

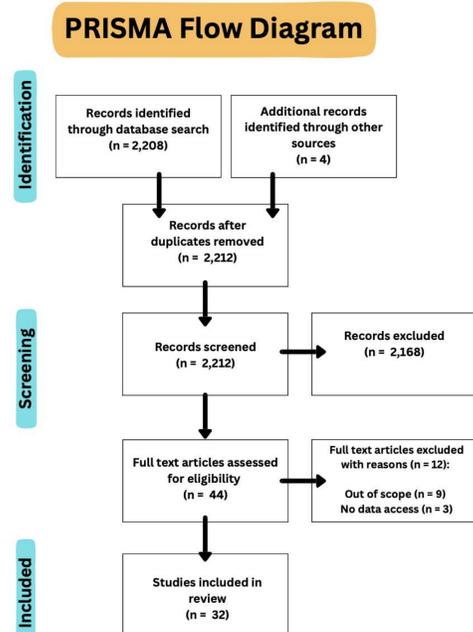
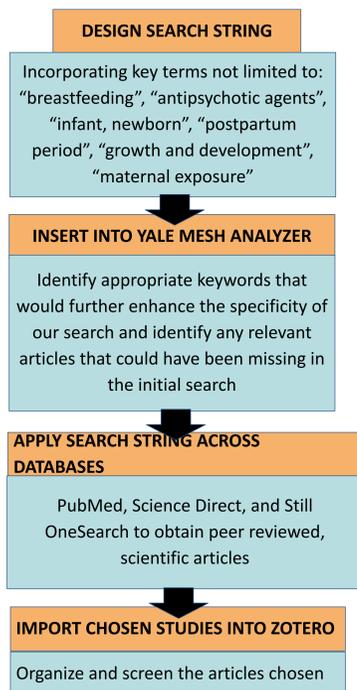
## Introduction

- Women in the postpartum period face a heightened risk of perinatal mood and anxiety disorders (PMADs), including postpartum depression, postpartum anxiety and more rarely postpartum psychosis [1].
- Data shows that 20-25% of women in the postpartum period will experience some kind of PMAD, with disproportionately higher rates observed among racially and ethnically minoritized groups, and those facing socioeconomic disadvantage [1,2].
- The risk of postpartum psychosis is greatest within the first 4 weeks after delivery and occurs in approximately 1-2/1000 childbirth [3].
- Untreated PMADs are associated with impaired mother-infant bonding, lower rates of breastfeeding, poor infant growth and development, and long-term psychiatric morbidity risk for both mother and baby [2].
- This review synthesizes current evidence on the neurodevelopmental and physical health outcomes of infants exposed to first and second generation antipsychotics through breast milk.

## Objectives

1. Assess the newborn safety of various first (FGA) and second generation antipsychotic (SGA) use while breastfeeding postpartum.
2. Analyze the neurodevelopmental and physical health outcomes of infants exposed to FGAs or SGAs through breastfeeding.
3. Help provide an understanding of the relative safety of the medications used to treat PMADs in order to make informed, evidence-based decisions that support infant well-being and maternal mental health.

## Methods



## Results

### Neurodevelopment

- **CASE 1:** Three breastfed infants, whose mothers were taking typical agents haloperidol and chlorpromazine, demonstrated no neurological deficits based on the Amiel-Tison assessment, which is a series of three neurological assessments completed on high-risk infants between 32 weeks to 6 years of age [6].
- **CASE 2:** In a study of a mother one week postpartum, a beginning dose of 2 mg of daily risperidone was given and later increased to 3 mg after 10 doses. She breastfed her child 6 times daily. The child was then seen five weeks later by a pediatric neurologist, who did not observe any adverse effects. Another follow up was conducted after three months of breastfeeding on risperidone and the examination was normal [7].
- **CASE 3:** More cases of mothers on 1, 3, 4, and 6 mg/day of risperidone found no long-term physical or neurological abnormalities between 3-12 months of age [7].
- **Overall,** existing studies do not demonstrate significant neurological impairment associated with antipsychotic exposure through breast milk.

### SGAs:

#### Risperidone (RIS)

- Relative infant dose (RID) between 2.3%-4.7% [8].
- One case report [9] studied a woman diagnosed with undifferentiated schizophrenia, who took 4-5 mg of RIS throughout all 5 of her pregnancies. All subsequent infants were breastfed for 20-24 months, and no adverse consequences were seen in any of the children. In fact, the oldest three children who were aged 26, 23, and 22 years old had completed their education and were currently employed at the time of publication. The youngest two were 15 and 19 years of age and were achieving normal educational and occupational milestones into adolescence and adulthood.
- Most reported infants showed normal development, and no sedation or feeding problems at follow ups ranging from 3-12 months [7].

#### Olanzapine (OLZ)

- RID between 0.28-2.24% [9].
- In one study, six breastfed infants whose mothers were taking OLZ at doses ranging from 2.5 - 20 mg daily consistently reported no significant adverse effects nor effects found on detailed medical testing [9].
- 4/7 infants had a normal birth weight and term birth, displayed normal weight, height, and DASII scores (Developmental Assessment Scales for Indian Infants), which assessed head and chest circumference, as well as mental development in 1-3 month intervals [3].
- Upon examination of the manufacturer's safety registry, 82.3% (84/120) experienced no negative outcomes. The remaining infants experienced nonspecific, transient symptoms such as irritability (2%), tremor (2%), somnolence (4%), and insomnia (2%) [10].

#### Quetiapine (QTP)

- RID from 0.02% to a maximum of 0.1% [11,12].
- One study noted delayed developmental and mental milestones, constipation, and sedation were observed in 17 infants breastfed by mothers on atypical antipsychotics, but that these effects were due to the presence of other factors such as low birth weight, higher maternal age, and in-utero exposure to both QTP and phenytoin [3].
- In general, the majority of studies have shown that QTP has minimal effects on prolactin levels and normal development in infants [13], displaying a favorable profile for use.

### FGAs:

#### Haloperidol (HAL)

- 3 children were breastfed for 6-8 months, whose development was considered age-appropriate at 16 months and 8 years of age [14].

#### Chlorpromazine (CPZ)

- One study of 7 infants who were breastfed for 3 to 4 months displayed normal behavior, emotional wellbeing, blood counts, as well as liver function tests after being followed for periods of 5 to 16 months, until the age of 4 [15].
- A small prospective study found evidence of psychomotor decline at 12-18 months of age in 2 of 4 infants taking both HAL and CPZ, further highlighting the potential risks associated with polypharmacy while breastfeeding [16].

## Conclusion

- Among FGAs, haloperidol and chlorpromazine have the most reassuring, though still limited, data in lactation.
- Among SGAs, current evidence suggests that most antipsychotics, particularly quetiapine and olanzapine, pose a low infant risk to breastfed infants through data demonstrating low RIDs, minimal breast milk transfer, and very low risk of short or long-term developmental and physical harm.
- There are concerns regarding clozapine use with breastfeeding due to risk of agranulocytosis and infant sedation, discouraging its use.
- Most reported side effects are often mild or transient and associated with other confounding factors such as polypharmacy, prenatal medication exposure, or prematurity.
- Decisions regarding antipsychotic use with breastfeeding require careful, individualized approach balancing the need for maternal stability with the available data regarding infant safety. When considering antipsychotic compatibility with lactation, potential risks of medication exposure must be weighed against the potential harms of untreated mental illness.
- It is important to note that when a patient has achieved psychiatric stability on a particular antipsychotic, continuation of that regimen is generally preferred due to the possible symptom relapse or decompensation that can occur with change

## Limitations/Future Directions

- Research specifically examining neurodevelopment is sparse and often involves very small cohort sizes.
- There is a lack of long-term follow up that expands beyond the 3-12 month follow ups, reinforcing the need for more longitudinal studies that explore a larger population size.
- The presence of confounding variables such as maternal illness severity and concurrent use of multiple psychotropic medications are inconsistently controlled for in existing studies.
- Many of the existing studies were outdated, with several foundational reports published decades prior. This can create a gap in understanding given today's standards of prescribing practices and new adverse effects discovered.
- Equity-related limitations are evident. Historically, studies have disproportionately enrolled well-educated white women, leaving significant gaps in understanding how antipsychotic exposure during breastfeeding affects racially and ethnically minoritized populations, as well as those facing social or economic disadvantage.

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