02 - Psychosis during pregnancy and postpartum

Psychosis during pregnancy and postpartum

Prescribing in pregnancy and breastfeeding CHAPTER 7 Psychosis during pregnancy and postpartum Pregnancy does not protect against psychotic relapse and psychosis during pregnancy predicts postpartum psychosis.13 The incidence of postpartum psychosis is 0.1–0.25% in the general population (around 1–2 psychiatric hospitalisations per 1000 births). Women with bipolar disorder have an increased risk of postpartum psychosis with around one in five experiencing a psychotic relapse postpartum.14 There is a high risk of relapse in women with a family history of postpartum psychosis or a personal history of postpartum psychosis.15 The risk of postpartum psychosis for women with a previous episode of illness, a diagnosis of bipolar disorder type 1 or schizoaffective disorder, and genetic loading for postpartum psychosis, bipolar 1 or schizoaffective disorder, can be as high as 50%. The mental health of the mother in the perinatal period influences fetal well-being, obstetric outcome and child development. The risks of not treating psychosis include harm to the mother and harm to the fetus or neonate (ranging from neglect to infanticide). First-generation antipsychotics ■ ■Some specific malformations have been reported with individual agents. However, first-generation antipsychotics (FGAs) are unlikely to be major teratogens.16 ■ ■Most initial data originated from studies that included primarily women with hyperemesis gravidarum (a condition associated with an increased risk of congenital malformations) treated with low doses of phenothiazines. The modest increase in risk identified in some of these studies, along with the absence of clear clustering of congenital abnormalities, suggested that the condition being treated may be responsible rather than drug treatment. ■ ■In a large American study including over a million women, no meaningful increase in the risk of major malformations or cardiac malformations was seen in 733 women prescribed an FGA.17 A 2023 study of nearly 6.5 million women (6371 prescribed an FGA) in the USA and Nordic countries found that antipsychotics were not major In all pregnant women ■ ■Ensure that parents are as involved as possible in all decisions ■ ■Prescribe as few drugs as possible (both simultaneously and in sequence) and use the lowest effective dose ■ ■Be prepared to adjust doses as pregnancy progresses and drug handling is altered. Dose increases are frequently required in the third trimester11 when blood volume expands by around 30%. Plasma level monitoring may be helpful, where available. Hepatic enzyme activity also changes markedly during pregnancy. CYP2D6

activity is increased by almost 50% by the end of pregnancy while the activity of CYP1A2 is reduced by up to 70%12 ■ ■For patients with SMI, discuss with the patient a referral to specialist perinatal services ■ ■Ensure adequate fetal screening by liaison with obstetric services ■ ■Be aware of potential problems with individual drugs around the time of delivery ■ ■Inform the obstetric team of psychotropic use and possible complications and where appropriate liaise with the neonatology team ■ ■Monitor the neonate for withdrawal effects after birth ■ ■Document all decisions (including the plan for medication)

716 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 7 teratogens. In the same study, the authors reported an observed increased risk of cardiac malformations with (the rarely used) chlorprothixene, which the authors suggest should be viewed as a safety signal for further study.18 ■ ■There may be an association between haloperidol and limb defects (based on a small number of cases) but, if real, the risk is likely to be extremely low and it has not been replicated in larger studies. ■ ■An increased risk of gestational diabetes19 and possibly preterm birth20 has been reported. A prospective study that included 284 women who took an FGA during pregnancy concluded that preterm birth and low birth weight were more common with FGAs than second--generation antipsychotics (SGAs) (or no antipsychotic exposure).21 In addition to this, 20% of neonates exposed to an FGA in the last week of gestation experienced early somnolence and jitteriness. ■ ■A higher risk of postpartum bleeding in vaginal delivery and a higher placenta to birth weight ratio has been reported.22 ■ ■Neonatal dyskinesia has been reported with FGAs.23 ■ ■Neonatal jaundice has been reported with phenothiazines.24 ■ ■An increased risk (greater in late pregnancy exposure) of neonatal withdrawal symptoms, neurological disorders and persistent pulmonary hypertension has been reported. The absolute risk is low, and the effects appear to be predominantly mild and transient.25 Prolonged neonatal hospital stay after birth has been reported.22 Second-generation antipsychotics ■ ■Some specific malformations have been reported with individual agents. However, SGAs are unlikely to be major teratogens.16 ■ ■In a large American study, no meaningful increase in the risk of major malformations or cardiac malformations was seen in 9258 women prescribed an SGA. In this same study a small increase in absolute risk of malformations was seen with risperidone. The authors suggested that this particular finding should be interpreted with caution and be seen as a possible safety signal that requires further investigation.17 In a separate study of 214 women taking an SGA, the absolute risk of major malformation was estimated to be 1.4% (1.1% in the control group).17 Another American study which analysed data from the National Birth Defects Prevention Study reported an association between SGA use in early pregnancy and conotruncal heart defects, tetralogy of Fallot, anorectal atresia/stenosis and gastroschisis. The study included over 22,000 cases and over 11,000 controls. Notably (and this may explain the findings in relation to SGAs), women exposed to SGAs were more likely to report pre-pregnancy obesity, illicit drug use, smoking and alcohol use and use of other psychiatric medications during pregnancy.26 A 2023 study of nearly 6.5 million women (21,751 prescribed an SGA) in the USA and Nordic countries reported that antipsychotics were not major teratogens. In the same study there was an observed increased risk of oral clefts with olanzapine and gastroschisis and brain anomalies with all SGAs, which the authors suggested should be viewed only as safety signals for further study.18 ■ ■A prospective study of 561 women who took an SGA during pregnancy concluded that SGA exposure was associated with increased birth weight, a modestly increased risk of cardiac septal defects (possibly due to screening bias or co-exposure to selective

Prescribing in pregnancy and breastfeeding CHAPTER 7 serotonin reuptake inhibitors [SSRIs]) and, as with FGAs, withdrawal effects in 15% of neonates.20 ■ ■Available data do not suggest that lurasidone is a major teratogen.27 ■ ■Olanzapine has been associated with lower birth weight and increased risk of intensive care admission,28 a large head circumference29 and macrosomia30 (the last of these is consistent with the reported increase in the risk of gestational diabetes24,29,31,32). ■ ■Neonatal seizures may be more likely to occur with clozapine31 than with other SGAs. There is a single case report of maternal overdose resulting in fetal death24 and there are theoretical concerns about the risk of agranulocytosis in the fetus/ neonate.24 Overall, pharmacovigilance data do not indicate that clozapine is less safe in pregnancy than other antipsychotics.33 Clozapine is included by the UK National Institute for Health and Care Excellence (NICE) in medications that may be prescribed in pregnancy. Lower mean adaptive behaviour scores have been reported in infants exposed to clozapine in utero compared with risperidone, quetiapine or olanzapine. A higher rate of disturbed sleep and lability were reported in clozapine- exposed infants in the same study.34 On the balance of evidence available, clozapine should usually be continued during pregnancy. Clozapine plasma level monitoring may be beneficial,35 especially if there are changes in smoking habits. ■ ■An increased risk of gestational diabetes has been reported for SGAs19 and possibly preterm birth,20 low birth weight36 and postpartum bleeding in vaginal delivery. The risk of gestational diabetes may be greatest with clozapine, olanzapine and quetiapine,37 and aripiprazole may not be associated with an increased risk.38 In a population-based study of over a million women, an increased risk of caesarean section, large for gestational age and preterm birth were reported in women prescribed an SGA compared with no antipsychotic. The risk of caesarean section and large for gestational age was higher with SGAs than with FGAs.39 Maternal mental illness and lifestyle may also be important factors in the risk for gestational diabetes.40,41 A lower risk with SGAs compared with FGAs has also been reported19 and other studies did not report increased risk of metabolic complications.36 ■ ■An increased risk (greater in late pregnancy exposure) of neonatal withdrawal symptoms, neurological disorders and persistent pulmonary hypertension has been reported. The absolute risk is low, and the effects appear to be predominantly mild and transient.37 ■ ■Quetiapine has a relative low rate of placental passage.42,43 One study of antipsychotic use in Finland showed a higher risk of increased postpartum bleeding in vaginal delivery, prolonged neonatal hospitalisation stay and a higher placenta to birth weight ratio with antipsychotics use. Quetiapine was the most commonly used antipsychotic in this study.22 ■ ■The manufacturers of cariprazine have advised against its use in pregnancy because of an increased risk of malformations noted in animal studies. It should probably be avoided. Antipsychotic use and longer-term neurodevelopment The effect of antipsychotics on longer-term neurodevelopment is unclear.44 A small prospective case–control study reported that babies who were exposed to SGAs in utero had delayed cognitive, motor and social–emotional development at 2 and 6 months old but

 not at 12 months.45 The clinical significance of this finding is unclear. No significant adverse effect on IQ or neurodevelopmental functioning was shown in a small study of school-aged children following exposure to antipsychotics during pregnancy.46 A cohort study of 667,517 children did not show an association between maternal antipsychotic prescription and poorer standardised test performance in language and mathematics in schoolchildren.47 Two large cohort studies have reported increased risk of attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) associated with maternal mental illness but not with prenatal antipsychotic exposure.20,48 A smaller study reported no increased risk of psychiatric disorders in children born

to women who continued antipsychotics in pregnancy.49 A 2022 birth cohort study found antipsychotics to not be causally associated with neurodevelopmental disorders although there was a safety signal for aripiprazole, which requires further study.50 Recommendations for psychosis in pregnancy are outlined in Box 7.2. Box 7.2 Recommendations – psychosis in pregnancy ■ ■Overall, the data do not allow an assessment of relative risks associated with different agents and certainly do not confirm absolutely the safety of any particular drug. However, the high risk of adverse outcomes for the mother and child associated with untreated maternal illness should be noted ■ ■Patients with a history of psychosis who are maintained on antipsychotic medication should be advised to discuss a planned pregnancy as early as possible ■ ■Women should be supported to minimise the risks in pregnancy from smoking and alcohol and drug misuse. Women should be referred to appropriate services such as smoking cessation clinics and addictions services ■ ■Drug-induced hyperprolactinaemia may prevent pregnancy. Consider switching to an alternative drug if hyperprolactinaemia occurs and a pregnancy is planned ■ ■If a pregnant woman is stable on an antipsychotic and likely to relapse without medication, advise her to continue the antipsychotic.51 Switching medication is generally not advised owing to the risk of relapse ■ ■When initiating an antipsychotic consider using the antipsychotic that has previously worked best for the woman, after discussion of benefits and risks.43 This may minimise fetal exposure by avoiding the need for higher doses and/or multiple drugs should relapse occur ■ ■Be clear of the indication for each drug, use the lowest effective dose and prescribe as few drugs as possible both simultaneously and in sequence. Do not continue medication that is not effective ■ ■Advise pregnant women taking antipsychotic medication about diet and monitor for excessive weight gain ■ ■Women taking an antipsychotic during pregnancy should be monitored for gestational diabetes. In the UK, NICE recommends women are offered an oral glucose tolerance test ■ ■In the UK, NICE recommends avoiding depot preparations in a woman who is planning a pregnancy, pregnant or considering breastfeeding, unless she is responding well to a depot and has a previous history of non-adherence with oral medication51 ■ ■The Australian Centre of Perinatal Excellence (COPE) recommends a 13- or 18–20-week ultrasound for women taking antipsychotics in the first trimester52 ■ ■Antipsychotic discontinuation symptoms can occur in the neonate (e.g. crying, agitation, increased suckling). This is thought to be a class effect.53 When antipsychotics are taken in pregnancy it is recommended that the woman gives birth in a unit that has access to paediatric intensive care facilities.21 Some centres used mixed (breast/bottle) feeding to minimise withdrawal symptoms ■ ■Document all decisions

---

Revision #1
Created 2026-01-04 20:17:09 UTC by Omar Ayman
Updated 2026-01-04 20:17:09 UTC by Omar Ayman