Psychiatric Care for the Perinatal Woman

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When I was a boy and I would see scary things in the news, my mother would say to me, 'Look for the helpers. You will always find people who are helping.' To this day, especially in times of 'disaster,' I remember my mother’s words, and I am always comforted by realizing that there are still so many helpers - so many caring people in this world.

- Fred Rogers
Public health urgency

“People don't care how much you know until they know how much you care”

— Theodore Roosevelt
The 2019 report, “Fostering Healthy Mental, Emotional, and Behavioral Development in Children and Youth,” began on a more somber note. Even though the mental health professions have developed many effective treatments for mental disorders, the prevalence of these disorders is not declining. The 2019 report points out that “rates of depression, suicide, and self-harm among young people have actually been increasing: in 2015, suicide was the second most common cause of death among young people aged 15 to 24, and between 2005 and 2014, the proportion of adolescents experiencing a major depressive episode increased from 8.7 percent to 11.3 percent.”
Investigators and clinicians support treating depression during pregnancy to mitigate depression’s effects on both the mother and her child. For example, exposure to depression during the fetal period has been shown to increase the risk for depression in offspring at age 16 by 4.7 times compared with unexposed offspring, even when the mother recovered from depression after birth. The relationship between maternal depression and child developmental adversity is a continuum that begins during pregnancy.

Even subtle problems in fetal brain development can predispose the child to mental illness in adulthood. Thus, the quality of the fetal environment during sensitive periods can dictate the vulnerability of individuals to a broad array of diseases across the lifespan. Fetal programming is widely accepted as part of the inheritance of obesity, metabolic disease, and diabetes.

Maternal Depression: a Lifecycle Lens

Psychiatry and Obstetrics: An Imperative for Collaboration

M. Camille Hoffman, M.D., M.Sc., Katherine L. Wisner, M.D., M.S.
Adult Diseases Associated with Childhood Adversity Dominate U.S. Health Care Costs

Four of the top eight most costly diagnoses: total $670 billion per year

- $294 billion
- $237 billion
- $99 billion
- $40 billion

Asthma #8 MOST COSTLY
Depression #5 MOST COSTLY
Diabetes #2 MOST COSTLY
Cardiovascular Conditions #1 MOST COSTLY

SOURCES: WATERS, G. (WILKEN INSTITUTE, 2018); GREENBERG ET AL. (2015); AMERICAN DIABETES ASSOCIATION (2018)

U.S. Life Expectancy Declined In 2020

- Hispanic: 70.2 years (1.1 years)
- White: 78.9 years
- Black: 73.5 years (1.6 years)
- 74.7 years

*Note: 2020 estimates are based on provisional data from January through June.

Source: CDC
Credit: Carole Nanobang, Jsh/NPR
ACE Study

- Dr. Vincent Felliti & Dr. Robert Anda
- Study to examine how childhood events affect adult health
- 17,000 participants
  - Middle class
  - Middle aged
  - 75% white
  - 40% with college degrees
  - All with jobs and good health care
- 10 Adverse Childhood Experiences (ACEs)
The three types of ACEs include:

**ABUSE**
- Physical
- Emotional
- Sexual

**NEGLECT**
- Physical
- Emotional

**HOUSEHOLD DYSFUNCTION**
- Mental Illness
- Incarcerated Relative
- Mother treated violently
- Substance Abuse
- Divorce

WHAT IMPACT DO ACEs HAVE?
3 Realms of Adverse Childhood Experiences

1. Household
- incarcerated family member
- physical and emotional neglect
- domestic violence
- maternal depression
- emotional and sexual abuse

2. Community
- discrimination
- historical trauma
- substandard schools
- structural racism
- lack of jobs
- substandard wages
- poverty
- lack of social capital and mobility
- food scarcity
- poor housing quality and affordability

3. Environment
- climate crisis
- record heat & droughts
- wildfires & smoke
- record storms, flooding & mudslides
- sea level rise
- natural disasters
- tornadoes & hurricanes
- volcanic eruptions & tsunamis
- earthquakes
- pandemic
An estimated 61.5% of adults and 48% of children in the United States have been exposed to ACEs, with more than one-third of these having multiple exposures.

Children ages 0-3 are particularly vulnerable.
Genetics and ACEs

Epigenetic Programming: A Putative Neurobiological Mechanism Linking Childhood Maltreatment and Risk for Adult Psychopathology

Brendan C. McKinney, M.D., Ph.D.

https://doi.org/10.1176/appi.ajp.2017.17101094

Epigenetic Programming: A Putative Neurobiological Mechanism Linking Childhood Maltreatment and Risk for Adult Psychopathology

Brendan C. McKinney, M.D., Ph.D.
Population Attributable Risk of ACEs

Adapted from ACE Interface 2013
Table 4. Relationship of the Adverse Childhood Experiences (ACE) Score to Having Attempted Suicide During Childhood/Adolescence or Adulthood*  

<table>
<thead>
<tr>
<th>ACE Score†</th>
<th>Child/Adolescent</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)‡</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>0 (3100)</td>
<td>5 (0.2)</td>
<td>1.0</td>
</tr>
<tr>
<td>1 (2280)</td>
<td>6 (0.3)</td>
<td>1.4 (0.4-4.6)</td>
</tr>
<tr>
<td>2 (1358)</td>
<td>17 (1.3)</td>
<td>6.3 (2.3-17.3)</td>
</tr>
<tr>
<td>3 (n = 821)</td>
<td>16 (1.9)</td>
<td>8.5 (3.1-23.5)</td>
</tr>
<tr>
<td>4 (n = 521)</td>
<td>15 (2.9)</td>
<td>11.9 (4.3-33.3)</td>
</tr>
<tr>
<td>5 (n = 313)</td>
<td>12 (3.8)</td>
<td>15.7 (5.4-45.3)</td>
</tr>
<tr>
<td>6 (n = 149)</td>
<td>12 (8.1)</td>
<td>28.9 (9.8-85.1)</td>
</tr>
<tr>
<td>≥7 (n = 87)</td>
<td>12 (13.8)</td>
<td>50.7 (17.0-151.4)</td>
</tr>
</tbody>
</table>

Total (n = 8629) | 95 (1.1) | 203 (2.4) |

*Odds ratio adjusted for sex, race, education level, and age at survey. CI indicates confidence interval.
†The trend for increasing risk of attempted suicide at all levels of the ACE score is significant (p < 0.002) for both groups.
‡From wave 2 only, n = 8629.
Maternal Suicide

Psychiatric disorders are associated with an elevated risk of maternal mortality from suicide, which was responsible for 20% of deaths during pregnancy or the first year postpartum.

An American study from Colorado found that deaths related to psychiatric disease were the eighth most common cause of maternal death, more common than hemorrhage or complications of anesthesia, and when combined with drug overdose they were the leading cause of maternal mortality.

Most suicides in the postpartum period occurred between 9 and 12 months postpartum and that the perinatal suicides were by highly lethal means (such as via firearm), suggesting that limiting follow up to 1, 3 or 6 months postpartum is insufficient. Intimate partner violence in half of the postpartum mothers who died by suicide.
### Perinatal Mortality in the United States

<table>
<thead>
<tr>
<th>Category</th>
<th>NH Black</th>
<th>Other</th>
<th>NH White</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Deaths</td>
<td>43.5</td>
<td>14.4</td>
<td>12.7</td>
<td>11</td>
</tr>
<tr>
<td>per 100,000 births</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>NH Black</th>
<th>AI/AN</th>
<th>NH/PI</th>
<th>Hispanic</th>
<th>NH White</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant Deaths</td>
<td>11.4</td>
<td>9.4</td>
<td>7.4</td>
<td>5</td>
<td>4.9</td>
<td>3.6</td>
</tr>
<tr>
<td>per 1,000 live births</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Black mothers are 3 to 4 x more likely to die in pregnancy than White mothers

Black babies are twice as likely to die than White babies in the first year

Black women with advanced degrees are more likely to have a baby die than a white woman with less than an 8th grade education

Education and poverty do not explain the gap in infant mortality

More than half of pregnancy-related maternal deaths occur after delivery.
Admissions to a Psychiatric Hospital: 2 Years Pre- and Post-Delivery

4th Trimester Project
- Shift cultural norms and assumptions
- Actively support health goals of all mothers and families
- Better prepare health care professionals to care for families
- Establish more equitable health care systems
- Help build ‘villages’ of support and resources
- Lift up the experiences of all women, with special attention to centering women of color and others whose opinions and perspectives have often been overlooked or ignored.

https://newmomhealth.com
40% of women do not attend a pp visit

ACOG Presidential Task Force on Redefining the Postpartum Visit, May 2018
Finding new solutions for racial health gaps

With help from Blue Cross, the U will be at forefront in addressing troubling health disparities.

By EDITORIAL BOARD, Star Tribune | MARCH 21, 2021 — 6:00PM

A painful but pioneering infant mortality study is a challenge we “can’t walk away from,” as Minnesota DFL Rep. Kelly Morrison, who’s also a physician, aptly put it during a recent legislative briefing.

Black babies in the U.S. have long been at much higher risk of dying than white newborns. But a study from a team that included two University of Minnesota researchers yielded a stunning finding: The hospital death rate for Black infants drops by a third when a Black doctor cared for them during the critical period after delivery. The study garnered national headlines last year and appeared in one of the world’s most prestigious scientific journals — and rightfully so. The distressing differences in infant mortality have long been a shameful public health crisis. The findings provide a groundbreaking perspective on the roots of this racial gap and should drive innovation to close it.

The work to do this is just beginning, but a timely $5 million donation will ensure that it will continue. Blue Cross Blue Shield of Minnesota has commendably provided a sizable gift to establish the Center for Antiracism Research for Health Equity at the U’s School for Public Health.

Rachel Hardenman, an associate U professor renowned for her research on reproductive health equity, will lead this new center. Along with the U’s Aaron Sojourner, she was one of four authors on the study linking Black infants’ health to having a Black doctor. The study yielded critical questions that still need to be answered about why the provider’s race matters.
“In 2020, we saw Minnesota become a national epicenter for racial injustice, under some of the most tragic and heartbreaking conditions imaginable,” said Craig Samitt, president and chief executive officer at Blue Cross and Blue Shield of Minnesota. “In order to transform our state, inspire change and improve health, we can’t just say the right things – we must do the right things. We believe that Blue Cross’ investment in the creation of the Center for Antiracism Research for Health Equity will serve as a catalyst to advance health equity and dismantle racism from the structure and fabric of our society.”
How childhood trauma affects health across a lifetime

Childhood trauma isn't something you just get over as you grow up. Pediatrician Nadine Burke Harris explains that the repeated stress of abuse, neglect and...
Serve and return interactions shape brain architecture.

When an infant or young child babbles, gestures, or cries, and an adult responds appropriately with eye contact, words, or a hug, neural connections are built and strengthened in the child’s brain that support the development of communication and social skills. Much like a lively game of tennis, volleyball, or Ping-Pong, this back-and-forth is both fun and capacity-building. When caregivers are sensitive and responsive to a young
Stillface = Toxic Stress
Bessel Van der Kolk “what we see most of in our offices is from interpersonal trauma”

TABLE 1

Developmental Trauma Disorder

A. Exposure
- Multiple or chronic exposure to one or more forms of developmentally adverse interpersonal trauma (e.g., abandonment, betrayal, physical assaults, sexual assaults, threats to bodily integrity, coercive practices, emotional abuse, witnessing violence and death).
- Subjective experience (e.g., rage, betrayal, fear, resignation, defeat, shame).

B. Triggered pattern of repeated dysregulation in response to trauma cues
- Dysregulation (high or low) in presence of cues. Changes persist and do not return to baseline, not reduced in intensity by conscious awareness.
- Affective
- Somatic (e.g., physiological, motoric, medical)
- Behavioral (e.g., re-enactment, cutting)
- Cognitive (e.g., thinking that it is happening again, confusion, dissociation, de-personalization)
- Relational (e.g., clinging, oppositional, distrustful, compliant)
- Self-attribution (e.g., self-hate, blame)

C. Persistently Altered Attributions and Expectancies
- Negative self-attribution
- Distrust of protective caretaker
- Loss of expectancy of protection by others
- Loss of trust in social agencies to protect
- Lack of recourse to social justice/retribution
- Inevitability of future victimization

D. Functional Impairment
- Educational
- Emotional
- Peer
- Legal
- Vocational
SENSE OF SELF AND OTHER, PERSONAL NARRATIVE: developmental trauma IS brain damage

• “the default mode network
• is the major resting network
• of the brain”
• -R. Lanius
Leaf approach to mental health, healthcare, and substance abuse

“Physical” leaves:
- Fatigue
- Migraines
- Irritable bowel
- Endometriosis
- Joint Pain
- Insomnia

“Mental” leaves:
- Depression
- Anxiety
- Eating disorders
- Substance Abuse
- Marital strain
- Parenting strain
EMOTIONS ARE PHYSICAL

Vagus Nerve

PNAS 2014
Body-Brain stress and PTSD

Yehuda et al. 2015
ACEs (Without Intervention) Predict Health Outcomes

- 3 or more categories of ACEs:
  - 60% increased risk of autoimmune disease (lupus, multiple sclerosis, RA, type 1 diabetes)
- 4 or more categories of ACEs:
  - 2.5x more likely to be diagnosed with cancer, lung disease
  - 4.5x more likely to face depression, Alzheimer’s
  - 12x more likely to attempt suicide
- 6 or more categories of ACEs shortens individual’s lifespan by 20 years

What Was Causing Health Concerns in Adults Who Faced Early Adversity?

- Were these individuals simply more likely to have poor health habits?
- People with an ACE Score of 7 or more who didn’t drink or smoke, weren’t overweight or diabetic, and didn’t have high cholesterol still had a 360% higher risk of heart disease.
Microglia: The Powerhouse Cell that Links our Physical and Mental Health

- Microglia: long thought to be a boring “housekeeper” cell that simply carts away dead neurons.
- Recent discovery: microglia are immune cells and function as the white blood cells of the brain.
- Microglia are easily activated by stressors!
- When microglia detect a threat – toxic stress, emotional trauma, pathogens, infections – microglia can morph into “Pac Man-like cells” and eat away at and destroy even healthy synapses, and change neural pathways.
- Biological basis of mind-body connection.

- When triggered by chronic stressors, microglia can destroy necessary synapses.
- Too much pruning – not enough connectivity – can result in neuropsychiatric disorders years later.
- In healthy, nurturing environments, microglia are Angels of the brain (secrete nutrients to stimulate healthy neurons to grow, create new synapses, strengthen brain connectivity).
- In unhealthy or toxic environments, microglia are brain’s untimely Assassins.
- For nearly a century science missed the power, peril, and promise of this tiny brain cell.
Vulnerability to shifts in reproductive hormones in pregnancy and childbirth

Estrogen and progesterone receptors throughout the brain and can modulate genomic and non-genomic mechanisms

Allopregnenolone GABA(α) receptors

Distinct neurobiological patterns of mothers with PPD on fMRI

Alterations in HPA axis during pregnancy such as CRH release by placenta

First-onset postpartum thyroid autoimmune disorders often coincide with postpartum mood disorders

Markers of inflammation associated with postpartum mood disorders, e.g. IL-6

First pregnancies are more often linked to postpartum disorders, including postpartum psychosis and preeclampsia, suggesting a common etiology of psycho-neuro-immune dysregulation
Maternal IL-6 during pregnancy can be estimated from newborn brain connectivity and predicts future working memory in offspring

Marc D. Rudolph, Alice M. Graham, Eric Feczko, Oscar Miranda-Dominguez, Jerod M. Rasmussen, Rahel Nardos, Sonja Entinger, Pathik D. Wadhwa, Claudia Buss & Damien A. Fair

*Nature Neuroscience* 21, 765–772(2018) | Cite this article

3291 Accesses | 92 Citations | 280 Altmetric | Metrics

**Abstract**

Several lines of evidence support the link between maternal inflammation during pregnancy and increased likelihood of neurodevelopmental and psychiatric disorders in the offspring.
Neurodevelopment: The Impact of Nutrition and Inflammation During Infancy in Low-Resource Settings

Nancy F. Krebs, Betsy Lazoff and Michael K. Georgieff
Pediatrics April 2017, 139 (Supplement 1):556-558, DOI: https://doi.org/10.1542/peds.2016-2828G

**Inflammation**
- Immature microbiome and immune system
- Acute transient (e.g., respiratory, intestinal) or chronic infection (e.g., HIV, TB)
- Environmental exotoxins, gut permeability, translocation of pathogens/toxins
- Early gut colonization by pathogenic organisms
- Nutrition-related immune deficits
- Toxic stress (i.e., excessive and prolonged activation of physiologic stress response systems)

**Individual and Environmental Risk Factors**
- Context of LRS
- Genetics, epigenetics, microbiota, temperament, and health status
- Prenatal and birth history: exposure and influences
- Unstable living situation, family stressors and conflict, poor quality of caregiving and impaired attachment
- Poor physical or mental health of caregivers
- Low literacy and/or education of caregivers
- Limited stimulation and opportunities for exploration ("functional isolation") and poor sleep
- Poor hygiene, food safety, sanitation, and water quality
- Food insecurity (e.g., lack of access to a diverse, safe, and nutritionally adequate diet)
- Natural disasters, weather extremes, pollution, medications, and toxins
- Trauma, stress, and violence
- Limited access to appropriate health care
- Age-specific risks to infectious agents (e.g., breastfeeding, weaning, crawling, hand-to-mouth behavior)

**Neurodevelopment**
- Atypical growth and structure, period of rapid brain development
- Altered developmental trajectory in multiple domains (e.g., cognitive, language, executive function, self-regulation, sensory, motor, emotional, and social)
- Effects in distinct regions and processes
- Susceptibility to nutritional deficiencies and adverse exposures dependent on timing, severity, frequency, duration, and individual modifiability factors
- High metabolic and nutritional requirements

**Nutrition**
- Nutrition is a biological variable (affects and is affected by health and disease)
- Minimal undernutrition and deficiencies
- Prenatal undernutrition/stress
- Feeding practices (e.g., exclusive or non-exclusive breastfeeding, complementary feeding)
- Malnutrition (e.g., micronutrient and protein-energy deficiencies)
- Altered nutrient use
- Unhealthy growth: underweight (low weight-for-age), wasting (low BMI), stunting (low height-for-age) and overweight/obesity
- Infections (e.g., HIV, TB) increase nutritional needs

**Figure 1**
Relationships among individual and environmental risk factors, inflammation, nutrition, and neurodevelopment for infants in LRS. TB, tuberculosis.
Resiliency findings/PACES

- Positive Childhood Experiences Score: The PCEs score included 7 items asking respondents to report how often or how much as a child they: (1) felt able to talk to their family about feelings; (2) felt their family stood by them during difficult times; (3) enjoyed participating in community traditions; (4) felt a sense of belonging in high school (not including those who did not attend school or were home schooled); (5) felt supported by friends; (6) had at least 2 nonparent adults who took genuine interest in them; and (7) felt safe and protected by an adult in their home.
Results Remission of maternal depression after 3 months of medication treatment was significantly associated with reductions in the children's diagnoses and symptoms. There was an overall 11% decrease in rates of diagnoses in children of mothers whose depression remitted compared with an approximate 8% increase in rates of diagnoses in children of mothers whose depression did not. This rate difference remained statistically significant after controlling for the child's age and sex, and possible confounding factors.
60% of women with postpartum depression do not seek help

THE PRIMAL SCREAM
How Society Has Turned Its Back on Mothers
This isn’t just about burnout, it’s about betrayal.

THIS IS A PRIMAL SCREAM
It’s not just the working from home, the record unemployment or the remote schooling. This is a mental health crisis, too.

By Jessica Grove
Postpartum Mood and Anxiety Spectrum

Blues
Depression
Bipolar

PP Mood Disturbance

Excessive worry/insomnia
GAD
Panic d/o
OCD
PTSD

PP Anxiety Conditions

PP Psychosis
Postpartum psychiatric disorders

- Epidemiology Pregnancy
  - 11% for depressive disorders and 15% for anxiety disorders.

- Epidemiology Postpartum (point prevalence):
  - depression disorder 12-20%
  - anxiety disorder 12%

- These disorders should not be confused with the so-called Baby Blues, which are usually described as transient, mild mood and anxiety symptoms that often persist for ≤2 weeks and usually resolve spontaneously with no sequelae.

- Further, antenatal anxiety and depression are two of the greatest risk factors for PPDs. Inadequate social support and a history of adverse life events increase the risk of PPDs.
Postpartum Disorders: Overview

- Biological factors might have greater role in postpartum bipolar illness whereas psychosocial risk factors might play greater role in depressive disorders.

- Continuing medication is protective in only a subset of postpartum women and discontinuing medication does not guarantee that women will relapse.

- PPD is often a trigger for onset of a chronic major depressive disorder, with almost 1 in 3 women continuing to struggle with depressive symptoms at least 4 years after delivery.
Rapid vs. Gradual Discontinuation

- Gradual (n = 27)
- Abrupt (n = 35)

Time to 50% recurrence:
- 22 weeks (95% CI: 16-38 weeks)

Risk of Recurrence in Pregnant Women with Bipolar Disorder who Continued vs Discontinued any Mood Stabilizer

N = 89; Bipolar Types I and II
- Maintain (n = 27)
- Discontinue (n = 62)

- Median time to recurrence > 40 weeks (95% CI: indeterminate)
- Median time to recurrence 9.0 weeks (95% CI: 8-13 weeks)

Mechanisms of Postpartum Psychiatric Disorders

- Sleep
- Psychosocial
- Neuroimmune
- Hormonal
- Genetics

S. Melzer-Brody et al., 2018
Admissions to a Psychiatric Hospital: 2 Years Pre- and Post-Delivery
Hospitalisation in postpartum period

Munk-Olsen, 2009
The perinatal woman with bipolar disorder

Weeks at risk after lithium discontinuation

Postpartum Psychosis: Overview

- Prevalence: 0.1 to 0.2% of postpartum women
- 75% have onset within 2 weeks postpartum
- Spectrum of symptoms involving losing touch with reality — symptoms can be subtle or very dramatic
- Delirium, confusion, memory impairment, irritability
- Paranoia, delusions, hallucinations

- Medical emergency
- Risk of harm to mother and infant, including 4% risk of infanticide

- Risk for maternal suicide is significantly elevated among depressed perinatal women, and maternal suicides account for up to 20% of all postpartum deaths, making it one of the leading causes of maternal mortality in the perinatal period.
Postpartum psychosis

- Postpartum psychosis, which is an umbrella term for disorders recorded as, for example, mania, mixed episodes, psychotic depression or psychosis not otherwise specified (not a recognized diagnosis in ICD10 or DSMV).

- Postpartum OCD particular diagnostic challenge—thoughts are highly distressing for the mother
Management of Postpartum psychosis

- Largest study (68 patients) showed stepwise sequence with short-term benzodiazepines, antipsychotics and lithium. 98.4% recovery.
- Another study (34 patients, many of whom had catatonia) treated with ECT
- Antipsychotics not protective against relapse.
- Lithium monotherapy was protective against relapse for at least a year postpartum.
- Lamotrigine used for bipolar depression, some use perinatally. Some evidence can help stabilize mood if woman does not tolerate lithium. Most likely in combination with benzodiazepines and SGAs.
Mother-Baby Day Hospital; early evidence of where the streams meet, opportunities for generational trauma healing

- Adverse Childhood Experiences
  - History of at least 3 ACEs: 70%
  - History of at least 5 ACEs: 47%

<table>
<thead>
<tr>
<th>Reproductive Status</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Pregnant</td>
<td>12%</td>
</tr>
<tr>
<td>More than one year PP</td>
<td>10%</td>
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<tr>
<td>0-12 months PP</td>
<td>78%</td>
</tr>
<tr>
<td>Married/Partnered</td>
<td>70%</td>
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<tr>
<td>Public Insurance</td>
<td>44%</td>
</tr>
<tr>
<td>College or beyond</td>
<td>50%</td>
</tr>
<tr>
<td>Lack of social support</td>
<td>88%</td>
</tr>
<tr>
<td>First-time mom</td>
<td>51%</td>
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</table>

N. Erickson and H. Kim (in progress)
Screening and Risk Assessment for Mood Disorder in the Perinatal Woman
Psychiatrists should be aware of the reproductive options for women and be prepared to have informed discussions with their patients about pregnancy or planning to become pregnant. Contraceptive use, including hormonal contraceptives, should be integrated into psychiatric care.

Treatment of Psychiatric Conditions in Pregnancy Starts With Planning

Kimberly A. Yonkers, M.D.

It may seem unusual that a psychiatric journal would include an article with guidance on contraception. However, more women than men suffer from non-substance-related psychiatric disorders. These women are more likely to become pregnant unintentionally or without planning. This leads to higher rates of pregnancy complications, including maternal mortality. Therefore, it is essential for psychiatrists to discuss contraception with their patients, especially those who are reproducing. This approach is in line with the American Psychiatric Association's guidance on the treatment of psychiatric conditions in pregnancy.
It is well established that women with both common mental disorders and severe mental illness have an increased risk for adverse obstetric and pregnancy outcomes, including preterm births and impairments in foetal growth. Furthermore, women with severe mental illness also have increased risks of pre-eclampsia, antepartum and postpartum haemorrhage, placental abruption and stillbirths. It is also increasingly clear that these risks are elevated regardless of pharmacotherapy during pregnancy suggesting causality beyond medication. This is unsurprising, given the higher prevalence of well-established obstetric risk factors among women with perinatal mental illness, including distal risk factors (such as domestic violence, and poor or delayed antenatal care) and proximal risk factors (such as obesity, gestational diabetes, hypertension and smoking).
Does patient have a positive or negative EPDS screen and a positive MDQ (7 co-occurring symptoms with or without impairment)?

Yes

Did the patient endorse item 5 (history of Bipolar Disorder diagnosis) on the MDQ?

Yes

Does the patient have an effective past or current psychotropic regimen?

Yes

- Rule-out postpartum psychosis
- Consider starting an antidepressant

No

- Start lithium OR a second-generation antipsychotic such as aripiprazole or lurasidone, which have less risk for weight gain

No

Does patient have a positive EPDS and negative MDQ screen?

Yes

- Recommend starting medication
- Discuss risks and benefits of pharmacotherapy versus illness exposure to the fetus in utero
- Optimize dose to reduce residual symptoms

No

- Discuss the risks of an untreated illness and plans to address symptom worsening

Clark and Wisner 2018
Figure 2 | Management of first-onset PPDs. Management of postpartum psychiatric disorders (PPDs) should take into account the diagnosis (such as psychosis, anxiety or depression), symptom severity and, with regards to mood and anxiety disorders, whether the mother is breastfeeding. *At any step in the treatment pathway, electroconvulsive therapy (ECT) can be considered for severe and/or treatment-refractory cases.
# Bipolar Mood Episodes Postpartum

<table>
<thead>
<tr>
<th>Clinical Group and Type</th>
<th>BD-I (N=479)</th>
<th>BD-II (N=641)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depression</td>
<td>19.21</td>
<td>28.71</td>
</tr>
<tr>
<td>Mania/hypomania</td>
<td>7.93/1.25</td>
<td>0/2.34</td>
</tr>
<tr>
<td>Mixed states</td>
<td>1.25</td>
<td>2.50</td>
</tr>
<tr>
<td>Anxiety or panic</td>
<td>6.47</td>
<td>0.94</td>
</tr>
<tr>
<td>Psychosis</td>
<td>1.25</td>
<td>0.00</td>
</tr>
<tr>
<td>All episodes</td>
<td>37.99</td>
<td>34.49</td>
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</tbody>
</table>

Factors increasing the probability of a diagnostic change from major depressive disorder to bipolar disorders (general, not only perinatal)

- Earlier age at onset (i.e. <25 years)
- Presence of psychosis
- Atypical depression (e.g., hyperphagia or hypersomnia)
- Number of depressive episodes (i.e. three or more previous episodes)
- A family history of bipolar disorders, an extensive family loading of psychopathology, or both
- Non-response to antidepressants or the induction of hypomanic symptoms by antidepressant treatment
- Mixed features
- Pattern of comorbidity (e.g. substance use disorder and migraine) and polymorbidity (three or more comorbid conditions)

(McIntyre et al. Lancet 2020)
Poor Sleep Quality Predicts Severity of Postpartum Depression

by MGH Center For Women’s Mental Health on September 22, 2014 in Postpartum Psychiatric Disorders, Psychiatric Disorders During Pregnancy

All women are at risk for postpartum depression (PPD), and there is growing evidence to suggest that poor sleep during pregnancy and the postpartum period may be a risk factor for the development of depression. A recent longitudinal study supports the hypothesis that disrupted sleep may contribute to the emergence and extent of postpartum depression symptoms.


Insomnia in pregnancy is prevalent

- 84% of pregnant women report having one or more sx of insomnia at least a few nights each week.
- 30% report that they rarely or never get a good night’s sleep during pregnancy
- Pts can develop a phobia about insomnia, particularly as birth is getting closer

National Sleep Foundation, Sleep in America Poll 2007
General management guidelines for non-psychotic psychiatric disorders

- Identify somatic comorbidities and optimize their management.
- Check the mode of delivery, whether complications were present and whether delivery was experienced as traumatic. In the case of post-traumatic stress symptoms, consider specific treatments.
- Assess for suicidal thoughts and intrusive thoughts of harm towards the baby.
- Consider the safety of the baby and whether the mother can provide care for the baby if she is alone or whether other adult supervision is required.
- Ask the mother about her attitude towards her baby and observe maternal–child interactions. Consider specific treatments with signs of problematic interactions or bonding.
- Review the feeding pattern of the baby. Address problems with breastfeeding or bottle feeding.
- Provide strategies to preserve sleep, such as finding another person to feed the infant at night.
- Assess psychiatric history before starting treatment. Review the nature and effectiveness of past treatments and restart previous effective treatment when appropriate.
Decision Making about Medication
You are not alone
Redleaf Center for Family Healing

Mission: To embrace and strengthen young children, parents, and families

We will foster mental health, supportive relationships, and parent capacity through a multi-generation integrative model of care based in research, lived experience, and social justice.

Clinical Services: Expansion of the Mother-Baby Program’s outpatient mental health and parenting services for pregnant women and families with children ages 0-5 years old

Integrative Health Services: Holistic nutrition program with teaching kitchen and other integrative services including mindful movement classes and the healing arts

Childcare Center: Drop-in childcare for children of HHS patients and back-up childcare for HHS staff

Training and Research: To understand and disseminate two-generation, integrative, trauma-healing practices

Trauma-Informed Network and Learning Lab: To develop and share trauma-informed models of care
Risk/Benefit/Alternatives Discussion

• What is known/unknown about risks of untreated illness in your patient

• What are known/unknown risks of treatment options to patient(mother) and fetus/baby

• “Parenthood is a journey into the unknown but together we can try to make decisions which reduce the overall risk.”

• Framework of assessing risk above baseline for both pregnancy and psychiatric illness.
“Best Practices”

- Share information:
  - medical knowns and unknowns (data, use your resources!)
  - Ask what the patient thinks is best for herself and her family
- Decrease the sense of “black or white”
- Think ahead
- Create a sense of options and working together, continuously weighing risks to mother and fetus/newborn and working to decrease the risk for both
Guiding principles

• Make treatment recommendations based on:
  – Severity of underlying disorder
  – History of treatment response
  – Individual patient preference
Barriers and Challenges

- Stigma of mental health and psychiatric illness in general
- Lack of timely intervention with knowledgeable providers
- Aversion to taking medication - mostly fear based due to lack of knowledge
- Negative feedback from support system on symptoms or use of medications
- Sometimes providers are quick to offer a prescription without listening which disrupts the therapeutic alliance
Pharmacologic Treatment in Perinatal Depression

The American Psychiatric Association and American Congress of Obstetrics and Gynecology both recommend either psychotherapy or antidepressant medication as first-line treatment for mild to moderate perinatal depression.
Risk of Relapse with Medication Discontinuation

The rule of thumb for treating perinatal women is that one size does not fit all, and each patient should have an individualized discussion with her provider about the risks of medication weighed against her own risks of not taking medication during pregnancy or lactation. Women who decide they want to come off medications should do so with the supervision of a physician, and ideally preconceptionally. Abrupt medication discontinuation has been associated with high relapse rates. In a prospective sample of 201 euthymic women on stable doses of antidepressants at the time of conception, 68% who discontinued medications during pregnancy experienced relapse of symptoms, and 60% of those who stopped their medication restarted it later in pregnancy. Predictors of relapse included having 4 or more prior depressive episodes and suffering illness for more than 5 years. The most judicious approach is to use the least amount of medication that helps a woman feel better and keeps her well. As noted, it is important to recognize that higher dosages are often required than pre-pregnancy dosages owing to increased blood volume and increased metabolism during pregnancy. Managing sleep and comorbidities, while providing a multidisciplinary treatment approach, will improve outcomes with medication treatment of perinatal depression.
SSRIs in Pregnancy

- There have been conflicting data about SSRI exposure during pregnancy and the potential risk of small for gestational age, preterm delivery, and spontaneous abortion. These risks have been associated with perinatal depression itself and the risk may lie with the illness rather than exposure.

- Most current data looking at exposure to all SSRIs show no consistent information to support specific teratogenic risks.

- Up-to-date publication examining a cohort of more than 3 million women, and adjusting for potential confounding variables, concluded a very small increased absolute risk for PPHN (persistent pulmonary hypertension) with SSRI exposure (adjusted odds ratio of 1.28 for SSRIs vs 1.14 for non-SSRIs).
Poor Neonatal Adaptation Syndrome (PNAS)

- Most common of the potential adverse effects of taking SSRI in pregnancy, estimated to occur in up to 30% of exposed babies
- Usually short lived with a median duration of 3 days
- 75% complete resolution by 5 days
- Reports of adaptation signs lasting up to 4 weeks
- **Premature babies** are more vulnerable to PNAS

- Symptoms can vary greatly in severity and can manifest as a range of symptoms, including irritability, respiratory distress, hypoglycemia, feeding difficulties, increased or decreased tone, sleep disturbance, and, more rarely, seizures, prolonged QT interval, or cardiac arrhythmias.
Autism/Long-term development and fetal exposure to SSRIs

The risk for autism spectrum disorders associated with SSRI exposure during pregnancy is controversial. Maternal depression has been found to be potentially neurotoxic, and is a considerable confounding variable. Some studies have shown potential risk for autism spectrum disorders with SSRI exposure however, when adjusted for confounders, including the risk of maternal depression, statistical significance is usually lost. Other developmental outcomes that must be considered with perinatal exposure to psychotropic medications include language, growth, and motor development. Review of available data demonstrates no effects of in utero SSRI exposure on head circumference, weight, or length during the first year of life. Examination of the literature on IQ and behaviors of sibling pairs in mother’s with and without SSRI exposure during pregnancy showed that the child’s IQ was predicted by maternal IQ. Maternal depression has an impact on problematic behaviors in the children. Last, a longitudinal study of the development in children within utero SSRI exposure found no differences in mental indices; psychomotor scores were mildly lower during the first year of life, and then normalized thereafter.
If the Relative Infant Dose is less than 10%, most medications are quite safe to use. The RID of the vast majority of drugs is < 1%.

(from Medications and Mothers’ Milk)
Breastfeeding is promoted by all major medical groups for the first year of the child’s life to improve both maternal and infant health outcomes. Therefore, to minimize stress on the mother, for most medications pumping and dumping (ie, pumping and then throwing out all milk while taking a medication or after taking the medication throwing out the first pump of milk after taking the medication) is not advised. However, there may be cases where the risk–benefit ratio supports this practice, such as in the case of a treatment agent that may have high likelihood of passing into breast milk. As noted, the amount of medication exposure in breast milk is thought to be far less than exposure during pregnancy through transplacental passage. Data from the National Institutes of Health have demonstrated that SSRIs are compatible with breastfeeding. It is important to collaborate with the infant’s pediatrician when a mother is taking a psychotropic medication during lactation, and to monitor the infant for sedation, proper weight gain, and achievement of developmental milestones. For any medication other than lithium, the literature does not support checking infant blood levels. For questions, an important resource is LACTMED, https://toxnet.nlm.nih.gov/newtoxnet/lactmed.html, a database from the National Institutes of Health, with information on medication patients may have taken during pregnancy.
Lithium Treatment during Pregnancy

Congenital malformations Fetal exposure to lithium has been associated with an increased risk for cardiac abnormalities. The risk for Ebstein’s anomaly with first trimester exposure is 1 (0.1%) to 2 in 1000 (0.2%)

Folate supplementation with 5 mg reduces the risk and severity of congenital heart disease by suppressing lithium-induced potentiation of a signaling pathway that inhibits genes important to initiating cardiogenesis.
No other congenital malformations have been associated with lithium exposure.

For women with first trimester exposure, fetal echocardiography and a level 2 ultrasound examination is recommended at 16 to 18 weeks of gestation to evaluate for anomalies
LITHIUM, ATYPICAL ANTIPSYCHOTICS, AND LAMOTRIGINE: DATA REGARDING LONG-TERM EFFECTS ON CHILDREN’S DEVELOPMENT

Recent literature has shown that lithium’s association with cardiac malformations is smaller than previously thought and must be weighed against the risks of the illness itself. Although limited, data for lithium and second-generation antipsychotics indicate effects are reassuring with regards to child development. Despite some earlier concerns, subsequent studies have suggested that lamotrigine is not associated with an increased risk of congenital malformations. The long-term safety profile of lamotrigine during pregnancy is promising. In a review that included 8 studies, lamotrigine had no adverse outcomes on infant IQ or neurodevelopment.
Resources: medical literature

- S. Melzer-Brody et al., *Postpartum Psychiatric Disorders*, Nature Reviews 2018
- M. Kimmel et al., *Pharmacologic Treatment of Perinatal Depression*, Obstet Gynecol Clin N Am 2018
- C. Bethell et al., *Positive Childhood Experiences and Adult Mental Health,…*, JAMA Pediatrics 2019
- L. Howard and H. Khalifeh, *Perinatal Mental Health: a review of the progress and challenges*, World Psychiatry 2020
Preface

Treatment of Peripartum Mental Health Disorders: An Essential Element of Prenatal Care

Constance Guilie, MD, MSCR
Roger B. Newman, MD
Editors

Obstetricians and Gynecologists are acutely aware of the prevalence of maternal mental health disorders and the impact they can have on maternal, fetal, and newborn health and child development. Sadly, fewer than half of pregnant women with a mental health illness are identified in clinical settings. Among women who are identified, only 15% receive mental health treatment, fewer than 10% receive adequate treatment, and less than 5% achieve remission from their illness.
Resources medical literature

Welcome to NCRP, an online, interactive curriculum designed to teach reproductive psychiatry to mental health professionals – either within an educational program or self-guided. Please navigate using the tabs above to learn more.
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Dosage Range</th>
<th>Unique Considerations/Indications</th>
</tr>
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<tbody>
<tr>
<td><strong>SSRIs</strong></td>
<td></td>
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</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft, Serafem</td>
<td>50–200 mg, increase by 25 mg or 50 mg, for very anxious patients 12.5 mg</td>
<td>Due to half-life small, even negligible amounts transmitted into breast milk.</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>20–80 mg, increase by 10 mg or 20 mg</td>
<td>Longer half-life → withdrawal less likely if doses are missed, but also longer to get out of the system if there are adverse effects, likely greater amount in breast milk, thought to be more activating.</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Celexa</td>
<td>20–40 mg, increase by 10 mg or 20 mg</td>
<td>FDA Drug Safety Communication that &gt;40 mg could result in a life-threatening heart arrhythmia.</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro</td>
<td>10–20 mg, increase by 5 mg or 10 mg</td>
<td>Older data demonstrated potential for a 1.5- to 2.0-fold increase risk in cardiovascular malformations, leading to a 2005 warning. Recent data show no consistent information to support teratogenic risks.</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil, Pexeva, Brisdelle</td>
<td>10–60 mg, increase by 10 mg or 20 mg, CR in 12.5 mg doses</td>
<td>More often used for treatment of obsessive compulsive disorder.</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Luvox, Faverin, Fervarin, Floxyfiral, Dumyrox</td>
<td>25–150 mg, increase by 25 mg</td>
<td>More often used for treatment of obsessive compulsive disorder.</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Venlafaxine</td>
<td>Effexor, Effexor XR</td>
<td>37.5–375.0 mg, increase by 37.5 mg</td>
<td>Older and most data available.</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Cymbalta, Irenka</td>
<td>20–120 mg, increase by 20 mg, 30 mg</td>
<td>No studies currently available on use in pregnancy examining neither teratogenic risks nor available data about long-term developmental outcomes.</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>Savella</td>
<td>100 mg BID–200 mg, increase by 12.5 mg, 25 mg, 50 mg</td>
<td>No studies currently available on use in pregnancy examining neither teratogenic risks nor available data about long-term developmental outcomes.</td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>Pristiq, Khedezia</td>
<td>25–400 mg</td>
<td>No studies currently available on use in pregnancy examining neither teratogenic risks nor available data about long-term developmental outcomes. No evidence &gt;50 mg is helpful.</td>
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**Other antidepressants: Their own unique mechanisms of action**

<table>
<thead>
<tr>
<th>Buproprion</th>
<th>Wellbutrin SR, Wellbutrin XL, Zyban, Aplenzin, and Forfivo XL</th>
<th>150–450 mg, increase by 150 mg, SR BID dosing</th>
<th>Not to exceed 450 mg owing to an increased risk of seizure, greater concern for seizure in those with a history of seizure or those engaging in purging behaviors. Helpful for smoking cessation and even evidence for lower prematurity risk for smokers. May help ADHD and other addictive disorders, such as overeating.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazapine</td>
<td>Remeron</td>
<td>15–45 mg, increase by 7.5 mg, 15 mg</td>
<td>Antiemetic effects in addition to antidepressant and anxiolytic effects, and helps with sleep and decreased appetite.</td>
</tr>
<tr>
<td>Trazodone, nefazodone</td>
<td>Oleptro, Desyrel, Serzone</td>
<td>50–400 mg, ½ tablet (25 mg)–100 mg for sleep</td>
<td>Sleep aid at lower dosages, higher dosages more antidepressant effects. No differences in the rate of major malformations.</td>
</tr>
</tbody>
</table>

**Tricyclic TCAs**

<table>
<thead>
<tr>
<th>Desipramine, nortriptyline</th>
<th>Norpramin, Pamelo, Aventyl</th>
<th>Dose varies for each TCA</th>
<th>Less anticholinergic, so less orthostatic hypotension and constipation, which are common in pregnancy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxapine, imipramine, doxepin, clomipramine, trimipramine, amitriptyline, protriptyline</td>
<td>Asendin, Tofranil, Sinequan, Silenor, Anafranil, Sumontil, Vivactil, Elavil, Vanatrip</td>
<td>Dose varies for each TCA, blood levels are possible to obtain</td>
<td></td>
</tr>
</tbody>
</table>

**MAOIs**

| Isocarboxazid, phenelzine, selegiline, tranylcypromine | Marplan, Nardil, Emsam, Parnate | Dose varies for each MAOI | Requires special diet, interacts with some medications to cause life-threatening hypertensive crisis. |

*(continued on next page)*
<table>
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<tbody>
<tr>
<td>Mood stabilizer and antidepressant</td>
<td></td>
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<tr>
<td>Lamotrigine</td>
<td>Lamictal</td>
<td>&gt;50 mg, start at 25 mg daily and increase by 25 mg every 2 wk to decrease risk of Stevens-Johnson syndrome</td>
<td>Some evidence to use for augmentation in treatment-resistant depression, OCD, and, therefore, possibly obsessive compulsive symptoms of perinatal depression, and for mood dysregulation and aggressive behaviors of borderline personality disorder, which is often comorbid with depression.</td>
</tr>
<tr>
<td>Atypical antipsychotics (ariprazole, quetiapine, olanzapine, risperidone, ziprasidone, lurasidone, paliperidone)</td>
<td>Abilify, Seroquel, Zyprexa, Risperdal, Geodon, Latuda, Invega</td>
<td>With augmentation of depression resulted in modest but statistically significant increased likelihood of remission during 12 wk of treatment compared with switching to bupropion monotherapy; small study found less likely to have a postpartum mood episode.</td>
<td></td>
</tr>
</tbody>
</table>
| Lithium | | Increase by 150 mg, 300 mg; Therapeutic blood level 0.4–0.8 for depression augmentation, 0.8–1.2 for mood stabilization | Helpful for monotherapy and augmentation of unipolar depression, and postpartum psychosis in addition to Bipolar Disorder. Increases the likelihood of maintaining mood stability during pregnancy and preventing postpartum relapse as does immediately restarting postpartum.

**Abbreviations:** ADHD, attention deficit hyperactivity disorder; BID, 2 times per day; CR, controlled release; FDA, US Food and Drug Administration; MAOI, monoamine oxidase inhibitor; OCD, obsessive-compulsive disorder; SNRI, Serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; XR, extended release.

- All treat depression and anxiety, higher dosages needed for anxiety, Black Box warning for use in children secondary to an increased risk of suicidal thoughts at initiation (still used to treat depression, anxiety, which will decrease risk of suicide), increase dosage for 1 week for menses for premenstrual mood worsening or anxiety.
- Some providers may increase to 250 mg or 30 mg.
- Treat depression and anxiety, and have also shown to be effective treatments for chronic pain.
- First discovered in the 1950s, revolutionized treatment of depression and preceded SSRIs, but are associated with higher mortality rates owing to overdose.
- Helpful for chronic pain.
- Gracious and Wisner indicate a use in patients with atypical depression that have not otherwise responded.
Resources: web-based

- Womensmentalhealth.org
- Postpartum.net
- 4th Trimester Project
- Lactmed
- Hales’s Medications & Mother’s Milk
- MothertoBaby
- Reprotox.org
- PACES Connection
- NCRPtraining.org
- Harvard Center on the Developing Child
- Redleaf Center for Family Healing (HCMC)
- Masonic Institute for the Developing Brain (U of MN)