optimally in self-care, to have lower levels of psychosocial supports during pregnancy and after delivery, and to be more vulnerable to intimate partner violence (Ben-Sheetrit et al. 2018, Nidey et al. 2022b, Simmons et al. 2022). They are also likely to experience more adverse determinants of health more generally during this critical period (Ben-Sheetrit et al. 2018, Nidey et al. 2022b, Simmons et al. 2022). Maternal mental health problems, particularly well-studied with respect to postpartum depression, have been associated with lower perceived parental efficacy, less positive perceptions of infant behavior (e.g., greater perceptions of fussiness), reduced bonding activities (e.g., less breastfeeding, playing with, reading, or talking to infants), and lower probability of infants having vaccinations or well child visits on time while also having a higher probability of using urgent care or emergency services (McFarland et al. 2011, Gobel et al. 2018, Ramsauer et al. 2018, Slomian et al. 2019). These factors are also likely to be associated with adverse general and mental health impacts on offspring.

Conclusion

Overall, substantial evidence links perinatal mental and substance use disorders to adverse outcomes for offspring, including greater risks of stillbirth and infant mortality, prematurity, impaired growth, NAS, NICU or hospital admissions, and enduring cognitive, behavioral, and emotional problems. The evolving literature is heterogeneous with respect to ascertainment of comorbid psychiatric and other health conditions, social determinants of health, and other relevant factors and how these factors were included in the analyses. The duration of maternal mental and substance use disorders is often not well-specified such that ability to isolate the impact of mental and substance use disorders during the antenatal or postpartum period on childhood development may be confounded by the persistence of these problems beyond the perinatal period. Finally, even well-controlled studies cannot exclude the impact of shared genetic vulnerability on risk for adverse health outcomes. Clearly, much more work is needed to elucidate the link between mental and substance use disorders and offspring health. Nevertheless, to the extent that mental and substance use disorders are associated with adverse offspring outcomes, the research questions whose answers will have the greatest individual and public health significance relate to better understanding the range of mental health treatments and other supports and resources that most effectively mitigate these risks and the best means to enhance access for those individuals who most need them.



CLINICAL MANAGEMENT

Mental and substance use disorders are common conditions that complicate pregnancy and have deleterious effects on pregnant and postpartum individuals and their infants, particularly when left undetected or untreated/undertreated (ACOG 2023a, ACOG 2023b). They are the leading cause of maternal mortality, exceeding all other causes of death during the perinatal period (Troost et al. 2021). Of these deaths, 84% are preventable (Troost et al. 2021). Despite the prevalence and burden of mental and substance use disorders during the perinatal period, they are often undertreated (Marcus et al. 2003, Carter et al. 2005, Smith et al. 2009, Rowan et al. 2012, Byatt et al. 2015, Ford et al. 2017, Matthews et al. 2021). Individuals from groups that have been marginalized (e.g., women of color, women from low socioeconomic backgrounds) are less likely to receive adequate care and have worse overall outcomes compared with majority populations (Primm et al. 2010). In addition to the treatment access gap, the number of available psychiatric providers cannot keep pace with the growing psychiatric needs of perinatal individuals (Costa 2016). Many clinicians specializing in psychiatry but not reproductive or perinatal mental health specifically are hesitant to provide clinical care in this population (Weinreb et al. 2014, Webb et al. 2021a). Evidence shows that training often focuses on potential treatment risks to the fetus rather than on the benefits of pharmacologic management of psychiatric disorders to both the mother and the fetus (Gjerdingen et al. 2007, Griffen et al. 2021b). Systemic barriers, including lack of exposure to perinatal mental and substance use disorder treatment during provider training, lack of access to specialists, and fear of litigation over medication management, also contribute to rates of undertreatment in this population (Gjerdingen et al. 2007, Griffen et al. 2021b).


Mental and substance use disorders are common conditions that complicate pregnancy and have deleterious effects on pregnant and postpartum individuals and their infants, particularly when left undetected or untreated/undertreated.

To improve health outcomes, it is imperative that healthcare providers implement existing evidence-based strategies to prevent, detect, refer, and appropriately treat patients suffering from perinatal mental and substance use disorders (Gjerdingen et al. 2007, Griffen et al. 2021b). As such, this section provides a review of high-yield, clinically relevant information for behavioral health clinicians, and has the primary goal of serving as a resource for any clinician involved in the prevention, screening, and treatment of psychiatric diagnoses in perinatal individuals.

PREVENTION

Risk factors for perinatal mental and substance use disorders are described in fuller detail elsewhere [Page 20]. Briefly, these include a prior history of mental or substance use disorders, a history of abuse (e.g., physical, sexual), unintended pregnancy, pregnancy during adolescence, stressful life events, intimate partner violence, low socioeconomic background, lack of social support, and obstetric complications (Vesga-Lopez et al. 2008, Biaggi et al. 2016, Howard et al. 2020). Ideally, prevention and intervention strategies should be made available to any pregnant individual with any of these risk factors.

Prevention of perinatal mental and substance use disorders is critical because currently the U.S. healthcare system is reactive. The system is built to treat patients after an illness manifests rather than to




prevent illnesses before they reach clinical threshold, resulting in what is known as the “prevention gap” (Jorm et al. 2019). Because of this, healthcare resources are primarily allocated to treatment rather than prevention, resulting in unnecessary suffering and excessive costs to healthcare systems and society.

Shifting focus to preventing perinatal mental and substance use disorders before they occur is essential, especially because empirical evidence demonstrates that prevention efforts could reduce maternal morbidity and mortality as well as healthcare spending (Porter 2009, Knapp et al. 2011, Mihalopoulos et al. 2015). It is encouraging that several initiatives are starting to move in that direction. For instance, the Biden Administration’s agenda for maternal mental health includes an explicit goal to eliminate coverage gaps by encouraging states to expand Medicaid coverage from 60 days to a full 12 months postpartum and ensuring that the federal government serves as a model employer for maternal health coverage (House 2022). Other federal efforts include the launch of a 24/7 national support hotline for pregnant individuals and new mothers facing mental health challenges (1-833-943-5746 or 1-833-9-HELP4MOMS) and expansion of insurance coverage to include midwifery and doula care (House 2022). Further, under the 2010 Affordable Care Act, the Maternal, Infant, and Early Childhood Home Visiting Program provides federal funding and oversight, highlighting maternal mental health as a measured outcome (HRSA 2023).

Prevention of perinatal mental and substance use disorders is critical because currently the U.S. healthcare system is reactive.

Numerous prevention interventions are available for perinatal populations with mental and substance use disorders. Interventions that focus on stress reduction and building community support can alleviate the risk for developing or exacerbating mental and substance use disorders both during pregnancy and the postpartum period. Although broadly addressing all perinatal mental and substance use disorders is critical, efforts thus far have primarily focused on the prevention of depression and anxiety.

A systematic review designed to inform the U.S. Preventive Services Task Force assessed existing interventions for preventing perinatal depression categorized as counseling, health system interventions, physical activity, education, social support, infant sleep, debriefing of the birth experience, other behavior-based approaches, antidepressants, and supplements (O'Connor et al. 2019a). The largest effects were found for the cognitive-behavioral therapy (CBT)–based Mothers and Babies program and the interpersonal therapy (IPT)–based programs Reach Out, Stand Strong Essentials for New Mothers (ROSE). The Mothers and Babies program has specific goals to create a healthy physical, social, and psychological environment for participants and their infants (McFarlane et al. 2017). The ROSE program is targeted at stress management, developing a social support system, managing role transitions and associated changes, and addressing types of interpersonal conflicts common around childbirth (Berry et al. 2021). A novel dyadic prevention counseling intervention, the Practical Resources for Effective Postpartum Parenting program targets maternal well-being, infant behavior, and maternal infant bonding (Werner et al. 2016). It has demonstrated efficacy in at-risk populations, including those with subthreshold symptoms of depression or anxiety as well as those from disadvantaged backgrounds. The Task Force concluded that counseling had the highest strength of evidence among the various interventions, with a “moderate” rating. Treatment with antidepressants showed some evidence of effectiveness but lacked a sufficient evidence base to be recommended (Force et al. 2019).




Pregnant individuals with risk factors for poor birth outcomes and subsequent psychiatric illness may benefit from doula services, which may help minimize the detrimental impact of SDOH on their pregnancy and childbirth experience (Viguera et al. 2007). Doulas can offer security for pregnant individuals who lack social support and are generally isolated (Viguera et al. 2007). Doulas ensure that patients understand clinical terms and procedures, which facilitates more positive birthing experiences (Viguera et al. 2007). They can also assist in strengthening the connection between individuals and their babies during the perinatal period. A small qualitative study (N=13) exploring low-income pregnant individuals' experiences with a doula highlighted positive (maternal–infant) outcomes in domains of agency, personal security, respect, knowledge, and connectedness (Viguera et al. 2007).

Home visiting programs are comprised of trained social workers, nurses, and early childhood education specialists who meet routinely in homes of pregnant and postpartum individuals with young children (Sandstrom 2019). Currently, all 50 states have some form of home visitation programs targeting maternal mental health. These are funded by federal, state, and county maternal and child health programs, boards of education, community-based organizations, and philanthropy (HHS , HRSA 2023).

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Data show that 2 models, Healthy Families of America and Parents as Teachers, have resulted in promising improvements (Challacombe et al. 2017). Healthy Families of America (<https://www.healthyfamiliesamerica.org>) is a U.S. social program dedicated to child abuse and neglect prevention that promotes healthy parent–child relationship development. The program conducts an initial evaluation to assess for risks such as single parenthood, history of mental illness, and socioeconomic stress. It also assesses for opportunities to strengthen family functioning over the course of weekly in-person or virtual home visits during pregnancy through the first 5 years of the child's life. Parents as Teachers supports first-time parents of newborns by educating parents and families on early child development and supporting healthy well-resourced home environments during pregnancy until the start of kindergarten (Parents_as_Teachers_National_Center 2018). Both programs are associated with improvements in maternal and child health, positive parent–child interactions, child development and school readiness, intimate partner violence, family economic sufficiency, family connection, and utilization of community resources (Tandon et al. 2018). Additional research is needed to clarify the ideal timing and intensity of preventive care delivery during the perinatal period to optimize effectiveness in preventing psychiatric illnesses. Lastly, developing tailored training materials for practitioners (and possibly also for lay people) as well as promoting research to determine best practices for larger-scale telehealth-, internet-, and smartphone-based implementation strategies could help address disparities access to care.

Another important prevention target is insomnia. Insomnia is common among pregnant, postpartum, and lactating persons in general and for those with co-occurring mental disorders in particular (Hashmi et al. 2016, Meers et al. 2022). Ensuring proper sleep is imperative for preventing psychiatric relapse and managing current episodes of illness. Attention to good sleep habits, also called sleep hygiene, is key. Effective approaches to sleep hygiene include setting consistent sleep times; avoiding stimulating activities, such using electronics before bedtime; sleeping in a cool and dark room; avoiding large meals,



alcohol, and caffeine near bedtime; and exercising regularly during waking hours, although not near bedtime (Irish et al. 2015, Chow 2022). Insomnia should be addressed as early as possible to prevent worsening of sleep as well as other psychiatric and general medical conditions.

Insomnia should be addressed as early as possible to prevent worsening of sleep as well as other psychiatric and general medical conditions.

RISKS OF UNTREATED PERINATAL MENTAL AND SUBSTANCE USE DISORDERS

Mental and substance use disorder treatment is challenging in general but even more so during the perinatal period. Patients and healthcare providers face multiple barriers to treatment, including lack of training on screening and referral as well as stigma (e.g., stigma among healthcare providers, self-stigma among patients) (Knaak et al. 2017, Webb et al. 2021b). These barriers loom largest for populations who have been marginalized by race, socioeconomic status, and additional social stigmas, which can deter them from help seeking (Iturralde et al. 2021).

Many psychiatrists and behavioral health clinicians caring for perinatal persons as well as their partners worry about the effects of psychotropic medication on the fetus and possible long-term effects on brain development and behavior (Kalfoglou 2016, Eakley et al. 2022). Consequently, pregnant persons are often encouraged to decrease medication dose or discontinue psychotropic medication altogether throughout pregnancy and lactation (Kalfoglou 2016, Eakley et al. 2022). These recommendations are often made without taking into consideration the potential risk of recurrence of psychiatric symptoms and the short- and long-term effects of relapse and recurrence on the mother and her child.


What follows below are brief descriptions of the evidence of the impact of untreated and undertreated mental and substance use disorders in the perinatal period.

Depression

Untreated depression can have serious consequences. In a meta-analysis on the risk of depression relapse during pregnancy (N=518), risk of relapse following antidepressant discontinuation was 1.74 times higher compared with women who continued their antidepressant (95% confidence interval [CI] 0.97–3.10, P=0.06) and was even higher among women with severe or recurrent depression (risk ratio [RR] 2.30, 95% CI 1.58–3.35) (Bayrampour et al. 2020a). Pregnant women with untreated depression are also 3 times more likely to be hospitalized and to experience obstetric and other health complications such as low maternal weight gain, increased risk for preterm birth, low birth weight, and increased rates of tobacco, alcohol, and other substance use (Li et al. 2009, Yonkers et al. 2009, Jahan et al. 2021).

Bipolar Disorder

The risk of relapse in bipolar disorder, particularly during pregnancy and postpartum, is very high—approximately 30%–50%—and can increase the likelihood of other adverse outcomes, including suicide, infanticide, and substance use and other high-risk behaviors (Wesseloo et al. 2016a, Salim et al. 2018) (Epstein et al. 2015a). Individuals who discontinue mood stabilizers during pregnancy are twice as likely to relapse compared with individuals who continue treatment (Viguera et al. 2007). Recurrence rates have



been reported to be as high as 71% in patients who discontinue mood stabilizers during pregnancy (Viguera et al. 2007). A systematic literature review of 37 articles found the risk of postpartum relapse was significantly higher among women with bipolar disorder who discontinued medication during pregnancy versus those who used prophylactic medication during pregnancy (66% vs 23%, $P < 0.001$) (Wesseloo et al. 2016b) Another small study ($N = 26$) similarly found women who discontinued lamotrigine during pregnancy had a 100% relapse rate versus 30% ($P < 0.0001$) among the women who continued the medication (Newport et al. 2008).

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Anxiety and PTSD

If untreated, anxiety disorders, including PTSD and symptoms of trauma, can have adverse effects on families and children (Araji et al. 2020). Untreated anxiety disorders and panic attacks in perinatal populations are associated with preeclampsia, cervical dyskinesia, placental abruption, premature rupture of membranes, fetal distress, low birth weight, lower gestational age, and reduced Apgar scores as well as an increased risk of substance use (Rubinchik et al. 2005) Untreated PTSD specifically is associated with increased risk of preeclampsia, low birth weight, gestational diabetes, and preterm birth (Shaw et al. 2017, Padin et al. 2022).

Obsessive-Compulsive Disorder


Little research has examined the effects of untreated obsessive-compulsive disorder (OCD) or discontinuing OCD treatment during pregnancy. It stands to reason that pregnant persons with OCD who do not receive treatment are at an elevated risk for experiencing the negative health consequences associated with the disorder. Briefly, those include a greater risk of preterm birth and low birthweight (Uguz et al. 2015). Further, OCD during pregnancy can lead to pregnant persons engaging in more frequent fetal monitoring, excessive reassurance seeking from obstetric providers, and avoiding normal activities they erroneously believe will lead to fetal demise. Attachment and bonding between parent and infant may become disrupted, with potential adverse impact on infant development (Challacombe et al. 2017).

Psychosis Spectrum Disorders

Psychosis relapse is a significant threat to the mother and child when untreated or undertreated. The cumulative 10-month relapse rate has been reported to be 53% in patients with schizophrenia who discontinue medications, compared with 16% in patients who continue treatment (Gilbert et al. 1995).

Substance Use Disorders

Untreated substance use disorders (SUDs) increase the risk of adverse events associated with substance exposure during the perinatal period. For example, prenatal opioid misuse increases risk for fetal seizures,



diminished fetal growth, preterm birth, fetal/neonatal withdrawal, and fetal death (O'Donnell et al. 2017). Alcohol abuse during pregnancy confers an increased risk of miscarriage, stillbirth, preterm birth, sudden infant death syndrome, and fetal alcohol spectrum disorder (Bailey et al. 2011). Despite as many as 70% of dispensaries recommending cannabis for nausea during pregnancy (Dickson et al. 2018), prenatal cannabis exposure is associated with preterm birth, low birthweight, and neonatal intensive care unit (NICU) admission (Marchand et al. 2022). Finally, tobacco use during pregnancy is linked to miscarriage, stillbirth, preterm delivery, and low birthweight as well as childhood asthma and visual problems; even passive exposure to tobacco during pregnancy doubles the risk for stillbirth (Gould et al. 2020).

Tobacco use during pregnancy is linked to miscarriage, stillbirth, preterm delivery, and low birthweight as well as childhood asthma and visual problems; even passive exposure to tobacco during pregnancy doubles the risk for stillbirth.

Literature exploring the potential adverse effects of tapering or discontinuing medication for opioid use disorder (MOUD) during the perinatal period is scarce. A systematic review of methadone and buprenorphine discontinuation during pregnancy (N= 15 studies) found discontinuation rates vary widely, from 26% to 64% (Wilder et al. 2015). In a national database analysis from Australia (N=2,993), women with OUD who initiated methadone treatment at least 1 year prior to delivery and continued during pregnancy experienced better fetal outcomes—including a lower risk of being admitted to the NICU, reduced prematurity, and earlier engagement in postnatal care—than women who did not initiate methadone until 6 months prior to delivery (Burns et al. 2007). A retrospective cohort study in Massachusetts (N=2,314) found discontinuation of MOUD before delivery was associated with a 1.79 increased risk (95% CI 1.52–2.12) of being incarcerated during pregnancy or after delivery (Schiff et al. 2021).


Insomnia

Untreated insomnia during the perinatal period poses negative health risks to the mother and offspring. These include but are not limited to preeclampsia, growth retardation, increased labor, preterm birth, cesarean delivery, low birth weight, and gestational diabetes, (Reichner 2015, MacKinnon et al. 2022). Insomnia in pregnancy is also associated with an increased risk of maternal suicidal ideation and postpartum depressive symptoms (Reichner 2015, MacKinnon et al. 2022).

SCREENING

One in 5 individuals will develop a perinatal mental or substance use disorder (Vesga-Lopez et al. 2008). These rates far exceed other obstetric complications of pregnancy. For example, the prevalence rates for gestational diabetes and preterm birth are 2%–6% and 12.7%, respectively (Werner et al. 2016, Deputy et al. 2018). Even though evidence-based treatments for perinatal mental and substance use disorders are available, these disorders often go untreated (Byatt et al. 2015).

Screening is a critical first step to facilitating early identification and subsequent assessment and, if needed, treatment (Byatt et al. 2019). Mental and substance use disorders are the leading causes of maternal mortality, exceeding all other causes of death during the perinatal period (Troost et al. 2021).



Untreated perinatal mental and substance use disorders are associated with numerous adverse outcomes, such as child abuse and neglect, discontinuation of breastfeeding, and family dysfunction (Earls et al. 2019a). Infants born to pregnant individuals with untreated mental and substance use disorders are more likely to experience compromised dyadic relationships, potentially leading to attachment disorders and developmental delays that are associated with brain changes visible through magnetic resonance imaging (Earls et al. 2019a).

Given the maternal mortality crisis in the United States, which is increasingly being fueled by mental and substance use disorders (Troost et al. 2021), many healthcare professional associations recommend perinatal mental health screening (Byatt et al. 2020a). For instance, the American College of Obstetrics and Gynecology (ACOG), American Psychiatric Association (APA), American Academy of Pediatrics, and the U.S. Preventive Services Task Force recommend screening for mental and substance use disorders during the first half of pregnancy, second half of pregnancy, and postpartum period (Wisner et al. 2013, Siu et al. 2016, 2017, Kendig et al. 2017b, 2018, Byatt et al. 2018, Earls et al. 2019b, ACOG 2023a, ACOG 2023b) . Screening in pediatric settings is recommended at 1-month, 2-month, 4-month, and 6-month well-child visits (Byatt et al. 2020b).

An interdisciplinary approach to screening during routine obstetric visits through pregnancy, postpartum, and well-baby visits with pediatric clinicians in postpartum is recommended.

To facilitate evidence-based treatment, screening needs to be performed by perinatal healthcare professionals. Successfully identifying those who may need treatment is vital for increasing treatment rates. Thus, an interdisciplinary approach to screening during routine obstetric visits through pregnancy, postpartum, and well-baby visits with pediatric clinicians in postpartum is recommended. Of note, healthcare providers should be mindful that screening tools are not diagnostic. That is, screeners cannot be used to determine whether a person has a mental or substance use disorder. Rather, screeners are used to indicate which patients have a possible or probable mental or substance use disorder and thus require formal psychiatric evaluation to determine or rule out diagnosis.

Screening for Depression

Healthcare providers need to screen for depression multiple times over the course of the perinatal period to optimally identify individuals with symptom onset before, during, and after pregnancy. Sixty percent of individuals with postpartum depression (PPD) exhibit symptoms during or before pregnancy.¹ Peak of onset of symptoms is typically at 6 weeks after delivery for major depression and 2–3 months after delivery for minor depression (Byatt et al. 2019). Another peak for depression occurs at 6 months postpartum (Earls et al. 2019a). Thus, screening for depression repeatedly over the course of the perinatal period is critical.

Regarding which measures to use, the Nine-Item Patient Health Questionnaire is a self-report depression screen that is widely used, highly validated, and easily accessible. The Edinburgh Postnatal Depression Scale (EPDS) is a 10-item self-report screening tool that is also valid for use during pregnancy and postpartum (Kroenke et al. 2001).



Screening for Bipolar Disorder

During the perinatal period, there is an elevated risk for new-onset bipolar disorder or disease recurrence (Masters et al. 2022). The U.S. Preventative Services Task Force recommends screening once for bipolar disorder in the first half of pregnancy (Masters et al. 2019). Screening for bipolar disorder is especially recommended before prescribing an antidepressant to pregnant individuals who screen positive for depression, as per the Council of Patient Safety and the APA (Byatt et al. 2018, ACOG 2023a).

The Composite International Diagnostic Interview is a clinician administered, 3- item screener that takes approximately 3 minutes to administer and screens for bipolar spectrum disorders.⁷ Another validated and widely used tool is the Mood Disorders Questionnaire—a self-report, 15-item questionnaire that takes an estimated 5 minutes to complete.⁹

Screening for Anxiety Disorders

Anxiety is often under-detected in perinatal populations in part because symptoms like general worry, fatigue, irritability, tension, concentration difficulties, and insomnia are typical during pregnancy and postpartum and thus may not be considered signs of a potential mental health issue (Misri et al. 2015). Also contributing is the tendency of birthing parents to underreport the intensity of their anxiety and its full impact on their lives.

The U.S. Preventive Services Task Force (USPSTF) recommends screening pregnant and postpartum persons for anxiety disorders.

The U.S. Preventive Services Task Force (USPSTF) recommends screening pregnant and postpartum persons for anxiety disorders (USPSTF 2023). The General Anxiety Disorder is a 7-item self-report screener for anxiety symptoms that is widely used in clinical populations (Zhong et al. 2015). Additional screeners for anxiety include the Depression, Anxiety, and Stress Scale and the Perinatal Anxiety Screening Scale, which are 21- and 31-item, respectively, self-report screeners (Somerville et al. 2014). The EPDS was initially developed for postpartum depression but includes a 3-item subscale that also can be used to effectively screen for anxiety symptoms (Somerville et al. 2014).

Screening for Obsessive-Compulsive Disorder

The perinatal period is an especially vulnerable time for first-episode or reemergence of OCD (Russell et al. 2013). Unfortunately, routine screening for perinatal mental disorders typically does not include screening for OCD.

The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) is the gold standard assessment tool for detecting both presence and severity of OCD symptoms in the general population and can be used in perinatal populations as well (Goodman et al. 1989). It can be administered by clinician interview or as a self-report measure. The Perinatal Obsessive-Compulsive Scale (POCS) is another self-report scale that includes a 16-item version to be administered during pregnancy and a 33-item postpartum version (Lord et al. 2011). Other validated OCD screening instruments include the Parental Thoughts and Behaviors Checklist, which has recently been modified as a self-report measure (Abramowitz et al. 2006, Thiseus et al. 2019).



Screening for Trauma and Posttraumatic Stress Disorder

There are no current guideline recommendations for posttraumatic stress disorder (PTSD) screening even though patients often do not share their diagnosis/symptoms of PTSD with their obstetric or gynecology provider (Powers et al. 2020). The Perinatal Post-Traumatic Stress Disorder Questionnaire can be helpful as a diagnostic tool for persons who may have perinatal PTSD (Cirino et al. 2019). The PTSD Checklist-5 has shown reliability, validity, and diagnostic utility for PTSD screening and may be used with perinatal populations (Vignato et al. 2017). ACOG also includes a screener for PTSD in its perinatal mental health toolkit (<https://www.acog.org/programs/perinatal-mental-health/patient-screening>).

Screening for Psychosis Spectrum Disorders

There are no current guideline recommendations for screening for psychotic disorders during the perinatal period. However, because psychotic symptoms can occur during the perinatal period and can have serious adverse consequences, healthcare providers should still screen for these disorders. Brief validated screening tools include the PRIME Screen—a 12-item, self-report measure that takes about 3 minutes to complete—and the Prodromal Questionnaire–Brief Version, a 21-item, self-report tool that takes approximately 7 minutes to complete (Addington et al. 2015, Zhong et al. 2018b).

Screening for Substance Use Disorders

Substance use warrants high priority for screening as well. Many healthcare professional organizations, including ACOG (ACOG 2017), APA (APA 2019), American Academy of Family Physicians (AAFP 2021), the Alliance for Innovation on Maternal Health (AMCHP 2020), and the USPSTF (USPSTF 2020), recommend universal screening of perinatal women for substance use with validated instruments (ACOG 2008, AIM 2021). Ideally, this should occur at the initial obstetric visit. If positive, screening should be continued at subsequent visits in pregnancy and postpartum, and biological testing should be considered only with the patient’s consent and in compliance with state mandates (Committee on Substance et al. 2011, Jones et al. 2014, 2017, Ecker et al. 2019). However, using urine or blood specimens as the primary method for screening is not recommended because of the risk of false positives, the potential legal ramifications (i.e., state laws) of a patient producing a positive test, and the inability of biological tests to provide other important information, such as frequency and severity of use (Price et al. 2018).

The Parents, Partners, Past and Pregnancy (4P’s) screen, a brief 4-item tool, was developed for detecting substance use disorders in pregnant individuals.

The Parents, Partners, Past and Pregnancy (4P’s) screen, a brief 4-item tool, was developed for detecting substance use disorders in pregnant individuals (Chasnoff et al. 2007). It has been shown to have strong sensitivity and specificity and has been widely employed (Chasnoff et al. 2007). ACOG supports the use of the 4P’s screener, the National Institute on Drug Abuse Quick Screen, and, for women younger than 27 years, the Car, Relax, Alone, Forget, Friends, Trouble screen (2017). The Alliance for Innovation on Maternal Health offers a substance use bundle to guide clinicians in screening and treating perinatal patients for substance use disorders (<https://saferbirth.org/psbs/care-for-pregnant-and-postpartum-people-with-substance-use-disorder/>).



Screening for Insomnia

Any perinatal patient reporting sleep difficulties should be screened for insomnia. A general physical examination and testing for other medical conditions (e.g., obstructive sleep apnea) may be warranted (Bazalakova 2017, Meers et al. 2022). Frequently used and validated measures include the Insomnia Severity Index and the Sleep Condition Indicator (Felder et al. 2020a). Both are self-report questionnaires that can be administered rapidly.

PHARMACOLOGIC MANAGEMENT

Any decision to initiate or continue psychotropic medication during pregnancy should consider the patient's current symptoms or risk for symptom recurrence or exacerbation based on epidemiologic data and the patient's clinical history. For example, patients with frequent episodes, a declining course, or a history of severe symptoms in prior pregnancies are more likely to become ill during the pregnancy and postpartum period (Meltzer-Brody et al. 2018a). The effects of psychotropic exposure during the perinatal period on the fetus's development also must be specifically weighed against the risk of no treatment or undertreatment, including the risk of suicidal or homicidal ideations, in the pregnant individual during this time. International guidelines recommend that psychiatric treatment plans involve collaborative decision-making, including a full discussion of the potential risks and benefits of implementing and foregoing treatment (2021a).

The effects of psychotropic exposure during the perinatal period on the fetus's development also must be specifically weighed against the risk of no treatment or undertreatment, including the risk of suicidal or homicidal ideations, in the pregnant individual during this time.

Healthcare providers should prescribe the minimally effective dose of psychotropic medication during pregnancy, considering perinatal pharmacokinetics and pharmacodynamics. Yet they also should avoid undertreatment, with the goal of treating the condition until remission occurs. An increase in plasma volume and decrease in plasma protein binding can alter the apparent volume of distribution of medication, and renal excretion of medication is increased due to an increase in the glomerular filtration rate (Ke et al. 2018). Because of this, plasma concentrations of many psychotropic medications decrease during pregnancy. Medication doses may need to be increased in the second and third trimester to maintain adequate control of psychiatric symptoms (Betcher et al. 2020). Within approximately 11 weeks after delivery, metabolism reverts to prepregnancy levels, which often requires dose reductions of psychotropic medication (Anderson 2005, Betcher et al. 2020).

The extent and rate of placental medication transfer is highly dependent upon the physiochemical properties of the medication (Al-Enazy et al. 2017). Healthcare providers should consider patient preference, individual disease and treatment response characteristics, medical comorbidities, and metabolic and sedative side-effect profiles before deciding to switch psychotropic medication in pregnant patients. For example, a medication may have a small increased risk of adverse fetal outcomes, but if it is effective, the risk for symptom exacerbation due to a change in medication often outweighs the risk of exposure to the treatment. In other words, the principal clinical objective is to minimize infant exposure to the risks of both unmedicated maternal psychiatric disorder and the psychotropic medication.



Antidepressants

Selective Serotonin Reuptake Inhibitors


Recent meta-analyses have found no association between prenatal selective serotonin reuptake inhibitor (SSRI) exposure and overall risk of birth defects (Reefhuis et al. 2015, Gao et al. 2018). However, some concerns with specific SSRIs have emerged. For example, isolated studies have reported an increased risk of cardiovascular malformations associated with paroxetine, fluoxetine, and sertraline (Berard et al. 2007, Louik et al. 2007, Gao et al. 2017).

A few studies have systematically assessed child development following prenatal SSRI exposure, observing no differences in cognitive, language, or motor development or behavior with the exception of 1 study reporting minor transient differences in fine motor skills (Nulman et al. 1997, Nulman et al. 2002, Casper et al. 2003, Oberlander et al. 2004, Oberlander et al. 2007, Nulman et al. 2012). In addition, rapidly emerging literature has examined whether there is an association between prenatal antidepressant exposure and childhood autism. Although the results appear mixed, closer inspection suggests an ascertainment bias due to ethnic disparities in healthcare access among studies using a population-based control group; indeed, studies mitigating this bias with a discordant sibling comparator group demonstrated no connection between fetal antidepressant exposure and autism diagnosis (Vega et al. 2020).

Data regarding the impact of prenatal antidepressant exposure on rates of miscarriage, preterm delivery, and low birth weight are decidedly mixed with some reporting an association with poor obstetric outcomes, whereas others have not (Pastuszak et al. 1993, Chambers et al. 1996, Kulin et al. 1998, Einarson et al. 2001, Simon et al. 2002, Einarson et al. 2003, Chun-Fai-Chan et al. 2005, Sivojelezova et al. 2005, Oberlander et al. 2006, Ross et al. 2013, Eke et al. 2016, Venkatesh et al. 2016b, Chang et al. 2020, Vlenterie et al. 2021). Multiple recent meta-analyses found an association between prenatal antidepressant exposure and preterm delivery and low birth weight (Ross et al. 2013, Huang et al. 2014b, Huybrechts et al. 2014, Eke et al. 2016, Chang et al. 2020, Vlenterie et al. 2021). However, interpretation is complicated by other reports that maternal depression and anxiety during pregnancy increase risk for preterm birth and low birth weight (Jarde et al. 2016, Grigoriadis et al. 2018, Dadi et al. 2020, Ghimire et al. 2021). As a result, no definitive conclusions can be drawn as to whether antidepressant use during pregnancy adversely impacts fetal growth or the timing of delivery.

Finally, neonatal adaptation syndrome (NAS), manifested by a variable constellation of transient respiratory, cardiovascular, gastrointestinal, motor, and/or central nervous system symptoms, has been reported in studies of perinatal SSRI use (Moses-Kolko et al. 2005). A recent meta-analysis confirmed an association between prenatal SSRI exposure and NAS; however, the authors noted the low quality of studies hindered their ability to draw firm conclusions (Kautzky et al. 2022).

Concern has also been raised regarding a potential connection between late-pregnancy SSRI exposure and persistent pulmonary hypertension of the newborn (PPHN). A lone study supporting an association between SSRI exposure and PPHN led the U.S. Food and Drug Administration (FDA) to issue a Public Health Advisory regarding this reported link in July 2006 (Chambers et al. 2006, FDA 2006). However, the FDA issued an update 5 years later noting that conflicting studies make it “unclear whether use of SSRIs during pregnancy can cause PPHN” (FDA 2011). Two meta-analyses reported a significant association



between SSRI exposure and PPHN, with 1 estimating the increased PPHN risk attributable to SSRI as 6.19 per 10,000 live deliveries reported (Masarwa et al. 2019, Ng et al. 2019).

Of note, the above-described studies on PPHN risk are all limited by confounding by indication. To account for this, a cohort study restricted their analysis to women with a diagnosis of depression and used propensity score stratification to address additional confounding by illness severity (Huybrechts et al 2015). Investigators found no increased odds of PPHN for women exposed to SSRIs (adjusted OR 1.12, 95% CI 0.95–1.31) or non-SSRI antidepressants (adjusted OR 1.01, 95% 0.76–1.35). In secondary analyses, they restricted the sample by excluding preterm infants and infants with congenital cardiac malformations or lung abnormalities. In doing so, they found an increased odds of PPHN for SSRIs (adjusted OR 1.28, 95% CI 1.01–1.64) but not for non-SSRI antidepressants (adjusted OR 1.14, 9% CI 0.74–1.74).

In summary, data suggest there may be an increased risk of PPHN associated with SSRI exposure during pregnancy. Regardless of any potential association, the absolute risk of PPHN is low (approximately 1–2 per 1000 additional cases of PPHN). Even so, this small risk should be balanced against the significant risks associated with untreated depression.

Serotonin-Norepinephrine Reuptake Inhibitors

Pregnancy safety data for serotonin-norepinephrine reuptake inhibitors (SNRIs) are increasing. Studies examining venlafaxine during pregnancy have reported higher malformation rates (Einarson et al. 2001, Polen et al. 2013, Anderson et al. 2020). Two duloxetine studies did not find evidence of increased birth defect risk (Einarson et al. 2012, Ankarfeldt et al. 2021). To date, there are no reports regarding birth defect rates associated with desvenlafaxine or levomilnacipran.


Pregnancy safety data for serotonin-norepinephrine reuptake inhibitors (SNRIs) are increasing.

There has been only one controlled study of developmental effects of prenatal SNRI exposure, reporting no cognitive or behavioral differences among children exposed to venlafaxine during pregnancy (Nulman et al. 2012). In addition, SNRIs have been linked to hypertension during pregnancy, particularly at higher doses (Einarson et al. 2001, Masarwa et al. 2019). One study reported an increased risk for hypertensive disorders of pregnancy in association with prenatal venlafaxine therapy, with a 6-fold increase among those receiving venlafaxine at doses exceeding 187.5 mg per day (Newport et al. 2016). Like the SSRIs, SNRI exposure linked to a small increase in risk for persistent pulmonary hypertension of the neonate (Einarson et al. 2001, Masarwa et al. 2019). Despite the inconsistent data, it may be preferable to continue an effective SNRI, as with any antidepressant in pregnancy, if the patient is deemed likely to experience a recurrence or worsening of illness.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) were widely used during pregnancy before the advent of the SSRIs. Although early studies raised concerns regarding malformation risk in association with TCAs, subsequent large-scale studies and meta-analyses have found no evidence of increased malformation risk (Altshuler et al. 1996, McElhatton et al. 1996, Vasilakis-Scaramozza et al. 2013).

No adverse neurodevelopmental effects were reported in two studies of prenatal TCA exposure (Nulman et al. 1997, Nulman et al. 2002). However, a variety of fetal and neonatal complications have been reported in association with prenatal TCA exposure, including tachypnea, tachycardia, cyanosis, irritability,



hypertonia, clonus, and spasm (Eggermont 1973, Misri et al. 1991, Ter Horst et al. 2008, Nijenhuis et al. 2012). In addition, studies have shown that TCA exposure is linked to a small increase in risk for persistent pulmonary hypertension of the neonate (Masarwa et al. 2019, Munk-Olsen et al. 2021). Importantly, this literature is older and marked by significant methodological limitations.

Atypical Antidepressants

Pregnancy safety data are limited for the atypical antidepressants (i.e., bupropion, mirtazapine, nefazodone, trazodone, vilazodone, and vortioxetine). Malformation rates following prenatal exposure to bupropion, trazodone, nefazodone, and mirtazapine are consistent with population norms (McElhatton et al. 1996, Einarson et al. 2003, Chun-Fai-Chan et al. 2005, Djulus et al. 2006, Cole et al. 2007, Boucher et al. 2008, Smit et al. 2015, Winterfeld et al. 2015). There are no published data on prenatal vortioxetine or vilazodone exposure. Neurodevelopmental and neonatal outcome data following prenatal exposure to atypical antidepressants are lacking (Holland et al. 2017, Kautzky et al. 2022).

Mood Stabilizers

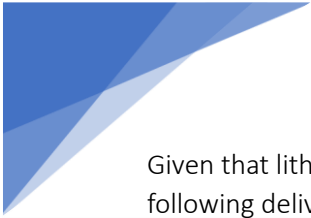
Lithium

A gold standard treatment, extensively studied, and used for over 70 years in the treatment of bipolar disorder, lithium is now considered a first-line treatment for bipolar I disorder in the perinatal period (Epstein et al. 2015a, Poels et al. 2018, Tondo et al. 2019, Uguz 2020). As with any medication used during pregnancy, postpartum, and lactation, it is important to weigh the risk–benefit ratio and use the least effective dose of lithium. The emphasis should be on “effective” dosing to avoid undertreatment. Because lithium is such an effective mood stabilizer, especially for bipolar mania, and may decrease suicide risk, lithium should be in the clinician’s toolbox for perinatal or lactating persons with bipolar disorder (Riblet et al. 2022).

As with any medication used during pregnancy, postpartum, and lactation, it is important to weigh the risk–benefit ratio and use the least effective dose of lithium.

Although there is an increased risk of Ebstein’s anomaly—a congenital fetal cardiac defect of the tricuspid valve—with lithium use during the first trimester compared to the general population, the absolute risk is quite low. Risk does appear to increase with increased dosages (i.e., >900 mg daily), but this risk must be weighed against its benefits, as lithium prevents relapse (Fornaro et al. 2020). A high-resolution ultrasound with detailed fetal cardiac scanning at 16–20 weeks gestational age is recommended to monitor cardiac development. In a prospective study of 99 children born to mothers with bipolar disorder, lithium was not linked to neuropsychological dysfunction in prenatally exposed offspring ages 6–14 years of age (Poels et al. 2018).

Lithium levels should be carefully monitored during pregnancy and the dosage adjusted as needed. Lithium elimination increases with pregnancy and remains elevated for several weeks after pregnancy. Even small decrements in the lithium serum level can increase the risk of relapse (Clark et al. 2022). In addition, although the absolute risk of Ebstein’s anomaly is relatively low, it is also recommended that individuals taking lithium in pregnancy have an ultrasound to evaluate fetal cardiac anatomy (Poels et al. 2018).



Given that lithium has several notable side effects, mother and offspring should continue to be monitored following delivery. For example, lithium can induce thyroid disorders and renal toxicity (Batt et al. 2022). As noted earlier, patients with bipolar disorder are already prone to thyroid disorders, so monitoring for this potential side effect is even more critical in pregnant and lactating people with bipolar disorder who are taking lithium. In addition, pregnant individuals taking lithium should be seen by a high-risk obstetrician, and care should be coordinated across obstetric, psychiatric, and pediatric healthcare providers.

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Discontinuation of lithium in the days immediately leading up to delivery to minimize neonatal cardiac, hepatic, neuromuscular (e.g., hypotonia), renal, respiratory, and thyroid complications has been recommended but remains controversial and could precipitate relapse. Maintaining usual dosing during labor and delivery is often warranted (Fornaro et al. 2020).

Lamotrigine

Lamotrigine is among the most extensively studied psychotropic medicines for pregnancy safety showing no increase in malformation rates, neonatal complications, or adverse neurodevelopmental outcomes (Cunnington et al. 2011). It has become the first-line treatment for pregnant and nonpregnant patients with bipolar II disorder, especially bipolar depression, although its efficacy as a monotherapy for bipolar mania is lower than that of lithium (Epstein et al. 2015b). Pregnancy registry data has demonstrated no increase in malformation rates or any other untoward outcomes (Cunnington et al. 2011). Of note, lamotrigine levels may be dramatically decreased, on the order of 200% or greater, and dosing may need to be increased significantly as pregnancy progresses (sometimes just a few weeks into the first trimester) due to estrogen's induction of glucuronidation—the major pathway of lamotrigine metabolism. Additionally, there is a great deal of individual variability in lamotrigine metabolism, likely due to genetic variation; thus, serum drug level monitoring is recommended (Clark et al. 2013a). As such, lamotrigine is not useful for the treatment of bipolar mania and only offers limited prophylaxis against recurrence of mania (Cunnington et al. 2011). With dramatic downward shifts in estrogen following delivery, and if dosing was increased during pregnancy, dosing should be quickly readjusted to pre-pregnancy doses and levels monitored (Clark et al. 2013b, Clark 2020).

Other Miscellaneous Mood Stabilizers

Several other mood stabilizers commonly used for the treatment of bipolar disorder, especially those of the antiepileptic class, have been associated with negative outcomes during pregnancy, postpartum, and lactation. For example, valproic acid is associated with a significantly increased risk of neural tube defects, several other organ major malformations, and reduced IQ and neurodevelopmental disorders (e.g., ADHD, autism spectrum disorders)(Koren et al. 2006). Valproic acid is contraindicated in pregnancy and should not be used among persons of child-bearing age (Epstein et al. 2015b, Anmella et al. 2019) or only as a last resort(Macfarlane et al. 2018, Heinonen et al. 2022a) . Carbamazepine and oxcarbazepine similarly increase the risk of neural tube defects and other organ malformations, including urinary tract malformations. As such, barrier methods of contraception (e.g., condoms, copper IUD) is necessary to avoid unintended pregnancy as the enzyme-inducing properties of these drugs render hormonal



contraception less reliable (Reddy 2010, Kennedy 2017). Topiramate is associated with cleft/facial palate malformations (Wlodarczyk et al. 2012). Use of antiepileptics during pregnancy, postpartum, or lactation should be undertaken with extreme caution and only after extensive informed consent, careful deliberation of the risk–benefit ratio for the individual patient, and careful documentation thereof, as these medications may be the only ones that have controlled the patient’s bipolar disorder and possibly co-occurring seizure disorders (Khan et al. 2016).

Antipsychotics


Placental passage of antipsychotics is incomplete. The passage ratio is highest for olanzapine followed by haloperidol, risperidone, and quetiapine, which has the lowest cord blood levels after quetiapine exposure (Newport et al. 2007). Data on prenatal exposure and placental passage of other second-generation antipsychotics and their impact on neurodevelopmental outcomes are scant.

Use of promethazine, chlorpromazine, haloperidol, perphenazine, trifluoperazine, loxapine, thioridazine, flupenthixol, or fluphenazine has not been found to increase the rate of congenital malformations (Diav-Citrin et al. 2005). An epidemiologic study from Denmark suggests that the overall risk for miscarriage and stillbirths is approximately 2-fold in women exposed to an antipsychotic during pregnancy, but others found rates of miscarriage and stillbirth were no different than in pregnancies without first- or second-generation antipsychotics (Habermann et al. 2013). Existing studies suggest in utero exposure to aripiprazole, olanzapine, or quetiapine are not associated with increased risks of major congenital malformations, but exposure to risperidone or paliperidone carries a minimally increased risk (Cohen et al. 2018, Damkier et al. 2018). Overall, data on teratogenic risks after prenatal exposure to antipsychotics are insufficient to allow for definitive conclusions about their safety in pregnancy.

If a patient is taking an antipsychotic that is effective, the benefits of continued treatment often outweigh the risks.

Preterm birth, low birth weight, neonatal jaundice, and postnatal intestinal obstructions are more common in infants exposed to first-generation antipsychotics than in nonexposed infants (Gentile 2010, Galbally et al. 2014). Second-generation antipsychotics have been reported to carry an increased risk for fetal distress as well as low and high infant birth weight (Jablensky et al. 2005, Galbally et al. 2019, Betcher et al. 2020). Olanzapine exposure may result in greater rates of infant low birth weight or high birth weight, as well as a higher rate of neonatal intensive care admissions (Newport et al. 2007). A transient delay in cognitive, motor, social-emotional, and adaptive function has been noted in infants exposed to second-generation antipsychotics, but this delay may remit by age 1 (Peng et al. 2013). Furthermore, a large epidemiologic study in Hong Kong found no associations between prenatal antipsychotic exposure and a later diagnosis of attention-deficit/hyperactivity disorder (ADHD) or autism spectrum disorder (Wang et al. 2021).

If a patient is taking an antipsychotic that is effective, the benefits of continued treatment often outweigh the risks (Galbally et al. 2014). Because neonates exposed to first-generation or second-generation antipsychotics in the last gestational week are at higher risk of adverse postnatal outcomes, delivery should be planned in a setting that has access to NICUs. In the first 72 hours after birth, infants should be



monitored closely for poor NAS, which often presents with nonspecific symptoms such as mild autonomic, respiratory, neurologic, or gastrointestinal symptoms. These symptoms typically last 2–6 days and most commonly resolve without treatment. Extrapyramidal symptoms, such as decreased sucking reflex, dystonia, motor restlessness, abnormal movements, increased muscle tone, and primitive reflexes, also can occur (Heinonen et al. 2022a). Somnolence and seizures have also been observed (Heinonen et al. 2022a). For mild symptoms, observation on the maternity ward is preferred, as it enhances bonding between mother and child. Infants with severe neonatal abstinence syndrome should be admitted to an intensive care unit.

Medications for Substance Use Disorders

Medications for Opioid Use Disorder (MOUD)


MOUD has emerged as a vital component of managing opioid, alcohol, and tobacco addiction and is recognized as the standard of care for opioid use disorder. Whereas opioid detoxification during pregnancy is discouraged due to high relapse rates, MOUD as a perinatal maintenance strategy is highly recommended. MOUD includes treatment with an opioid agonist (i.e., methadone or buprenorphine) or an opioid antagonist (i.e., naltrexone).

Opioid agonist treatment during pregnancy contributes to better engagement in obstetric care, reduced infection risk, normal fetal growth, and reduced fetal/neonatal mortality (Jones et al. 2008, Zhao et al. 2020b). However, prenatal MOUD is not without risk. Several studies, although not all, have reported higher malformation rates among methadone exposed children (Wurst et al. 2016, Zedler et al. 2016, Kelty et al. 2017, Cleary et al. 2020). Buprenorphine, however, is not associated with malformation risk (Wurst et al. 2016, Zedler et al. 2016, Kelty et al. 2017).

Opioid agonist treatment during pregnancy contributes to better engagement in obstetric care, reduced infection risk, normal fetal growth, and reduced fetal/neonatal mortality.

Obstetric complications, including preterm birth, low birth weight, and neonatal withdrawal, are more frequent among patients receiving methadone or buprenorphine but less frequent and less severe than patients continuing to misuse opioids during pregnancy (Mozurkewich et al. 2014, Tran et al. 2017, Minozzi et al. 2020). Whereas rates of neonatal withdrawal are similar among buprenorphine- and methadone-exposed neonates, the severity and duration of withdrawal is markedly lower among those exposed to buprenorphine (Jones et al. 2010). Moreover, methadone has been associated with neonatal arrhythmias and QTc prolongation (Hussain et al. 2007, Parikh et al. 2011). Finally, among 96 mother–child dyads enrolled in a randomized controlled trial examining opioid-agonist pharmacotherapy during pregnancy, prenatal exposure to neither methadone nor buprenorphine exhibited any deleterious impact upon cognitive and language development, temperament, or sensory processing through 3 years of age (Kaltenbach et al. 2018).

There are some special considerations when using buprenorphine, a partial agonist, during pregnancy. First, when initiating buprenorphine during the latter half of pregnancy, continuous antenatal monitoring is advised, as individuals with opioid use disorder must be permitted to experience moderate symptoms of withdrawal before buprenorphine can be safely started. In addition, because buprenorphine may



interfere with post-delivery pain management, lowering the buprenorphine dose several days before delivery may be considered (Kampman et al. 2015).

There are 2 commercially available opioid antagonists in the United States. Naloxone is used only for emergency treatment of opioid overdose and has no role in MOUD (Wermeling 2015). The other, naltrexone, is used in MOUD for recovery from both opioid use disorder (in a long-acting injectable form) and alcohol use disorder (in an oral form) (Srivastava et al. 2018).

Two studies indicate that naltrexone-exposed neonates have a lower risk of abstinence and shorter length of hospitalization than neonates whose mothers were treated with methadone or buprenorphine (Wachman et al. 2019, Towers et al. 2020). However, there is concern that initiation of naltrexone during pregnancy may lead to intrauterine fetal withdrawal (Kelty et al. 2017, Minozzi et al. 2020). This was not observed in 1 study, however (Towers et al., 2020).

Naltrexone therapy proximate to delivery poses a challenge for postdelivery pain management (Terplan et al. 2018). However, this concern can be obviated by discontinuing oral naltrexone therapy as little as 3 days before delivery (Towers et al. 2023). For this reason, the long-acting injectable formulation should be transitioned to oral naltrexone at least 1 month prior to anticipated delivery.

Alcohol Use Disorder

Medications for the management of alcohol use disorder include naltrexone, acamprosate, and disulfiram. Reproductive safety data for these agents is limited; consequently, they are not routinely encouraged for use during pregnancy despite the risks of prenatal alcohol use (Rolland et al. 2015, Reus et al. 2018, Thibaut et al. 2019). Some studies have suggested that continuing naltrexone or acamprosate may be considered for individuals stable on these agents prior to conception (Rolland et al. 2015, Reus et al. 2018).

The reproductive safety data for acamprosate is limited to a single retrospective study reporting no association with congenital malformations, low birth weight, or neonatal complications (Kelty et al. 2019). In a literature review of alcohol use disorder pharmacotherapy during pregnancy, disulfiram was associated with an increased risk for fetal malformation (Kelty et al. 2021). The risk to the fetus of the “disulfiram reaction” has led to a recommendation to discontinue disulfiram during pregnancy, even among those already effectively treated with it prior to conception (Rolland et al. 2016). Neurodevelopmental effects of fetal exposure to acamprosate and disulfiram have not been studied.

Smoking Cessation

Pregnant individuals often require pharmacologic treatment to stop smoking (Myung et al. 2012, 2020). Smoking cessation medications include bupropion, varenicline, and nicotine replacement therapy (NRT). Despite the limited and sometimes conflicting safety data regarding their use during pregnancy, ACOG recommends offering smoking cessation medication (2020).

Smoking cessation medications are not considered a major teratogen; however, evidence for other perinatal outcomes is inconclusive. Compared with continued smoking, several studies have not demonstrated either a protective or harmful impact of therapy with bupropion, varenicline, or NRT (Turner et al. 2019, Patnode et al. 2021, Taylor et al. 2021). Relative to bupropion and NRT, varenicline’s reproductive safety data remains sparse.



Other Medications

Insomnia

Insomnia is common among pregnant and postpartum persons. Literature support for the use of insomnia medications during pregnancy and postpartum is lacking. Treatment of insomnia should be individualized (McLafferty et al. 2022). The benefits, risks, side effects, and alternatives of using pharmacotherapy should be considered and documented in the medical record for each patient and their offspring. Use of the smallest effective dose for the shortest duration is recommended.

Benzodiazepines and Related Medication

There have been some reports of adverse pregnancy/neonatal outcomes including neonatal NICU admission due to prenatal benzodiazepine use, but these studies lack proper controls (Freeman et al. 2018, Grigoriadis et al. 2020, Huitfeldt et al. 2020). Data on benzodiazepine use during the first trimester do not suggest an association with major malformations (n=1053) (Szpunar et al. 2022). However, other studies have shown that fetal exposure to benzodiazepine is associated with neonatal toxicity if higher doses are taken proximate to delivery and neonatal withdrawal if higher doses are taken on a regular basis proximate to delivery (Creeley et al. 2019, Grigoriadis et al. 2020). Furthermore, animal studies raise concern for cognitive impairment following prenatal exposure (Gonzalez-Maciel et al. 2020). For the treatment of anxiety, other first-line medications, such as monotherapy with SSRIs, should be optimized before using benzodiazepines to minimize risk. However, low-to-medium potency agents with no active metabolites (e.g., lorazepam, oxazepam) are preferred when a benzodiazepine must be used during pregnancy (Iqbal et al. 2002).

Hypnotic Benzodiazepine-Receptor Agonists

There are few studies in pregnant, postpartum, or lactating individuals for hypnotic benzodiazepine-receptor agonists, also referred to as Z-drugs (e.g., zolpidem, zopiclone, zaleplon). Zolpidem does cross the placenta by about a minimum of 50% but clears from the fetus rapidly (Chaudhry et al. 2018). As with benzodiazepines, there does not appear to be a solid link between Z-drugs and major congenital malformations (Grigoriadis et al. 2022, Lee et al. 2022). There may be some association with Z-drugs and outcomes such as risk of preterm birth, low birth weight, and small for gestational age, but research documenting this finding is marked by significant study limitations, warranting further study (Grigoriadis et al. 2022, Lee et al. 2022). In the Norwegian Mother and Child Cohort Study (N=36,401), behavioral problems with Z-drugs or benzodiazepines were not significantly different from nonexposed offspring at 5 years of age (Sundbakk et al. 2019).

Antihistamines

Antihistamines are very commonly used by pregnant persons, especially for nausea, vomiting, and itching, but also for the treatment of anxiety and insomnia (Kar et al. 2012). Example medications include diphenhydramine, hydroxyzine, and doxylamine. The bulk of the evidence supports no association between antihistamines and major malformations or other adverse pregnancy outcomes (1994a, Li et al. 2013, Hansen et al. 2020). However, there have been some studies that have found various antihistamines are associated with certain malformations and adverse outcomes (Shenai et al. 2018, Biffi et al. 2021).

Trazodone

Trazodone is frequently used for the treatment of insomnia in general psychiatric practice. Data on use of trazodone during pregnancy is reassuring but limited to a multicenter, observational prospective cohort study of 221 trazodone-exposed pregnancies in the first trimester (Chaudhry et al. 2018, Dao et al. 2023).



Melatonin

Data on melatonin and its use during pregnancy are limited and controversial. It is generally recommended that melatonin be used in a limited fashion during pregnancy and lactation (1994b, Chaudhry et al. 2018). In fact, Chaudhry and colleagues (2018) advised against the use of melatonin during pregnancy given the lack of clinical data and concerns raised by animal studies. Emerging studies may help shed light on the safe use of melatonin during pregnancy (Health 2020)

Pharmacologic Management of Postpartum Depression and Psychosis

Because of their association with serious adverse events, including maternal suicide as well as neonaticide/infanticide, separate discussion of the pharmacologic management of postpartum depression and psychosis specifically is warranted.


Postpartum Depression

Postpartum depression is a major risk to both mother and child and is one of the most common complications that arise from pregnancy and childbirth (Frieder et al. 2019). However, much of its treatment is simply derivative of strategies for the treatment of major depressive disorder. SSRIs are the most widely prescribed antidepressants for postpartum depression given available data on safety, efficacy, and lactation (Kroska et al. 2020). A summary of the literature identified sertraline as a potentially effective treatment for postpartum depression (Frieder et al. 2019). In addition, the authors noted possible benefits of SSRIs as a whole, psychotherapy, and nortriptyline. However, the quality of studies conducted in postpartum depression is low to moderate, making it difficult to derive firm conclusions about effectiveness and safety (Chow et al. 2021).

SSRIs are the most widely prescribed antidepressants for postpartum depression given available data on safety, efficacy, and lactation.

One drawback to SSRIs is the common 4–6-week lag needed to achieve therapeutic effect. A distinguishing physiological feature of postpartum depression compared to depression at other times in a woman's life is the central role of reproductive hormones. One such hormone, allopregnanolone—a major metabolite of progesterone, is a neuroactive steroid and modulator of GABA-A receptors, which fluctuates in concert with progesterone. Specifically, allopregnanolone increases steadily throughout pregnancy, reaching peak levels in late pregnancy, and drops precipitously at childbirth (Brunton et al. 2014). Animal, correlational, and hormone manipulation studies suggest the presence of a subgroup of individuals who are especially sensitive to the hormonal fluctuations associated with reproductive events (Mohler 2012). For this group, the decline in allopregnanolone at childbirth may play a role in the development of postpartum depression (Molyneaux et al. 2014b). As such, recent investigations have focused on the development of novel treatments that specifically address hormonal fluctuations that may trigger postpartum depression in susceptible persons.

In March 2019, the FDA approved brexanolone as the first pharmacologic treatment designed specifically for postpartum depression (FDA 2019) It was developed based on the hypotheses implicating hormonal fluctuations as the primary postpartum depression trigger. Brexanolone is an exogenous formulation of allopregnanolone. Approval was based on data from an initial open-label study and 3 randomized



controlled trials demonstrating efficacy of brexanolone in reducing depression in postpartum women using validated depression severity scales (Meltzer-Brody et al. 2018b). These results were both clinically and statistically significant (Meltzer-Brody et al. 2018b). In the trials, brexanolone treatment consisted of a 60-hour continuous intravenous infusion designed to restore allopregnanolone levels to third trimester pregnancy levels. Although most study participants experienced no adverse events, 5% experienced excessive sedation or sudden loss of consciousness, which led to the decision to implement a Risk Evaluation and Mitigation Strategy (REMS) protocol (Meltzer-Brody et al. 2018b, FDA 2019). Based on this adverse reaction, another caregiver is required to be present if the baby is present during treatment.

Brexanolone infusion for postpartum depression has been shown to be highly effective, but since it requires a REMS protocol, there must be a strong infrastructure and resources to establish the treatment protocol. Howard et al. reported on their implementation of a brexanolone program in a large obstetric hospital and discuss key elements for success, including obtaining cooperation from multiple departments (e.g., billing, education, pharmacy, contracting, institutional leadership, and psychiatry) as well as performing outreach to obstetric providers; using tightly designed protocols; and implementing frequent structured communication among key members of clinical and nonclinical teams (Howard et al. 2022c). Because of the high cost of brexanolone, obtaining preauthorization is imperative and is usually granted when patients meet criteria.


Brexanolone infusion for postpartum depression has been shown to be highly effective, but since it requires a REMS protocol, there must be a strong infrastructure and resources to establish the treatment protocol.

Howard and colleagues also noted that patients responded positively to the treatment with an absence of adverse events, although 1 patient did report sedation, which did not interfere with her completion of the infusion (Howard et al. 2022c). They also found women with a more anxious type of depression reported an initial anxiolytic effect of the medication, followed by an antidepressant effect. Nine patients continued breastfeeding throughout the infusion, based on the Drugs and Lactation Database that notes that brexanolone is not likely to cause adverse outcomes given low oral bioavailability and low amounts detected in breastmilk (2006).

Postpartum Psychosis

Postpartum psychosis is a medical emergency that has been associated with suicide and infanticide and requires immediate attention (Osborne 2018). Given its low prevalence of 1–2 in 1,000, empirical data informing treatment decisions are limited to observational studies. Use of lithium for postpartum psychosis is generally supported by these studies (Doucet et al. 2011). Because postpartum psychosis is associated with infanticide and suicide, psychiatric hospitalization is generally indicated. If there is acute concern about the safety of the mother or baby, hospitalization is indicated. Longer term treatment of this condition includes pharmacotherapy and sometimes requires electroconvulsive therapy.

In studies evaluating prevention of postpartum psychosis, the initiation of high-dose lithium immediately following delivery has the strongest evidence (Luykx et al. 2019). Other evidence-based options include olanzapine and benzodiazepines (Luykx et al. 2019). 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 (Bergink et al. 2016); (Luykx et al. 2019).

Pharmacologic Management and Breastfeeding

The choice of whether to breastfeed can be complicated for mothers with mental and substance use disorders, as psychotropic medication can be transferred from mother to child via breastmilk. The decision for breastfeeding should be made after an individual risk–benefit analysis that weighs severity and frequency of symptoms of the maternal psychiatric disorder, the level of family support, the woman’s general adherence to treatment, and the ability to closely monitor the newborn (Meltzer-Brody et al. 2018a). Importantly, neonates have low hepatic enzyme activity and low glomerular filtration and tubular secretion rates, which may result in higher than anticipated drug exposures.

Antidepressants

In general, the benefits of taking antidepressants typically outweigh the risks, even during breastfeeding.

Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs are the most extensively studied medications with respect to breastfeeding safety, documenting medication concentrations in breast milk and infant plasma, and reports of infant well-being. There are now published studies of lactation safety for all SSRIs, including citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. Among these, only a few isolated adverse effects have been reported (Lanza di Scalea et al. 2009, Alwan et al. 2016). Long-term neurobehavioral studies of infants exposed to SSRI antidepressants during lactation warrant continued examination. The pharmacokinetic profiles of breast milk excretion are best defined for sertraline paroxetine, escitalopram, and fluoxetine, consistently indicating the level of infant SSRI exposure via lactation is markedly lower than the level of fetal exposure via transplacental passage during pregnancy (Stowe et al. 1997, Stowe et al. 2000, Suri et al. 2002, Stowe et al. 2003, Weisskopf et al. 2020).

SSRIs are the most extensively studied medications with respect to breastfeeding safety, documenting medication concentrations in breast milk and infant plasma, and reports of infant well-being.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Breastfeeding data for SNRIs remain limited. The best studied are venlafaxine/desvenlafaxine, for which 4 studies found relative infant doses of 6.8%–8.1%, which is within the notional 10% presumed safety level (Ilett et al. 1998, Newport et al. 2009, Rampono et al. 2011, Schoretsanitis et al. 2019). Two small duloxetine studies reported relative infant doses of less than 1% during lactation (Lobo et al. 2008, Boyce et al. 2011). There are no published lactation data for levomilnacipran.

Tricyclic Antidepressants (TCAs)

TCAs were once widely used during lactation. The only adverse event reported to date is respiratory depression in a nursing infant exposed to doxepin, leading the authors to conclude that doxepin should be avoided but that most TCAs are safe for use during breastfeeding (Matheson 1985). This clinical finding is paralleled by the pharmacokinetic data indicating that infant plasma concentrations are considerably higher for doxepin than for other TCAs (Wisner et al. 1996).



Atypical Antidepressants

Breastfeeding data for the atypical antidepressants are also limited. Best studied is mirtazapine, which has a low relative infant dose and has been associated with no adverse effects on the infant during lactation (Klier et al. 2007, Kristensen et al. 2007, Tonn et al. 2009, Smit et al. 2015). Breastfeeding data for bupropion and trazodone are each limited to a single case report, with both reporting extremely low rates of excretion into breastmilk (Verbeeck et al. 1986, Briggs et al. 1993). There are no published lactation data for vilazodone or vortioxetine.

Mood Stabilizers

Valproic acid, carbamazepine, oxcarbazepine, topiramate, and lamotrigine are considered safe during breastfeeding (Heinonen et al. 2022b). However, caution should be taken since valproic acid and carbamazepine have been linked to liver and blood cell abnormalities in breastfed infants (Heinonen et al. 2022a). Although controversial, there is some evidence that lithium can be used safely during breastfeeding, with close monitoring for lithium toxicity in the newborn (Sprague et al. 2020, Heinonen et al. 2022b).

In general, if a patient is taking an antipsychotic and it is effectively controlling their symptoms, discontinuation during breastfeeding would not be recommended.

Antipsychotics

In general, if a patient is taking an antipsychotic and it is effectively controlling their symptoms, discontinuation during breastfeeding would not be recommended. Infant laboratory monitoring for antipsychotic medication levels is not routinely indicated, but breastfeeding should be discontinued if there is suspicion that the child is experiencing adverse effects from nursing exposure to antipsychotic medications (Brunner et al. 2013). The most commonly reported adverse effects in infants exposed to antipsychotics are somnolence, irritability, tremors, and insomnia (Brunner et al. 2013).

Medication for Opioid Use Disorder (MOUD)


New mothers who are stable on opioid agonist therapy and abstinent from illicit opioid use are encouraged to breastfeed in the absence of other contraindications, such as maternal human immunodeficiency virus infection (2017). Lactation studies of buprenorphine and methadone have reported no adverse effects and low levels of infant exposure, with relative infant doses of 0.2% and 2.1%, respectively (Lindemalm et al. 2009, Bogen et al. 2011). In addition, breastfeeding during methadone therapy has been reported to reduce the severity and duration of neonatal withdrawal (McQueen et al. 2019). The lone case report of naltrexone use during lactation reported a relative infant dose of 1.1% (Chan et al. 2004).

Alcohol Use Disorder Medication

To our knowledge, there are no published reports at the time of this publication regarding the use of acamprosate or disulfiram during lactation.

Smoking Cessation Medication

Over half of individuals who abstain from tobacco during pregnancy resume smoking within 6–12 months after delivery (2020); thus, postpartum treatment with smoking cessation agents is often warranted. Studies of bupropion report a low level of infant exposure (i.e., relative infant dose of 2.0%; Hale 2019).



However, there has been a report of seizure in an infant exposed to bupropion during breastfeeding (Chaudron et al. 2004).

Data regarding the risks of NRT during lactation are sparse. In 1 report, nicotine levels in breastmilk among women using a 21 mg patch were equivalent to those in smoking women, but levels were 70% lower among those using a 7 mg patch (Ilett et al. 2003). There are no known lactation studies with other NRT formulations, such as lozenges or gum. There are no published reports regarding the use of varenicline during lactation.

NONPHARMACOLOGIC MANAGEMENT

Although pharmacologic management of perinatal mental and substance use disorders is often important to reduce symptoms and prevent relapse, it is also critical to ensure that individuals and their families have adequate support and are offered nonpharmacologic treatments as appropriate. This includes helping patients and their loved ones access psychotherapy, support groups, and alternative treatments.

Psychotherapy

Depression


Although pharmacologic treatments often play a critical role in treating perinatal depression, nonpharmacologic management also can be used. A meta-analysis of 43 studies suggests a large effect of psychological treatments in improving depressive symptoms among pregnant and postpartum women, indicating psychological treatments are significantly associated with improved depressive symptoms among pregnant and postpartum women (Cuijpers et al. 2021). In the 14 studies reporting outcomes at 1 year follow-up, the effect size dropped to moderate but remained significant ($g=0.40$). In addition to improving depressive symptoms, psychotherapies in the meta-analysis also were associated with improvements in social support, anxiety, functional impairment, parental stress, and marital stress (Cuijpers et al. 2021).

Although pharmacologic treatments often play a critical role in treating perinatal depression, nonpharmacologic management also can be used.

Another meta-analysis of nonpharmacologic treatments for perinatal depression, including such as CBT, IPT, and yoga (N=21 randomized controlled), found CBT and IPT were effective in reducing depressive symptoms versus controls, with IPT showing even greater effects than CBT (Jiang et al. 2022). However, yoga had no effect on improving depressive symptoms compared with controls.

Anxiety Disorders

CBT helps patients develop connections between their thoughts, feelings, and behaviors. More specifically, CBT looks at psychological problems through the lens of learned patterns of unhelpful or maladaptive thinking and behavior (Chand et al. 2023). If psychological problems are rooted in unhelpful ways of thinking (e.g., cognitive distortions, maladaptive thinking), treatment focuses on challenging and changing those thinking patterns and supporting more adaptive, healthier thought patterns. A wide range of interventions can be used with CBT, and successful treatment requires the collaboration of the patient and clinician to target those strategies intentionally to best support individual needs.



CBT is well-established in the literature as an effective evidence-based approach to treat anxiety disorders in perinatal populations (Maguire et al. 2018). In the general population, improvement rates are estimated to vary from 34% to 68% (Misri et al. 2015). Although the effectiveness in postpartum patients seems to vary, it is suggested that CBT should be among the first treatments offered to pregnant and breastfeeding persons with anxiety disorders due to the potential benefits in contrast with other psychotherapy approaches (Marchesi et al. 2009). Li et al. conducted a systematic review and meta-analysis of 77 studies that used CBT to treat perinatal depression, anxiety, and stress. Investigators found CBT-only (i.e., CBT without other types of intervention) had both short- and long-term efficacy for the reduction of perinatal anxiety symptoms (Li et al. 2022). They also found that an in-person group format was superior to in-person individual format for short-term effects on perinatal anxiety. This may speak to the importance of social connection and belonging during the postpartum period. Given long-term improvements observed across studies, authors speculated that when patients continue to use CBT techniques taught during treatment, they were able to continue making improvements.


CBT is well-established in the literature as an effective evidence-based approach to treat anxiety disorders in perinatal populations.

There is also significant evidence that supports the use of IPT in the treatment of perinatal anxiety. IPT focuses on relieving symptoms by improving interpersonal functioning; rather than focusing on the past (e.g., issues from childhood), IPT addresses current problems and relationships. More specifically, perinatal IPT focuses on addressing 4 interpersonal problems that are common in pregnant and postpartum people—role transitions, interpersonal disputes, grief, and interpersonal deficits. A meta-analysis of 45 studies explored the use of IPT for perinatal women and found IPT was associated with a significant improvement in anxiety as well as depression, social support, relationship quality/satisfaction, and adjustment (Bright et al. 2020). IPT is the preferred option for perinatal patients wanting to improve social support and relationship quality (Bright et al. 2020). Bright and colleagues also observed a trend of individual IPT showing a greater reduction of anxiety symptoms than group IPT. One of the benefits to IPT is that it has wide adaptability. It can be provided in all treatment settings, including outpatient clinics, hospitals, and community treatment centers. Additionally, IPT has demonstrated effectiveness across modalities, including individual and group in-person formats and online (Kang et al. 2020b).

Support groups can be a valuable alternative to individual psychotherapy for perinatal patients with anxiety. Many postpartum support groups meet weekly or biweekly and are facilitated by a mental health professional trained to support postpartum needs. Although specific support group goals vary, one of the chief aims is to help group members feel accepted, understood, and validated in their experiences. Support groups can provide a more affordable and sustainable alternative to individual therapy. They can also offer new parents an opportunity for increased social connections and emotional validation from other people experiencing similar challenges. Although not all support groups are formally identified as psychotherapy, there is evidence suggesting that group-based care and other group activities that promote positive social networks and holistic support may provide the most benefit, compared with interventions that focus on individual support (Collins et al. 1993, Hetherington et al. 2018).

Obsessive Compulsive Disorder (OCD)

Many perinatal patients opt for nonpharmacologic treatment to minimize medication exposure to the



fetus or breastfeeding infant. Fortunately, interventions such as exposure and response prevention (ERP) and cognitive therapy have been shown to be highly efficacious in the treatment of OCD.

Many perinatal patients opt for nonpharmacologic treatment to minimize medication exposure to the fetus or breastfeeding infant.

CBT combined with ERP is an effective, evidence-based, time-limited, and structured treatment approach for OCD in the general population and should be used as first-line treatment of perinatal OCD (Koran et al. 2007). Both treatments require a high degree of motivation and focus on the participation of the patient, which may be challenging given the near-universal presence of sleep deprivation among new parents in addition to the presence of other comorbid conditions. The cognitive requirements of participating in CBT can be challenging for individuals with perinatal OCD due to the severity of their symptoms. Further, many postpartum parents experience sleep deprivation, particularly those who are exclusively breastfeeding (Ruan et al. 2022). To maximize benefit from ERP and/or CBT, many patients with OCD may concurrently require pharmacologic intervention.

Posttraumatic Stress Disorder (PTSD)


Individual trauma-focused psychotherapy is a first-line treatment for perinatal PTSD. Trauma-focused psychotherapies may vary in specific therapeutic content but generally all share core features of supporting patients, helping them better understand and manage traumatic experiences, and teaching patients cognitive restructuring (Furuta et al. 2018). A systematic review and meta-analysis of trauma-focused psychotherapies for postnatal women—including exposure therapy, expressive writing, trauma-focused CBT, eye movement desensitization and reprocessing, and other psychological approaches (N=11 studies)—found all were effective at reducing PTSD symptoms up to 6 months postpartum (Furuta et al. 2018). All studies analyzed used trauma-focused psychotherapies that had been adapted to patients’ postpartum needs.

Psychosis

To our knowledge, there are no psychotherapy modalities that specifically target perinatal psychosis. Nonetheless, psychotherapies can be useful in helping patients with safety planning, coping with diagnosis and symptoms (especially hallucinations and delusions), enhancing their support system, and managing certain nonpsychotic symptoms, such as insomnia (Osborne 2018, Forde et al. 2019, Medalia et al. 2019). Cognitive therapies for psychosis can help remediate impairments with attention, memory, and emotional processing (Medalia et al. 2019). Group-based CBT also may be a useful adjunctive to pharmacotherapy and in some patients with schizophrenia could help target specific symptoms related to overall functioning and social skills, but overall evidence is considered weak and inconsistent (Guaiana et al. 2022).

Insomnia

Many pregnant persons would prefer to avoid medication as much as possible during pregnancy and lactation. Fortunately, CBT for insomnia (CBT-I) is an evidence-based, highly supported psychotherapy that is widely considered the first-line treatment in U.S. and international clinical guidelines for the management of insomnia (Qaseem et al. 2016, Riemann et al. 2017, Wilson et al. 2019, Edinger et al. 2021, Morin et al. 2021). The small number of CBT-I trials conducted in pregnant persons report significant improvements in insomnia severity, sleep efficiency, and sleep quality (Tomfohr-Madsen et al.



2017, Felder et al. 2020b). Additionally, a cross-sectional survey of pregnant women (N=187) in Canada found patients strongly preferred CBT-I over pharmacotherapy or acupuncture (51% vs 12% vs 37%, respectively, $P < 0.001$) and that CBT-I was perceived as a more credible treatment than pharmacotherapy ($P < 0.001$) (Sedov et al. 2017).

Neuromodulation

Neuromodulation treatments affect brain circuits through use of electromagnetic stimulation that leads to improved mood and other psychiatric symptoms (Lewis et al. 2016b). These treatments include but are not limited to deep brain stimulation (DBS), electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and transcranial direct current stimulation (tDCS). These treatments are known to be very effective for depressive disorders, but growing evidence suggests their effectiveness with many other mental illnesses. These treatments are currently not used first line and are typically reserved for more treatment-resistant disorders, although there are exceptions (Conroy et al. 2021). Further, this may not be the case in the future, as these treatments—both in terms of technology and protocols—become more advanced and as research progresses.


Because neuromodulation is nonpharmacologic, it could be highly advantageous for perinatal persons looking to avoid medication.

Because neuromodulation is nonpharmacologic, it could be highly advantageous for perinatal persons looking to avoid medication. In individuals with treatment-resistant disorders who still require adjunctive therapy with psychotropic medication, the doses and number of required medications may be reduced with use of neuromodulation. To date, neuromodulation therapies also appear to be safe in pregnancy and postpartum, although further research is warranted, as many studies to date have small sample sizes and other methodological issues, and many study protocols exclude perinatal persons (Kim et al. 2015b, Pacheco et al. 2021).

Neuromodulation treatments should be considered in the treatment armamentarium of any psychiatrist or other clinician treating perinatal persons. As with any treatment, there are risks, benefits, and side effects that must be weighed against the significant risks of untreated mental disorders that can affect both the mother's and offspring's health and well-being (e.g., preterm birth, low birth weight, impaired attachment, developmental delay). As more evidence mounts, neuromodulation treatments may eventually surpass the use of psychotropics as effective interventions that are less prone to major side effects and complications for pregnant, postpartum, or lactating patients.

Electroconvulsive Therapy (ECT)

ECT has been utilized for over 80 years and is considered one of the most, if not the most, effective treatment for depressive disorders (Kim et al. 2015b). ECT has the advantage of being effective for several disorders, including major depressive disorder, bipolar disorder, schizophrenia, and many others (Rose et al. 2020). In cases of acute life-threatening mental illness, for both the mother and her unborn child, ECT is considered a clear choice (Ward et al. 2018). For example, individuals experiencing postpartum psychosis are at high risk for suicide and/or infanticide, and ECT should be considered as a first-line treatment for these individuals (Focht et al. 2012).



ECT is safe in all trimesters of pregnancy (Calaway et al. 2016, Coshal et al. 2019). Some possible adverse events in pregnancy are vaginal bleeding, abdominal pain, and miscarriage. Special precautions, such as fetal monitoring before, during and after ECT; ultrasound and fetal stress testing; and collaboration with obstetrics specialists, are suggested but require more study (Ward et al. 2018, Rabie et al. 2021).

Transcranial Magnetic Stimulation (TMS)

Growing evidence suggests that TMS is as effective in terms of response and remission as psychotropic medication for the treatment of depression in nonpregnant patients and most likely in the peripartum state, although the number of combined peripartum study participants remains low (Kim et al. 2019, Liu et al. 2020, Peng et al. 2020, Lee et al. 2021). Side effects are usually considered minimal and are generally well-tolerated (Chail et al. 2018). For perinatal patients who refuse or cannot tolerate medication, TMS is a viable alternative (Kim et al. 2015b, Ganho-Avila et al. 2019). Major advantages are the lack of sedation required and the ability of patients to return to usual activity immediately after each treatment (Cox et al. 2020). Disadvantages include the requirement for frequent treatment (e.g., daily and over several weeks), but newer technology provides hope for reducing this burden. Long-term safety in perinatal populations will require continued surveillance and research, although no major adverse events have been reported to date (Cole et al. 2019).

Because tDCS is a completely noninvasive brain stimulation technique, it has a very favorable safety profile for perinatal populations.

Transcranial Direct Current Stimulation (tDCS)

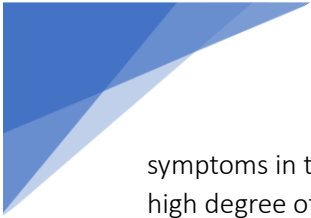
Because tDCS is a completely noninvasive brain stimulation technique, it has a very favorable safety profile for perinatal populations. There are some positive early study results (Konstantinou et al. 2020), but currently the evidence is insufficient to recommend tDCS for the treatment of psychiatric illness in these patients (Kurzeck et al. 2018).

Deep Brain Stimulation (DBS)

DBS is being used increasingly for the treatment of several psychiatric illnesses (Holtzheimer et al. 2011, Graat et al. 2017). However, it remains an extremely uncommon treatment used only for the most intractable forms of depression or OCD. Most trials exclude patients who are pregnant or planning to become pregnant. A literature review including data from 29 pregnancies with DBS implants who became pregnant demonstrated no association with perinatal complications (King et al. 2022). This is encouraging and reassuring for patients who may become pregnant during treatment but is insufficient to recommend routinely at this point. There is also insufficient data on effects during postpartum and lactation. As the use of DBS becomes more common and occurs in younger populations, including those of reproductive age, more data likely will become available.

ALTERNATIVE MANAGEMENT

Complementary or adjunctive interventions (e.g., mind–body practices; biologically based, manipulative/movement-based practices; traditional healing practices) are often utilized in the perinatal period. A national study among pregnant and postpartum women found a significant proportion (37% pregnant, 28% postpartum) reported that they had used a complementary intervention to manage their



symptoms in the last 12 months (Birdee et al. 2014). Overall, although anecdotal evidence may suggest a high degree of efficacy, there are limited well-designed studies that focus on perinatal populations and inconclusive results regarding complementary interventions.

Lifestyle Interventions

There is some promising evidence that supports targeted lifestyle interventions to help reduce anxiety symptoms in perinatal patients. Lifestyle interventions can include exercise, targeted nutrition, yoga, massage, and stress reducing activities (Kołomańska et al. 2019).

Some of the most highlighted “alternative” complementary interventions include supplements/vitamins, aromatherapy, herbs, bright light therapy, and acupuncture.

Complementary Treatments

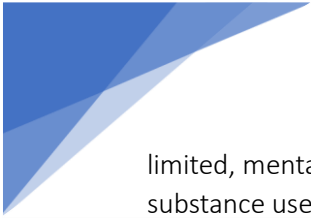
Complementary interventions have yielded inconclusive results in the literature. Some of the most highlighted “alternative” complementary interventions include supplements/vitamins, aromatherapy, herbs, bright light therapy, and acupuncture (Smith et al. 2019). Given the lack of empirical, peer-reviewed research on the use of these interventions in the perinatal population, all birthing people should coordinate with their medical provider(s) to determine the safety of an intervention before initiation.

One of the more commonly utilized complementary interventions is placentophagia. Placentophagia is the ingestion of the placenta and afterbirth components released during and after parturition (Mota-Rojas et al. 2020). Human maternal placentophagy is a relatively new practice, having only become better known in Western cultures during the 1970s. Currently, it is used predominantly by White, middle class, married women, often in the form of placental encapsulation (Botelle et al. 2020). Individuals who choose placentophagy tend to report doing so in support of mood stabilization, enhancing recovery from birth, and increasing milk production. However, there is no strong evidence to support a clinically significant impact of this practice on perinatal anxiety or depressive symptoms (Botelle et al. 2020).

Conclusion

Despite the high prevalence and significant individual and public health burden of mental and substance use disorders in perinatal individuals, clinicians may not be aware of recent evidence supporting effective interventions or of the best strategies for preventing and managing these disorders. Although there are risks involved in prescribing psychotropic medication to perinatal populations, in some patients, the risk of not treating the disorder can result in equally or potentially even more serious negative effects to the mother and offspring. Initiating or continuing psychotropic medication is often a complicated decision, and clinicians must be prepared to provide guidance to patients in these cases. This requires clinicians to stay informed on current evidence for and against perinatal medication use (e.g., antidepressants) so they can provide patients with the most accurate and timely information possible.

The lack of randomized clinical trials to establish the usefulness and risks of pharmacologic and nonpharmacologic treatments remains a major limitation. As highlighted by the USPSTF recommendations, more studies are needed on the use of validated tools for risk assessment, including established perinatal depression screening tools. Additionally, there is a lack of existing clinical practice guidelines as well as research on identifying and mitigating risks of other psychiatric illnesses. Although empirical evidence to guide healthcare providers and patients toward the best course of treatment is



limited, mental health professionals must not shy away from treating perinatal patients with mental and substance use disorders and in fact have a responsibility to help patients make the most informed decisions for themselves and their offspring. This section aims to provide readers with current evidence regarding pharmacologic and nonpharmacologic treatments to help make evidence-based recommendations to patients.



VULNERABLE AND UNDERSERVED POPULATIONS

A universal, one-size-fits-all approach to the mental health care of pregnant individuals is not rooted in evidence-based practice. It is critical to acknowledge that vulnerable populations within the demographic of pregnant individuals present unique risk factors, which can potentially trigger an escalation of existing mental health issues or lead to the emergence of new symptoms related to mental and substance use disorders. Therefore, the implementation of culturally competent care becomes indispensable. Such an approach not only facilitates active engagement of these individuals in their mental health care but also significantly enhances the likelihood of improved health outcomes for both the parent and their offspring.

ADOLESCENTS


Adolescent pregnancy is a public health concern that is linked to numerous adverse maternal and fetal outcomes (Hodgkinson et al. 2014a, Laurenzi et al. 2020a). Adolescent perinatal patients are often overlooked in receiving timely psychiatric diagnosis and intervention (or referral for treatment) (Hodgkinson et al. 2014a, Laurenzi et al. 2020a). This section aims to improve healthcare practitioners' understanding of the scope and seriousness of mental and substance use disorders among adolescent perinatal patients as well as the empirical evidence supporting the prevention and treatment of mental and substance use disorders in these patients.

Adolescent perinatal patients are often overlooked in receiving timely psychiatric diagnosis and intervention (or referral for treatment).

Epidemiology

Despite a significant decline in teen pregnancy since the early 1990s, the US continues to have the highest teen birth rate of industrialized nations. Adolescents from racial and sexual minorities, families with low socioeconomic status, and unsafe neighborhoods have a higher proportion of teen pregnancy, as are youth who are experiencing homelessness, are involved with the welfare system, abuse substances, and are involved with the justice system (Coleman-Cowger et al. 2011, Khurana et al. 2011, Helfrich et al. 2013, Case et al. 2015, Salas-Wright et al. 2015, Maness et al. 2016, Salas-Wright et al. 2016, Abdelaal et al. 2018, Decker et al. 2018, Aparicio et al. 2019, CDC 2021). Additional factors for adolescent pregnancy include having a partner in a gang, history of running away, cognitive delay or learning disability, parents being divorced or separated, having an absentee father, and exposure to an incarcerated family member (Maness et al. 2016).

Adolescent mothers are at high risk of adverse pregnancy outcomes, such as preterm delivery and low birth weight (Kawakita et al. 2016, Anderson et al. 2018a). Birth defects may disproportionately affect children of very young mothers who may be less likely to take folic acid (Case et al. 2015). Risk factors for preterm delivery and low gestational weight include higher cortisol levels, lower body mass index, depressive and substance use disorders, residing in higher poverty and unsafe neighborhoods, prenatal insurance status, maternal diabetes and hypertension, and intent of pregnancy (Spicer et al. 2013, Baker



et al. 2014, Ahmadi-Montecalvo et al. 2016, Coley et al. 2016, Felder et al. 2017, Abdelaal et al. 2018, Anderson et al. 2018b).

The timely diagnosis and treatment of adolescent depression may help not only with adolescent well-being but also with prevention of teen pregnancy (Garwood et al. 2015). The timing of depression onset relative to age at sexual debut is associated with teenage pregnancy (Vafai et al. 2020). Compared with those with no depression onset, girls who experienced depression onset in the same year as their sexual debut have been found to be more likely to have a first pregnancy. Approximately 7-35% of teen mothers planned or wanted their pregnancy, and those who report a desire for pregnancy and attempting pregnancy have reported symptoms of hopelessness and low self-worth (Fedorowicz et al. 2014, Case et al. 2015). Depression may significantly decrease positive communication with primary care practitioners and interfere with personal pregnancy prevention (Carvajal et al. 2012).


The timely diagnosis and treatment of adolescent depression may help not only with adolescent well-being but also with prevention of teen pregnancy.

Trauma and Interpersonal Violence

A history of trauma is associated with adolescent motherhood, and adolescent mothers have reported high levels of comorbid traumatic experiences impacting perinatal mental health and physical health, including sexual abuse, intimate partner violence (IPV), physical violence, emotional adversity, loss of caregiver or sibling, and community violence or urban social stress (Noll et al. 2011, Walsh et al. 2015, Killian-Farrell et al. 2020, Anastas et al. 2021, Laursen et al. 2022). There are particularly high rates of IPV among adolescents who are pregnant or parenting, and adolescent mothers report higher levels of perpetrating IPV, including psychological abuse (52.7%–85.7%) and physical conflict (24%–56%), than being a victim of psychological or verbal abuse (38.6%–80%) and physical assault (10.1%–40%) (Sue Newman et al. 2011, Madkour et al. 2014, Toews et al. 2014, Lewis et al. 2017b, Buzi et al. 2020). However, adolescent mothers are more likely to report physical injury from IPV than inflicting injury (7% vs 4%) (Buzi et al. 2020). Subsets of adolescent mothers, such as those currently or previously involved in the foster care or juvenile justice system, report high rates of IPV (62%) and fear of it, including non-partner sexual violence, incapacitated rape, and reproductive coercion, which was associated with alcohol or drug use before sex and partnering with older men (Herrman et al. 2017, PettyJohn et al. 2021).

IPV experienced by adolescent mothers during the perinatal period is also associated with many adverse infant health across the infant's first year, including lower birth weight and preterm birth, poor or fair nutrition ($P<0.01$), lack of regular primary health care practitioner ($P<0.001$), being behind on childhood immunizations ($P<0.001$), missing regular well-child check-ups ($P<0.001$), routine emergency room use ($P<0.05$), and child maltreatment, which may perpetuate an intergenerational cycle of trauma ($P<0.001$) (Madkour et al. 2014, McGuigan 2018)

In a study examining the effects of child maltreatment and adolescent pregnancy on late adolescent depressive symptomatology, participants with a history of childhood maltreatment who had pregnancies in adolescence (both birth and no birth outcomes) demonstrated significantly greater depressive symptoms than maltreated individuals who did not experience an adolescent pregnancy (Russotti et al.



2020). This effect remained after controlling for prior depressive symptoms, peer and maternal relationship quality, and romantic relationship violence (Russotti et al. 2020).

With regards to impact of delivery on trauma, studies have recommended assessing for acute stress and posttraumatic stress in adolescents with unmet birth expectations or stress, which have been found to be related to poor pain management, fear of dying, delivery complications, history of prior trauma, and higher depressive symptoms (Anderson et al. 2014, Anderson et al. 2018b, Anderson et al. 2022).

Juvenile Justice-Involved Youth

Justice-involved youth who intend to become pregnant or have a positive attitude toward future pregnancy are more likely to exhibit symptoms concerning for depression, hyperactivity, impaired self-control and self-esteem, and trauma symptoms (Gray et al. 2016, Rosen et al. 2022). There may also be differences in pregnancy rates among youth that are court-involved versus incarcerated, with almost 13% of court-involved juveniles in one study reporting a current or prior pregnancy compared to estimates of over 30% for detained or incarcerated female juvenile offenders (Khurana et al. 2011).


Although multiple guidelines suggest that reproductive health counseling should occur routinely, and research showing GSM individuals desire this counseling, recent studies indicate that only a minority of GSM adolescents and young adults have these discussions with their healthcare teams.

Sexual and Gender Minority Adolescent

Compared to heterosexual adolescents, sexual and gender minority (SGM) adolescents or those who are unsure of their identity are more likely to exhibit sexual risk behaviors and to experience or be involved in an adolescent pregnancy (Everett et al. 2019, Goldberg et al. 2022a, Tabac et al. 2022, Everett et al. 2023). Studies show that sexual orientation disparities in teen hormonal contraception use and pregnancy have persisted despite general rates of teen pregnancy declining dramatically (Charlton et al. 2013). Although multiple guidelines suggest that reproductive health counseling should occur routinely, and research showing GSM individuals desire this counseling, recent studies indicate that only a minority of GSM adolescents and young adults have these discussions with their healthcare teams (Reed et al. 2011, Everett et al. 2016, Greenfeld et al. 2016, May et al. 2016, Mosovsky et al. 2016, Obedin-Maliver et al. 2016, Ruppel et al. 2017, Leonard et al. 2022). Further, utilization rates of fertility preservation are low among transgender adolescents (Nahata et al. 2017). Enriched communication training for healthcare practitioners is necessary to provide a skilled workforce for GSM adolescents and young adults. Dedicated training for practitioners and programs increasing access are important goals for improving care. The need for additional research is also critical.

Perinatal Depression

Adolescent mothers and their children are at high risk for depression and its associated negative educational, social, health, and economic outcomes. Adolescent mothers face unique challenges compared to adult mothers, including fear, transition difficulties, feelings of overwhelm and confusion,




low self-esteem, peer rejection, a sense of abandonment and isolation, and concerns about derailment of educational aspiration that may put them at higher risk of parental stress and depression (Raley et al. 2012, East et al. 2014, Venkatesh et al. 2014a, Barassi et al. 2022). Adolescents in general are a high-risk group for perinatal depression (Walker et al. 2019, Franta et al. 2022). Indeed, the incidence of postpartum depression among adolescents ages 15–19 years is double the rate of mothers older than 25 years, with prevalence ranging from 14%–53% compared to 6.9%–16.7% (Anderson et al. 2015, Buzi et al. 2015, Dinwiddie et al. 2018, Nowak et al. 2022). Risk factors for perinatal depression among adolescents during pregnancy and the postpartum period include parental stress, prior history of depression, negative view of the pregnancy, excessive gestational weight gain in adolescents that entered pregnancy overweight or obese, early breastfeeding difficulties, history of sexual, physical, or community violence, socioeconomic hardship, and limited familial and partner social support (Tzilos et al. 2012, Meltzer-Brody et al. 2013, Nunes et al. 2013, Siegel et al. 2014, Venkatesh et al. 2014b, Buzi et al. 2015, Recto et al. 2017a, Cunningham et al. 2018, Sipsma et al. 2018, Hymas et al. 2019).

The prevalence of depressive symptoms has been found to increase with adolescent maternal age, with lower prevalence in 12- to 13-year-olds compared to 16- to 17-year-old mothers (Brown et al. 2012). Similar to findings in adults, lower pregnancy intendedness and wantedness has been associated with parenting difficulties and depression (East et al. 2012, East et al. 2014, Whitworth 2017). Among women who had more positive adolescent pregnancy attitudes, women who had teen first births were actually less depressed in adulthood than women who had their first births as adults (Whitworth 2017).

Adolescent mothers experiencing homelessness may benefit from maternity group homes given low levels of familial and partner support in this population.

Adolescents with perinatal depression have been found to be at increased risk of substance use, birth complications, and impaired parenting ability with poor mother and child interactions (Siegel et al. 2014). In addition, their children may be more at risk for maltreatment and being developmentally behind compared to mothers who are not depressed (Whitson et al. 2011). Strong support systems—including stable familial, partner, neighborhood, and healthcare support during the perinatal period—have been identified as important factors contributing to healthy outcomes, such as lower levels of depressive symptoms and perceived stress in adolescent mothers (Brown et al. 2012, Huang et al. 2014b, Siegel et al. 2014, Solivan et al. 2015, Campbell-Grossman et al. 2016, Recto et al. 2020, Simons et al. 2020, Tung et al. 2021, Nowak et al. 2022). In fact, limited social support has been identified as a primary risk factor for depression compared to other demographic and obstetrical risk factors (Koleva et al. 2014). Father involvement, including seeing infants at least a few times each month, providing financial support, and being partnered with the infant’s mother, has predicted lower infant stress and buffers the impact of maternal depression (Edwards et al. 2012, Lewin et al. 2015). Stressful life events, most commonly financial in nature or related to moving, experienced by pregnant youth and their partners have been found to be significantly associated with depression (Divney et al. 2012). Relationship adjustment during pregnancy is significantly related to lower relationship attachment avoidance and anxiety, family support of the relationship, lack of IPV, and relationship equity (Kershaw et al. 2013). Insecure romantic attachment may be associated with development of depressive symptoms (Desrosiers et al. 2014).



Adolescent mothers experiencing homelessness may benefit from maternity group homes given low levels of familial and partner support in this population (Meadows-Oliver 2003). Peer support may also modulate anxiety and depressive symptoms, as high levels of social support from peers in combination with high sleep duration and quality were found to decrease depressive symptoms, and fluctuations in social networks elevate postpartum anxiety symptoms (Kazal et al. 2021, Yung et al. 2021). Online peer support, such as online teen pregnancy message boards, may alleviate some of the social isolation and stigma associated with youth pregnancy and parenting (Sherman et al. 2013). Peer support in a lactation consultant-peer counselor team or health promotion text blasts may also increase breastfeeding duration and healthcare behavior outcomes, such as recommended maternal and infant healthcare visits (Wambach et al. 2011, Brown et al. 2014).

Adolescent mothers who perceive attachment, trust, and maternal warmth from their own caregivers, particularly if they co-reside with their parent, have reported lower levels of depressive symptoms, and positive prenatal mood, which in turn is associated with lower preterm birth and perceived stress (Edwards et al. 2012, Siegel et al. 2014, Zeiders et al. 2015, Tung et al. 2021). The prevalence of depression may decrease in the postpartum period, which has been postulated to be due to increased social support (Edwards et al. 2012, Meltzer-Brody et al. 2013, Simons et al. 2020). Adolescent mothers with chronically high depressive symptoms, estimated to be around 10% in one study, may be more likely to endorse higher levels of pregnancy distress and social conflict and lower levels of perceived quality of social support (Simons et al. 2020).

Antenatal anxiety may impact caregiving behaviors in the postpartum period (Hipwell et al. 2016). The experience of pregnancy itself may also impact later parenting. Adolescents who had greater prenatal stress about physical symptoms of pregnancy or economic and social stressors during pregnancy had reduced maternal warmth and reduced verbal and physical affection and acceptance of child interests in the postpartum period (Scorza et al. 2021).

The Parenting Responsibility and Emotional Preparedness tool may help identify adolescent mothers at high risk of suboptimal parenting and poor child developmental outcomes.

Screening Tools for Diagnosis and Management

The Edinburgh Postnatal Depression Scale has been found to be highly accurate at identifying postpartum depression in adolescents (Venkatesh et al. 2014c). Of note, a systematic review found that the standard threshold score of 12 for detecting depression with this scale did not consistently identify all adolescents at high risk of developing perinatal depression, and a lower threshold score of 9 may be more appropriate (Barassi et al. 2022). In addition, it is important to screen at multiple time points during the postpartum period, as depressive symptoms at 3 months postpartum may predict later symptoms (Anderson et al. 2018b). The Parenting Responsibility and Emotional Preparedness tool may help identify adolescent mothers at high risk of suboptimal parenting and poor child developmental outcomes (Lanzi et al. 2012). Screening for comorbid disorders, such as eating disorders, is important, as there may be a remission in symptoms during pregnancy followed by postpartum relapse (Harrison et al. 2018).




Treatment of Mental Disorders

Although the evidence of their effectiveness is limited, interventions for the prevention of postpartum depression and other mental disorders in adolescent mothers include a range of psychosocial and psychological interventions, such as home visits, cognitive-behavioral therapy (CBT) psychoeducational intervention, infant massage training, perinatal educational programs, and the REACH program—an interpersonally oriented intervention offered in the prenatal period to prevent postpartum depression (Phipps et al. 2013, Sangsawang et al. 2019, Laurenzi et al. 2020b). Psychosocial interventions may also improve maternal outcomes for adolescent mothers by reducing the occurrence of low birth weight, improving maternal education and employment, and decreasing repeat adolescent pregnancies (SmithBattle et al. 2017, Laurenzi et al. 2020b). Preventative behavioral counseling, such as CBT and interpersonal therapy, offered to all pregnant adolescents has been proposed as a cost-effective intervention to prevent perinatal depression and subsequent adverse pregnancy outcomes (Franta et al. 2022). For adolescents with perinatal depressive symptoms, interpersonal psychotherapy, dialectical behavior therapy-informed skills groups, and motivational interviewing have been found to reduce rates of major depression (Lieberman et al. 2014, Kleiber et al. 2017).

Social media and internet-based interventions are being developed to decrease stigma and increase treatment-seeking behavior in adolescent mothers with postpartum depression.

Inaccessibility, lack of awareness of perinatal mental health programs, and poor mental health literacy have been identified as barriers to engagement in treatment (Muzik et al. 2016, Bledsoe et al. 2017, Recto et al. 2017a, Recto et al. 2017b, Recto et al. 2017c). Social media and internet-based interventions are being developed to decrease stigma and increase treatment-seeking behavior in adolescent mothers with postpartum depression (Logsdon et al. 2013, Cynthia Logsdon et al. 2018). Integrated mental health care programs in obstetric or pediatric medical homes may improve the identification and treatment of adolescent mothers in need of mental health care (Ashby et al. 2016, Booth et al. 2018). Mental health interventions for teen mothers need to incorporate pediatricians, who may be able to screen and initiate treatment for postpartum depression, deliver developmentally appropriate guidance, and provide support around breastfeeding (Moriarty Daley et al. 2013, Hodgkinson et al. 2014b, McPeak et al. 2015). Integrated clinic models, with social work and mental health services in a primary care setting, which utilize adapted parenting and life skills interventions, may improve maternal self-esteem, perceived parenting abilities and relationship with infants, and decrease rapid repeat teen pregnancy (Cox et al. 2019, Lewin et al. 2019). Home, telephone, and drop-in center-based services may decrease inaccessibility, particularly for homeless adolescent mothers and those at risk for homelessness (Conroy et al. 2016, Stevens et al. 2017, Aparicio et al. 2019).

Group prenatal care, such as CenteringPregnancy® Plus group prenatal care, may reduce depressive symptoms during the perinatal period compared to individual care, and adolescent mothers have reported a preference for group based interventions to decrease stress and depressive symptoms (Kinser et al. 2015, Felder et al. 2017). CenteringPregnancy® has also been found to increase compliance with prenatal and postpartum care, adequate weight gain during pregnancy, breastfeeding in addition to bottle feeding, and use of long acting, reversible contraception following delivery (Trotman et al. 2015). The



evidence-based, in-person, group CBT intervention Mothers and Babies is being adapted for adolescents and young adults (<25 years) to be delivered in a social media platform that might prevent perinatal depression (Gewali et al. 2021).

Trauma-informed programs, such as the coparenting counseling program Young Parenthood Program and the Safe Dates IPV prevention program, are being developed to support positive communications and decrease the occurrence of IPV in pregnant adolescents and their partners (Florsheim et al. 2011, Kan et al. 2021). Narrative exposure therapy has been proposed as a potential treatment of IPV-related posttraumatic stress disorder in parenting and pregnant adolescents (Volpe et al. 2016, Volpe et al. 2017).

Treatment may need to be tailored to the population. An intervention in Southwest Native American communities—Family Spirit—which utilized paraprofessionals in a home-visiting program found decreases in externalizing behaviors, depressive symptoms, and lower past month use of cannabis among adolescent mothers and their children up to 36 months postpartum and significantly greater parenting knowledge and self-efficacy (Barlow et al. 2013, Barlow et al. 2015).


For adolescents requiring inpatient psychiatric treatment during pregnancy, no adverse effects on pregnancy outcomes have been found (Fletcher et al. 2015).

Substance use among adolescents is a risk factor for unplanned pregnancy and subsequent fetal exposure with nearly 3 in 5 pregnant teens in the US reporting substance use within the previous 12 months.

Substance Use Epidemiology, Treatment, & Prevention

Substance use among adolescents is a risk factor for unplanned pregnancy and subsequent fetal exposure with nearly 3 in 5 pregnant teens in the US reporting substance use within the previous 12 months (Cavazos-Rehg et al. 2012, Salas-Wright et al. 2015, Dir et al. 2019). Adolescent mothers have reported higher levels of personal or peer substance use before sexual intercourse and pregnancy compared to other adolescents, and they are significantly more likely to meet criteria for substance use disorders, including those involving alcohol, cannabis, stimulants, and opioids (Cavazos-Rehg et al. 2012, Chapman et al. 2013b, Connery et al. 2014, Killebrew et al. 2014, Salas-Wright et al. 2015, Salas-Wright et al. 2016). Whereas some adolescent mothers continue using substances while pregnant, most reported use attenuates over the course of pregnancy, stops, and then resumes within 6 months after giving birth (Chapman et al. 2013b, Constantine et al. 2014, Salas-Wright et al. 2015, Anderson 2018).

Although pregnant adolescents have been found to be significantly less likely to have used 1 or more substances in the previous 30 days compared to nonpregnant adolescents, studies have found heterogeneity in substance use among adolescent mothers (Salas-Wright et al. 2016, Tung et al. 2020). Factors such as exposure to caregiver alcohol use, peer alcohol use, and drinking as a coping mechanism may be associated with higher risk for moderate-to-heavy drinking during the perinatal period (Salas-Wright et al. 2015). Male partner use of cigarettes and cannabis in the prenatal period has been found to significantly predict adolescent mother substance use in the postpartum period with psychological distress and low self-esteem being other factors involved in continued use (Chapman et al. 2013b, Desrosiers et al. 2016). Polydrug use has been associated with older age, more infrequent parental limit



setting, absence of mother or father in household, low parental warmth and positive reinforcement, and higher income adolescents in their first trimester of pregnancy (Salas-Wright et al. 2015, Salas-Wright et al. 2016). Substance use may vary by race/ethnicity, with White adolescent mothers being more likely to smoke cigarettes and use cannabis compared to Black adolescent mothers, who may be more likely to drink alcohol and use other drugs (Chapman et al. 2013b). There is a dearth of studies on Hispanic adolescent mothers. Substance use, especially alcohol and illicit drug use, has been found to be associated with depression among adolescent mothers in the antenatal and postpartum period (Tzilos et al. 2012, Chapman et al. 2013b). Pregnant adolescents with parental support and engagement in school may be significantly less likely to use substances (Salas-Wright et al. 2015). Adolescents with substance use in addition to bipolar disorder had significantly higher rates of pregnancy and abortion over the past 12 months (Siegel et al. 2014).

Prevention efforts including screening for substance use in all healthcare settings, and if present, utilizing motivational interviewing plus parent training and case management, have been shown to significantly reduce pregnancy rates in adolescents. For pregnant adolescents with opioid use disorder, the benefits of treating with opioid agonist treatment, including buprenorphine or methadone, are thought to outweigh the risks of potential harm to the fetus and unknown impact on adolescent development (Spada et al. 2020). Long-term follow-up studies of offspring of adolescent mothers have found increased behavioral dysregulation and early sexual behavior following cigarette and cannabis use during pregnancy, respectively, in addition to a significant likelihood of additional in utero exposure to alcohol and cannabis use (Cornelius et al. 2012, De Genna et al. 2015)

Conclusion

Adolescent mothers have identified physical and structural factors, such as power and stigma, in addition to individual factors as impacting well-being and overall mental health during and after pregnancy (Lucas et al. 2019). Although the long-term mental health outcomes of teen pregnancy remain unclear, social factors have emerged as possible targets of interventions (Xavier et al. 2018). In terms of future directions, a socioecological framework and multigenerational life course perspective may be helpful for considering additional upstream risk factors that impact the risk of adolescent pregnancy and mental health outcomes of expectant and parenting teens (Buzi et al. 2015, Tebb et al. 2022).

IMMIGRANTS & REFUGEES

Pregnant and postpartum refugees and immigrants face unique risk factors for psychiatric problems due to decreased access to perinatal care, migration difficulties, legal status stress, and trauma. About one-third of migrant women from low–middle income countries are estimated to have perinatal depression (Fellmeth et al. 2018). The background of trauma often found with refugees/immigrants may increase the risk for posttraumatic stress disorder (PTSD) and postpartum depression (Fazel et al. 2005). Compared to women of other migrant groups, women with asylum seeker and refugee status have worse perinatal mental health and obstetric outcomes, higher child mortality, and preterm birth (Heslehurst et al. 2018, Adjei Boakye et al. 2023). Health outcomes differ based on country of origin, healthcare access in the host country, immigration status, length of residence, political context, and legal status stress, amongst other factors. However, the need for individualized, culturally sensitive perinatal care and social support is apparent cross-culturally. This section describes the special considerations in mental health and substance use disorder care of perinatal patients during premigration, migration, and resettlement.



Premigration/Migration

Trauma, including sexual/gender-based violence, can increase the risk of PTSD. Certain groups—including but not limited to children; members of the lesbian, gay, bisexual, transgender, queer, and intersex community; and women—may be in vulnerable situations and at risk for more systematic violence and discrimination. Feelings of desperation with regards to border crossings can lead to repeated attempts and may escalate the dangers of migration. Aside from being potential victims of violence, perinatal immigrants may endure physical demands of the elements; travel on cargo freight trains or crowded boats; and treacherous walks before arriving at a destination. In refugee camps and detention facilities, reproductive health can be compromised by decreased access to perinatal care and contraceptives, increased exposure to unsanitary conditions, and an increased risk of infectious diseases. Migrant workers often cope with separation from family, nonoptimal working conditions, inequitable pay, and insufficient protections.

The background of trauma often found with refugees/immigrants may increase the risk for posttraumatic stress disorder (PTSD) and postpartum depression.


Acculturation/Resettlement

Acculturation difficulties can affect depressive and anxiety symptoms during the perinatal periods (D'Anna-Hernandez et al. 2015, Preciado et al. 2017, Lara-Cinisomo et al. 2019b). Resettlement can lead to feelings of optimism but also grief over loss of cultural norms and supports. Immigrants may cope with difficulty accessing health care. They may also face discrimination both at their country of destination and in countries traveled through. Shifts in traditional roles may occur if family members go missing or are lost.

Health trends can depend on the degree of acculturation to the host country. Some studies show a health advantage for immigrants, supporting the initial “healthy immigrant” phenomenon. Perinatal substance use (e.g., tobacco use, alcohol use) is less common in most immigrant groups compared to U.S. born counterparts (Shellman et al. 2014, Hoyt et al. 2019). Pregnancy-related hypertension in most available studies appears to be less prevalent in immigrants (Mogos et al. 2017). Data from the Early Childhood Longitudinal Birth Cohort (N=7,000) shows that immigrants are also less likely to gain excessive weight during pregnancy or have elevated body mass index prior pregnancy. This trend depends on length of residence in the US (Green et al. 2021). Regarding prenatal parameters, other studies have found differences in rates of breastfeeding, physical activity, use of birth control, and birthweights amongst various immigrant groups compared with U.S. born women (Teitler et al. 2012, Xaverius et al. 2012, Shellman et al. 2014, Fleuriet et al. 2015, Miller et al. 2016b, Hoyt et al. 2019, Araneta et al. 2020).

Immigration and Postpartum depression

Acculturative stress, especially marginalization, can contribute to postpartum depressive symptoms (Alhasanat-Khalil et al. 2019, Luis Sanchez et al. 2020). Some estimates show 20%–45% of immigrant mothers are diagnosed with postpartum depression after arriving in the host country; however, statistics may vary based on nativity, duration of residence, socioeconomic factors, host country, health status and social support (Collins et al. 2011, Shellman et al. 2014, Alhasanat et al. 2015, Tobin et al. 2015, Alhasanat et al. 2017, Tobin et al. 2018, Shovers et al. 2021). Reporting of postpartum depression may also depend



on traditional gender roles, cultural beliefs, and societal expectations of parenthood. Stigma, fear of judgement, limited awareness of postpartum depression, language barriers, and legal status stress can affect disclosure of symptoms (Sampson et al. 2017, Sampson et al. 2021). A common theme amongst individuals experiencing postpartum depression are feelings that social support was lacking (Tobin et al. 2015, Alhasanat-Khalil et al. 2018). This may also include the absence of desired postpartum traditions and a ritual support system (i.e., a “sitting month”) in their new environment (Son 2016, Ta Park et al. 2017, Han et al. 2020).

Optimizing Perinatal Psychiatric Care for Refugees and Immigrants

Culturally Competent and Culturally Responsive Services

Individualized, compassionate, culturally competent and responsive care from practitioners is nearly universally desired by refugee and immigrant patients to improve maternal mental health and infant well-being. This support can offset feelings of isolation and lack of control during the birthing process and the postpartum period in an unfamiliar system (Hill et al. 2012, Tobin et al. 2018, Ta Park et al. 2019, Trainor et al. 2020, Bamgbose Pederson et al. 2022, George et al. 2022, McClellan et al. 2022, Vo 2023). Similar supports are called for by immigrants experiencing pregnancy loss (Alaradi et al. 2022). Language proficiency differences have been associated with isolation, effects on self-esteem, lack of treatment access, and possibly higher prevalence of mental illness. Proper translation is vital to providing optimal perinatal care for refugees and immigrants (Montemitro et al. 2021).


Social Support

Having a social support network (e.g., a home visitor, mental health outreach worker), irrespective of the type is generally protective against perinatal depression across different racial and ethnic groups (Coburn et al. 2016, Hansotte et al. 2017, Logsdon et al. 2018, Pao et al. 2019, Luo et al. 2023). Rigorous studies are often lacking, but interventions providing social support usually report benefits. Published interventions include employing doulas familiar with the cultural and linguistic needs of perinatal immigrant patients to provide support during perinatal care. Ideally, a multidisciplinary effort including behavioral and nonbehavioral healthcare practitioners, translators, community advocates, policymakers, and public health advocates would provide a broad social support network for immigrant parents, which could increase the odds for positive outcomes and well-being (Clare et al. 2012).

Therapists providing support should be mindful of the impact of immigration stresses but also the person’s identity other than being an immigrant.

Feedback from patients and doulas emphasize the influence of language, culture, and beliefs on birth and prenatal care and outcomes (Kang 2014, LaMancuso et al. 2016, Mendel et al. 2021). In a randomized controlled trial of Hispanic mothers in Tennessee (N=188), receiving home health worker visits by peer mentors was associated with fewer depressive symptoms and decreased stress versus a minimal educational intervention (Lutenbacher et al. 2018). This translated to improved infant care and quality infant stimulation/engagement.

Therapists providing support should be mindful of the impact of immigration stresses but also the person’s identity other than being an immigrant. Moreover, traditional gender roles may influence mental



health and need for support. Attempts have been made to assess effectiveness of cognitive-behavioral therapy in immigrant pregnant women, and although some benefits have been observed, the degree of effectiveness is inconclusive, partially due to methodological issues (Le et al. 2011, Le et al. 2013, Le et al. 2021). Internet-based psychotherapy appears to benefit at least some immigrant groups, but rigorous studies are lacking (Green et al. 2021).

Medical and Mental Health Screenings


Recommended screenings for refugees and immigrant include those for infectious diseases (e.g., sexually transmitted infections, malaria, tuberculosis, intestinal parasitic infections), vaccinations, gender-based violence, and nutritional deficits. Data from the 1997–2011 National Birth Defects Prevention Study (n=28,385 cases, n=10,964 controls) show an increased risk in several birth defects when both parents are foreign born, including spina bifida, anotia/microtia, and diaphragmatic hernia (adjusted odds ratios range: 1.3–1.7) (Hoyt et al. 2019). Further, a smaller cross-sectional study of pregnant and/or lactating women (N=68) found higher docosahexaenoic acid and eicosapentaenoic acid consumption among U.S.-born women versus immigrant women (Nochera et al. 2011).

Screening for exposure to environmental toxins is important because these can affect reproductive health and infant outcomes. For instance, pregnant migrant workers may be exposed to pesticides hazardous to pregnancy health (Flocks et al. 2012). Immigrants also may have an increased risk of lead exposure from their home country, during migration, or in home household products, and pregnant women with increased lead levels are disproportionately foreign born (2006). Lead exposure can increase the risk of neurodevelopmental problems, gestational hypertension, and miscarriage (La-Llave-Leon et al. 2016). Lead also can be stored in the body long term, to be released in times of higher bone turnover, such as pregnancy and lactation (2012). Thus, the U.S. Centers for Disease Control and Prevention recommends lead screening of all refugee children and pregnant and lactating people (Alba et al. 2012).

Successful screening for mental disorders in immigrants and refugees requires attention to cultural differences in the presentation and expression of psychiatric symptoms and disorders.

Screening for female genital cutting is warranted, as this can provoke anxiety during delivery, cause feelings of shame, and lead to reactivation of trauma. A substantial number of asylum affidavits specific to female genital cutting claims also reported violence or trauma, including forced marriage and torture (Wikholm et al. 2020). Genital cutting can also increase the risk of obstetric complications, such as postpartum hemorrhage infection and perineal tears (Sarayloo et al. 2019). Patients also may be difficulty with intercourse and chronic pain (Pimentel et al. 2014, Hamid et al. 2018). Health care practitioners, including those in the US, may feel discomfort addressing female genital cutting in their patients and many lack the knowledge and training for managing such cases (Hamid et al. 2018). Although female genital cutting can occur worldwide, reports have clustered in Southeast Asia, the Middle East, and Africa (Wikholm et al. 2020). Healthcare practitioners should be especially vigilant for cases in these patient populations.

Successful screening for mental disorders in immigrants and refugees requires attention to cultural differences in the presentation and expression of psychiatric symptoms and disorders (Tobin et al. 2015). Screening tools appropriate for this population include the Refugee Health Screener-15, a widely used



questionnaire that has been translated to multiple languages and validated across several cultures (Hollifield et al. 2013, Johnson-Agbakwu et al. 2014, Hollifield et al. 2016, Fellmeth et al. 2018). It has been used to screen newly arrived refugees, including people seeking obstetric and gynecologic care (Johnson-Agbakwu et al. 2014). The postpartum depression Screening Scale and the Nine-Item Patient Health Questionnaire also have been validated in diverse samples (Beck et al. 2012). Of note, some patients may present with somatization instead of depressive symptoms, and relaxation techniques in some cultures may appear as agitation in others (Lanzara et al. 2018).

Legal Status Stress and Perinatal Mental and substance use disorders

Legal status and public policy surrounding immigration has important implications for access to prenatal care, especially for undocumented immigrants (Korinek et al. 2011)(Utah population database). Fear of deportation is associated with increased perinatal anxiety (Lara-Cinisomo et al. 2019c). More restrictive immigrant policies or criminalization are associated with an increased risk of preterm birth, especially in Black mothers born outside the US (Ro et al. 2020, Sudhinaraset et al. 2021). Medical care can be compromised when patients forego social services for fear of penalties due to immigration status. Legal status stress can also impact the experience parents have with their children. For instance, in a Medicaid claims analysis, Deferred Action for Childhood Arrivals eligibility of mothers was associated with decreased adjustment disorders and anxiety disorders among children (Hainmueller et al. 2017).


Legal status and public policy surrounding immigration has important implications for access to prenatal care, especially for undocumented immigrants.

Access to Care

Eligibility in programs and expansion of insurance coverage to include immigrants may improve access to mental health and perinatal care, thereby enhancing maternal and infant well-being. For example, immigrants who participated prenatally in a nutritional supplementation program with Women, Infants, and Children (N=9,083) were less likely to have infants with low birth weight (adjusted odds ratio 0.79, 95% CI 0.65–0.97, P=0.02) compared with infants of nonparticipants (Ettinger de Cuba et al. 2022). U.S. natality data from the National Center for Health Statistics from 2011–19 (N= 22,042,624) showed insurance coverage was associated with disparities in timely perinatal care, with U.S. born women being more likely to access timely prenatal care, whereas Asian and Hispanic immigrant women were not (Janevic et al. 2022). Similarly, state Medicaid expansion has been associated with increased health insurance coverage during pregnancy and early engagement in prenatal care among low-income women (Wherry et al. 2017). Expansion of Medicaid also is linked to increased rates of prenatal care including among women with low socioeconomic status and undocumented immigrants (Jain et al. 2022). The rollout of emergency Medicaid Plus in Oregon, for example, was not only associated with increased rates of prenatal care, diabetes screening, and healthcare utilization by undocumented immigrants but also increased well-child visits and vaccinations and improved health outcomes for infants (Swartz et al. 2017).

Research and Knowledge Gaps

Multiple research and knowledge gaps exist that, if addressed, could help improve psychiatric and obstetric health outcomes for perinatal refugees and immigrants. Rigorous studies are needed to identify more protective factors and assess the effectiveness of interventions for perinatal mental and substance



use disorders in this population. The role of mental health promotion and mental disorder prevention in the resettlement process should be better defined. Analysis of health trends that change with acculturation could help correlate risk factors with physiological markers for perinatal health outcomes (Lara-Cinisomo et al. 2016). Further stratification of data could uncover other disparities that may be overlooked. There is also a paucity of research on certain conditions of public health significance, such as postpartum psychosis and how it presents and is expressed in non-English-speaking perinatal patients (Naito et al. 2019). Currently, few peer-reviewed publications exist on internally displaced individuals, undocumented individuals, and groups in vulnerable situations that may be difficult to reach.

Conclusion

The role of immigration and migration in the psychiatric health of perinatal refugee and immigrant patients warrants more attention. Currently, psychiatric care is underutilized by immigrants, especially those who are undocumented (Garcini et al. 2021). Distress and psychiatric functioning related to nativity should be included in the assessment of perinatal immigrants and in the management of their mental and substance use disorders. Culturally responsive prevention and intervention strategies are sorely needed to ensure care is tailored to patients' unique needs and to give refugee and immigrant parents and their offspring the best opportunity to thrive.


INCARCERATED

Women represent a growing percentage of the U.S. prison population, with approximately 150,000 women incarcerated in 2020—a 475% increase since 1980 (Monazzam 2023). The impact of this is far reaching, as over half of women in prison have children under the age of 18, an estimated 3%–10% of incarcerated women are pregnant on admission to correctional facilities, and over 1,000 infants born to women in prison each year (Sufrin et al. 2019, Friedman et al. 2020, Sufrin et al. 2020a, 2021b). The aim of this section is to describe the psychiatric and psychosocial effects of incarceration and separation on perinatal patients and to demonstrate how perinatal support programs and interventions can help mitigate adverse psychiatric and obstetric outcomes in this population.

Incarcerated mothers have reported high rates of depression, substance use, and symptoms associated with thought disorders, with higher rates among those with a history of childhood physical abuse and parenting stress.

Risk of Mental and substance use disorders in Incarcerated Perinatal Patients

Incarcerated pregnant women are a particularly vulnerable population. The majority are from minority groups with low preincarceration rates of access to healthcare and higher rates of substance use, trauma, and poverty (Sufrin et al. 2015, Schlafer et al. 2019, Sufrin et al. 2019, Dargis et al. 2021). Studies have found low rates of screening for perinatal mood and anxiety disorders in the incarcerated pregnant population, yet pregnant women currently or recently incarcerated have reported levels of perinatal anxiety, depression, and substance use—particularly alcohol and tobacco—of up to 80% (BOJ 2006, Huang et al. 2012, Mukherjee et al. 2014, Meine 2018, Morse et al. 2019, Zhao et al. 2019). Incarcerated mothers have reported high rates of depression, substance use, and symptoms associated with thought



disorders, with higher rates among those with a history of childhood physical abuse and parenting stress (Milavetz et al. 2020). In an evaluation of a prison-based pregnancy and parenting support program at a women's state prison (N=58), approximately one-third of incarcerated women who gave birth in custody reported moderate-to-severe depressive symptoms following delivery, with higher rates among women with longer periods of separation from their infant due to longer sentences following delivery (Howland et al. 2021).

Incarcerated mothers have reported high rates of depression, substance use, and symptoms associated with thought disorders, with higher rates among those with a history of childhood physical abuse and parenting stress.


When considering the prevention and treatment of perinatal mental and substance use disorders, incarceration itself should be considered a risk factor. Women exposed to incarceration personally or via their partners in the year prior to delivery may be less likely to initiate prenatal care in the first trimester, with up to half reporting no prenatal care prior to incarceration; significantly high rates of partner abuse before and during pregnancy; smoking during their last trimester of pregnancy; and prescription opioid use during pregnancy (Huang et al. 2012, Dumont et al. 2014, Dumont et al. 2015, Testa et al. 2022).

Since the 1976 US Supreme Court ruling *Estelle v. Gamble* established health care as a constitutionally protected right for incarcerated people, best practices and standards of care have been published by several national medical organizations, including the American College of Obstetricians and Gynecologists (ACOG) (American College of et al. 2021). However, due to lack of oversight, such as with mandatory accreditation, there is variability in the following of best practices and standards of prenatal care, and tension exists between the punitive nature of incarceration and the reality of correctional facilities as a healthcare safety net (Ferszt et al. 2012, Kelsey et al. 2017, Knittel et al. 2022a).

Although incarceration may increase access to prenatal care in this vulnerable population, incarcerated women face unique challenges, such as the use of shackling in a population with high rates of past trauma and inadequate access to recommended nutrition, medication for opioid use disorders (MOUD), and comprehensive mental health care (Nair et al. 2021). In addition, despite the fact that more than three-quarters of incarcerated women are of child-bearing age, pregnancy screening on entry is not guaranteed, which may also delay prenatal care (Kelsey et al. 2017).

Anti-Shackle Legislation

Despite concerns that restraints in the form of handcuffs, belly chains, and leg shackles may endanger the health of the mother and child, they are still routinely used in practice during pregnancy, childbirth, and the postpartum period (Ferszt et al. 2012). Although there are exceptions allowing them for a perceived safety threat, healthcare workers may use them because of perceived facility rules or protocol for the care of incarcerated pregnant women (Goshin et al. 2019). The use of handcuffs are the most common, and incarcerated women in their first trimester are more likely to be shackled (Thomas et al. 2017). Societal attitudes including stigma and distrust have been found to impact treatment of incarcerated pregnant women, who may receive inconsistent treatment by both healthcare professionals and prison workers (Ferszt et al. 2012, Zust et al. 2013, Suarez 2021, Knittel et al. 2022a, Kramer et al. 2023). In addition,



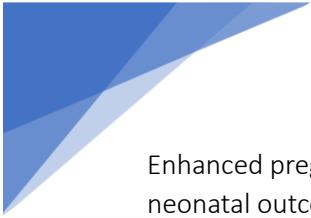
recommended nutrition, adequate rest, and attention to comfort, such as having a lower bunk, double mattress, and female identifying correction officer, are not guaranteed. Parenting and opportunities to facilitate early attachment are impacted by the availability of parenting units for pregnant women with extended, child-friendly visits, and women have reported few opportunities to foster connection with their children while incarcerated (Kennedy et al. 2020, Pendleton et al. 2021, Kramer et al. 2023).

Substance Use Disorders

Prenatal substance use exposure may be higher in infants born to incarcerated women, with a retrospective cohort study finding incarcerated women more likely to report prenatal alcohol and benzodiazepine use than nonincarcerated women (Drago et al. 2022). Illicit drug use, such as opioid use disorder, was reported by up to 36% of pregnant inmates in one study (Mukherjee et al. 2014). For infants experiencing neonatal abstinence syndrome (NAS), incarcerated mothers may be removed from them—prior to when symptoms of NAS peak and maternal support is needed—to return to prison. A retrospective cohort study of incarcerated pregnant people with opioid use disorder (N=279) found that only 40% received MOUD, and less than one-third (30%) were referred to a community practitioner to continue treatment on release (Knittel et al. 2022b). Jails and prisons require licenses to operate as healthcare facilities to provide evidence-based MOUD for pregnant women with opioid use disorder, and studies have found variability in screening for opioid use disorder, a lack of provision of MOUD for incarcerated pregnant women who enter jail on treatment or are initiated on it for opioid withdrawal, and treatment is often discontinued during the postpartum period and upon reentry to the community (Friedmann et al. 2012, Williams 2018, Peeler et al. 2019, Ahlbach et al. 2020, Sufrin et al. 2020b, King et al. 2021, Sufrin et al. 2022). Treatment has also been found to vary by region, with Northeast facilities and metropolitan settings more likely to provide MOUD in incarcerated pregnant women compared to jails in the South.

Impact of Incarceration on Attachment and Parenting

The impact of incarceration on the mother–baby dyad and parenting has been well-documented. Prior to incarceration, women are more likely to have custody and be primary caregivers of their children compared to men, and their children are often placed with maternal relatives, particularly grandparents, or in the foster care system during incarceration (Kubiak et al. 2012, Pendleton et al. 2021, Rose et al. 2022). For those with subsequent criminal justice involvement, the majority retain legal custody and only felony arrest is a significant predictor of foster care involvement (Kubiak et al. 2012). Incarcerated mothers have reported feelings of guilt, shame, inadequacy, and incompetence as a parent that is compounded by hardship in providing for their children on release (Dargis et al. 2021, Rose et al. 2022). The impact on attachment may be exacerbated by the incarcerated parent’s own experience of separation from their caregiver as a child and insecure attachment. Barriers such as distance, variability in visitation and contact policies, and caregiver of the children may pose significant barriers to parenting while incarcerated (Dargis et al. 2021). In addition to their mental health impact, stressors related to parenting have been associated with greater difficulty adjusting to the prison environment and misconduct. Studies have shown infants of incarcerated women are significantly less likely to be fed breastmilk and have longer unadjusted lengths of stay following delivery than infants born to unincarcerated women (Dumont et al. 2014, Drago et al. 2022, Schmitt et al. 2022, Wouk et al. 2022).



Enhanced pregnancy services, such as doula support, have been proposed to improve maternal and neonatal outcomes among incarcerated pregnant women (Dahl et al. 2020, Shlafer et al. 2021). Women who received evidence-based lactation support in the prenatal period from doulas were significantly more likely to initiate breastfeeding. Although many prisons are supportive of breastfeeding and lactation among incarcerated women, there is inconsistent implementation of institutional practices and policies, and structural barriers and biases may be a factor (Asiodu et al. 2021).

In addition to job training, educational support, anger management, and substance abuse programs, parenting classes and non-parenting programs that incorporate issues involving family may have a positive impact on self-confidence and self-efficacy (Gilham 2012, Tenkku Lepper et al. 2018, Koons-Witt et al. 2021, Phillips et al. 2022). Parenting classes that aim to help manage distress related to separation from children and improve communication with children and current caregivers may decrease distress and improve communication during incarceration (Loper et al. 2010).

Children who co-reside in prison nursery units during their first 18 months of life have been found to have significantly lower levels of anxiety and depression in preschool compared to children who lived with an alternate caregiver.

The impact of forced separation on early attachment has been in part mitigated by the implementation of prison nurseries in correctional facilities in at least 8 U.S. states (Carlson 2018). Children who co-reside in prison nursery units during their first 18 months of life have been found to have significantly lower levels of anxiety and depression in preschool compared to children who lived with an alternate caregiver (Goshin et al. 2014, Fritz et al. 2015). In addition, prison nursery programs may improve early attachment as well as reduce recidivism or return to prison custody (Byrne et al. 2010, Campbell et al. 2012, Carlson 2018, Tuxhorn 2021). Out-of-prison nursery programs, in which an incarcerated pregnant woman is transferred during her last trimester, are also emerging as programs to increase mother–infant attachment and bonding to impact child development (Kwarteng-Amaning et al. 2019). For prisons without prison nurseries, doulas may also provide support around separation following delivery (Shlafer et al. 2015).

Incarcerated women have reported that pregnancy and planning to breastfeed represents a new start in terms of motherhood, and prison nurseries may remove a barrier to breastfeeding—a potential component of maternal identity and attachment (Huang et al. 2012).

Policies and programs to support incarcerated pregnant women may include doulas, supplemental nutrition, work modifications, prenatal healthcare services, anti-shackling policies, adoption, and abortion services, parenting classes, prison nurseries, breastfeeding support, and parenting classes (Pendleton et al. 2020). Problem-solving parole courts, or Reentry Courts, have also been proposed as an alternate to traditional parole to aid in mother–child reunification (McGrath 2012, Western et al. 2018). Additionally, programs that help formerly incarcerated mothers secure stable housing may have a positive impact on close and regular contact between parents and children (McGrath 2012, Western et al. 2018). Finally, primary care clinics, which function as reentry transition clinics, may increase access to prenatal care following release (Morse et al. 2019).



Conclusion

The mental health and substance use disorder treatment needs of incarcerated perinatal persons are high. However, perinatal psychiatric screening and treatment are not routinely offered in U.S. prisons. Programs and policies that reduce separation between mothers and offspring, promote mother–child bonding, and increase access to supportive perinatal care (e.g., via doulas, breastfeeding support, visitation rights) while incarcerated could help mitigate the risk of adverse psychiatric outcomes and improve obstetric and fetal outcomes.

INFERTILITY


Depression, anxiety, and emotional distress are prevalent in patients experiencing infertility. Some studies estimate that up to 19.5% of women and nearly as many men undergoing infertility treatment are diagnosed with a psychiatric disorder (Bhat et al. 2016). In another study, 40% of women and about 15% of men met criteria for MDD during treatment (Holley et al. 2015). Patients may also experience anger, shame, stigmatization, loneliness, relationship strains, and trauma especially when there is pregnancy loss. This section calls greater attention to these risks and underscores the importance of support, screening, and access to care for patients experiencing infertility and undergoing assisted reproductive technology (ART).

Psychiatric Outcomes of Infertility and ART

Poorer quality of life, along with increased anxiety and depression, are commonly reported in patients who experience infertility, are undergoing in vitro fertilization (IVF) treatment, or have difficulty maintaining a pregnancy (Ross et al. 2011, Gourounti 2016, Stevenson et al. 2016, Boulet et al. 2017, Crawford et al. 2017, Swift et al. 2021). During treatment, fertility medication (i.e., clomiphene, letrozole, and gonadotropins) has the potential to affect mood, although published studies on this relationship are limited (Stenbaek et al. 2015, Gonzalez-Rodriguez et al. 2020). In a small study of women undergoing their first ART cycle (N=83), women with state neuroticism were more susceptible to mood fluctuations and emotional distress during ART, regardless of the type of gonadotropin-releasing hormone agonist or antagonist received (Stenbaek et al. 2015). Causes of infertility include diminished ovarian reserve, hyperprolactinemia, anatomical problems, cancer, low body mass index, poor nutrition, and polycystic ovary syndrome. Some of these conditions, such as polycystic ovary syndrome and cancer, may be independently associated with depressive symptoms (Dokras 2012).

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Patients may experience distress due to repeated intrusive procedures and stressful waiting periods, including for pregnancy test results following embryo transfer. As ART is associated with twins or multiple births, patients may face additional obstetric complications, such as preterm birth, which in turn could



increase the risk of psychiatric distress. Trauma symptoms can be exacerbated in patients experiencing infertility who have previous trauma (Hahn et al. 2021). Pregnancy loss or unsuccessful IVF can lead to grief and regret that may be impactful enough to warrant emotional support interventions or formal counseling (McBain et al. 2019, Huang et al. 2022, Swift et al. 2022). During the 2019 pandemic, a substantial number of patients receiving IVF treatment also reported feeling distress and increased anxiety due to cancellations or delays in infertility treatments (Vaughan et al. 2020, Lawson et al. 2021).

During the postpartum period, patients who conceive via infertility treatment do not appear to be at an elevated risk of postpartum depression (PPD) compared with those who conceive naturally. However, depression and anxiety symptoms may be more concentrated during pregnancy in patients who had recurrent failed cycles of treatment. It has also been suggested that postpartum depression may differ based on type of treatment, but data on this relationship are sparse. For instance, in the 2012-19 Pregnancy Risk Assessment Monitoring System, conceiving via fertility-enhancing drugs only was associated with an increased risk of postpartum depression symptoms versus conceiving via ART (OR 2.00, 95% CI 1.24–3.24, $P < 0.01$) (Barber et al. 2022). Factors such as neonatal intensive care unit stay, smoking, stressful life events, and unintended pregnancy do appear to increase the odds of developing postpartum depression (Lynch et al. 2014a).


Among couples experiencing infertility, discord and sexual dysfunction may be present. Similarly, depressive and anxiety symptoms are often higher in couples—and in women in particular—who are unable to conceive (Pasch et al. 2016). Despite this, couples are not routinely referred to psychiatric services or referred for counseling/couples therapy (Wichman et al. 2011, Pasch et al. 2016, Pasch et al. 2017).

Stress and Infertility

Whereas infertility can cause stress, evidence is unclear whether stress can cause infertility (Matthiesen et al. 2011, Rooney et al. 2016, Nicoloro-SantaBarbara et al. 2018, Purewal et al. 2018, Gleason et al. 2021, Negris et al. 2021). Proposed mechanisms include physiologic changes associated with the depressed/stressed state, such as perturbation of the hypothalamus-pituitary-adrenal axis, elevated prolactin levels, and thyroid dysfunction. It is also uncertain whether psychiatric illness—including in the father—affects infertility. In a secondary analysis of data from 2 large randomized trials of couples undergoing non-IVF infertility treatment ($n=1,650$ women, $n=1,608$ men), women with infertility who had male partners with active MDD experienced decreased pregnancy rates (RR 0.44; 95% CI 0.20–0.98) (Evans-Hoeker et al. 2018). However, this relationship was not observed among women with active MDD. The relationship between PTSD and time to conception has also been investigated but is not conclusive (Wamser-Nanney 2020).

Male infertility comprises a significant number of infertility cases, but their experience of loss is not as well-studied and requires further research.

Researchers have attempted to identify reliable markers of stress (e.g., allosteric load, oxidative stress, cytokine levels, salivary cortisol/alpha amylase) on pregnancy outcomes for individuals undergoing infertility treatment, but these have been performed mostly in small samples and are inconclusive. Such



biomarkers remain exploratory or academic in nature and cannot currently be used to reliably predict psychiatric outcomes (Younis et al. 2012, Lynch et al. 2014b, Barrett et al. 2018, Haimovici et al. 2018).

Male infertility comprises a significant number of infertility cases, but their experience of loss is not as well-studied and requires further research (Petok 2015). Additionally, more research is needed regarding the psychiatric impact of male infertility on his partner's well-being and emotional functioning. There is also sparse literature on psychiatric outcomes of offspring conceived by infertility treatment (Kasman et al. 2020).

Cancer is a specific stressor that can compound the psychiatric effects of infertility. Patients with cancer often face the concomitant threat of infertility and can experience problems accessing psychiatric services even though depressive and anxiety symptoms commonly arise in the cancer population (Zebrack et al. 2013, Lawson et al. 2014). Stressful, time-sensitive decisions may include whether to pursue fertility preservation. The high cost of fertility preservation and lack of insurance coverage for these procedures are additional burdens that can negatively affect patients' mental health (Lawson et al. 2014). Counseling and/or consultation with a psychiatrist or other behavioral healthcare practitioner is recommended and may help increase life satisfaction, decrease emotional distress, and improve coping with decision-making processes (Deshpande et al. 2015).


Detecting Mental and substance use disorders During Infertility Evaluation

Patients with psychiatric symptoms may first present to nonbehavioral health practitioners, such as obstetricians, gynecologists, or fertility clinic practitioners (Greenwood et al. 2018). Psychiatric problems may be detected during the evaluation of the patient's infertility (Hanson et al. 2017). Although most reproductive healthcare practitioners acknowledge that psychiatric issues and distress can impact patients pursuing IVF, formal screening for depression and anxiety is not routinely performed. Reasons for this are unclear. In a cross-sectional exploratory study of healthcare practitioner perspectives on screening for psychological conditions in women with infertility (N=86), lack of time and lack of familiarity with treatment recommendations appeared to contribute to discomfort with screening (Hoff et al. 2018). Investigators noted that practitioners who did not screen were more often from private practice clinics as opposed to academic centers (Hoff et al. 2018).

Screening for substance use disorders in people undergoing fertility treatment is particularly important because substance exposure can impact ART and IVF success in addition to affecting patients' mental health and physical well-being.

Infertility evaluation may also lead to discovery of an eating disorder given that excessively low or high body mass index can decrease chances of conceiving and carrying to birth (Langley 2014, Micali et al. 2014, Cousins et al. 2015, Hecht et al. 2022). Encouragingly, a meta-analysis of 5 studies found patients recovered from anorexia nervosa do not have different odds of childbirth than the general population (Chaer et al. 2020).

Screening for substance use disorders in people undergoing fertility treatment is particularly important because substance exposure can impact ART and IVF success, in addition to affecting patients' mental



health and physical well-being. Some patients may be at an increased risk for self-medicating depression, anxiety, and distress in general with substances (Wright 2017). Recent studies on substance use in individuals undergoing infertility treatment have focused on the impact of caffeine, alcohol, tobacco, cannabis, and opioids, as per the following:

- Caffeine: In most studies, consumption of caffeine does not have definitive effects on IVF outcomes, such as live birth rate or conception (Abadia et al. 2017, Minguez-Alarcon et al. 2018).
- Alcohol: Evidence generally suggests adverse effects of alcohol use on IVF outcomes. Although not conclusive, it is typically recommended that patients avoid alcohol before ART and during pregnancy, given the risk of birth defects and fetal loss from other studies (Rossi et al. 2011, Rooney et al. 2014, Dodge et al. 2017, Minguez-Alarcon et al. 2018).
- Tobacco: There is compelling evidence that smoking tobacco adversely affects IVF outcomes, including live births per cycle, clinical pregnancy rate per cycle, number of retrieved oocytes, average fertilization rate, and miscarriage rates per pregnancy (Budani et al. 2018, Kasman et al. 2018, Zhang et al. 2018).
- Cannabis: Studies show mixed results as to the adverse effects of cannabis in fertility outcomes or conception, but because a number of adverse obstetric outcomes have been observed in pregnancy and given the potentially prolonged fetal exposure from cannabis stored in the tissues, patients should avoid cannabis during infertility treatment (Nassan et al. 2019).
- Opioids: A review of prescription opioid use during fertility treatment suggests an increase in pregnancy loss in the setting of acute opioid use; however, this remains inconclusive due to limited data and heterogeneity in methodology (Flannagan et al. 2020).

Interventions

Meeting the psychiatric needs of patients experiencing infertility involves optimizing both psychotherapy and pharmacotherapy (Roussos-Ross et al. 2018). This section primarily covers psychotherapy and other nonpharmacologic interventions. For a discussion of the role of pharmacotherapy in managing perinatal mental and substance use disorders, see the clinical management section [Page 39].

Pharmacotherapy

Evidence on whether psychotropics affect fertility is not definitive. Antipsychotics have the potential of inducing hyperprolactinemia, which can lead to amenorrhea and menstrual cycle disruptions by affecting the hypothalamic-pituitary-gonadal axis (Edinoff et al. 2021). There are limited animal and human data suggesting adverse effects of psychotropics on sperm parameters, such as quantity and mobility (Worly et al. 2015). In trials with participants undergoing non-IVF infertility treatment, antidepressants other than selective serotonin reuptake inhibitors were associated with higher rates of first trimester pregnancy loss, but data were not conclusive and absolute number of miscarriages were small (Evans-Hoeker et al. 2018). Healthcare practitioners also should consider that exacerbation of psychiatric illness by stopping psychotropic medication may lead to patients dropping out of infertility treatment and that untreated or poorly controlled psychiatric symptoms can increase the risk of adverse obstetric and fetal outcomes [Page 20].



Communication, Counseling, and Other Nonpharmacologic Interventions

Patients experiencing infertility may derive some relief of anxiety and distress with even brief contact with their physician after embryo transfer. Enabling self-compassion and encouraging expression rather than suppression of emotions also can be beneficial (Steuber et al. 2015, Hoyle et al. 2022, Shah et al. 2022). Feedback from healthcare practitioners suggests improvements are needed in patient communication, including communicating the uncertainty of treatment success, treatment duration, and costs. In some instances, clinician awareness of their own feelings towards the success of the procedure could be useful in enhancing patient support (Klitzman 2018).


Studies support the integration of psychiatric support and psychiatric/behavioral healthcare practitioners into infertility treatment teams.

Psychological counseling and emotional support are important for patients struggling with infertility. A meta-analysis of psychological interventions for women experiencing infertility (N=2,752) found group psychological interventions were associated with improvements in depression, anxiety, infertility stress, and relationship strain (all P's=0.000) (Warne et al. 2022). In some studies, there was also an association with improvements in rates of conception and group psychological treatment (OR 2.42, 95% CI 2.03–2.87, P=0.000), although the mechanism of action is unclear (Warne et al. 2022). Another meta-analysis of psychological interventions for individuals with infertility (N=58 studies from around the world) found the relationship between treatment and outcomes was moderated by geographic location, with the largest effects reported in studies in the Middle East (Hedge's $g=1.40$ vs $g=0.23$ among studies outside the Middle East, $P<0.001$) (Dube et al. 2023). However, studies were likely confounded by bias and evidence was rated as low to moderate.

Studies support the integration of psychiatric support and psychiatric/behavioral healthcare practitioners into infertility treatment teams (Polshuck et al. 2014, Domar 2015). Mobile apps and online applications could potentially help increase access to care and decrease psychological distress during infertility treatment; however, rigorous data on the efficacy of digital treatments are sparse (Meyers et al. 2021).

For couples experiencing infertility, some studies showed improvements in depression and anxiety with cognitive-behavioral therapy (CBT) (Peterson et al. 2011, Abdollahpour et al. 2022). However, degree of effectiveness was often difficult to ascertain due to methodological variation. Additional interventions—including CBT, mind–body interventions, group psychotherapy, acceptance and commitment therapy, and emotionally focused couples therapy—have been proposed for couples during critical times, such as while awaiting pregnancy result after embryo transfer (Peterson et al. 2011, Ying et al. 2016, Brigance et al. 2020).

Finally, complementary interventions, such as acupuncture, have been linked to improved emotional well-being for individuals undergoing infertility treatment (Clark et al. 2013c, Hullender Rubin et al. 2022). Music therapy, yoga, and other mind–body interventions also have been associated with reduced psychological distress (LoGiudice et al. 2018, Mahmoud et al. 2022). However, heterogeneity between



studies and confounding factors need to be addressed in future research before firm conclusions can be made about their efficacy.

Disparities in Infertility Treatment Access and Ethical Dilemmas

More research is needed examining barriers to infertility treatment for individuals who desire it and the psychiatric effects of being unable to obtain treatment. In some studies, patients who pursued and had access to infertility treatment generally reported better life satisfaction and self-esteem than those who did not seek treatment, despite the potential for loss and failure (Greil et al. 2011, McCarthy et al. 2011). These disparities may also depend on socioeconomic, educational, cultural, and demographic factors. According to the National Survey of Fertility Barriers (N=4,712), over half (58.1%) of women in need of infertility treatment do not actually meet with a physician to discuss infertility (Greil et al. 2016). Because most studies about infertility are conducted among fertility clinic populations, the struggles of patients with infertility who do not or cannot seek fertility help may not be as well-represented in the current literature.

Healthcare practitioners should be mindful of ethical situations related to infertility treatment that could have psychiatric repercussions, such as high-order multiple births, egg freezing and egg banking, and third-party preproduction.


Healthcare practitioners should be mindful of ethical situations related to infertility treatment that could have psychiatric repercussions, such as high-order multiple births, egg freezing and egg banking, and third party preproduction (Leyser-Whalen et al. 2012, Swanson et al. 2021). With more aggressive fertility treatment, the chances for higher-order births may increase, which may increase the risk of obstetric complications and in turn psychiatric distress (Hamilton et al. 2018). Egg banking or egg freezing, especially for nonmedical reasons (e.g., due to advancing age, due to desires to delay childbearing), has been the subject of ethical debate and could lead to patients experiencing distress or feelings of alienation (Robertson 2014, Harwood 2015, Borovecki et al. 2018).

Conclusion

Patients experiencing infertility, including those undergoing infertility treatment to conceive, face an elevated risk of psychiatric outcomes, including depression, anxiety, and general distress. Infertility treatments are complex, costly, and are often prolonged, with uncertain outcomes in terms of achieving pregnancy and childbirth. Healthcare practitioners should be vigilant for patients in need of treatment or referral—especially nonbehavioral healthcare practitioners, who are likely to be on the front lines of treating these patients and may be the first to recognize symptoms and need for care.

INTIMATE PARTNER VIOLENCE

Intimate partner violence (IPV)—defined by the U.S. Centers for Disease Control and Prevention (2022) as abuse or aggression occurring in the context of a romantic relationship—is a serious and pervasive public health problem. For the subset of persons who experience IPV during the perinatal period, IPV carries a



risk of substantial physical and psychological harm not just to the victim but the fetus and infant as well. Pregnancy is a vulnerable time in which IPV often begins or increases in severity and frequency, yet perinatal IPV remains underdetected. This section aims to help behavioral healthcare practitioners better understand the crucial role they play in early identification and intervention. In addition to offering (or referring patients to) formal psychiatric treatment for mental and substance use disorders and impairing symptoms, practitioners can leverage multiple strategies to help educate, support, and empower individuals experiencing perinatal IPV to enhance their safety and well-being.

Epidemiology of Perinatal IPV


IPV includes a wide range of violent, abusive, controlling, or aggressive behaviors, such as physical violence (e.g., striking, slapping, pushing), sexual abuse (e.g., attempted or completed rape), stalking (e.g., obsessive unwanted attention or contact), emotional abuse (e.g., insults, coercion), and efforts to control or manipulate a birthing person's reproductive health (e.g., refusal to wear a condom, attempting to impregnate a person who does not want to be pregnant) (Chisholm et al. 2017, Hahn et al. 2018). Meta-analyses of worldwide rates of IPV during pregnancy indicate that, in North America, the prevalence of any IPV is approximately 20%, IPV involving physical violence is 9%, psychological abuse is 29%, and sexual abuse is 9% (Roman-Galvez et al. 2021). In the US specifically, rates range from approximately 9% to 15% for all types of IPV during pregnancy, 21% for IPV at 3 months postpartum, 16% at 6 months postpartum, 18% at 12–18 months postpartum, and 13% at 24 months (Mojahed et al. 2021).

Mental Distress and Other Consequences of Perinatal IPV

Perinatal IPV is associated with numerous adverse mental health outcomes during pregnancy and postpartum, including substance misuse and substance use disorders, eating disorders, sleep-wake disorders, depression, OCD, and PTSD (Desmarais et al. 2014, Chisholm et al. 2017, Hahn et al. 2018). Other mental health-related outcomes include low self-esteem, suicidal ideation, and suicide attempt (Alhusen et al. 2015b, Chisholm et al. 2017, Campbell et al. 2021). Women exposed to perinatal IPV have triple the risk of being a victim of attempted or completed homicide compared with women who do not experience perinatal IPV (Hahn et al. 2018). Many women experiencing perinatal IPV have a lifetime exposure to IPV, which further increases the risk of poor mental health outcomes (Hahn et al. 2018). Perinatal IPV also is associated with general medical conditions that often have psychiatric comorbidities, such as chronic pain, which is associated with depression and substance use disorders, and irritable bowel syndrome and other gastrointestinal dysfunctions, which are linked to anxiety disorders (Alhusen et al. 2015b, Chisholm et al. 2017).

Perinatal IPV also is associated with general medical conditions that often have psychiatric comorbidities, such as chronic pain, which is associated with depression and substance use disorders, and irritable bowel syndrome and other gastrointestinal dysfunctions, which are linked to anxiety disorders.

Women exposed to IPV during and after pregnancy may engage in behaviors that can harm themselves and their fetus/infant, such as using tobacco or alcohol, missing perinatal care visits, failing to gain adequate weight during pregnancy, engaging in sexual risk-taking, and having poor nutritional intake



(Alhusen et al. 2015b, Chisholm et al. 2017). Consequently, perinatal IPV has been linked to multiple obstetric and birth complications, including utero-placental injury from hypothalamic-pituitary-adrenal axis dysregulation, vaginal bleeding, dehydration, membrane rupture, miscarriage, stillbirth, preterm birth, low birthweight, and small for gestational age (Alhusen et al. 2015b, Donovan et al. 2016, Chisholm et al. 2017, Hahn et al. 2018).

Risk Factors

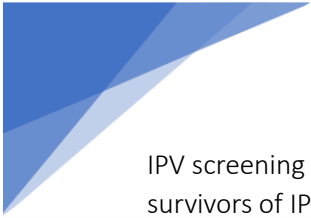
Women with a heightened vulnerability for perinatal IPV include those of younger age, women of color (especially non-Hispanic American Indian/Alaska Native and non-Hispanic Black women), those with unintended pregnancies, women from low socioeconomic backgrounds (e.g., Medicaid recipients), single women, and women with low educational attainment (Alhusen et al. 2015b, Bianchi et al. 2016, Chisholm et al. 2017).

In a nationally representative sample of women with pregnancy-related hospitalizations (Greely et al. 2022), IPV was most observed among non-Hispanic White and non-Hispanic Black women (56.7% and 17.6%, respectively). Non-Hispanic Black women had the highest risk of intrauterine fetal demise (odds ratio [OR] 7.69, 95% confidence interval [CI] 2.56–12.85), and Hispanic women demonstrated the highest risk of intrauterine growth restriction (OR 3.33, 95% CI: 1.47–7.14) and miscarriage (OR 12.5, 95% CI 4.55–23.33).

Racial and ethnic disparities also exist in fatal and nonfatal perinatal IPV, with women of color experiencing a greater risk of victimization versus non-Hispanic White women (Kivisto et al. 2022). For example, findings from the National Violent Death Reporting System show non-Hispanic White women who are pregnant are 2.7 times more likely to experience intimate partner homicide than non-Hispanic White women who are nonpregnant. However, Hispanic women who are pregnant have a 4.4 greater risk and non-Hispanic Black women have an 8.1 greater risk of intimate partner homicide than their nonpregnant cohorts (Kivisto et al. 2022).

Screening and Assessment

Although its prevalence and effects are well-documented, perinatal IPV is not universally screened for as a standard of care. Findings from the 2009–15 Pregnancy Risk Assessment Monitoring System (PRAMS) indicate that barely half (51%) of the pregnant women surveyed who reported perinatal IPV received healthcare practitioner counseling (Kapaya et al. 2019). Another study of PRAMS data, this time from 2016–19, found among all women surveyed who gave birth (N = 158,338), two-thirds (66%) were not screened for IPV prior to pregnancy, 30% were not screened during pregnancy, and 48% were not screened postpartum (Kozhimannil et al. 2023). Reasons for not receiving an IPV screen were either because the woman did not attend a perinatal care visit or because she was not screened for IPV during the visit. Women who lacked perinatal health care visits were significantly more likely to be Spanish-speaking Hispanic, American Indian/Alaska Native, Medicaid recipients at childbirth, and without insurance at childbirth (Kozhimannil et al. 2023). Women who did attend perinatal care visits but were overlooked for screening were significantly more likely to be non-Hispanic White, rural residents, and with private insurance (Kozhimannil et al. 2023). Thus, both marginalized and advantaged persons are at risk for being overlooked for IPV screening during perinatal care visits.



IPV screening can effectively identify pregnant and nonpregnant women who are current victims or survivors of IPV (Chisholm et al. 2017, Force et al. 2018). Consequently, the U.S. Preventive Services Task Force recommends screening vulnerable adults—including women of reproductive age—for IPV (Force et al. 2018). The American College of Obstetrics and Gynecology also recommends screening for IPV during prepregnancy counseling sessions (American Society for Reproductive et al. 2019).

Both marginalized and advantaged persons are at risk for being overlooked for IPV screening during perinatal care visits.

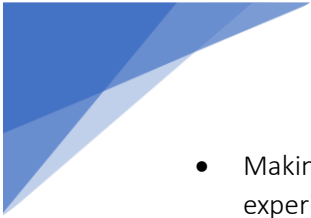
Although there is no consensus gold standard measure currently in place, there are several validated screening tools healthcare practitioners can use for rapid identification of perinatal IPV cases (Chisholm et al. 2017). These include the Abuse Assessment Screen: the Humiliation, Afraid, Rape, Kick measure; the Hurt/Insult/Threaten/Scream screener; the Extended Hurt/Insult/Threaten/Scream tool; the Partner Violence Screen; the Ongoing Violence Assessment Tool; and the Woman Abuse Screening Tool (Force et al. 2018, Hahn et al. 2018). Many of these assessments contain 5 or fewer questions and can be administered quickly and easily in busy clinical settings. Screening should occur at the first prenatal care appointment and during each trimester (Drexler et al. 2022).

Not all measures will assess for all forms of IPV, especially reproductive coercion, and thus may need to be supplemented with additional questions (Hahn et al. 2018). Questions about IPV should address specific behaviors (e.g., “Has your husband ever forced you to have sex with him when you did not want to?”) rather than be vague and general (e.g., “Does your boyfriend ever mistreat you?”) (Hahn et al. 2018). Many screening tools are also heteronormative and have been largely validated in mostly White populations/Anglo cultures (Hahn et al. 2018). Clinicians should be mindful of the need to supplement with questions adapted to the woman’s relationship and culture. Further, women from marginalized groups—such as racial/ethnic, gender, and sexual minorities—might feel mistrustful of law enforcement and the healthcare system and thus feel hesitant to disclosure IPV, either verbally or through screeners (Rodriguez et al. 2009, Hulley et al. 2023).

Patients who screen positive for IPV need assistance with safety planning, especially those in imminent danger (Bianchi et al. 2016, Hahn et al. 2018). Effective safety planning includes strategies for how to stay safe within a relationship (e.g., finding safe spaces within the home/having an escape plan), how to safely exit a relationship (e.g., identifying a local women’s shelter or other safe housing), and how to maintain safety after leaving a relationship (e.g., how to file a restraining order/order of protection) (Hahn et al. 2018).

Healthcare settings and practitioners can help improve screening practices and remove barriers to screening by (Bianchi et al. 2016):

- Developing clearly articulated written policies about the routine use of perinatal IPV screening, including which screening tools will be used and when screening will be conducted;
- Creating written procedures for how screening will take place and what follow-up should be taken for patients who screen positive (e.g., identify community support agencies for referral);
- Teaching staff about how to create safety plans with patients who screen positive;

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- Making sure the healthcare setting is a safe environment conducive to patients disclosing their experiences with IPV (e.g., building trust and rapport with patients, learning empathic listening skills, using a culturally sensitive and culturally responsive approach to care);
 - Ensuring healthcare practitioners receive clinical guidelines and recommendations from federal agencies and women’s health experts about the importance of perinatal IPV screening; and
 - Where possible, incorporating perinatal IPV screening into staff training opportunities to ensure they are knowledgeable about signs and symptoms of perinatal IPV.

Treatment Approach

As noted earlier, women experiencing perinatal IPV have an elevated risk of psychiatric illness, including anxiety disorders, depression, OCD, and PTSD (Desmarais et al. 2014). Given this, there may be a high need for formal psychiatric treatment or psychological counseling among this population. In addition to providing evidence-based care for specific mental disorders, clinicians should offer patient-centered, tailored, multicomponent interventions for IPV that involve education about IPV and its effects, safety planning, instrumental support (e.g., connecting patients to IPV-related resources and social services), and goal setting (Jack et al. 2019, Tobin-Tyler 2022). Clinicians should also prioritize creating care environments that are conducive to perinatal patients feeling comfortable seeking treatment for IPV—specifically, settings that convey empathy, support, warmth, privacy, and trust for all patients regardless of their socioeconomic status, demographics, or life circumstances (Tobin-Tyler 2022).

Treatment for patients experiencing perinatal IPV should take a trauma-informed approach that ensures their safety, confidentiality, and privacy (Drexler et al. 2022). Trauma-informed cognitive-behavioral therapy and standard cognitive-behavioral therapy have demonstrated effectiveness among women experiencing IPV (Hameed et al. 2020, Jackson et al. 2020), but more research is needed to determine outcomes in perinatal populations specifically (Jackson et al. 2018).

Treatment for patients experiencing perinatal IPV should take a trauma-informed approach that ensures their safety, confidentiality, and privacy.

A systematic review of interventions for IPV during pregnancy found home visitation and supportive counseling programs helped reduce the odds of physical, emotional, and sexual IPV (ORs range 0.47–0.92), with multifaceted interventions showing greater effects than single interventions (Van Parys et al. 2014). Empowerment-based interventions have also shown promise. For example, the Domestic Violence Enhanced Home Visitation Program (DOVE) is a brief empowerment intervention that uses community health nurse prenatal/postpartum home visitation (Sharps et al. 2016). It consists of six 15- to 25-minute sessions focused on education (e.g., the cycle of violence, risk factors for intimate partner homicide), safety planning, and locating community-based IPV resources. DOVE has been associated with a significant decrease in IPV from baseline to 24 months postpartum ($P < 0.001$), as measured by the gold standard Conflict Tactics Scale (Sharps et al. 2016). Other studies utilizing an empowerment approach that similarly emphasize education, safety planning, and autonomous decision-making have also shown to help decrease IPV over time (Chisholm et al. 2017). However, these studies are small in number, underscoring the importance of further developing the evidence base for perinatal IPV interventions.



Conclusion

The perinatal period is a time of increased vulnerability to IPV. Unaddressed IPV can have serious consequences for victims and their offspring, including attempted and completed suicide and homicide. Numerous validated screening tools exist to help healthcare practitioners better detect and actively respond to IPV in perinatal patients. Interventions should prioritize patient safety and comfort and, if needed, should include formal treatment (or referral to treatment) for mental and substance use disorders.

PREGNANCY LOSS

Pregnancy loss is a traumatic event associated with distressing emotions and mental disorders, which are often overlooked in the clinical picture. Some of the major psychological effects of pregnancy loss include depressive disorders, anxiety disorders, posttraumatic stress disorder (PTSD), feelings of shame and stigma, and relationship strain. Although occurring frequently in the pregnant population, the psychiatric effects of pregnancy loss often are underrecognized and untreated, leaving parents without the necessary resources and support to ensure healthy coping in the aftermath of loss.


Patients benefit from healthcare practitioners who are engaged with them about the mental health aspects of their loss and are equipped with resources and tools to help them manage their grief and other psychosocial sequelae.

Whereas grief is an expected response to loss, it is important to identify those persons for whom symptoms become overwhelming, disruptive, and impairing or are otherwise in need of treatment. The aim of this section is to help clinicians recognize the risk factors that may contribute to negative psychiatric and psychosocial outcomes in this population as well as how to intervene if psychiatric screening and intervention are needed. Patients benefit from healthcare practitioners who are engaged with them about the mental health aspects of their loss and are equipped with resources and tools to help them manage their grief and other psychosocial sequelae.

Terminology

The term pregnancy loss broadly refers to loss of a fetus due to spontaneous abortion or miscarriage (Prager et al. 2021). The American College of Obstetrics and Gynecology (ACOG) defines early pregnancy loss as that occurring at less than 20 weeks gestations (American College of et al. 2018, Dugas et al. 2023). Pregnancy loss occurring at 20 weeks or later is considered late pregnancy loss. About one-quarter (26%) of all pregnancies and 10% of all clinically recognized pregnancies end in miscarriage (American College of et al. 2018, Dugas et al. 2023).

For the purposes of this section, pregnancy loss will also include stillbirths and neonatal deaths. Stillbirth, also sometimes termed fetal death, refers to delivery of a fetus lacking any signs of life, marked by an absence of breathing, pulsation of the umbilical cord, or purposeful movements of voluntary muscles (American College of et al. 2020). Stillbirths are also relatively common, occurring in approximately 1 out



of every 160 deliveries in the US (American College of et al. 2020). Approximately 23,600 stillbirths at 20 weeks of gestation or later occur each year (American College of et al. 2020). The World Health Organization defines neonatal death, also sometimes called newborn death, as death occurring within the first 28 completed days of life, with early neonatal death occurring between days 0–7 of life and late neonatal death happening between days 7–28 (Pathirana et al. 2016). Almost three-fourths (73%) of neonatal deaths occur in the first 7 days of life (Pathirana et al. 2016).

Finally, this section also includes in the discussion of pregnancy loss the death of a fetus due to therapeutic abortion. Therapeutic abortion refers to termination of pregnancy due to medical necessity (Watson 2018).

Psychiatric Effects of Pregnancy Loss


Pregnancy loss is associated with a significant increase in the odds of certain mental disorders and symptoms, including but not limited to depressive disorders, anxiety disorders, and PTSD (Gold et al. 2014, Daugirdaite et al. 2015, Gold et al. 2016, Christiansen 2017, Hunter et al. 2017, Farren et al. 2018, Westby et al. 2021, Herbert et al. 2022).

Numerous systematic reviews and meta-analyses confirm the relationship between pregnancy loss and an increased risk of psychiatric outcomes. A systematic review and meta-analysis of mental health sequelae of perinatal loss found, compared to controls, a 2.14 increased risk of depressive disorders ($P < 0.001$) and a 1.75 increased risk of anxiety disorders ($P < 0.001$) (Herbert et al. 2022). A systematic review of mental health outcomes (in parents after stillbirth similarly found a significantly higher risk of short- and long-term depression, anxiety, and PTSD compared with controls (relative risk [RR] ranged 1.74–6.70), in some cases up to 3.5 years following the stillbirth (Westby et al. 2021).

Parents who experience pregnancy loss may report feeling stigma, shame, and pressure from society not to talk about the loss openly but rather to keep their feelings and experiences a secret, which can intensify their grief and loneliness.

Also common in pregnancy loss are psychosocial sequelae that do not rise to the level of a clinical mental disorder but nonetheless can be impairing or distressing, and thus could be a reason for seeking formal treatment, support, and/or resources. For instance, following stillbirth, parents often experience a complex range of difficult emotions and stressors, such as anxiety over surviving children in the family, avoiding or suppressing grief, chronic pain and fatigue, having difficulties at work (and as a result, financial challenges), negative changes in one's body image, reduced quality of life, and increased substance use (Burden et al. 2016). Parents who experience pregnancy loss may report feeling stigma, shame, and pressure from society not to talk about the loss openly but rather to keep their feelings and experiences a secret, which can intensify their grief and loneliness.

Data from the National Survey of Family Growth shows the experience of miscarriage or stillbirth significantly increases the risk of a relationship dissolving compared with pregnancies that end in live birth (hazard ratio [HR] 1.22–1.40, P-value ranges 0.001–0.007) (Gold et al. 2010). In another nationally representative survey of 3,461 women who had ever been previously pregnant and married, women with



a history of stillbirth were significantly more likely to be divorced, separated, or widowed at the time of interview than women who had experienced live births ($P < 0.01$) (Shreffler et al. 2012).

Risk Factors

Multiple contributors increase the likelihood of mental distress following pregnancy loss. Among the most common predictors is prior pregnancy loss, which greatly increases the odds of developing depression, anxiety, and PTSD following a subsequent lost pregnancy (Giannandrea et al. 2013, Nynas et al. 2015). A perceived lack of paternal support is associated with a 4 times higher risk (adjusted OR 4.67, 95% CI: 2.73–8.00) of experiencing depression or anxiety following stillbirth compared with receiving paternal support (Lewkowitz et al. 2022). Other risk factors include a history of infertility or multiple previous attempts to conceive, pregnancy loss at a later gestational stage, not having any living children, social isolation, positive psychiatric history, preexisting relationship strain/low satisfaction with the relationship, and lacking good coping skills (Nynas et al. 2015, Farren et al. 2018). Demographically, miscarriage has been associated with greater rates of depression among younger women, women of color, and women from lower socioeconomic backgrounds (Nynas et al. 2015, Farren et al. 2018). For example, the risk of depression following pregnancy loss is more than 2 times higher for Black women compared with non-Black women (adjusted OR 2.48, 95% CI: 1.28–4.81) (Shorter et al. 2021).


Demographically, miscarriage has been associated with greater rates of depression among younger women, women of color, and women from lower socioeconomic backgrounds.

Unique Populations

For certain populations, the traumatic experience of pregnancy loss, and the inability to seek services to help cope with such loss, may be compounded by additional stressors and barriers, such as those related to their marginalized status in society. Understanding the unique needs and challenges faced by special populations could inform the development of tailored interventions and services as well as a heightened awareness among healthcare practitioners of the need to screen and, if appropriate, treat (or offer referrals to) these patients.

For example, among lesbian, gay, bisexual, transgender, queer, and other sexual and gender minority patients, access to mental health services and social support can be limited due to stigmatization within the healthcare system and society as a whole (Lacombe-Duncan et al. 2022). Inequalities exist in the availability and accessibility of pregnancy loss services for other marginalized populations as well, including rural dwellers and people from low-income backgrounds (Domogalla et al. 2022). Black women often experience race-related stressors that can hinder their ability to seek and access formal treatment for pregnancy loss, such as discrimination and bias from healthcare practitioners (Langley-Evans et al. 2022). A qualitative study of Black urban women with recent pregnancy loss noted the importance of receiving support from other Black women who had experienced the same loss, as well as the perceived benefits of relying on spiritual beliefs to cope with their trauma (Fenstermacher et al. 2019).

Scant literature addresses fathers' experiences of pregnancy loss, and, not surprisingly, existing studies note a lack of grief-related resources for men (Horstman et al. 2021, Robinson et al. 2022). Thus, it is



imperative that healthcare practitioners avoid handling pregnancy loss as solely a “woman’s issue” (Horstman et al. 2021).

Psychiatric Evaluation and Monitoring Following Pregnancy Loss

Healthcare practitioners play a pivotal role in recognizing and addressing mental health needs following pregnancy loss. They should be highly vigilant for mental health struggles following pregnancy loss, especially in high-risk patients, and can engage with patients by proactively asking about their mental health symptoms and needs, reviewing patients’ medical charts for past trauma (including previous pregnancy loss), and providing education, resources, and referrals (Nynas et al. 2015, Panches et al. 2019, Wool et al. 2019, Davoudian et al. 2021).

Validated screening tools, such as the Patient Health Questionnaire-2 for assessing depression, can be easily integrated into busy clinical scenarios and offer healthcare practitioners a quick and simple way to determine whether formal mental health evaluation is warranted.


Primary and specialty care practitioners (e.g., emergency department healthcare practitioners) should be suspicious of and proactively screen for mental disorders and symptoms in patients who have recently experienced pregnancy loss, as this can help reduce treatment delay (Grauerholz et al. 2021). Validated screening tools, such as the Patient Health Questionnaire-2 for assessing depression, can be easily integrated into busy clinical scenarios and offer healthcare practitioners a quick and simple way to determine whether formal mental health evaluation is warranted (Nynas et al. 2015). For validated assessments specific to grief from pregnancy loss, healthcare practitioners should consider administering the Perinatal Grief Scale, which is widely used and has been translated into multiple languages, and the Perinatal Grief Intensity Scale, which has not been used as extensively but is validated, short, and easy to score (Setubal et al. 2021).

Treatment Approach

Despite the overwhelming evidence on the deleterious psychiatric effects of pregnancy loss, these issues remain largely underrecognized by the healthcare system and society at large and untreated by healthcare practitioners. For instance, even when miscarriage aftercare services are present, they generally do not address bereavement, trauma, and other psychiatric sequelae (Ho et al. 2022).

Evidence from randomized controlled trials on nonpharmacologic interventions for mental disorders and symptoms following pregnancy loss is lacking (Murphy et al. 2012, San Lazaro Campillo et al. 2017). Qualitative research, observational studies, and literature reviews inform much of what is known about effective interventions. Successful strategies typically include (Randolph et al. 2015, Cuenca 2022, Jones et al. 2022b, Schoonover et al. 2022):

- Validating parents’ experiences and emotions through empathy, support, and normalizing their reactions;
- Helping parents process their grief and find healing through bereavement care, including helping them identify outlets for them to share their grief verbally and/or in writing;

- 
- Where appropriate, including the partner in pregnancy loss services;
 - Facilitating parents' access to community support resources (e.g., support groups) and interpersonal support systems (e.g., family, friends), especially resources that are specific to pregnancy loss rather than bereavement support in general;
 - Connecting parents with other individuals with a lived experience of pregnancy loss;
 - Providing education about grief and different grieving styles; or
 - Encouraging parents to identify and engage in remembrance activities, if desired.

Psychoeducation is also an important intervention for this population (Ho et al. 2022). Research suggests patients who have experienced pregnancy loss desire information about why their miscarriage or stillbirth occurred and its potential impact on future pregnancies (Nynas et al. 2015, Ho et al. 2022). Patients can also benefit from discussions about stigma and self-blame, which are common experiences and, if unaddressed, can exacerbate feelings of grief, depression, and trauma.

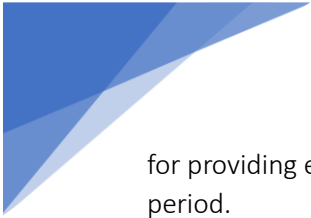
Finally, a trauma-informed approach to care should be considered, meaning one that emphasizes making patients feel safe to express their emotions and share their experiences; maximizes patient treatment choice and privacy; offers peer support as a form of collaboration with others with the shared experience of pregnancy loss; helps patients feel empowered and build resilience; and discusses ways patients can manage and overcome stigma (Cahill et al. 2021). Regardless of the interventions used, practitioners are also encouraged to take an interdisciplinary approach that involves collaborative care from obstetricians and gynecologists, primary care practitioners, nurses, psychiatrists, psychologists, and social workers. Although not all healthcare facilities are adequately resourced for this approach, doing so when possible, can help ensure patient-centered, family-oriented, holistic, and comprehensive care is provided (Kobler et al. 2011, Hiefner et al. 2021).

Conclusion

Pregnancy loss is a devastating event that results in many patients (and their partners) needing aftercare to help manage mental disorders and symptoms as well as general feelings of distress. Despite the high need for intervention, patients experiencing pregnancy loss are an overlooked group who can benefit from better clinician attention to screening and treatment needs. Although the literature is sparse, evidence suggests there are many approaches healthcare practitioners can use to help patients and partners improve their psychiatric functioning and well-being.

SEXUAL AND GENDER MINORITY PERSONS

Surveys indicate that lifetime pregnancy among assigned female at birth (AFAB) sexual and gender minority (SGM) individuals is not an uncommon experience. In a survey of postmenopausal cisgender sexual minority women (n=93,311), reports of at least one prior pregnancy ranged from 35% (lesbians) to 81% (bisexuals) (Stoffel et al. 2017). Among assigned female at birth gender minority adults, 12-17% report prior pregnancy (Light et al. 2018, Moseson et al. 2021). For AFAB SGM individuals, the perinatal period can be a time of increased stress and complexity. The intersection of gender and sexual minority status with the biological and psychosocial changes inherent in the perinatal period can create unique mental health challenges. These may include fear of discrimination within healthcare settings, lack of support from family and community, and difficulty in reconciling identities as new parents with gender and sexual identities (Kirubarajan et al. 2022). Understanding these intersectional experiences is crucial



for providing effective, inclusive healthcare and support for AFAB SGM individuals during the perinatal period.

Pregnancy Intentions among SGM Persons


Among AFAB SGM persons, prevalence of adolescent and unintended pregnancy is consistently higher than among their heterosexual and/or cisgender peers (Lindley et al. 2015, Goldberg et al. 2016, Coble et al. 2017, Nahata et al. 2020). A longitudinal cohort study over two generations demonstrated that while teen pregnancy rates dropped in a single generation, sexual orientation disparities in teen hormonal contraception use and pregnancy have persisted across two generations (Charlton et al. 2013). Girls who identified as lesbian, bisexual, or questioning were significantly more likely to not be using a method of contraception (AOR, 2.61; 95% CI, 1.31e5.19) compared with girls who identified as heterosexual (McCauley et al. 2014). Data from the National Survey of Family Growth revealed that adolescents who identify as bisexual, ages 15-21, were three times more likely to seek termination of pregnancy, an indicator of unwanted pregnancy (Tornello et al. 2014a). A survey of AFAB gender minority adolescents (n=923) found that 26% experienced unintentional pregnancies compared to 12% among their cisgender peers, although the rate of reported contraception use is close to the national average of 62% (Veale et al. 2016, Light et al. 2018).

Several studies found higher rates of unwanted pregnancy endorsed by sexual minority compared to heterosexual women.

Heightened risk for unintended pregnancy persists among AFAB SGM adults. Several studies found higher rates of unwanted pregnancy endorsed by sexual minority compared to heterosexual women (McCauley et al. 2015, Everett et al. 2016, Everett et al. 2017). Systematic review of the rates of abortion between sexual minority and heterosexual women, however, yielded conflicting results (Hodson et al. 2017). Among gender minority adults, one study reported that 54% of prior pregnancies were unintended (Moseson et al. 2021). Misconceptions on the effects of testosterone on reproductive capability are among the risk factors for unintended pregnancy (Gomez et al. 2020, Krempasky et al. 2020). A survey of gender minority adults (n=1694) found that 19% had attempted to terminate a pregnancy without clinical supervision by means such as physical trauma and substance abuse, citing desire for privacy, cost, and prior mistreatment by healthcare professionals as factors influencing their decision (Moseson et al. 2022).

Perinatal Mental and Substance Use Disorders Among SGM Persons

SGM persons are more than twice as likely as their cis-gendered, heterosexual peers to experience depression, anxiety, trauma, and substance misuse in their lifetime (Bostwick et al. 2010, Gmelin et al. 2022). These disparities extend to the perinatal period. In one sample, over one-third (35.6%) of sexual minority women scored in the clinical range for perinatal depression on the Edinburgh Postnatal Depression Scale (Marsland et al. 2022). By comparison, the rates of depression among all women during pregnancy, the postpartum period, or both is estimated between 10-20% (Ko et al. 2017). History of victimization and trauma are also trend higher among SGM persons. For example, bisexual and lesbian women were more likely than heterosexual young women to report having been forced to have sex by a male partner. (Tornello et al. 2014b, Charlton et al. 2019).



Sexual minority women are more likely to report substance use—including binge drinking, smoking, and cannabis use—than heterosexual women prior to pregnancy (Limburg et al. 2020). Smoking during pregnancy is more common among sexual minority than heterosexual women (Hartnett et al. 2021). In a national study, sexual minority women had higher odds (AOR = 2.29, 95% CI = 1.61, 3.27) of using cigarettes during their third trimester of pregnancy when compared with heterosexual individuals in the fully adjusted models (Beck et al. 2021).

The prevalence of perinatal mental and substance use disorders among AFAB gender minorities is unknown. In general, due to the historical exclusion of SGM individuals in surveillance research, current estimates rates likely represent an underestimation of the real scope of perinatal mental health issues in this population.

Factors Influencing Perinatal Mental Health in SGM People

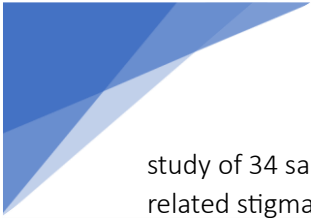
Several intertwined factors influence perinatal mental health in SGM person, including: 1) psychological factors, such as stress, trauma, and stigmatization; (2) social factors, such as support networks, acceptance, and societal attitudes; (3) healthcare disparities and discrimination; and (4) biological factors related to pregnancy itself (Kirubarajan et al. 2022).

Psychologically, SGM individuals often grapple with minority stress, a unique form of chronic stress related to experiences of stigma, prejudice, and discrimination. This stress can be exacerbated in the perinatal period, a time often associated with intensified gender roles and increased healthcare interactions. Sexual minority women report multiple barriers to becoming mothers, including the logistics of starting a family, financial strain of adoption and pregnancy, losing or lack of social and family support, unsupportive laws and politics, and fear of discrimination from society (Wall 2011).

Psychologically, SGM individuals often grapple with minority stress, a unique form of chronic stress related to experiences of stigma, prejudice, and discrimination. This stress can be exacerbated in the perinatal period, a time often associated with intensified gender roles and increased healthcare interactions.

Acceptance from family and friends, access to supportive networks, and the wider societal climate towards SGM people can significantly influence mental health outcomes. Positive social support can buffer against poor mental health, while discrimination and isolation (compromised social support) can increase risk. An investigation of posts from an online forum for lesbian mothers with postpartum depression identified several common themes, including feelings of invisibility and social rejection from heterosexism (Alang et al. 2015). A qualitative study of lesbian mothers with postpartum depression found increased experience of heterosexism/homophobia from healthcare practitioners and family as well as negative changes to the couple relationship (Maccio et al. 2012).

Largely ignored by research, co-parents may also experience perinatal distress. A study among 24 self-identified lesbian non-gestational mothers found the experience of preconception, pregnancy, and new motherhood for nonbiological lesbian mothers is complicated by the lack of biological and legal substantiation to the infant, few role models, and limited social support (Wojnar et al. 2014). In another



study of 34 same-sex female couples, among the pregnant mothers, personal experiences of sexuality related stigma, social support, and sexual identity disclosure were all associated with individual wellbeing (Tornello et al. 2022). In contrast, among the non-pregnant mothers, wellbeing was unrelated to their personal experiences of sexuality stigma. Instead, the non-gestational mothers' wellbeing associated with the gestational mother's reports of sexual identity centrality and affirmation and support from friends (Tornello et al. 2022).

Healthcare disparities also play a pivotal role. In recent decades, social acceptance of SGM individuals has increased (Flores 2014) while legal barriers to relationship recognition and parenthood have declined (Moore et al. 2013). Nevertheless, many SGM individuals often face barriers to care, including discrimination, lack of culturally competent care, and in some cases, outright denial of services (Rounds et al. 2013). SGM persons frequently report a lack of understanding from their healthcare practitioners regarding capacity or intentions for pregnancy (Hudak 2023). A study found that few sexual minority women experience internalized conflict between their sexual minority identity and pregnancy, instead experiencing imposed conflict from heterosexism and discrimination experience in healthcare encounters (Dyer et al. 2022). These factors can result in delayed or inadequate care, contributing to poorer mental health outcomes.

SGM persons frequently report a lack of understanding from their healthcare practitioners regarding capacity or intentions for pregnancy.

For masculine-identified sexual minority women and AFAB gender minority persons, the gendered nature of pregnancy can create a conundrum (Ryan 2013). For AFAB gender minority persons, cessation of gender affirmation hormones to facilitate pregnancy and lactation or exposure to fertility treatments may exacerbate gender dysphoria due to regression of masculinization. However, many gender minority pregnant persons, facial hair may persist even with cessation of testosterone, which may these individuals a target for discrimination, harassment, and violence. The use of breast binders may hinder lactation and increase the risk for mastitis. These factors may influence an individual's preferences regarding pregnancy care and delivery. In a small sample of AFAB gender minorities (n=8), preference for caesarean delivery was noted as vaginal delivery associated with worsened gender dysphoria (Light et al. 2014).

Lastly, although this section focuses on AFAB SGM parents, it is important to note that assigned male at birth (AMAB) SGM individuals and couples that become parents via adoption or surrogacy are also at heightened risk for perinatal mental distress. One study looking at the association among wellness, sexual orientation, and level of outness found that gay male parents (versus female parents) reported greater need for social acceptance given possible differences in perceived internalized homophobia (Lassiter et al. 2017). Another study examining the predictors of parenting stress among 230 gay adoptive fathers suggests the importance of social support and a positive gay identity in facilitating successful parenting outcomes among gay adoptive fathers (Tornello et al. 2011). Failed adoption or surrogacy matches is not uncommon for prospective SGM parents (Goldberg et al. 2022b). A study found that the grief that gay men experience after the adoption failure is akin to that of pregnancy loss among heterosexual people (Johnson 2022).



Perinatal Outcomes

There is limited, mixed evidence regarding perinatal, obstetrical, and neonatal outcomes by SGM status. In a population-based cohort study of live birth hospitalizations in California, sexual and/or gender minority parents accounted for 6802 (0.3%) of live births over the 5-year study period (Berrahou et al. 2022). The most common sexual and/or gender minority parental structures were mother-mother (n=4310; 63% of the group) and father-father (n=1486; 22% of the group). Compared with parents giving birth in the mother-father structure (n=2,055,038; 91%), a higher proportion of parents giving birth in the sexual and/or gender minority group were aged ≥ 35 years, White, college-educated, and had commercial health insurance. Although likely underreported overall, the proportion of those who used assisted reproductive technology was much higher in the sexual and/or gender minority group (1.4%) than in the mother-father group (0.05%).


Unintended pregnancy associates with poor pregnancy outcomes, including miscarriage, stillbirth, low birthweight, and neonatal mortality.

In a study of birth certificate data from the state of Massachusetts, people in same-sex marriages who gave birth had perinatal outcomes related to decreased fetal growth and preterm birth that were like those of their peers in different-sex marriages (Downing et al. 2021). Use of assisted reproductive technology was associated with decreased fetal growth and increased risk of preterm birth for infants with different-sex parents but not for infants with same-sex parents (Downing et al. 2021). One study found that mother-mother parental structure was associated with a higher risk of multifetal gestation, labor induction, postpartum hemorrhage, severe morbidity, and non-transfusion severe morbidity compared with mother-father parental structure (Leonard et al. 2022). Gender minority parents in any partnership were not at a significantly elevated risk of any adverse obstetrical or birth outcome considered in this study (Leonard et al. 2022). Another study of gender minority pregnant persons found no trend in complications (Light et al. 2014).

Unintended pregnancy associates with poor pregnancy outcomes, including miscarriage, stillbirth, low birthweight, and neonatal mortality (Hall et al. 2017). Although differential rates of unintended or unwanted pregnancy across lifespan in AFAB SGM individuals, evidence for association between pregnancy intention and these outcomes in the SGM population is understudied.

Affirming Care

Healthcare practitioners are uniquely positioned to make the transition to parenthood easier by fostering an environment neutral to sexual orientation or gender identity (e.g., avoiding assumptions about pregnancy capacity or intent, inclusive language on intake forms) (Brennan et al. 2014). Affirming, inclusive care must also incorporate cultural sensitivity and respect for privacy and autonomy (Hoffkling et al. 2017, Fix et al. 2020, Moseson et al. 2021). Ongoing communication between different disciplines can facilitate an integrative approach, where physical, psychological, and social aspects are all considered (Light et al. 2017, Griggs et al. 2021, Lampe et al. 2021, Roosevelt et al. 2021, Ruderman et al. 2021, Gedzyk-Nieman et al. 2022).



Healthcare practitioners must have a thorough understanding of the unique experiences, challenges, and health disparities that the SGM community faces. This can be achieved through ongoing professional education and training, as well as personal reflection on biases and stereotypes. Clinicians often report inadequate knowledge as to SGM reproductive health. This is particularly true of gender minority reproductive health and options, such as the impact of cross-sex hormones on fertility (Hoffkling et al. 2017, Maxwell et al. 2017). Education and training can alleviate practitioner fears of offending and inadequacy that can precipitate patient distrust and avoidance of care (Krempasky et al. 2020, Forsberg et al. 2022). For example, gender minority patients have voiced a need for effective contraception counseling about options that minimize gender dysphoria (Agenor et al. 2020, Gomez et al. 2020).

Healthcare practitioners are uniquely positioned to make the transition to parenthood easier by fostering an environment neutral to sexual orientation or gender identity (e.g., avoiding assumptions about pregnancy capacity or intent, inclusive language on intake forms).

The American Psychiatric Association recommends comprehensive screening for mental health issues during the perinatal period, considering factors such as prior mental health history, exposure to trauma, substance use, and family history of psychiatric illness. These guidelines apply universally, but for SGM individuals, further consideration should be given to factors such as experiences of stigma or discrimination, which can contribute to mental health issues in the perinatal period.

Research into interventions and therapies specifically beneficial to the SGM population in the perinatal period is lacking. Cognitive-behavioral therapies (CBT) have demonstrated effectiveness across a range of mental health issues and can be adapted to address the unique needs of SGM individuals during the perinatal period. CBT can assist in mitigating the effects of stigma, enhancing coping strategies, and building resilience. For example, a modification of CBT known as acceptance and commitment therapy (ACT) focuses on helping individuals accept their experiences and commit to actions that align with their values. This approach can be beneficial for SGM individuals who may be struggling with internalized stigma or difficulties related to their identity. Furthermore, interpersonal psychotherapy (IPT), which focuses on improving interpersonal relationships and communication, may also be effective for SGM individuals who may be experiencing social isolation or difficulties related to their sexual or gender identity. Importantly, such interventions should always be delivered in a manner that respects and acknowledges the individual's identity and experiences.

Psychoeducation is another crucial aspect of best practice approaches. This involves educating SGM individuals about common perinatal mental health issues, their causes, the importance of seeking help, and available treatments. Psychoeducation can also extend to family members and friends to enhance understanding and support of SGM individuals during pregnancy and beyond.

Conclusion

Providing the highest standard of care to SGM individuals during the perinatal period entails treating mental health symptoms. In addition, the standard of care to this population must address the underlying factors that contribute to mental health symptoms, such as stigma, discrimination, and social isolation.

BEHAVIORAL HEALTH EDUCATION AND TRAINING

The U.S. behavioral healthcare workforce is inadequately trained to screen, evaluate, treat, and prevent perinatal mental and substance use disorders. Most of these providers have not received focused training on women’s mental health in general or perinatal mental health specifically during their education or as practicing clinicians. This section addresses the pressing need to expand the education and training of the behavioral healthcare workforce, including current gaps in training and how future directions can potentially help close these gaps. Training in perinatal mental and substance use disorders can help increase the likelihood perinatal patients receive evidenced-based and culturally responsive care, which can help improve maternal and offspring outcomes and reduce suffering.

ACCREDITATION AND TRAINING REQUIREMENTS

Accreditation and training requirements across behavioral health disciplines do not include mandates in women’s mental health or perinatal mental health. This is true for psychiatry, advanced practice nursing (e.g., psychiatric nursing), psychology, mental health counseling, and social work. The lack of accreditation requirements, focused curriculum, and supervised clinical rotations in perinatal mental and substance use disorders contributes to perinatal patients with psychiatric needs being overlooked and undertreated. Further, wide variability in accreditation and training standards across behavioral health disciplines means patients do not have universal access to a workforce fully prepared to provide evidenced-based care for persons coping with or at risk for perinatal psychiatric illness.

Accreditation and training requirements across behavioral health disciplines do not include mandates in women’s mental health or perinatal mental health. This is true for psychiatry, advanced practice nursing (e.g., psychiatric nursing), psychology, mental health counseling, and social work.

What follows below are brief descriptions of how each behavioral health discipline addresses—or fails to address— perinatal mental health in its training. Note that fully describing the credentialing steps and standards of each behavioral health profession is beyond the scope of this section. Readers interested in such information are encouraged to visit the following websites:

Program	Weblink
Accreditation Council for Graduate Medical Education’s (ACGME) overview of psychiatry training requirements	https://www.acgme.org/specialties/psychiatry/overview/
National Organization of Nurse Practitioner Faculties (NONPF)	nonpf.org
American Association of Colleges of Nursing’s (AACN) – FAQ Webpage	https://www.aacnnursing.org/Essentials/FAQ
National Task Force Standards’ Frequently Asked Questions	https://cdn.ymaws.com/www.nonpf.org/resource/resmgr/2022/ntfs/_20220616_ntfs_faq_.pdf
American Psychological Association’s-Licensing Requirements	https://www.apa.org/gradpsych/2004/01/get-licensed

American Counseling Association’s-Licensure And Certification	https://www.counseling.org/knowledge-center/licensure-requirements/accreditation-licensure-and-certification-defined
Association of Social Work Boards	https://www.aswb.org/
Council on Social Work Education	https://www.cswe.org/

Psychiatry

The ACGME does not mandate adult psychiatry residents demonstrate competency in women’s mental health or perinatal care (ACGME). Accordingly, most psychiatry residency programs offer limited training opportunities, if any at all. In a survey of 50 psychiatry residency program directors, about 40% reported no requirement for training in reproductive psychiatry (Coverdale et al. 2018, Osborne et al. 2018). Of those that did, the content, depth, and quality of information was highly variable. Furthermore, women’s mental health education focused primarily on didactic learning as opposed to meaningful clinical experiences (Coverdale et al. 2018, Osborne et al. 2018).

Advanced Practice Nursing

Most advanced practice nurses (APRNs) who specialize in psychiatry/mental health practice as generalists rather than specialists. Several national nursing organizations influence the development and implementation of nursing programs, including APRN programs. These include:

- AACN, which establishes the standards for nursing education and serves as the voice of academic nursing at the baccalaureate level and beyond (<https://www.aacnnursing.org/About-AACN/Who-We-Are>);
- Commission on Collegiate Nursing Education (CCNE), an autonomous agency that provides accreditation of nursing programs based on nationally recognized standards (<https://www.aacnnursing.org/CCNE-Accreditation/Who-We-Are>) and is an arm of AACN; and
- NONPF, a national organization whose mission is to “optimize quality and cultivate leaders in nurse practitioner education” (<https://www.nonpf.org/page/1>).


It is unclear whether any of these organizations have set benchmarks for a minimal number of clinical practice hours in a specialty, including perinatal care. In addition, none of these groups have specific accreditation requirements focused on perinatal mental and substance use disorders.

Each state mandates what is required to maintain APRN licensure. This is generally maintained by continuing medical/nursing education in the specialty. It is therefore difficult to enumerate the number of APRNs who specialize in any mental health specialty, including perinatal mental health.

Psychology

Consistent with other healthcare accrediting bodies, accreditation in psychology does not require trainees to demonstrate competencies in women’s mental health in general or in perinatal populations specifically (APA 2015). This applies to psychology doctoral students, predoctoral interns, and postdoctoral fellows.

Although not required for accreditation, some doctoral graduate programs, predoctoral internships, and postdoctoral psychology training programs offer evidence-based coursework and/or clinical rotations in



women's and perinatal mental health. Unfortunately, formal data on the frequency or content of didactic and clinical training in these areas are lacking. Data are also lacking, and needed, on the extent to which psychology graduate students, interns, postdoctoral fellows, and licensed psychologists feel well-trained and competent to evaluate, treat, and prevent perinatal mental and substance use disorders.

At the time of this writing, there are 115,248 licensed psychologists in the United States and Canada, but the percentage of those who provide general or specialized care in women's health or perinatal mental health is unknown (<https://asppbcentre.org/spotlight/number-of-licenses>). In addition, there appear to be no U.S. states that require continuing education on maternal mental health, unlike requirements for mandated workshops on suicide assessment, child abuse, and other areas of high public health importance.

Mental Health Counseling

Licensed mental health counselors include professional counselors, mental health counselors, and clinical professional counselors. Accreditation requirements in the area of perinatal mental health for these behavioral healthcare professionals is lacking. Consequently, few mental health counselors appear to be formally trained in perinatal-specific aspects of assessing, diagnosing, and treating mental and substance use disorders.

Social Work

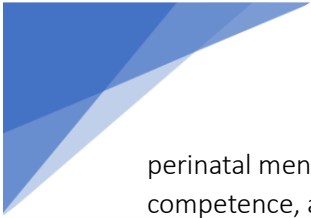
The Council on Social Work Education sets the core competencies required for social work education. These core competencies are applied across specialty curricular guides developed by a task force composed of national content experts. The accreditation process requires trainees demonstrate competencies in engaging, assessing, and intervening with individuals, families, groups, organizations, and communities, but it does not specifically refer to targeted populations, such as perinatal patients.

Nonbehavioral healthcare practitioners

Although this section is primarily focused on behavioral healthcare practitioners, it is useful to briefly reflect on the mental health training among nonbehavioral healthcare practitioners likely to encounter perinatal patients with psychiatric illness, such as obstetricians, gynecologists, primary care providers, and family medicine providers.

Although the ACGME does not require competency in women's mental health for obstetrics and gynecology (OB/GYN) residents, a survey of 239 OB/GYN program directors found 84% of programs that responded to the survey offered didactics on psychiatric topics taught by OB/GYN faculty (Garbarino et al. 2019a). The likelihood of having a greater overall count of mental health didactics was higher for programs that reported didactics conducted by psychiatrists. The majority of OB/GYN program directors (81%) did not feel that OB/GYN residents are "fully equipped" to identify patients' psychiatric needs (Garbarino et al. 2019a).

Similarly, a survey of American family medicine physicians, OB/GYNs, and social workers who practice in community clinics at academic medical centers (N=118) found that only 40% were "somewhat comfortable" with managing perinatal mood and anxiety disorders (Puspitasari et al. 2021). Relatedly, a systematic literature review of 11 studies on family physicians' perceptions of caring for patients with



perinatal mental and substance use disorders found physicians frequently reported a lack of confidence, competence, and training in perinatal mental and substance use disorders (Noonan et al. 2018). Physicians were more likely to screen for perinatal mental and substance use disorders if they had received training in postpartum depression during residency or were knowledgeable about postpartum depression from reviewing empirical literature. Physicians who received training in postpartum depression did so mainly through residency or through independent literature searches rather than through formal nonresidency didactics, such as continuing medical education programming or fellowships (Noonan et al. 2018).

These studies suggest that, like their behavioral health colleagues, most nonbehavioral healthcare practitioners also are ill-equipped to care for perinatal patients with psychiatric illness, including management with psychotropics (Viguera et al. 2002). This training gap further underscores the importance of having available for consultation and referral a well-trained workforce of behavioral health specialists with didactic and clinical experience in this area. Indeed, a recent call to action from clinical, research, and public health experts in the field of reproductive mental health urged clinician educators to enhance curricula for obstetricians and gynecologists with topics such as engaging patients in mental health care, taking a psychiatric history, assessing risk and level of care needed, referral strategies, and first-line interventions, including pharmacotherapies and nonpharmacotherapies (Hutner et al. 2021).

CONSEQUENCES OF AN UNTRAINED BEHAVIORAL HEALTH WORKFORCE

The lack of training in perinatal mental and substance use disorders in the U.S. behavioral healthcare workforce has adverse downstream effects on patients and families. The most obvious consequence is that patients who need treatment are not able to receive it in a timely manner, which can harm the health of the pregnant individual and their offspring. The negative maternal and fetal outcomes associated with perinatal mental and substance use disorders and the effects of untreated perinatal psychiatric illness are discussed at greater lengths in other sections.

The lack of training in perinatal mental and substance use disorders in the U.S. behavioral healthcare workforce has adverse downstream effects on patients and families.

In addition to obstetric complications and adverse health outcomes, poor access to evidence-based treatment for perinatal persons increases the risk of illness relapse or recurrence during subsequent perinatal periods as well as a risk of harm to self or others, including the baby (Sakalova et al. 1975, Earls et al. 2010, Luca et al. 2020). Indeed, one of the most serious potential outcomes of untreated perinatal mental or substance use disorders is an elevated risk of suicidal ideation and attempt, especially among patients with depression, psychosis, or substance abuse (Zhong et al. 2018b, Calthorpe et al. 2021). Similarly, although rare, maternal neonaticide, infanticide, and filicide have been documented in some women who are acutely psychotic, including with psychotic depression, as well as women with other forms of severe mental illness, such as severe substance use disorders, schizophrenia, and delusional disorders (West 2007, Flynn et al. 2013, Milia et al. 2022).



Psychiatry and Advanced Practice Nursing

The dearth of psychiatrists and APRNs with expertise in perinatal populations raises concerns about patients' ability to receive appropriate, evidence-based pharmacotherapy for mental and substance use disorders. A literature review of 19 studies found healthcare providers—including psychiatrists and APRNs—tended to overestimate the risks of psychotropic medication during pregnancy, and that community mental health providers often discharged perinatal patients from their care or instructed them to discontinue medication (Osborne et al. 2015a). Additionally, the percent of providers who reported “some level” of confidence in prescribing antidepressants to perinatal patients varied greatly, from 33.3% to 78.1%, suggesting that patients are not universally receiving the same standard of care (Eakley et al. 2022). In a systematic literature review of family physicians' perceptions of caring for patients with perinatal mental and substance use disorders, one study found 25% of family physicians avoided prescribing not just antidepressants but all psychotropic medication to perinatal patients with psychiatric symptoms, and the most common reason for avoiding antidepressant use was lack of training (Noonan et al. 2018). Anecdotally, an all-too-common scenario encountered by reproductive psychiatrists is restarting medications that have been stopped by other healthcare providers.

The dearth of psychiatrists and APRNs with expertise in perinatal populations raises concerns about patients' ability to receive appropriate, evidence-based pharmacotherapy for mental and substance use disorders.

The lack of access to evidenced-based medication management for perinatal persons is especially critical for individuals with a history of serious mental illness. For instance, in a meta-analysis on the risk of depression relapse during pregnancy (N=518), risk of relapse following antidepressant discontinuation was 1.74 times higher compared with women who continued their antidepressant (95% confidence interval [CI] 0.97–3.10, P=0.06) (Bayrampour et al. 2020b). An even higher relative risk (2.30, 95% CI 1.58–3.35) was observed among women with severe or recurrent depression (Bayrampour et al. 2020b). Relapse rates in persons with schizophrenia who discontinue antipsychotic medication is high, at 52% over approximately 6 months (Emsley et al. 2013).

Additionally, due to lack of education/training as well as misinformation in the media (e.g., social media), pregnant persons and their psychiatrists may be biased towards not treating or undertreating psychiatric disorders during pregnancy and lactation (Battle et al. 2013, Robinson et al. 2015). This can lead to increased obstetric complications and neuropsychiatric sequelae for the offspring (DiPietro et al. 2006, Brockington et al. 2011, Malm et al. 2015).

Of note, licensed psychologists can prescribe psychiatric medications in 6 states (i.e., New Mexico, Louisiana, Illinois, Iowa, Idaho, and Colorado) as well as in the Commissioned Corps of the U.S. Public Health Service, the Indian Health Service, the U.S. military, and the U.S. territory of Guam. Improving prescriber training and knowledge about working with perinatal patients should extend beyond that for psychiatrists and advanced practice nurses to also include psychologists.



Psychology, Mental Health Counseling, and Social Work

Because psychologists and mental health counselors are formally trained in the clinical diagnosis and nonpharmacologic treatment of persons with psychiatric illness. However, their lack of formal perinatal training means their pregnant and postpartum patients may experience delays in timely and appropriate diagnosis and nonpharmacologic care. As noted above, psychologists also can play a role in psychiatric medication management for perinatal persons. Further, social workers often help patients navigate systems and services that nonbehavioral healthcare practitioners may be less conversant in, such as those pertaining to insurance, childcare, schooling, employment, housing, transportation, and public benefits (e.g., Temporary Assistance for Needy Families; Women, Infants, and Children). Without social workers trained in perinatal patient needs, those patients will likely experience delays in accessing a full range of community-based resources and services.

Few studies have addressed the gaps and barriers to perinatal mental health training across behavioral healthcare fields and their impact.


Individuals and families especially vulnerable to perinatal mental and substance use disorders include those coping with infertility, pregnancy complications, pregnancy loss, pregnancy during and after cancer and other significant physical conditions, incarceration, intimate partner violence, birth-related trauma, and obstetric or neonatal complications (see the section on vulnerable populations [Page 68]). These patients likely will continue to experience significant challenges accessing highly effective services without a well-trained workforce. In addition, unless the behavioral healthcare field makes a focused effort to train providers from underrepresented groups (e.g., racially and ethnically diverse populations, gender and sexual minority individuals), underserved patients likely will continue experiencing limited access to providers who come from their communities, which can affect patient trust and satisfaction with care.

GAPS IN AND BARRIERS TO TRAINING ON PERINATAL MENTAL AND SUBSTANCE USE DISORDERS

Few studies have addressed the gaps and barriers to perinatal mental health training across behavioral healthcare fields and their impact. Existing research suggests barriers can be conceptualized as those related to providers, programs, and organizations/healthcare systems. These are somewhat fluid, as certain barriers may overlap categories; for instance, low provider comfort in addressing perinatal psychiatric illness is itself a provider-level barrier but is also partly related to lack of exposure and few training opportunities available, which is a program barrier.

Provider Barriers

Gaps in perinatal mental health care can be attributed somewhat to provider-level challenges. For example, psychiatry residents' discomfort with perinatal mental and substance use disorders is a known difficulty for some trainees, which may stem from gender bias and stigma (Coverdale et al. 2018). A qualitative study found psychiatry residents lack the confidence and resources to address the sexual and reproductive health of their patients with severe mental illness (Zatloff et al. 2020). Obstacles to providing this care included lack of training, discomfort with the topic, and limited time to address this topic during clinic visits. When residents did provide this care, it mostly pertained to medication changes (Zatloff et al.



2020). Literature reviews also suggest healthcare providers lack comfort and experience in pharmacotherapy for perinatal patients specifically (Noonan et al. 2018, Eakley et al. 2022).

Program Barriers


Program barriers largely concern the lack of training opportunities available and disparities in training opportunities that do exist (e.g., opportunities mostly being offered at large, well-funded, urban institutions). For instance, research suggests psychiatry residencies are lagging in teaching trainees about reproductive psychiatry. In a 2015 survey, Osborne and colleagues found that only 59% of residency programs required some training in reproductive psychiatry, and only 36% believed that residents should be competent in this area (Lauren M et al. 2015, Osborne et al. 2015b). Most psychiatry residency training programs that have curricula on women’s mental health are located in urban areas, which creates disparities for trainees and patients in suburban and rural areas (Coverdale et al. 2018). Similarly, within APRN programs, there are difficulties finding and contracting with clinical sites that offer didactic and clinical exposure in perinatal care. Few psychology, mental health counseling, and social work trainees receive comprehensive training in women’s health/mental health in general and in perinatal mental health specifically, including education about providing services in perinatal settings such as neonatal intensive care units (NICUs), fertility clinics, and OB/GYN offices.

Most psychiatry residency training programs that have curricula on women’s mental health are located in urban areas, which creates disparities for trainees and patients in suburban and rural areas.

Psychiatrists and psychiatric nurse practitioners are less likely to be trained to provide integrated assessment and consultation in OB/GYN, family medicine, and pediatric settings compared with psychologists and other behavioral healthcare practitioners. Although recent efforts to increase training in the collaborative care model have increased the number of psychiatrists in ambulatory peripartum settings, and psychiatrists may provide evaluations in some perinatal settings (e.g., NICUs), the overall number is too few to address the psychiatric needs of all or most perinatal patients (Byatt et al. 2016).

Systemic and Organizational Barriers

Systemic and organizational barriers are commonly cited as a major reason for suboptimal perinatal mental and substance use disorder training across behavioral health disciplines. For instance, although there are a growing number of women’s mental health or reproductive psychiatry fellowship training programs available, these fellowships are not ACGME accredited and therefore lack consensus in required competencies. Another systemic barrier is the lack of qualified instructors and time built into training curricula (Coverdale et al. 2018, Osborne et al. 2018). Further, many programs currently do not have financial and material support to develop perinatal-specific curricula. Even when continuing education/continuing medical education opportunities in perinatal mental health are available, they are not always readily accessible. These programs can range from several days’ training to months-long intensive learning. Additionally, training fees can be substantial, ranging from hundreds to thousands of dollars.



Failure on the part of the education system to prioritize and value perinatal mental health as an important issue is a major hindrance. Osborne and colleague's (2018) survey of psychiatry residency program directors, offers insight into how this topic is perceived by training programs. Among residencies who reported offering some degree of training in reproductive psychiatry, a majority offered 1 hour of training or less across the entire 4-year curriculum on topics of perimenopause, premenstrual dysphoric disorder, perinatal eating disorders and anxiety disorders, and infertility. Most programs only offered 1–4 hours of training on topics of perinatal mood disorders, psychotic disorders, and substance use disorders as well as pharmacotherapy for perinatal patients (Osborne et al. 2018). When asked about their attitudes toward reproductive psychiatry training, only 40% agreed that all residents should be competent in this area, and only 13% agreed that interested residents should be given training opportunities in perinatal mental health—but with the caveat that such training should not be required for everyone (Osborne et al. 2018).


Poor collaboration between departments of psychiatry and OB/GYN is also problematic and has been cited as a barrier to training (Garbarino et al. 2019b). Integration of OB/GYN and psychiatric services is essential for training both groups of residents. Real-time experience with successful interdisciplinary collaboration for pregnant persons is a crucial skill and may be even more important when providing care to vulnerable populations, including pregnant persons with severe mental illness, with human immunodeficiency virus, and who are socioeconomically disadvantaged (Coverdale et al. 2015).

Poor collaboration between departments of psychiatry and OB/GYN is also problematic and has been cited as a barrier to training.

The timing of when opportunities are available can be an obstacle because professionals generally are not targeted early enough in their education to maximize their experiences with and exposure to this population. For instance, social workers can receive specialized trainings through hospital-based, in-service professional training programs and conferences (Smith et al. 2012, Choi et al. 2015). Although these improve education and applied skills, they target social workers after postgraduate education and professional licensing. Thus, there is a gap in specialized clinical education and skill development earlier in the career trajectory. In addition to gaps during graduate and postgraduate work, there are missed opportunities to educate all behavioral healthcare practitioners about perinatal mental health during the undergraduate and prelicensing periods.

Another systemic barrier concerns the lack of inclusivity in perinatal mental health broadly and in training opportunities specifically. Because perinatal mental health has often been regarded as a problem only experienced by cisgender women, nonbirthing people have often been disregarded in the literature, training curricula, and underrepresented as training faculty and researchers. These factors can create further gaps in access to quality providers for underrepresented groups.

Finally, research has shown evidence-based counseling modalities, specifically cognitive-behavioral therapy and interpersonal therapy, to be useful in treating perinatal mental and substance use disorders (Stamou et al. 2018, O'Connor et al. 2019b) (see the clinical management section [Page 39] for more discussion of evidence-based treatments). However, currently no higher education program in the United States exists to specifically train perinatal mental health professionals and, prior to 2019, there was no



extensive continuing education training that led to certification in perinatal mental health (Bray 2019). This reflects a lack of understanding of the urgency of this gap by educators and credentialing bodies.

TRAINING OPPORTUNITIES IN PERINATAL MENTAL AND SUBSTANCE USE DISORDERS

What follows below is a brief compendium of graduate and postgraduate training opportunities in perinatal mental health across behavioral healthcare fields. This is not intended to be a comprehensive listing of all opportunities available (e.g., a listing of opportunities in bachelor's programs is not within the scope of this section), and interested readers are encouraged to visit the websites of the professional credentialing bodies listed earlier for more information about existing programs and training opportunities.

Psychiatry

At the time of this writing, there are 12 women's mental health fellowships, most of which are situated within psychiatry, with 1 in OB/GYN. These fellowships focus primarily on reproductive psychiatry with a special emphasis on public sector psychiatry and trauma (Nagle-Yang et al. 2018).

The most common sources of perinatal psychiatry education outside of fellowships are online toolkits from sources such as the National Curriculum for Reproductive Psychiatry (NCRP) (<https://ncrptraining.org/>), which is a free, web-based, interactive curriculum that teaches the basics of reproductive psychiatry to mental health professionals. NCRP also offers a free year-long didactic series for Postgraduate Year-4 psychiatry residents in a reproductive psychiatry track or to interested psychiatry fellows. NCRP covers topics such as premenstrual mood disorders, infertility, pregnancy loss, and perimenopause, with a focus on diagnosis and management during pregnancy and postpartum.

The most common sources of perinatal psychiatry education outside of fellowships are online toolkits from sources such as the National Curriculum for Reproductive Psychiatry (NCRP), which is a free, web-based, interactive curriculum that teaches the basics of reproductive psychiatry to mental health professionals.

Many states and institutions have created their own online toolkits, primarily geared towards providers. The Massachusetts Child Psychiatry Access Program (MCAP) For Moms was a trailblazer in this area and grew out of a Massachusetts state-level program that created access to real-time perinatal psychiatric consultation, referrals, and case management support for providers across the state. The aim of the toolkit was to help improve the prevention, identification, and management of perinatal mental and substance use disorders. Although the toolkit is geared primarily towards obstetricians, it contains helpful information on screening, treatment, and referrals for psychiatrists and other behavioral healthcare practitioners caring for pregnant persons (Byatt et al. 2016).

Advanced Practice Nursing

Current sources of training for APRNs include the Perinatal Mental Health certification program sponsored by Postpartum Support International ([PSI] <https://www.postpartum.net/professionals/certification/>). The

cost of PSI training begins at \$425.00 for a 2-day training. To reduce travel costs, the course can be taken remotely, using Zoom. An additional course on advanced psychotherapy or advanced psychopharmacology must be completed at a cost of \$250.00. Learners also must submit documentation of 2 years' work experience with perinatal populations. PSI also offers multiple other certifications, as well as webinars and curricula, on numerous perinatal mental health topics, including pharmacotherapy (<https://www.postpartum.net/professionals/>).

Additionally, the American Association for Women's Health, Obstetric and Neonatal Nurses publishes a Compendium of Postpartum Care (<https://www.awhonn.org/education/compendium/>) that includes evidence-based guidelines for practice for nurses in both inpatient and outpatient settings (AWHONN 2019).

Psychology

Below is a list of selected psychology training opportunities in women's health and perinatal mental health. Click on each link to learn more about the training program. Additionally, some predoctoral internships and postdoctoral fellowships in the U.S. Department of Veterans Affairs offer specialized clinical training in women's health, including the VA Washington DC Healthcare System (<https://www.va.gov/washington-dc-health-care/work-with-us/internships-and-fellowships/psychology-training-programs/>). Relatedly, the VA San Diego Healthcare System offers a postdoctoral fellowship in women's health, which also provides advanced training in this area for social workers and nurses (<https://www.mirecc.va.gov/CESAMH/WomensHealth.asp>).

Psychology Doctoral Programs

Program	Weblink
Drexel University	https://drexel.edu/coas/academics/graduate-programs/psychology/doctorate-clinical-psychology/
Stony Brook University	https://www.stonybrook.edu/commcms/psychology/clinical/index.php#Accreditation
University of Denver Graduate Program in Professional Psychology, infancy, and early childhood mental health specialization	https://psychology.du.edu/news/infant-and-early-childhood-mental-health-specialty

Psychology Pre-Doctoral Internship Programs

Program	Weblink
University of North Carolina School of Medicine, track focused on reproductive psychology	https://www.med.unc.edu/psych/reproductive-psychology-track-description-2022-2023/
University of Rochester College of Medicine and Dentistry	https://www.urmc.rochester.edu/psychiatry/education/psychology-internship-and-fellowship/doctoral-internship.aspx
Warren Alpert Medical School of Brown University	https://clinical-psychology.med.brown.edu/internship

Psychology Post-Doctoral Fellowships

Program	Weblink
Geisinger Commonwealth School of Medicine	https://www.geisinger.edu/education/residencies-fellowships/fellowships/adult-clinical-psychology-behavioral-medicine-fellowship
Harris Infant Mental Health Post-Doctoral Fellowship, Department of Psychiatry, University of Colorado School of Medicine	https://www.appic.org/Postdocs/Universal-Psychology-Postdoctoral-Directory-UPPD/Detail/id/2124
Women’s Health and Mental Health and NICU Psychology, Department of Psychiatry, University of Colorado School of Medicine	https://medschool.cuanschutz.edu/psychiatry/education-pillar/fellowships/harrisprogram
Postpartum Support International	https://www.postpartum.net/professionals/
American Society of Reproductive Medicine’s Mental Health Professional Group	https://connect.asrm.org/mhpg/education/new-item2?ssopc=1
National Perinatal Association’s National Network of NICU Psychologists	https://www.nationalperinatal.org/psychologists
American Psychological Association	https://www.apa.org/members/your-training
State Psychological Associations	https://www.apa.org/about/apa/organizations/asociations

Mental Health Counseling and Social Work

For counseling professionals and social workers, perinatal training programs are available through education and advocacy organizations as follows:

Program	Weblink
Postpartum Support International	https://www.postpartum.net/professionals/
Seleni Institute	https://www.seleni.org/
National Curriculum in Reproductive Psychiatry	https://ncrptraining.org/
National Perinatal Association	https://www.nationalperinatal.org/
Postpartum Action Institute	https://www.facebook.com/postpartumaction/
Postpartum Stress Center	https://www.postpartumstress.com/
Maternal Mental Health Now	https://www.maternalmentalhealthnow.org/
North American Society for Psychosocial Obstetrics & Gynecology	https://www.naspog.org/Welcome/Info
International Marcé Society for Perinatal Mental Health	https://marcesociety.com/
Interprofessional Training Conference On Infertility Counseling by Jefferson Medical College	https://www.facebook.com/JICC2023/



ONLINE TOOLKITS


A list of online toolkits focused on perinatal mental health and that can be useful across behavioral health professions follows below:

Program	Weblink
ACOG's Perinatal Mental Health Toolkit	acog.org/programs/perinatal-mental-health
Children's National Hospital's Perinatal Mental Health Toolkit for Pediatric Primary Care	https://www.dchealthcheck.net/documents/PMH%20Toolkit%20Spring%202020.pdf
First 5 Orange County Children & Families Commission's Orange County Perinatal Mental Health Toolkit	https://first5oc.org/wp-content/uploads/2021/08/OC-Perinatal-Mental-Health-Toolkit.2021_2022.FINAL_.pdf
Florida State University College of Medicine's Mothers' Mental Health	https://mothersmentalhealth.org/toolkits-for-clinicians/
Kansas Department of Health and Environment's Maternal and Child Health Integration Toolkits	https://www.kdhe.ks.gov/457/MCH-Integration-Toolkits
Maternal Mental Health Leadership Alliance Advocacy Toolkit	https://www.mmhla.org/advocacy-toolkit
MCAP For Moms' Provider Toolkits	https://www.mcpap.com/Provider/ScreeningNToolkits.aspx
Periscope Project's Perinatal Specialty Consult Psychiatry Extension Provider Toolkit	https://the-periscope-project.org/provider-toolkit/
Public Health Ontario's Perinatal Mental Health Toolkit for Ontario Public Health Units	https://www.publichealthontario.ca/-/media/documents/h/2018/hhdt-toolkit-perinatal-mental-health.pdf?sc_lang=en
UMass Chan Medical School's Lifeline4Moms Perinatal Mental Health Toolkit	https://www.umassmed.edu/lifeline4moms/products-resources/toolkits-and-apps/2019/11/lifeline4moms-perinatal-mental-health-toolkit/

Future Directions for Training in Perinatal Mental and Substance Use Disorders

It is essential that the behavioral healthcare field actively recruits, trains, and supports more providers with expertise in perinatal mental and substance use disorders. Tactics for doing so (discussed below) are generally applicable across the behavioral healthcare fields. Strategies specific to one field or another are noted accordingly.

The future of training in perinatal mental health lies in the creation of standardized competencies. For instance, in psychiatry, these competencies would need to be codified by the ACGME (Osborne et al. 2018). Given that over 80% of U.S. women will become pregnant at least once and over 50% of psychiatric patients are women, perinatal psychiatry should be elevated from a subspecialty to a required competency area for all general psychiatrists (Payne 2019). Furthermore, advanced training in perinatal mental health should be advocated for and formally recognized and accredited by each profession's respective credentialing bodies (e.g., the ACGME for psychiatry fellowships, the American Psychological Association and Association of Psychology Postdoctoral and Internship Centers for postdoctoral psychology fellowships) (Hudepohl et al. 2018).




Trainees need exposure to specific curricula on perinatal mental health at graduate and postgraduate levels (i.e., while working towards a degree as well as during residencies, internships, and fellowships) (Hudepohl et al. 2018, Osborne et al. 2018, Payne 2019). This requires giving trainees opportunities to build didactic and clinical skills in a variety of perinatal settings, including maternal-fetal medicine clinics, labor and delivery settings, antepartum units, and NICUs. In addition to learning core concepts related to screening, diagnosis, and treatment of mental and substance use disorders, trainees also can benefit from education on secondary topics likely to be of relevance to perinatal patients. These could include neonatal abstinence syndrome, brokering community resources, maternal advocacy, stigma reduction, promoting maternal–infant bonding, conducting comprehensive biopsychosocial screenings for intimate partner violence, and sexually transmitted infections (Mahoney et al. 2019). Graduate programs should create more learning opportunities through electives in perinatal mental health to improve understanding, awareness, intervention, and advocacy for this population (McCloskey et al. 2021). Proper formal education and training should also address the complexities of perinatal mental health and the family system (Broudy 2017).

Of note, stigma—including self-stigma—and negative experiences with the healthcare system (e.g., bias and discrimination from healthcare providers) can lead to some patients feeling uncomfortable disclosing their psychiatric symptoms (APA 2020). Improving behavioral healthcare practitioners’ confidence with perinatal mental and substance use disorders means teaching trainees to feel comfortable initiating these conversations. Training should also address how to establish rapport, facilitate trust, convey warmth and care, teach patients about confidentiality, and help patients feel safe discussing their symptoms and treatment needs.

Trainees can benefit from more exposure to integrated or collaborative care models that bridge the silos between behavioral healthcare practitioners, obstetricians, and other perinatal health experts.

Trainees need to develop advanced competencies in women’s mental health in general and perinatal care specifically, including perinatal mental health, psychosocial aspects of infertility, and mental health needs related to NICU care. Perinatal mental health competencies should include knowing when and how to screen for perinatal mental and substance use disorders, evidence-based pharmacologic and nonpharmacologic treatments, how and when to refer to other behavioral healthcare practitioners (e.g., referring to a psychiatrist or psychiatric nurse practitioner for medication needs, referring to a psychologist or counselor for psychotherapy, referring to a social worker to assist with obtaining food stamps), linking perinatal patients to community informational resources and community-based support, and how to engage in risk reduction or prevention efforts (e.g., how to help perinatal patients at risk for suicide or intimate partner violence with safety planning). Areas of specialty training could include perinatal mood and anxiety disorders, substance use screening and treatment, trauma-informed care, perinatal psychotherapy, and integrated models of care (Smith et al. 2012, Choi et al. 2015, Goodman 2015, Broudy 2017, Mahoney et al. 2019).

Trainees can benefit from more exposure to integrated or collaborative care models that bridge the silos between behavioral healthcare practitioners, obstetricians, and other perinatal health experts. Methods for implementing this approach, and examples of successful model care programs, have been described in



the literature and include combining mental and substance use disorder treatment in prenatal care visits, integrating access to behavioral health consultations and local referrals/resources into obstetric clinics, and creating maternal mental health outpatient clinics to coordinate services between obstetrics and behavioral healthcare practitioners (Goodman 2015, McLafferty et al. 2016, Hudepohl et al. 2018, Osborne et al. 2018, Payne 2019, Richards 2022). Training in integrated models should include both ambulatory and inpatient obstetric settings.

Professional development in perinatal mental and substance use disorders should be more feasible. Although there are resources for postgraduate education and training in perinatal mental health, they can be costly, and it may be difficult for new clinicians to allocate time and money to completing additional training immediately after finishing their schooling. Behavioral health professional societies (e.g., American Psychiatric Association, American Counseling Association) can play an important role in promoting certification for members by disseminating information about formally recognized training opportunities, such as PSI's certifications or the American Society of Reproductive Medicine's MHPG training and certification.

Lastly, behavioral healthcare professions should make efforts to address health inequities by recruiting and training providers from marginalized populations (e.g., persons of color, persons living in rural communities). Perinatal persons from racially or ethnically minoritized communities, immigrants and refugees, gender and sexual minority persons, people with disabilities, individuals with low socioeconomic status, and rural dwellers face marked barriers to psychiatric care (APA 2022, Mitra et al. 2022). Having a diverse and inclusive healthcare system that reflects the full range of patients it serves can help improve patient trust, satisfaction, and comfort and can help expand healthcare access for underserved groups (LaVeist et al. 2014).

Conclusion

Perinatal mental health is a topic of high public health importance, and this should be better reflected in the availability of training within and outside of academia. The lack of formal, structured training opportunities in perinatal mental health means behavioral healthcare practitioners are not adequately equipped to meet patients' needs, which in turn prolongs patient suffering. Implementing changes to the graduate and postgraduate education system is a complex undertaking that will require ample time, money, and resources. A significant attitudinal and cultural shift is likely also needed for the field to embrace and elevate perinatal mental health from its status as a non-priority topic.




CONCLUSIONS

Perinatal mental and substance use disorders are highly prevalent, undertreated, and consequential for the health and well-being of persons who are pregnant and postpartum and their offspring. In addition to the wide range of risk factors for mental and substance use disorders within the general population, physiological and psychosocial factors relevant to the perinatal period heighten vulnerability to the new onset or recurrence of mental health conditions during and after pregnancy. The barriers to perinatal mental health and substance use disorder treatment involve many of the same factors that impede such care for all individuals, including stigma on the part of individuals, communities, and healthcare professionals; lack of awareness; inadequate resources such as insurance and transportation; and the sheer complexity of the U.S. mental healthcare system. These barriers are generally greater among historically minoritized and vulnerable communities, contributing further to health disparities. Additional impediments include the lack of consistent mental health screening during the perinatal period as well as the often poor connection of screening to referral for evaluation and treatment; the paucity of mental healthcare professionals who have the expertise and willingness to treat individuals with perinatal mental and substance use disorders; and the often inadequate communication and care coordination that exist among multidisciplinary behavioral healthcare and nonbehavioral healthcare clinicians involved in the care of persons during and after pregnancy.

This white paper has underscored many of these challenges while highlighting the growing evidence base that supports the critical importance of screening, evaluation, and treatment of perinatal mental and substance use disorders. We believe that progress within the domains described below will meaningfully advance the health of birthing individuals and communities, including those most vulnerable to poor care and outcomes.

Defining the scope and impact of mental and substance use disorders: The field has benefitted from an increasing number of well-designed studies on the epidemiology of mental and substance use disorders. However, the literature is still limited and highly heterogeneous. In particular, the preponderance of studies focuses on the proportion of cases at a given time (prevalence) rather than the onset of new cases (incidence), thereby not separating conditions predating the perinatal period from new cases arising during this period, nor relapses during or after pregnancy from chronic, persistent conditions. Furthermore, methodologies for ascertaining cases are wide-ranging, including use of diagnostic codes in electronic health or billing records, threshold scores on symptom rating scales, or diagnoses made by semistructured interviews. Although this is not dissimilar from many other areas of mental health research, meta-analyses and systematic reviews that assess prevalence, incidence, or impact of perinatal mental health conditions need to more explicitly evaluate whether divergent findings are related to dissimilar approaches to case definition.


In addition, the bulk of studies on mental disorders focus on depression or anxiety, or an amalgam of the two, such as perinatal mood and anxiety disorders, which generally includes unipolar and bipolar disorders and anxiety disorders. More focus is needed on other conditions such as psychotic disorders, trauma and stress-related disorders, attention-deficit/hyperactivity disorder, OCD, and eating disorders, which also wield a major impact on the health of individuals and offspring during pregnancy and postpartum. Similarly, much of the work on the epidemiology of perinatal substance use disorders focuses, appropriately and critically, on alcohol, cannabis, and tobacco. More data are needed on opioid, stimulant, and poly substance use disorders as well as on patterns of substance use before, during, and after pregnancy.



Stratifying and understanding risk: In the context of limited healthcare resources, including for mental disorder screening and treatment, identifying individuals at greatest risk of new onset, worsening, or relapsing perinatal mental and substance use disorders is imperative to deploying resources to those who will need them most. More work is needed to identify individuals at highest risk during the perinatal period. This involves disentangling biological, psychological, and social determinants of health factors that contribute to risk for mental and substance use disorders broadly from those that may be relevant more uniquely during and after pregnancy. In the same context, further work is needed to better delineate mediators of risk that are causally and mechanistically linked to perinatal mental and substance use disorders from moderators of risk that may affect the strength and direction of other factors. Although a greater understanding of moderators as well as mediators will undoubtedly contribute to the development of better prevention and treatment strategies, increasing understanding of mediators will be particularly fruitful for defining promising biological, psychological, and social targets for intervention.

Developing standardized competencies and curricula related to perinatal mental health: Training programs across every behavioral health field including psychiatry, psychology, social work, mental health counseling, and advanced practice nursing, lack standardized required competencies in perinatal mental health. The often inadequate and patchy training received by behavioral health professionals at the graduate, postgraduate, and continuing education level is striking. The lack of priority given to perinatal mental and substance use disorders in behavioral health training programs across the country is an important instance of a broader historic inattention to women's health generally. Fortunately, this is changing but will require a concerted effort within each discipline to adopt standardized competencies within accredited training programs. As many current practitioners are beyond their formal training years, additional continuing educational opportunities as well as requirements, where relevant, for training in perinatal mental health as a component of recertification or license renewal are needed. The strongest single recommendation of this white paper is to enhance required training in perinatal mental health across all behavioral health disciplines as a unique and much-needed area of competence.

Expanding knowledge to support shared decision making: The evidence base on therapeutics continues to support the safety and efficacy during and after pregnancy of many of the medications, psychotherapies, and neuromodulation treatments that are evidenced based for mental and substance use disorders outside of the perinatal period. Exceptions include certain medications, such as valproic acid. In addition, pregnancy and breastfeeding may require enhanced monitoring of dosing and/or levels for other medications, such as lithium and lamotrigine. For most medication and nonmedication treatments, a well-informed risk–risk discussion needs to be central to care of individuals at risk for perinatal mental and substance use disorders. This includes reviewing the potential risks of treatment as well as the risks of discontinuing or withholding treatment. Whenever possible, for individuals with a known history of mental or substance use disorders, these discussions should take place during conception planning and certainly at the earliest point possible if an individual has already conceived. In addition, further research is needed on the risk–risk calculation related to use of medication for substance use disorders, including medication for opioid use disorder and nicotine replacement therapies. Finally, the care of individuals with mental or substance use disorders during the perinatal period is inherently multidisciplinary, typically involving obstetric practitioners, behavioral health practitioners, and pediatricians or family medicine practitioners. The traditional siloing of mental health care from other health care—which serves no patient well—serves individuals during the perinatal period particularly poorly given the elevated



potential for adverse health outcomes during and after pregnancy, particularly among historically marginalized and vulnerable groups.


Community engagement: In addition to factors such as lack of screening and referral and the lack of behavioral health practitioners with expertise in perinatal mental health, stigma, social determinants of health, and cultural factors contribute importantly to gaps in care for persons with perinatal mental and substance use disorders. Meaningful progress toward eradicating barriers to perinatal mental health care requires robust collaboration between community leaders and other stakeholders, community agencies and faith-based organizations, behavioral health professionals, and other health professionals to reduce stigma, promote awareness, share reliable information, and provide logistical assistance (e.g., transportation, childcare). The expansion of state programs providing mental health consultation to obstetricians, pediatricians, and other health professionals described in this white paper as well as bipartisan federal legislation related to perinatal mental health (<https://www.hassan.senate.gov/news/in-the-news/senator-hassans-bipartisan-bill-to-improve-maternal-mental-health-now-law-supported-by-leading-maternal-health-advocacy-group>) also represent important steps toward broadening access to perinatal mental health care.

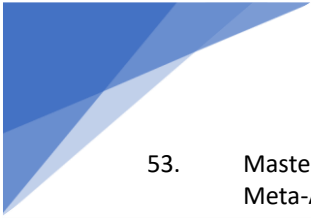
To paraphrase an oft-cited proposition attributed to psychiatrist Brock Chisholm, the first Director-General of the World Health Organization, without perinatal mental health there can be no true perinatal health. Access to high-quality mental health care during and after pregnancy is essential to optimal health outcomes for pregnant persons and their offspring. Efforts to promote awareness among healthcare professionals and within communities, reduce stigma, develop, and disseminate evidence-based prevention and treatment strategies, and dramatically expand the behavioral health workforce adequately equipped to provide care for perinatal mental and substance use disorders are urgently needed.





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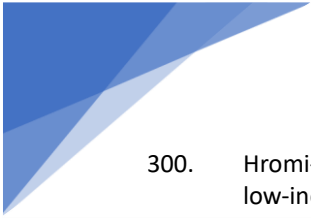
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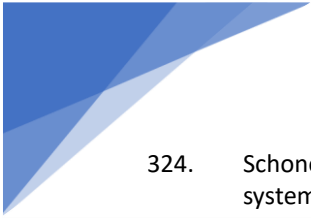
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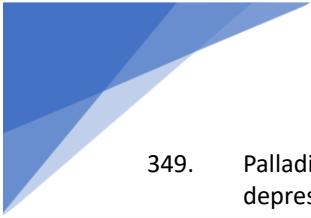
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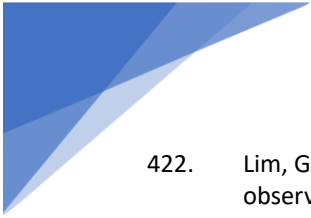
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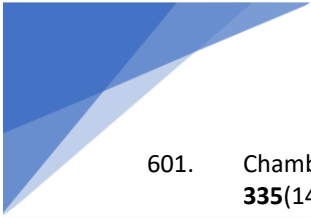
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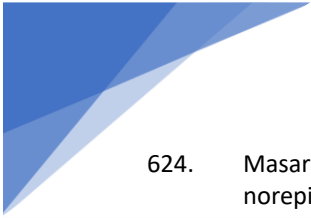
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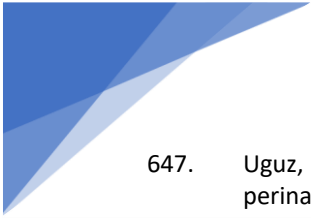
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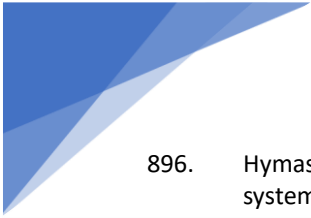
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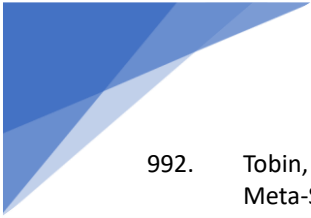
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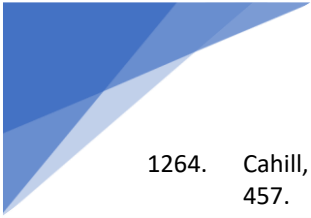
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