

### Women's Mental Health: Core Concepts for Community Psychiatry

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#### Introduction

Women's mental health is a broad term that refers to the biological, psychological, and social aspects of mental health that differentially affect women. Discoveries in women's mental health span biological sex differences pertaining to psychiatric practice, the influence of female reproductive hormone fluctuations on psychiatric conditions, and the impact of societal influences on the mental health of women. The study of women's mental health has grown tremendously over the past four decades in the context of important policy and advocacy efforts within the medical scientific community and resulting man-

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dates on the level of the National Institutes of Health (NIH) for inclusion of women in funded clinical research as well as for analysis of data by sex (Osborne et al. 2015). A sampling of important milestones includes the "postpartum onset specifier," first included in the DSM-IV. This was modified to the "perinatal onset specifier" in the DSM 5, an edition that also first formally acknowledged premenstrual dysphoric disorder (PMDD) as a distinct psychiatric diagnosis (American Psychiatric Association 2013). In 2015, in response to increased knowledge of how to understand potential risks of medications given during pregnancy, the Federal Drug Association (FDA) removed the misleading ABCDX categories and introduced a more comprehensive system to communicate reproductive safety data (Osborne et al. 2015). Finally, 2019 saw the first pharmacologic treatment approved specifically for postpartum depression, brexanolone (Powell et al. 2020).

While a full accounting of the field of women's mental health is beyond the scope of this textbook, this chapter aims to synthesize knowledge most applicable to the care of women living with severe mental illness (SMI) in a practical manner for community psychiatrists. The chapter is divided into two primary subsections. The first subsection covers aspects of women's mental health as they pertain to the reproductive lifespan, including sexual health, contraceptive care, preconception counseling,

perinatal care, and the perimenopause period. Each of these topics represents critical components of health with important considerations for women living with SMI. The second subsection covers three types of violence which disproportionately affect women and have pervasive effects on health: intimate partner violence, sexual assault, and sex trafficking. This section includes guidance on how to identify and respond to these experiences as encountered in clinical care.

A limitation of this chapter is that, while written to address the distinct needs of women within psychiatric treatment, the construct of "women's mental health" will not accurately capture many individuals who may be impacted by the outlined topics. Many people assigned female sex at birth do not identify as women, yet may experience pregnancy or menopause. Likewise, transgender females do not experience the same fluctuations in reproductive hormones as cisgender females. While a strong body of evidence exists to inform the critical need to reduce barriers and improve outcomes for LGBTQ+ individual across all domains of healthcare (Baptiste-Roberts et al. 2017), relatively little is known about the mental health impact of primary reproductive transitions for gender diverse populations (Hutner et al. 2021). While there is considerable momentum within the realm of women's health to move toward more gender-inclusive language (i.e., "reproductive and sexual health" rather than "women's health") (Stroumsa and Wu 2018), the implementation of this important concept has not been well-elucidated in women's mental health, which necessarily includes aspects of "womanhood" which are outside the domain of reproductive health. Nonetheless, it's likely that many of the subjects discussed in this chapter will be relevant to the care of individuals across the gender spectrum. For more information specifically on the clinical care of LGBT+ individuals, the reader may reference chapter "Clinical Issues and Programming for Sexual and Gender Minority Populations".

# Women's Mental Health Across the Reproductive Lifespan

#### **Sexual Health**

According to the World Health Organization, sexual health "requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence" (World Health Organization 2021a). Across the female reproductive lifespan, fluctuations in reproductive hormones, psychological symptoms, relationship factors, and psychosocial issues may impact sexual health in critical ways. Furthermore, pharmacologic treatment for psychiatric conditions may impact sexuality. Clinicians often do not inquire about sexual health, yet research demonstrates that patients wish to discuss sexual health with their psychiatrist (Barker and Vigod 2020).

Individuals with serious mental illness (SMI), including schizophrenia, bipolar disorder, and major depressive disorder, have similar sexual needs to the general population, but may present with distinct challenges (Barker and Vigod 2020). For those living with psychotic disorders, positive and negative symptoms, cognitive deficits, and medication side effects impact the capacity for intimate relationships and sexual functioning. Depression and anxiety affect the sexual response at multiple levels, with lower levels of desire and incentives for sexual behavior and diminished capacity for psychological and physical arousal (Basson and Gilks 2018). Individuals with bipolar disorder may engage in higher-risk sexual behaviors during the manic phase (Dell'Osso et al. 2009). Further, sexual trauma has been identified as one of the most potent risk factors for adult sexual dysfunction in the general population, affecting arousal, desire, orgasm, and pain (Bigras et al. 2021).

Treating a woman's sexual dysfunction involves a multimodal approach including ensuring psychiatric stability, using lowest effective doses of agents with limited sexual side effects,

Medication/	Mechanism of action	Sexual dysfunction risk	Potential strategies for mitigating risk
SSRIs	Blocks 5HT reuptake	High	Exercise prior to sexual activity Dose reduction Switch to alternative with fewer sexual side effects (vortioxetine, vilazodone, bupropion, mirtazapine, or desvenlafaxine) Augmentation with bupropion, aripiprazole, or vortioxetine
Antipsychotics	Antagonism of D <sub>2</sub> antagonism of 5HT <sub>2A</sub> , variable effects at 5HT <sub>1a</sub> , a <sub>1</sub> , a <sub>2</sub> , H <sub>1</sub> , M <sub>1</sub>	Low-medium	Dose reduction Switch to alternative with fewer sexual side effects such as aripiprazole or quetiapine

Table 1 Implications for sexual health by medication class

Basson and Gilks (2018), de Boer et al. (2015), Keepers et al. (2020)

and optimizing medical comorbidities such as vulvovaginal atrophy, diabetes, obesity, and hypothyroidism (Barker and Vigod 2020). Psychotropic medications often compromise sexual health, resulting in side effects and sexual dysfunction. See Table 1 for a summary of the common sexual implications of major classes of medications.

#### **Contraceptive Care**

Contraceptive information and services are a critical component of health. Individuals with psychiatric illness may be at particular risk for inadequate contraception or nonadherence to methods which require daily use, such as oral contraceptive pills (Barker and Vigod 2020). Psychiatrists should be prepared to have informed discussions about contraception with all female patients of reproductive age. This involves engaging patients in discussion of reproductive health goals and preferences, having knowledge of available contraceptive options, and understanding interactions between contraceptives and psychotropic medications.

#### Approach to Contraceptive Counseling

Providers must consider that women with SMI may have limited knowledge about sexuality and reproduction and carry misperceptions about contraception. The following approaches should be utilized:

- *Timing:* Provide counseling when patients are not acutely experiencing symptoms that would affect their ability to attend to, comprehend, retain, or evaluate the information presented.
- Presentation: Present information in a way that is accurate, simple, and clear. Supplement verbal counseling with simple written educational materials.
- Correct Use: Emphasize method-specific effectiveness rates, many of which are dependent upon correct use. Explain how psychiatric illness may interfere with correct use of certain contraceptives (i.e., severe mood disorder or psychosis affecting one's ability to take oral contraceptive medication daily or attending regular appointments for a subcutaneous injection).
- Partners: Effective use of some methods, like condoms, relies upon partner cooperation and support. Because some women may have difficulties negotiating contraceptive use before or during sex, it is important for providers to screen for intimate partner violence (IPV) and discuss contraceptive methods which do not depend on partner cooperation. Engage partners in contraceptive counseling when appropriate (Guedes et al. 2009).

## Contraceptive Methods and Considerations

The Medical Eligibility Criteria for Contraceptive Use developed by the Centers for Disease Control and Prevention is a comprehensive guide which rates contraceptive methods from most effective (Tier 1) to least effective (Tier 3) (Curtis et al. 2016). See Table 2 for a summary of contraceptive methods and ratings.

## Psychotropic and Contraceptive Drug Interactions

Pharmacologic interactions between psychotropic drugs and contraceptives exist for hormonal contraceptives (HCs). See Table 3 for a review of said interactions.

#### **Contraceptives and Mood Symptoms**

The effect of contraceptives on mood symptoms remains unclear (McCloskey et al. 2021). Data from randomized placebo-controlled trials suggest that women with psychiatric illness who use hormonal contraception have equal or lower rates of mood symptoms compared to non-users (Lundin et al. 2017). However, contraceptive discontinuation rates from perceived mood symptoms have been reported from 14% to 21% (Robinson et al. 2004). It is important to counsel on possible emergence of mood symptoms and discuss options to switch to other effective contraceptive methods (i.e., formulations with lower hormonal dosages or non-hormonal options such as the copper IUD). Drospirenone-containing oral contraceptive pills have been approved by the FDA for the treatment of mood symptoms occurring during premenstrual dysphoric disorder and could be considered for women with mood and anxiety disorders (Lopez et al. 2012). If mood symptoms emerge during particular phases of the menstrual cycle, extended cycle regimen or continuous dosing could be considered (Edelman et al. 2014).

#### **Preconception Counseling**

Preconception planning is a critical component of psychiatric care for all women of reproductive age. Approximately 50% of pregnancies are unplanned and women living with SMI are likely to be at increased risk for unintended pregnancy (Barker and Vigod 2020). Pregnancy is likely to

introduce additional risk for illness exacerbation, and medications prescribed for the treatment of psychiatric illness may be associated with obstetrical or neonatal risk at the earliest embryonic stages. The concept of preventative ethics, an aim to anticipate and prevent ethical dilemmas in the practice of healthcare, guides the psychiatrist to discuss family planning early in treatment and as a routine component of care during periods of illness stability (Miller 2009).

Psychiatrists should inquire about a patient's obstetrical history, plans for pregnancy, and contraceptive preferences and practices. Patients should be informed about potential risks of the underlying illness during the perinatal period, as well as the potential risks of prescribed medication to have teratogenic effects or increase obstetrical risk.

#### Impact of Psychiatric Illness on Fertility

While many patients may be concerned about how their psychiatric illness impacts their ability to conceive, current evidence suggests that the fertility rates of women with severe mental illness are equal to or approach that of the general population (Vigod et al. 2012). The exception to this general finding, however, is within the diagnostic domain of eating disorders. Anorexia and bulimia nervosa account for up to 60% of cases of anovulatory infertility (The ESHRE Capri Workshop Group 2006).

#### **Pharmacologic Treatment Planning**

Preconception treatment planning is best approached via a "risk-risk" analysis, in which the risks of potential pharmacologic treatments during pregnancy or lactation are weighed in conjunction with the risks of the underlying illness. This approach considers the potential for omission bias, defined as a discussion of the risks of commission (prescribing a medication) without a similar level of detail about the risks of omission (not prescribing a medication). In studies of medical decision-making, omission bias is common and likely to be based on an underlying belief on the part of a physician that introducing a risk is a stronger concern than failing to reduce a risk (Miller 2009).

**Table 2** Medical and psychiatric considerations for contraceptives

	Typical use failure rate <sup>a</sup>		Medical considerations	Potential psychiatric drug interactions	Psychiatric considerations
Tier I					
IUDs <sup>b</sup> Copper Progestin	0.1-0.8%	Replace every 3–10 years	_		Few adherence issues and reversible, preferable for SMI Hormone action is local (with progestin-IUDs); copper IUD is non-hormonal and may be preferable for women who have experience adverse somatic or psychiatric effects with hormonal contraception. Irregular bleeding patterns possible Inconspicuous, preferable for IPV
Progestin subdermal implant <sup>b</sup>	0.1%	Replace every 3 years	-	Not recommended with TCAs, MAOIs, St. John's wort, mood stabilizers, antiepileptics	Few adherence issues and reversible, preferable for SMI Irregular bleeding patterns possible Inconspicuous, preferable for IPV
Permanent methods Female sterilization Vasectomy	0.15– 0.5%	N/A – procedural			Present ethical concerns in women with SMI and cognitive impairment, especially in light of psychiatry's disturbing history in the eugenics movement (Roelcke 2019)
Tier II				·	·
Medroxyprogesterone acetate injection	4%	Injection every 3 months	Monitor for weight gain, truncal fat deposit, and peripheral glucose intolerance		Irregular bleeding patterns possible Less invasive than IUDs, may be preferred in cases of cognitive impairment where ethical considerations arise Inconspicuous, preferable for IPV but requires frequent health service visits

(continued)

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 Table 2 (continued)

	Typical			Potential	
	use failure rate <sup>a</sup>	Administration	Medical	psychiatric drug	Psychiatric considerations
Progestin-only oral contraceptives	7%	Daily at the same time	Efficacy reduced with delayed or missed doses	Not recommended with TCAs, MAOIs, St. John's wort, mood stabilizers, antiepileptics	Daily dosing at the same time requires higher level of cognitive functioning
Combined oral contraceptives	7%	Daily	Efficacy reduced with missed doses Not recommended for women <1 month postpartum OR women with cardiovascular risk factors, age >35 years, smokers, and with other estrogen contraindications due to risk of VTE, MI, and stroke	Not recommended with TCAs, MAOIs, St. John's wort; not optimal with mood stabilizers, antiepileptics, may need to monitor drug levels and adjust dosages as necessary if other methods are not feasible Can cause increased drug levels of clozapine	Extended-cycle preparations may be preferable for women with somatic and mood symptoms that are sensitive to hormonal fluctuation Menstrual suppression for hygiene management may be requested by women with disabilities or their caretakers COCs may have therapeutic benefit for hyperprolactinemia Daily dosing requires higher level of cognitive functioning
Transdermal hormonal patch	7%	Weekly replacement			
Vaginal ring	7%	Monthly replacement			
Tier III		-			
Male condom	13%	Single use	Dual use of	_	Significant adherence
Female condom	21%	Single use	condoms plus more effective methods should be routinely encouraged to avoid STI	-	issues, high effort, high user failure rates and need for partner compliance make these options not
Sponge, spermicide, diaphragm or cervical cap	14– 27%	Variable	_	_	optimal as first-line contraceptives Condoms should be encouraged as dual use to protect against STIs Acceptable when all other effective options are not feasible

 $<sup>^{</sup>a}$ Estimates are provided of probabilities of failure during typical use (which includes both incorrect and inconsistent use) (Trussell 2011)

<sup>&</sup>lt;sup>b</sup>IUDs and the progestin subdermal implant are long-acting reversible contraceptives (LARC) Curtis et al. (2016)

 Table
 3 Psychotropic
 and contraceptive
 drug interactions

#### Effect of HCs on psychotropics

- Clozapine concentrations increase when combined with HCs because of reduced activity of hepatic CYP P450 1A2, 2C19, and 34A enzymes. Clozapine doses must parallel the contraceptive regimen and be reduced in the active hormone phase, during which clozapine plasma concentration may increase 2–3× compared to the non-hormonal phase (Bookholt and Bogers 2014). Intrauterine devices, subdermal implant, and depot-medroxyprogesterone acetate are preferred, as these do not undergo the first-pass hepatic metabolism of HCs.
- Lamotrigine concentrations decrease when combined with HCs as ethinyl estradiol is a potent inducer of the uridine diphosphate glucuronosyltransferase (UGT) system. Clinicians should consider an increase in the maintenance dose of lamotrigine prior to initiation of a combined oral contraceptive (OCP), with further increases if clinically indicated. A baseline serum level of lamotrigine obtained prior to OCP therapy can provide a useful baseline for comparison later (Christensen et al. 2007; Reddy 2010).
- Valproic acid concentrations decrease when combined with HCs in a similar mechanism to lamotrigine. Additionally, ethinyl estradiol increases clearance of valproic acid (Herzog et al. 2009). Without dose adjustment, this may lead to decreased mood stability. Valproic acid is generally not recommended for women of childbearing age unless combined with a high-efficacy long-acting reversible contraceptive (LARC) due to risk of teratogenicity and neurodevelopmental effects (Meador et al. 2009; Weston et al. 2016).

#### Effect of psychotropics on HCs

- Carbamazepine reduces HC efficacy by increasing the production of sex-hormone-binding globulin, which tightly binds and reduces the concentration of free progestin (Dutton and Foldvary-Schaefer 2008).
   Intrauterine devices and depot-medroxyprogesterone acetate are preferred.
- Carbamazepine, oxcarbazepine, and St. John's wort reduce HC efficacy by inducing the CYP3A4 system, which increases the clearance of contraceptive steroids (including progestin) (Berry-Bibee et al. 2016; Davis et al. 2011; Hlengwa et al. 2020). Intrauterine devices and depot-medroxyprogesterone acetate are preferred.
- Lamotrigine reduces the blood concentration of progestin by approximately 20% in women taking HC; however it has not been shown to reduce HC efficacy (Sidhu et al. 2006). Intrauterine devices and depotmedroxyprogesterone acetate may be preferred.

Risks of untreated psychiatric illness vary broadly by illness and severity, but generally include impaired functioning, risk of suicide and hospitalization, poor prenatal care, increased substance use, preterm birth, postpartum depression or psychosis, and problems with attachment (Fitelson et al. 2021). Understanding associated risk for illness recurrence or exacerbation during pregnancy and in the postpartum period for specific psychiatric conditions is critical. In the setting of long-standing mental illness and treatments, clinicians should carefully review all aspects of the patient's history to confirm current diagnoses and indicated treatments, particularly in the setting of traumatic experiences or substance use. Important considerations when evaluating risk of untreated psychiatric illness include the severity of a patient's previous illness episodes, degree of recurrence in her illness history, level of psychosocial and familial support, degree of insight into symptoms, and access to medical and psychiatric care (Fitelson et al. 2021).

In considering the risks of the medication, clinicians must consider several questions. The first is, "What is likely to work for this patient?" Introducing a medication that has a high level of reproductive safety is not helpful if it doesn't allow the patient to achieve or maintain illness stability. Once medications with likely efficacy are identified, one must consider the overall level of data ("how much is known"), as well as "what is known" about its associated risk of teratogenicity, spontaneous abortion, obstetrical complications, neonatal complications, and adverse developmental outcomes. Consideration of safety in lactation should be considered from the start to avoid the need to switch medications during a high-risk period. Purposefully selected medications should be utilized at the lowest effective dose and, when possible, polypharmacy should be avoided. These principles are summarized in Table 4. Ultimately, the goal is to develop a treatment plan that best balances risk with efficacy. By including the patient, her family, and her treatment team in discussions about treatment planning, providers can minimize miscommuni-

**Table 4** General tenets perinatal psychiatry

Inquire about reproductive goals and contraceptive preferences as a component of routine care

Engage in preconception counseling with the goal of a treatment plan that best balances risk with efficacy

Confirm accuracy of historical diagnoses and indications for treatment

Engage patient in a risk-risk discussion which includes the risk of untreated/undertreated psychiatric illness vs. the risk of indicated medication

Consider risks associated with specific diagnoses

Consider severity of illness

Maximize non-pharmacologic treatments

Prioritize sleep

Consider the level of data when interpreting risk of medication

Utilize the lowest effective dose

Avoid polypharmacy when possible

cation and maximize the patient's treatment outcomes (Chisolm and Payne 2016).

It is important to note that a risk-risk analysis will almost always reveal elevated risk on both sides of the equation as treatment of illness during pregnancy is necessarily a situation with elevated risk. At times, this may lead to the false sense on either the part of the patient or the clinician that the well-being of the mother is at odds with the well-being of a developing fetus. In these circumstances, a helpful ethical construct to consider is that of relational ethics—the perspective that a mother's well-being and her baby's well-being are intertwined. Having a healthy and functioning mother is beneficial both for the developing fetus and future children; likewise a positive birth outcome, and a sense of security about the overall health and development of a child, is beneficial for mothers (Miller 2009).

#### **Perinatal Psychiatry**

As optimizing the treatment plan for women with psychiatric illness during the perinatal period is best accomplished in the preconception period, the general tenets of perinatal psychiatry are discussed in the preceding section. However, practically speaking, psychiatrists are likely to find themselves in the situation where a patient is

seeking advice about the optimal treatment plan once already pregnant. In these instances, there are additional factors to consider. A patient currently taking an effective medication may inquire about switching to a medication that is "safer" in pregnancy. However, switching medication during pregnancy may potentially increase reproductive risk by increasing the number of exposures during a pregnancy as well as increasing the risk for recurrence of illness (Chisolm and Payne 2016). In this context, consideration should be given to continuing an effective medication that the patient has already taken during this pregnancy. The timing of reproductive risk should also be considered in the context of the patient's pregnancy. Switching a medication based on teratogenic risk would not be an effective strategy once organogenesis is complete.

Breastfeeding is associated with multiple well-established benefits for both mother and infant; thus many women prefer to breastfeed. Psychiatrists should discuss infant feeding preferences with patients early in the process of preconception planning or treatment during pregnancy. Considerations in this discussion should include the benefits of breastfeeding as well as the potential risks due to her underlying illness or indicated medications. Strategies to effectively prioritize sleep in the setting of breastfeeding are critical and may include entailing support persons to bring the infant to breastfeed during the night while attending to other aspects of infant nighttime care (changing diapers, settling back to sleep, etc.) (Nagle-Yang et al. 2021a). Women with very limited supports or severe symptoms may not be able to safely breastfeed. Likewise, in some instances, the risks of indicated medications or underlying illness outweigh the benefits of breastfeeding. Providing support to women in navigating this complex decision may be a powerful intervention at a stressful time. Finally, regardless of how a woman chooses to feed her infant, psychiatrists should exercise caution in prescribing sedating medications to a patient caring for a young infant. When such medications are required, psychiatrists should recommend additional supports during nighttime feedings and provide guidance on safe sleep practices, as sedating medications are known to further increase the risk for sudden infant death syndrome associated with parentinfant bed sharing (Task Force on Sudden Infant Death Syndrome 2016).

The field of perinatal psychiatry has grown tremendously over the past few decades and has translated to increased knowledge of the phenomenology of psychiatric illness as well as associated risks. While a full accounting of this field is beyond the scope of this chapter, a summary of diagnoses and treatments most relevant to community psychiatrists is provided below.

#### Schizophrenia

#### **Prognosis in Perinatal Period**

Current data suggests that pregnancy is not protective for women with schizophrenia. Preconception illness severity and choices surrounding medication management are correlated with risk of relapse. The postpartum period is a high-risk period with increased risk for hospitalization throughout the first 6 postpartum months (Taylor et al. 2018).

#### **Risks of Not Treating**

Women with schizophrenia are at increased risk for obstetric complications including antepartum hemorrhage, low birth weight, placental abruption, intrauterine growth restriction, and preterm delivery (Tosato et al. 2017). These risks are likely multifactorial in etiology, and associations are confounded by higher rates of medical comorbidities and substance use and lower rates of prenatal care among women with this illness (Møller-Olsen et al. 2018). Of note, one study found that controlling for various maternal factors reduced differences in adverse pregnancy outcomes between women with and without schizophrenia; however those with an acute episode of psychosis during pregnancy remained at elevated risk even after these adjustments (Nilsson et al. 2002).

#### **Medication Treatments**

 Oral antipsychotics: Increasing data on second-generation antipsychotics (SGAs) is largely reassuring and does not support a significant association with congenital malformations, although one study did find a slight increase in cardiac malformations with risperidone specifically (Nagle-Yang et al. 2021b). Patients taking SGAs during pregnancy should be monitored for gestational diabetes, excessive maternal weight gain, and abnormalities in fetal growth (Park et al. 2018). While quetiapine is often preferred due to low placental passage rate and low breast milk transmission, caution should be exercised in breastfeeding due to potential sedating qualities (Nagle-Yang et al. 2021b). Newer medications (i.e., lurasidone) should be avoided in pregnancy when possible due to overall lack of data. Among first-generation antipsychotics, haloperidol has the highest level of data, and available data suggest this medication is not a major teratogen (Einarson and Boskovic 2009). Use of first-generation antipsychotics during late pregnancy has been associated with transient extrapyramidal symptoms in exposed neonates (Kulkarni et al. 2014).

- Clozapine: Clozapine merits special consideration given its role in treatment of schizophrenia in treatment-resistant cases or instances where alternate medication side effects of intolerable (Warnez and Alessi-Severini 2014). A recent review article by Mehta and Van Lieshout (2017) discussed the limitations of evaluating the safety of clozapine during pregnancy, including difficulty establishing a control group, lack of ability to control for comorbidities, and the role of polypharmacy. Thus, careful consideration of risks and benefits of treatment must be considered in the treatment of pregnancy patients. Based on review of approximately 200 case reports, Larsen et al. (2015) report there is no clear pattern of congenital malformations identified (Larsen et al. 2015). Clozapine is often considered a contraindication to breastfeeding due to high concentration in breast milk and risk for agranulocytosis in infants (Mehta and Van Lieshout 2017).
- Long-acting injectable antipsychotics: While the benefits of long-acting injectable (LAI)

antipsychotics are well established, there is a paucity of literature on the reproductive safety profile during pregnancy (Orsolini et al. 2021). Available data is limited to case reports on individual long-acting agents, which have not reported associated malformations (Ballester-Gracia et al. 2019). Some, but not all, case reports have reported adverse obstetrical or neonatal outcomes (Clinebell et al. 2017). These case reports are difficult to interpret due concurrent polypharmacy or missing information regarding potential confounding factors. While the weak level of data for LAI antipsychotics suggests that a switch to oral formulations in anticipation of pregnancy may be indicated, psychiatrists must consider the individual patient's treatment history, disease course, and previous medication trials. In the setting of a patient with a history of nonadherence to oral medication and a severe disease course, continuing an LAI antipsychotic as a component of a comprehensive treatment plan may be the strategy that best balances the risk of the underlying illness vs. the risk of the indicated medication. As LAIs bypass firstpass hepatic metabolism, it is theorized that they are less effected by pharmacokinetic changes of pregnancy and may offer more stable blood levels as pregnancy progresses (Nagle-Yang et al. 2021b).

#### Depression

#### **Prognosis in Perinatal Period**

Perinatal depression is the most common complication of childbirth and affects 15–20% new mothers (Osborne and Birndorf 2021). For women with a history of major depressive disorder, pregnancy is not protective against recurrence, and the postpartum period can be particularly high risk (Osborne and Birndorf 2021). Discontinuing previously effective maintenance medication increases the likelihood of illness relapse (Cohen et al. 2006).

Of note, the DSM 5 provides a "peripartum onset" specifier that can be applied to depressive, manic, or hypomanic episodes with onset during pregnancy or within 4 weeks postpartum (Sharma

and Mazmanian 2014). However, this time association remains controversial with evidence suggesting that mothers remain vulnerable to postpartum mental illness several months after delivery (Munk-Olsen et al. 2006a; Munk-Olsen et al. 2006b).

#### **Risks of Not Treating**

Left untreated, perinatal depression can have a pervasive impact on the health of the mother and her child. Depression during pregnancy is associated with adverse obstetrical outcomes such as preterm birth, low birth weight, operative delivery, and preeclampsia (Henshaw 2009). Depression during pregnancy also predicts postpartum depression, with well-established impact on parenting practices, infant and child development, and the mother-child relationship (McLearn et al. 2006).

#### Medication

SSRIs as a class have a high level of data to inform reproductive safety. Current data do not support associations with congenital malformations, although there is some mixed information specifically around paroxetine and cardiovascular malformations (Yonkers et al. 2014). SSRIs do show associations with a small increased risk for preterm delivery (as does untreated depression) and persistent pulmonary hypertension of the newborn (PPHN) (Grigoriadis et al. 2014). When used in the second half of pregnancy, they are associated with an increased risk for neonatal adaptation syndrome (Byatt et al. 2013). While sertraline is often considered first-line in the perinatal period due to the level of data available and its low breast milk transmission, all SSRIs are considered compatible breastfeeding with (Stewart and Vigod 2019).

#### **Bipolar Disorder**

#### **Prognosis in Perinatal Period**

Current research suggests pregnancy is not protective for women with bipolar disorder, and the postpartum period is particularly high risk (Di Florio et al. 2018). Women with bipolar disorder are 7x as likely to experience a first-time psychi-

atric admission and twice as likely to experience a psychiatric re-admission, for affective psychosis in the first postpartum month relative to postpartum healthy controls (Terp and Mortensen 1998). Data indicates that there is two times the risk of relapse in women who discontinue mood stabilizing medication during pregnancy compared to women who continued treatment (Viguera et al. 2007). Postpartum psychosis is a rare but serious condition that typically presents as a psychiatric emergency. While postpartum psychosis may occur outside of the setting of bipolar disorder, a personal or family history of bipolar disorder is one of the strongest risk factors for postpartum psychosis (Wesseloo et al. 2016).

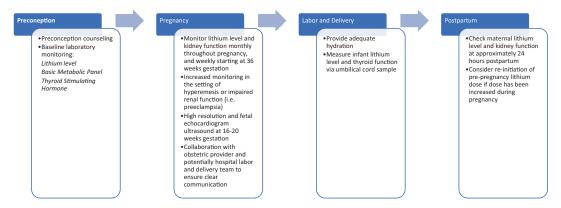
#### **Risks of Not Treating**

Women with bipolar disorder are at increased risk for a variety of obstetrical and neonatal adverse outcomes including preeclampsia, placental abnormalities, intrauterine growth restriction, low birth weight, preterm birth, and small for gestational age infant and neonatal hypoglycemia (Nagle-Yang et al. 2021a). As in the setting of maternal schizophrenia, studies examining outcomes among women with bipolar are often confounded by higher rates of substance use and obesity and decreased rates of prenatal care among women with bipolar disorder relative to the general population.

#### **Mood Stabilizers in Pregnancy**

· Lithium: Associations between lithium and cardiac malformations, most notably Epstein's malformation, have been reported since the 1970s. However, beginning in the 1990s epidemiologic studies suggested that the initial reports of risk were likely overestimations (Cohen et al. 1994). In recent years, several large-scale studies have dramatically increased knowledge on this topic and suggest that while lithium may have an association with cardiac or overall malformations, this risk is occurring at rates much lower than previously suggested and may be dose-dependent (with stronger associations at doses at or greater than 900 mg/ day) (Fornaro et al. 2020). As lithium is a highly effective treatment option for bipolar disorder, with increasing data to support its use for preventing postpartum mood episodes and postpartum psychosis in women with bipolar disorder, it is currently considered a viable option during the perinatal period for women when indicated.

- Physiologic changes in pregnancy which affect the pharmacokinetics of lithium include increased total body water content and increased glomerular filtration rate (GFR) (Pariente et al. 2016). Given the renal clearance of lithium (Oruch et al. 2014), changes in GFR can decrease lithium blood levels, making frequent serum monitoring important in assessing for adequate dosing and/or toxicity (Deligiannidis et al. 2014). Expert recommendations for lithium monitoring during the perinatal period are summarized in Fig. 1.
- Lamotrigine: Lamotrigine has a high level of largely reassuring data to inform reproductive risk (Nagle-Yang et al. 2021a). Thus, it is often considered a first-line approach to treatment of bipolar disorder in the perinatal period, particularly for women who have experienced a preponderance of depressive episodes. While earlier research by Holmes et al. (2008) of infants exposed to lamotrigine in the first trimester identified a small elevated risk of oral cleft palate or lip, a more recent large study incorporating data from over 10 million births did not identify an increased risk of cleft palate or overall malformation in infants with in utero exposure to lamotrigine (Dolk et al. 2016), and several international registries have reported no increase in risk for malformations with lamotrigine (Tomson et al. 2018).
- Increasing estrogen levels during pregnancy accelerate the metabolism of lamotrigine which correlates to decreased serum concentration of the medication (Clark et al. 2013). As there is not a clear consensus on the therapeutic level of lamotrigine for treatment of bipolar disorder, it is recommended to obtain a preconception therapeutic level in patients stabilized on lamotrigine. During pregnancy, some experts recommend monitoring monthly



**Fig. 1** Recommendations for lithium monitoring during the perinatal period (Nagle-Yang et al. 2021a; Wesseloo et al. 2017)

lamotrigine serum levels and, if clinically indicated, increasing the dose to maintain the patient's baseline therapeutic level (Clark et al. 2013). If the dose is increased during pregnancy, decreasing the dose by 25% after delivery is recommended to avoid toxicity, with subsequent decreases every 3–4 days until the patient is at preconception therapeutic dose (Clark and Wisner 2018).

Valproate: Valproate is considered a human teratogen with a 10% overall risk of major malformations and clear association with adverse developmental outcomes in children exposed in utero including reduced IQ, autism spectrum disorders, impaired verbal acquisition, and behavioral disturbances (Wieck and Jones 2018). Psychiatrists should avoid use of valproate in women of reproductive age. If valproate is necessary for treatment of bipolar disorder that has been refractory to other treatment options, counseling on these risks and providing guidance on highly-effective contraception is recommended (Khan et al. 2016).

#### Parenting While Living with SMI

Recent data suggest that women living with SMI are as likely as women in the general population to become pregnant, and most will experience motherhood (Vigod et al. 2012). Motherhood is a normative experience of adulthood and one that, for most, is a central component of identity and purpose. For women living with severe mental illness, the role of motherhood may provide an

increased sense of self-competence, meaning, and hopefulness or has the potential to reinforce feelings of stigma and shame (Hine et al. 2018). Despite the central role of parenthood in one's identity and connection to community, to date the experience of parenthood as a component of the mental health recovery model hasn't been well elucidated (Hine et al. 2018).

While many women living with SMI can successfully parent, mental illness is likely to have far-reaching impacts across domains of functioning, and as a group women with SMI demonstrate significant parenting challenges. Women with schizophrenia are more likely than healthy controls to display a passive or withdrawn parenting style, show interactional deficits with their infants, and lack knowledge of child development (Nagle-Yang et al. 2021b). Depressed mothers, relative to non-depressed mothers, are less likely to routinely talk with their child or adopt other age-appropriate safety and developmental practices such as using electric outlet covers, establishing daily routines, or limiting screen time (McLearn et al. 2006). Women who are experiencing sequelae of trauma may struggle with boundary distortions, difficulty with emotional regulation during parenting interactions, and diminished parenting supports (Noll et al. 2009). While there is a paucity of data regarding the parenting practices of mothers with bipolar disorder, children of parents with bipolar disorder are well-understood be at increased risk for mood disorders themselves (Axelson et al. 2015).

This risk is likely multifactorial and includes both genetic and environmental factors. Of note, families which include a parent with BD have been found to have lower levels of family cohesion and expressiveness and higher levels of conflict (Belardinelli et al. 2008).

When considering the care of mothers living with SMI, it is important to note that the rate of custody loss is high. Among women with mental illness, women with schizophrenia are at highest risk (Howard et al. 2003). Approximately half of women with this diagnosis will experience a period of custody loss, and fear of custody loss is a common experience in this population (Seeman 2012). Nonetheless, most women with SMI will raise or help to raise at least one child (Nicholson et al. 1998).

Support for parenting is a critical component of a comprehensive treatment plan for pregnant individuals and parents living with SMI. On the individual level, clinicians should acknowledge the centrality of the parenting role, even in situations in which a patient is not currently the primary parent. Positive, strength-based language balanced with acknowledgment of parenting challenges can move care toward a more personand family-centered model (Hine et al. 2018). Parents living with SMI should be informed about psychiatric advanced directives as a potential mechanism to plan for childcare in the event of an acute illness episode (Atkinson et al. 2004). A focus on building family and community supports is vital to increasing protective factors (Abel et al. 2005). Of note, in a study of structured interviews completed with women living with SMI, participants identified several ideas to improve services for mentally ill mothers, including greater availability of parenting support workers, support groups for mentally ill mothers, childcare facilities within mental health treatment centers, dedicated space within psychiatric hospitals for visits with children, and the availability of respite centers for periods of intense treatment needs (Diaz-Caneja and Johnson 2004).

There is also emerging evidence to support parenting interventions directly offered within psychiatric or general health settings. Let's Talk About Children is an intervention designed to be implemented in adult mental health settings and has shown improvement in child, parent, and family well-being, as well as a reduction in referrals to child protective services (Allchin et al. 2020). While not studied specifically with parents with SMI, other evidence-based programs have integrated mother-infant treatment into home visiting programs and group-based parenting programs (Muzik et al. 2015; Renshaw and Wrigley 2015).

#### Perimenopause

## What Is Perimenopause and Menopause?

The menopause transition, or perimenopause, typically begins in a woman's mid-40s and is defined as persistent variability in menstrual cycle length (Santoro et al. 2021). Female reproductive hormones fluctuate greatly, and menopausal symptoms are most intense during this period (Harlow et al. 2012). After 12 consecutive months of amenorrhea, a woman has officially entered menopause, the ovaries no longer produce estrogen, and there are no longer significant variations in hormone levels (Harlow et al. 2012). The average age of menopause is 51 years (ACOG 2018). Common menopausal symptoms include vasomotor symptoms, sexual complaints, insomnia, vaginal dryness, urinary changes, mood changes, and cognitive complaints (Santoro et al. 2015).

#### **Depression During Perimenopause**

Perimenopause is a period of increased risk for the development or recurrence of major depressive episodes. While women with a prior history of major depressive disorder are at highest risk for perimenopausal depression, women without any history of depression are two to four times as likely to develop depressive symptoms during perimenopause as compared to premenopausal periods (Gibbs and Kulkarni 2014). Depressive symptoms differ slightly during this period with more prominent irritability, anhedonia, and increased mood lability (Gibbs and Kulkarni

2014). Other more frequently reported symptoms include insomnia, impaired concentration, and memory complaints (Bromberger et al. 2007). As symptoms of depression can overlap with symptoms of menopause, the diagnosis of depression in this period can prove challenging.

As vasomotor symptoms are often a source of distress during this period, advising patients to speak with an ob-gyn about hormone therapy may also be appropriate. Of note, limited evidence suggests that estrogen therapy has antidewhen pressant properties utilized perimenopausal, depressed women (Soares 2017). While not recommended as primary treatment of severe or recurrent depression, some experts recommend that women with mild depression and bothersome vasomotor symptoms may benefit from a brief trial of estrogen prior to determining need for antidepressant treatment (Soares 2017).

The first-line treatment for perimenopausal depression is pharmacotherapy with an antidepressant medication (Maki et al. 2018). While desvenlafaxine is the only antidepressant to be studied in large-scale RCTs in peri- or postmenopausal women with depression, available evidence supports the use of SSRIs, SNRIs, and vortioxetine for treatment of depression in the menopause transition (Maki et al. 2018, 2019). While not well-studied in perimenopausal women, bupropion and vortioxetine are sometimes preferred due to a reduced potential for weight gain and sexual side effects and positive effects on cognition (Freeman et al. 2017). Selection of medication can also be guided by the presence of comorbid VMS. In one study, paroxetine followed by venlafaxine and then by fluoxetine have been shown to have the greatest reduction in VMS between 45% and 63% (Joffe et al. 2003), and more recent data supports vortioxetine for reduction in VMS on a similar scale (Freeman et al. 2017). Gabapentin and clonidine have also been shown to help reduce vasomotor symptoms by 54% and 20-37%, respectively (Joffe et al. 2003), so they may be useful for women with comorbid anxiety symptoms. Of note, the efficacy of antidepressants in the treatment of VMS occurs at the lower end of the dose

range for what is typical for treatment of depression, so titrating to a dose that adequately treats depression is likely to be effective for VMS as well (Santoro et al. 2015).

## Perimenopause and Women Living with Severe Mental Illness (SMI)

While it is well-established that women with a history of recurrent depression are at high risk for recurrence during perimenopause, recent evidence also suggests women with bipolar disorder are at increased risk for perimenopausal depression (Marsh et al. 2015). The estrogen hypothesis of schizophrenia has been discussed since the 1990s and posits that estrogen is protective against psychosis and that psychosis itself can influence hormones and disrupt the function of the hypothalamic-pituitary-gonadal (HPG) axis (Riecher-Rössler and Häfner 1993). From a clinical perspective, significant changes in the phenomenology of the illness among women in mid-life coincide with the menopause transition and lend support for the estrogen hypothesis. Women experience a second peak of onset for schizophrenia in midlife, with twice as many women developing the disease after the age of 40 relative to men (Riecher-Rössler et al. 2018). Women with an established diagnosis of schizophrenia are also at risk for a worsening of psychotic symptoms, longer hospital admission, and a need for higher doses of antipsychotics later in life (Brzezinski et al. 2017).

#### **Gender-Linked Violence**

#### **Intimate Partner Violence**

An estimated 30% of women worldwide over the age of 15 have experienced physical and/or sexual intimate partner violence (IPV) in their lifetime (Devries et al. 2013). Prevalence of IPV is estimated to be as high as 50% in pregnant women and women living with SMI (Hellmuth et al. 2013). It is the leading cause of homicide globally. For women, IPV carries several detrimental short- and long-term health sequelae, including depression, anxiety, PTSD, suicidal

behaviors, substance use disorder, detrimental pregnancy outcomes (i.e., low birth weight, miscarriage), economic hardship, and housing instability (Bacchus et al. 2018).

IPV includes physical violence, sexual violence, stalking behaviors, and psychological aggression by current or former partners. The cycle of IPV has been described as a pattern that begins with exerting control over the partner's activities which builds to an episode of violence (Beck 2016). A period of contrition and reconciliation follows the violence and defuses the tension, which produces hope in the person experiencing the violence and deters them from leaving. Violence may escalate over time and can involve coercive and threatening measures to keep the individual in the relationship or prohibit them from leaving. Other barriers to leaving the violent relationship include financial dependence, houselessness, childcare concerns, shame and guilt, real or perceived danger to self and children, isolation and lack of support, and past unsuccessful attempts at leaving.

The US Preventative Services Task Force (USPSTF) recommends that women of reproductive age be screened for IPV (Beck 2016). Reporting requirements vary by state, and clinicians should familiarize themselves with the laws in the areas in which they work. Evidence suggests that open, general survey questions, such as, "Have you been hit, kicked, punched, or otherwise hurt by someone within the past year? If so, by whom?" can appropriately identify up to 70% of women experiencing IPV (Beck 2016). The HITS screening tool (see Fig. 2) is well-established and demonstrates high sensitivity

How often does your partner:

- 1. Physically hurt you?
- 2. Insult you or talk down to you?
- 3. Threaten you with harm?
- 4. Scream or curse at you?

**Fig. 2** HITS screening tool. Scores are on a 5-point Likert scale: (1) never, (2) rarely, (3) sometimes, (4) fairly often, (5) frequently. Scores of >10.5 are positive. (Rabin et al. 2009)

(30–100% with lower end of range for men) and specificity (86-99%) (Rabin et al. 2009). It is important to empathically provide an assessment without judgment, document carefully, and reinforce that the individual does not deserve the behavior and is not responsible for the violence (Beck 2016). Interventions for IPV include referral to appropriate resources (i.e., hotlines, shelter, financial, legal services) and establishing a plan for safety inclusive of barriers for leaving and regular follow-up. Clinicians are best equipped to understand risk and tailor treatment planning by learning nuanced aspects of the range of behaviors. Risks for lethality include use or presence of weapons, strangulation attempts, and attempts to leave the relationship. It is advised that psychiatrists avoid prescribing sedating medications (i.e., benzodiazepines, sedative-hypnotics) that would impair an individual's ability to act quickly to protect themselves (Beck 2016).

#### **Sexual Assault**

Sexual assault is an umbrella term which encompasses multiple types of unwanted sexual contact such as rape, attempted rape, sexual touching, and forced oral sex (RAINN n.d.). Approximately 7.2% of women across the globe have experienced unwanted sexual contact (perpetrated by a non-partner) in their lifetime (Abrahams et al. 2014). A report by the World Health Organization found that 26% of women have experienced sexual violence by an intimate partner in their lifetime (WHO 2021b). Although sexual assault can be perpetrated by anyone, the majority of sexual assault is perpetrated by an individual known to the victim (Riggs et al. 2000).

Experiencing a sexual assault can have substantial impact on one's health. Survivors may develop posttraumatic stress disorder (PTSD), substance abuse, depression, and anxiety in the aftermath of sexual victimization (Ullman et al. 2013). Additionally, surviving a sexual assault is associated with an increased risk of developing a variety of psychopathologies including suicidality and disordered eating (Dworkin 2020).

Routine screening for sexual assault is recommended by the American College of Obstetricians and Gynecologists (Committee on Health Care for Underserved Women 2019). Barriers to disclosing sexual assault to clinicians include fear of being judged or blamed, perceived negative attitude of the provider, and lack of privacy. Conversely, factors that encourage disclosure of sexual assault include medical necessity of the disclosure, the positive attitude of the provider, perceived knowledge of the provider, and whether the provider directly queries about unwanted sexual experiences (Ahrens et al. 2009). Screening for sexual assault is crucial for clinicians to identify survivors and proceed with appropriate physical and mental health intervention or referral.

#### **Sex Trafficking**

The United Nations (UN) describes human trafficking as the recruitment and potential movement of vulnerable people using violence, deception, and/or threats for the purpose of exploitation (United Nations Office on Drugs and Crime 2000). The UN has reported that most human trafficking victims are women. Among more than 12,000 adult female victims of human trafficking, 77% were trafficked for sexual exploitation (United Nations Office on Drugs and Crime 2021).

Among sex trafficking victims, mental health concerns are prevalent. Approximately 37% of survivors have PTSD, 52% have depression, and 78% have clinically significant anxiety (Oram et al. 2012). Sex trafficking victims may also

exhibit aggression, social withdrawal, decreased self-esteem, and substance misuse (Simkhada et al. 2018). Perpetrators can utilize drugs to maintain control over their victims, and most survivors utilize substances while being trafficked (Lederer and Wetzel 2014).

Victims of sex trafficking may present to healthcare facilities with a myriad of physical health issues that may have been a direct result of victimization (i.e., headaches, fatigue, abdominal or back pain) (Zimmerman et al. 2003). Additionally, sexual abuse experienced within the context of human trafficking has many implications for women's reproductive and gynecologic health. Survivors may face concerns such as sexually transmitted infections, unsafe abortions, and infertility (Zimmerman et al. 2003, 2008). Multiple studies of sex trafficked women have found a high prevalence of HIV and other STIs (Wirth et al. 2013). When sex trafficking victims visit healthcare facilities for treatment of physical health concerns, the opportunity for clinicians to provide social resources and mental health services appears. Figure 3 outlines red flags that may indicate a victim of sex trafficking within a healthcare encounter. Recommended strategies for examining sex trafficking victims include separating the victim from the individual who has accompanied them, communicating with the victim directly, and using questions designed to ask about the victim's safety without using words that could upset the victim (i.e., "Do the people you live with treat you with kindness?") (Chesnay 2013). Not all victims will be receptive to help escaping from the sex trafficking environment due to fear for their own safety, for the safety of

**Fig. 3** Red flags that indicate a potential victim of sex trafficking (Shandro et al. 2016)

- 1) The individual accompanying the patient may appear reluctant to leave the patient alone with healthcare professionals.
- The patient has an inconsistent medical history and/or medical history that does not match presenting complaints.
- 3) Patients may be irritable or anxious, demonstrate flat affect, or have difficulty making eye contact.
- 4) Patients may not know their home address or not be in possession of their own identification cards.

others, or distorted loyalty to perpetrators (Myths, Facts, and Statistics | Polaris 2018).

#### Conclusion

Women's mental health is a robust area of psychiatry that has emerged in recent decades. Given significant sex differences apparent in the phenomenology of psychiatric disorders and the impact of reproductive hormone transitions on psychiatric care, women's mental health is an area of importance to community psychiatry. Women living with SMI are likely to have unique needs around sexual health and contraceptive counseling, and most will become pregnant and engage in motherhood. Community psychiatrists, experts in person- and family-centered care, are well-positioned to take a primary role in the healthcare of women through these major reproductive events. Essential skills include providing psychoeducation on contraceptive options in the context of psychiatric care, engaging in preconception counseling as a component of routine care, and assisting the patient in a collaborative discussion weighing the risks of underlying disease against the risks of indicated treatment during pregnancy and lactation. Further, as trusted members of a patient's healthcare team, community psychiatrists are ideally situated to consider the impact of gender-linked trauma in the biopsychosocial formulation of illness. Routine and purposeful screening for traumatic events within psychiatric care can create a safe space for women to disclose IPV or sexual assault and allow clinicians to provide a more wholistic treatment plan that considers critical safety supports as well as psychosocial treatments. Finally, as victims of sex trafficking face many barriers to disclosing their abuse, community psychiatrists should be aware of red flags that indicate an individual is being trafficked, be comfortable with methods to sensitively screen potential victims, and provide care in a traumainformed manner.

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