

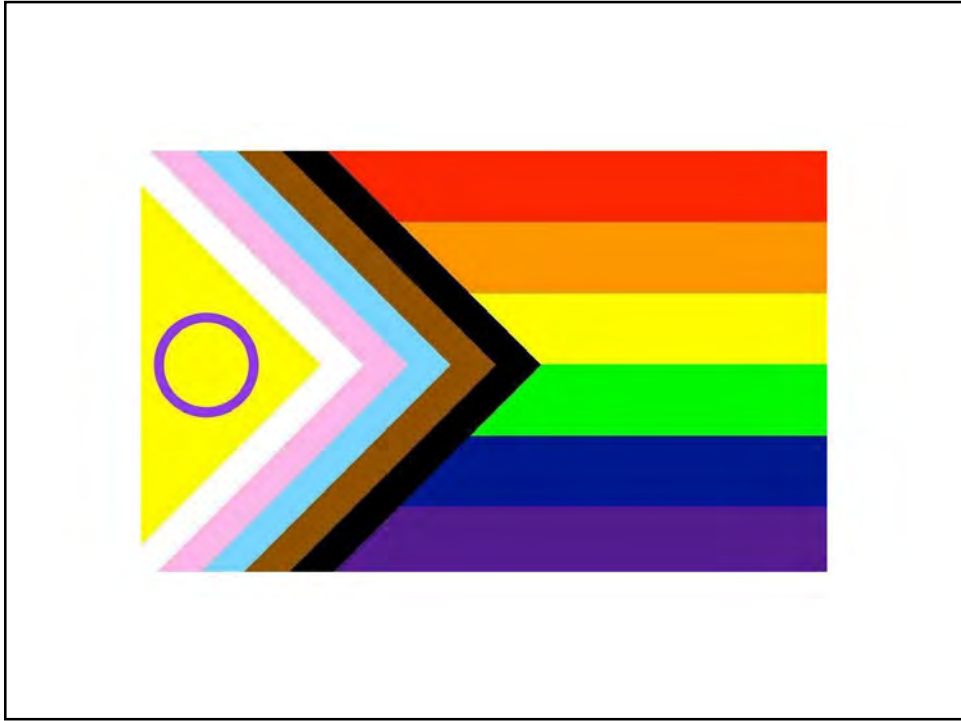


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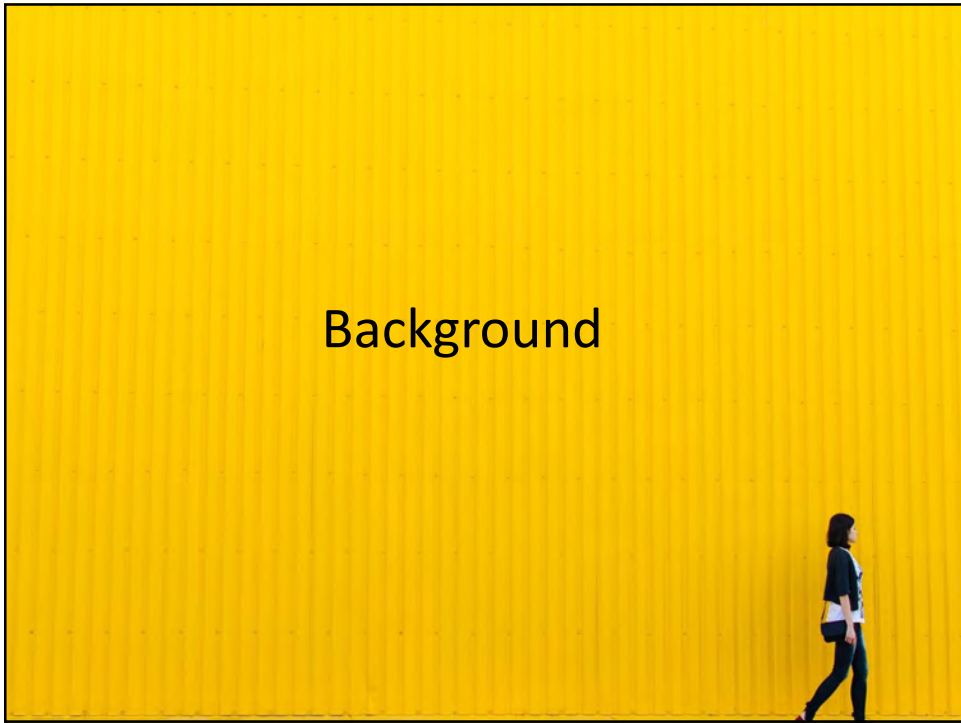
Objectives

Discuss	Discuss impact of maternal depression on breastfeeding
Describe	Describe impact of breastfeeding on maternal depression
Examine	Examine impact of antidepressant use on breastfeeding
Evaluate	Evaluate safety data on psychotropic medication use in lactation

2



3



4

What is Post-Partum Depression?

Difficulty with at least 5 of the following:

- Sleep
- Concentration or focus difficulty
- Low interest/Apathy**
- Appetite
- Guilt or Hopelessness
- Low Energy
- Psychomotor Slowing
- Low mood or feeling of sadness most of the time**
- Thoughts of death or suicidal thoughts

American Psychiatric Association. (2022). Depressive Disorders. In *Diagnostic and statistical manual of mental disorders* (5th ed., text rev.). <https://doi.org/10.1176/appi.books.9780890425787>

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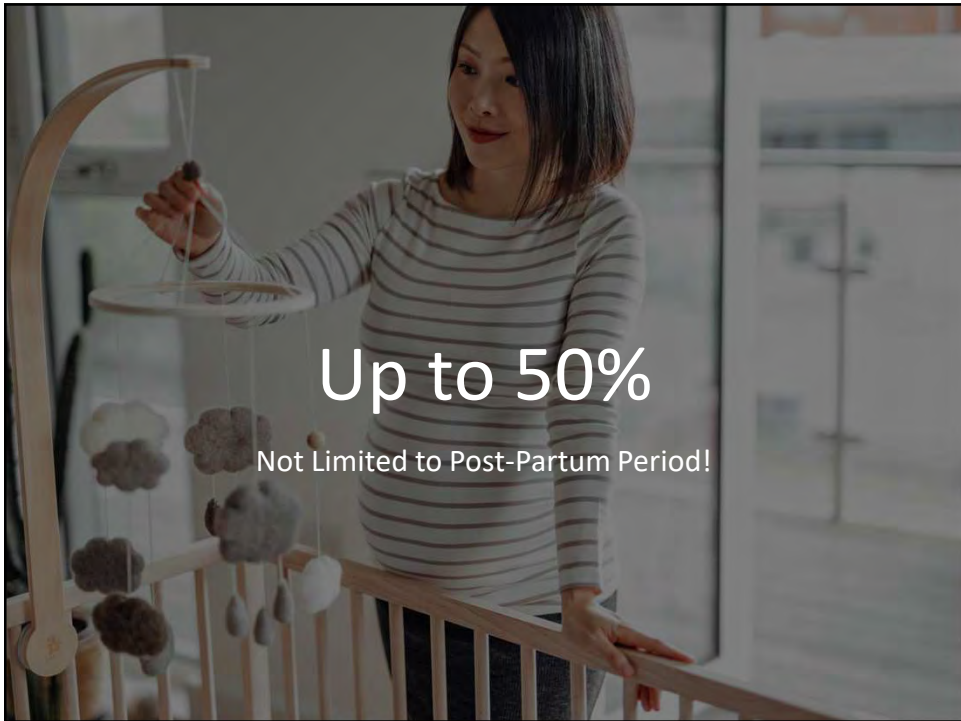
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10-20%

The most common medical complication of normal childbirth

7



Up to 50%

Not Limited to Post-Partum Period!

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Objective 1:
Discuss the impact of
maternal depression on
breastfeeding

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Depressed mothers experience:

- Less sensitivity to infant cues and ability to “read” their babies which can lead to problems in infant latching and establishment of breastfeeding routines.

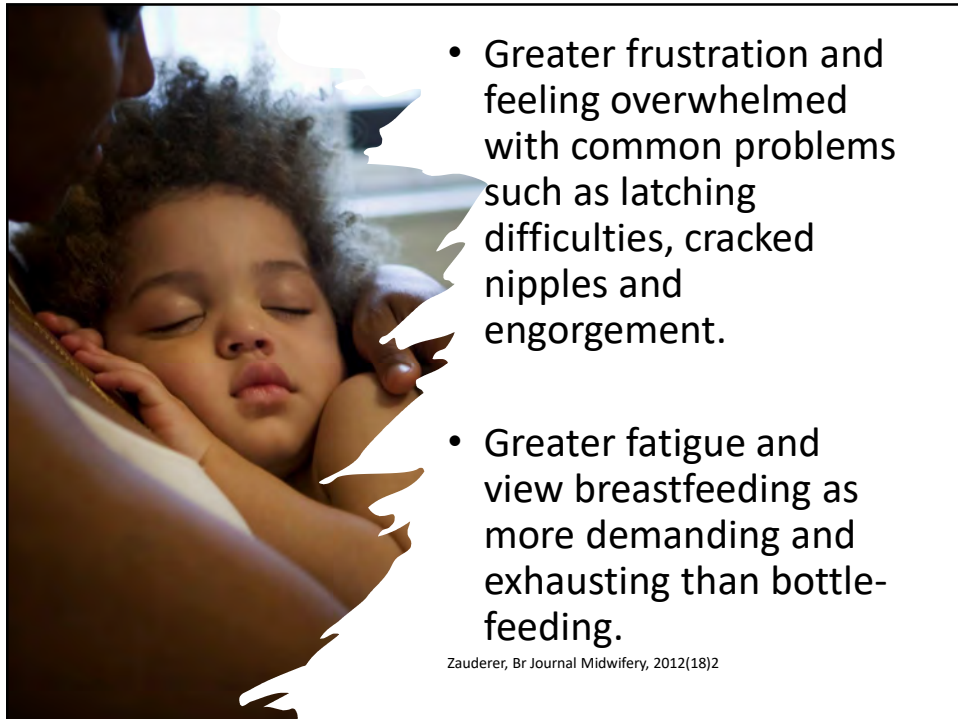
Murray, Child Development, 1996 (67)



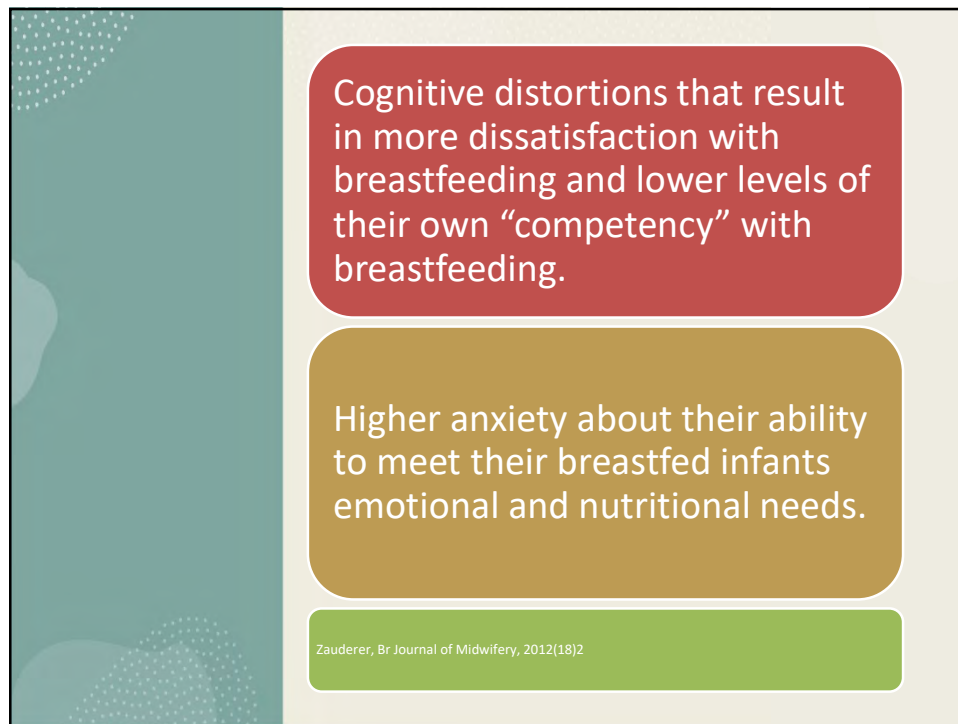
11

- Greater frustration and feeling overwhelmed with common problems such as latching difficulties, cracked nipples and engorgement.
- Greater fatigue and view breastfeeding as more demanding and exhausting than bottle-feeding.

Zauderer, Br Journal Midwifery, 2012(18)2



12

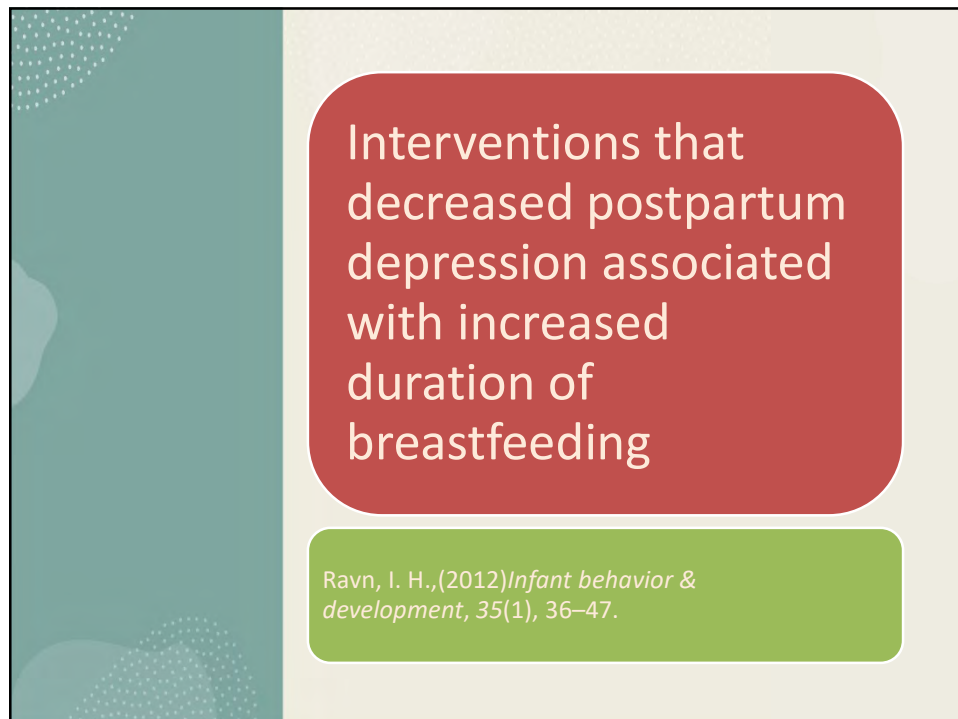
An infographic slide with a teal and light green background. It features three rounded rectangular text boxes. The top box is red and contains text about cognitive distortions. The middle box is gold and contains text about anxiety. The bottom box is green and contains a citation.

Cognitive distortions that result in more dissatisfaction with breastfeeding and lower levels of their own “competency” with breastfeeding.

Higher anxiety about their ability to meet their breastfed infants emotional and nutritional needs.

Zauderer, Br Journal of Midwifery, 2012(18)2

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An infographic slide with a teal and light green background. It features two rounded rectangular text boxes. The top box is red and contains text about interventions. The bottom box is green and contains a citation.

Interventions that decreased postpartum depression associated with increased duration of breastfeeding

Ravn, I. H.,(2012)*Infant behavior & development*, 35(1), 36–47.

14

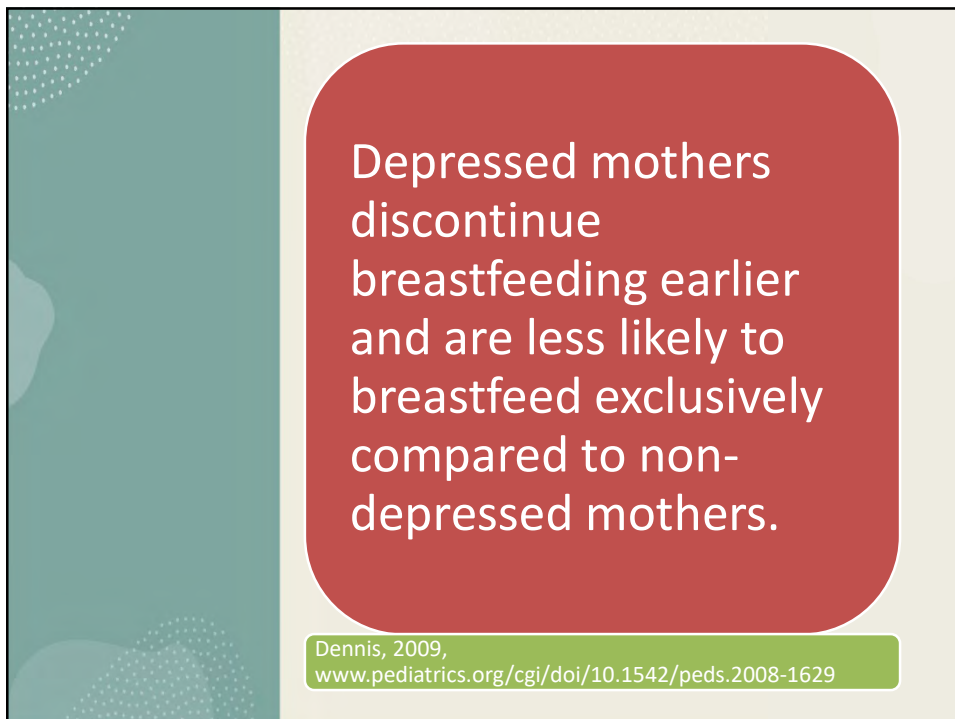


Women who are depressed during pregnancy are significantly less likely to attempt breastfeeding.

82% vs. 94%

- Green, *Perinatal Psychiatry*, UK: Gaskell;1994(180-198)

15



Depressed mothers discontinue breastfeeding earlier and are less likely to breastfeed exclusively compared to non-depressed mothers.

Dennis, 2009,
www.pediatrics.org/cgi/doi/10.1542/peds.2008-1629

16

PPD associated with lower breastfeeding initiation and earlier cessation of breastfeeding

Seimyr, J. Psychosom Obstet. Gynaecol 25 (1) (2004)

17

Australian study 1745 new mothers:

18% experienced PPD.

Onset was before 8 weeks postpartum in 60% of women and after 8 weeks in 40%.

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Median duration of breastfeeding:

- 26 weeks for early-onset depression
- 28 weeks for later-onset depression
- 39 weeks for non-depressed

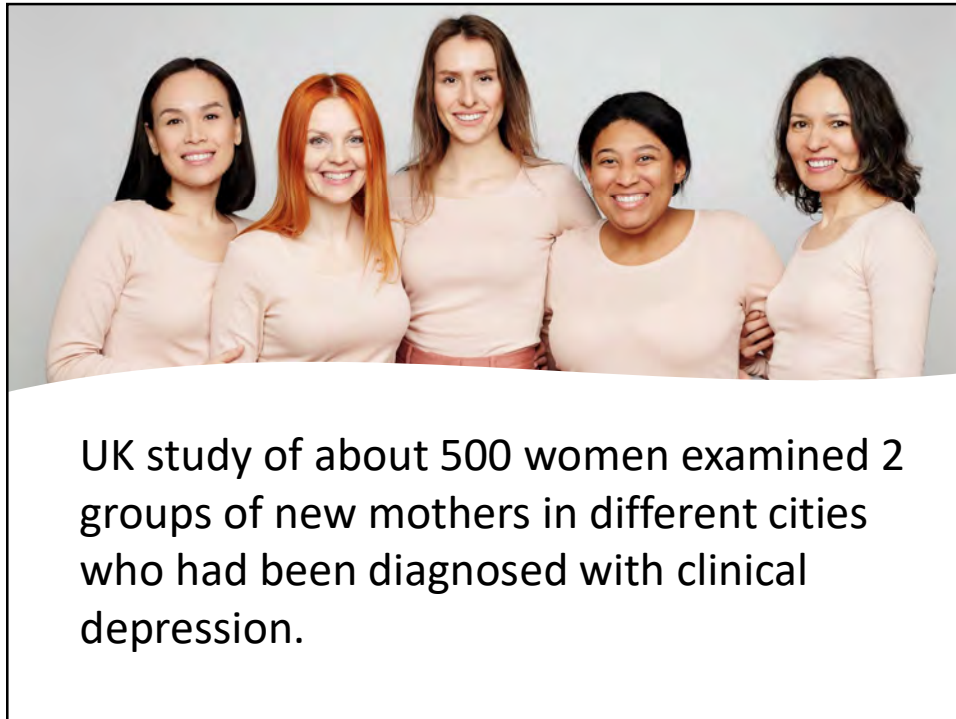
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Depressed mothers stopped breastfeeding, on average, 3 months earlier than non-depressed mothers.

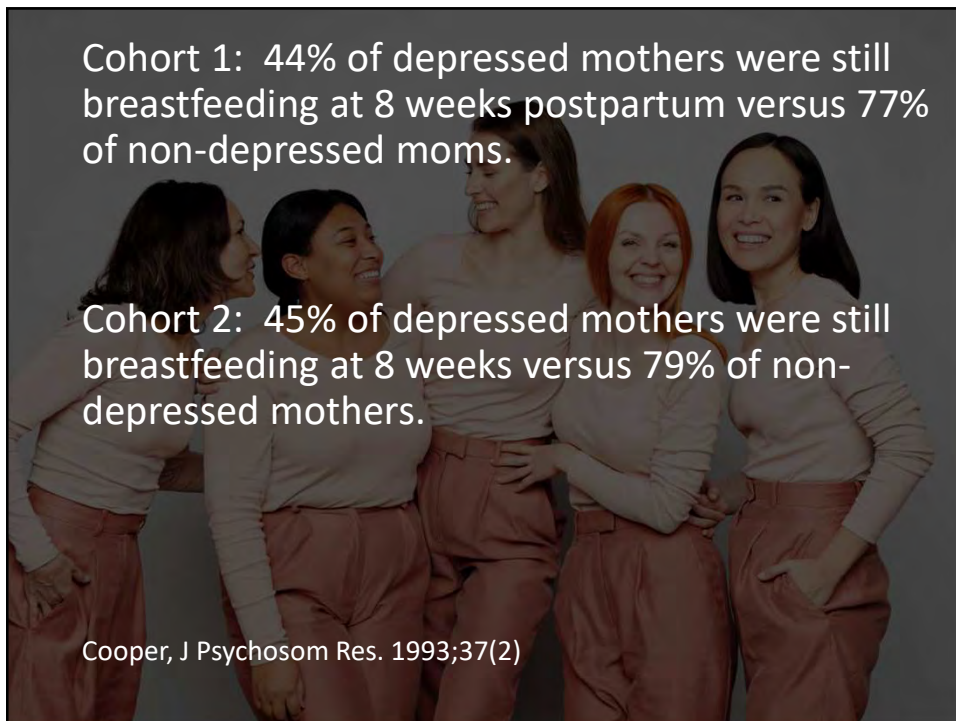
The study adjusted for confounding variables and found a significant association with PPD.

Henderson, Birth, 2003;30(3) 175-180

20



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22



23

In a US study, a "failed" breastfeeding attempt at the 6-week postpartum visit was the only factor associated with an elevated depression rating score (EPDS) in low income urban group of women.

Ferguson, Am J Obstet Gynecol 2002;186(5)

The inability to establish breastfeeding in the first few weeks postpartum should prompt a depression screening of the new mother.

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No study has specifically evaluated interventions to support breastfeeding mothers who are experiencing PPD.

We do not know what interventions would be most effective in improving infant-feeding outcomes in depressed women.

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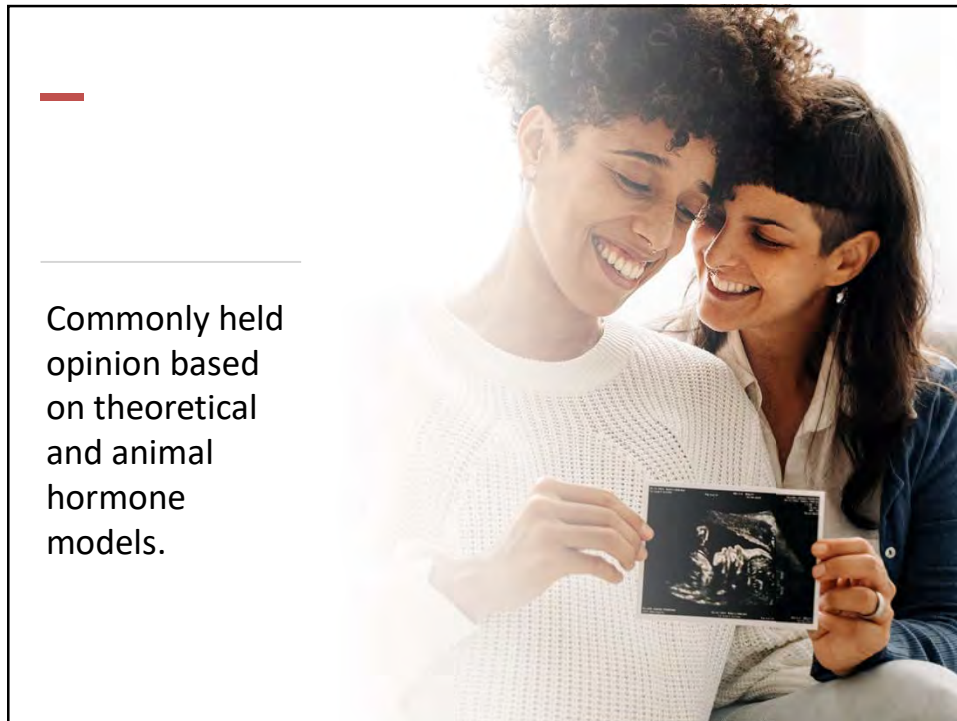
Objective 2:
Describe impact of
breastfeeding on maternal
depression

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Does
breastfeeding
protect
mothers from
developing
postpartum
depression?



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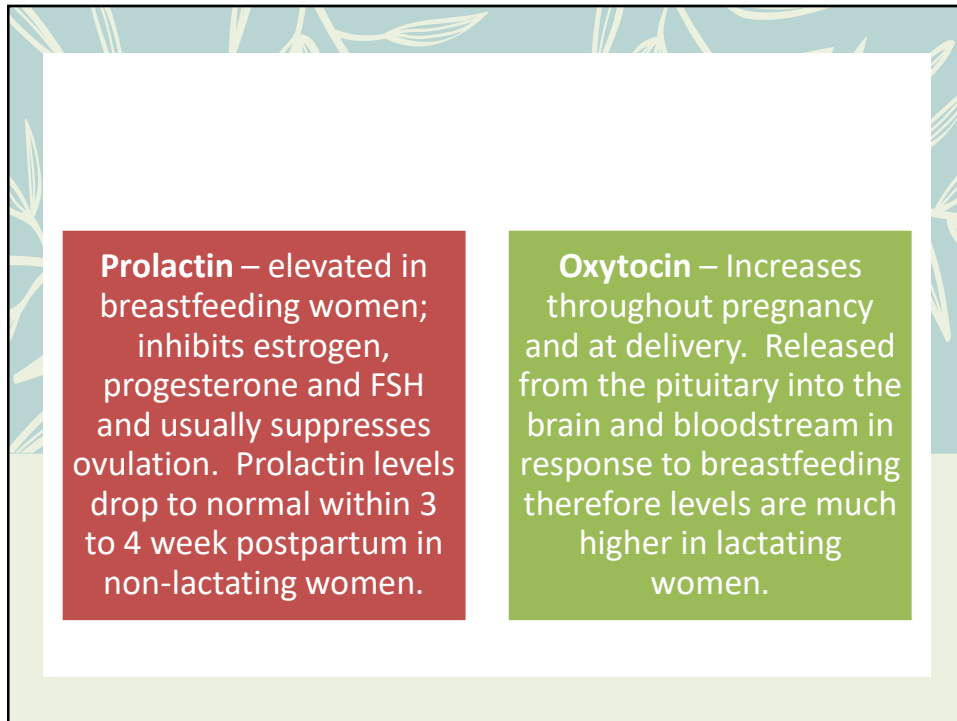


Commonly held opinion based on theoretical and animal hormone models.

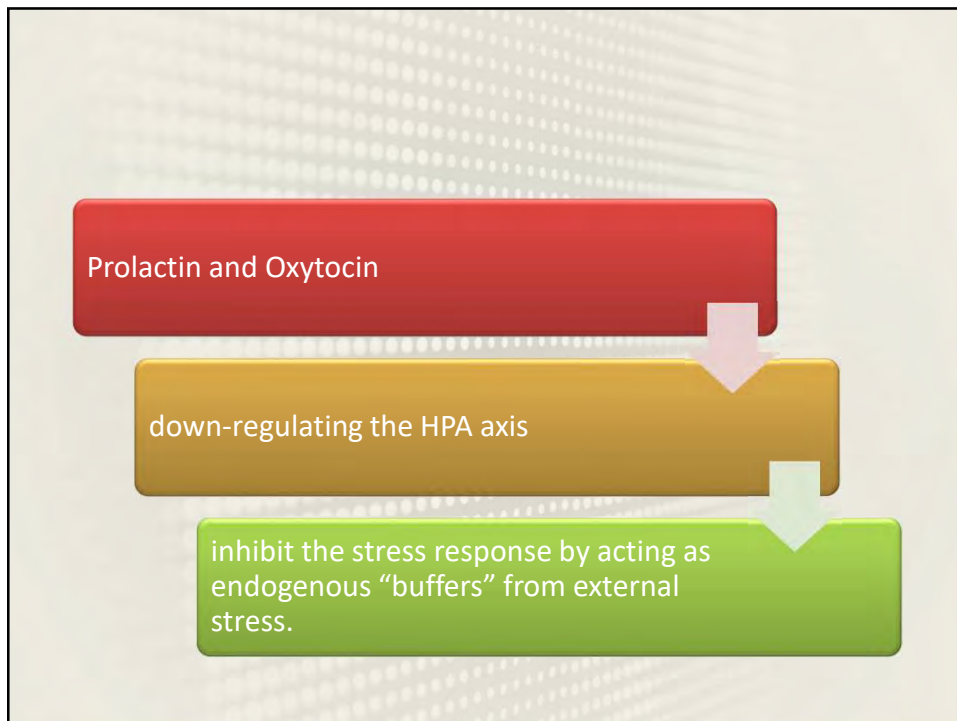
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Currently, there are no specific guidelines on the role of breastfeeding in the management of PPD.

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Oxytocin


associated with successful mother-baby bonding in mammals and this bond is theorized to help make women more resilient and less susceptible to depression.

33



BF may decrease the stress response
(Mezcappa, 2004, Kendall-Tackett, 2007)

34




Decreased stress and cortisol stress response when comparing breastfeeding vs non breastfeeding mothers

(Henriches et a, 2001, Groer and Davis 2006)

35

BF reduces neuroendocrine responses to stress, a factor less associated with symptoms of PPD



Groer and Morgan, 2007

36

Adrenocorticotrophic hormone and cortisol levels in BF mothers significantly lower than in controls

(Handlin et al., 2009)

37

Let's take a look at two prospective studies....



38

Study of 594 Canadian mothers.

- Assessed mothers' feeding method and depression scores (EPDS) at 1, 4 and 8 weeks postpartum.
- No relationship was found between method of infant-feeding feeding one week postpartum and development of depression at weeks 4 or 8 postpartum.

Dennis, Acta Paediatr, 2007;96(4)

39

205 mothers from California were followed for 2 years postpartum and were assessed prenatally and at 3,6,12, and 24 months postpartum for feeding method and depression.

Study took into account confounding variables for breastfeeding and PPD: maternal age, income, education, marital status, preterm birth status, ethnicity and social support.

Hahn-Holbrook, Arch Women's Mental Health; 2013(16)

40

Results

Maternal depression levels at 3, 6 and 12 months did **not** differ between lactating and non-lactating women. The results were unaffected by the confounding variables.

At 3 months postpartum, mothers who were exclusively breastfeeding did **not** have less depression than bottle-feeding mothers

- the time when the differences in oxytocin and prolactin levels between the two groups is highest.

41

Results (cont.)

Consistent with other studies, women who had *depression during pregnancy* breastfed for a short duration – they weaned an average of 2.3 months sooner than non-depressed women.

Prenatal depression also predicted more use of supplemental formula while women were breastfeeding compared to non-depressed women.

42

Results (cont.)

The only positive finding was that the *frequency* of nursing at 3 months predicted less maternal depression at 6, 12 and 24 months postpartum.

Low frequency was defined as 4 feeding per day and high frequency was defined as 9 per day.

Women with high frequency of feeding at 3 months postpartum had less depression develop over the subsequent 21 months compared to women with low frequency breastfeeding at 3 months postpartum.

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The findings need to be replicated and a randomized study design is not possible and correlation does not mean causation.

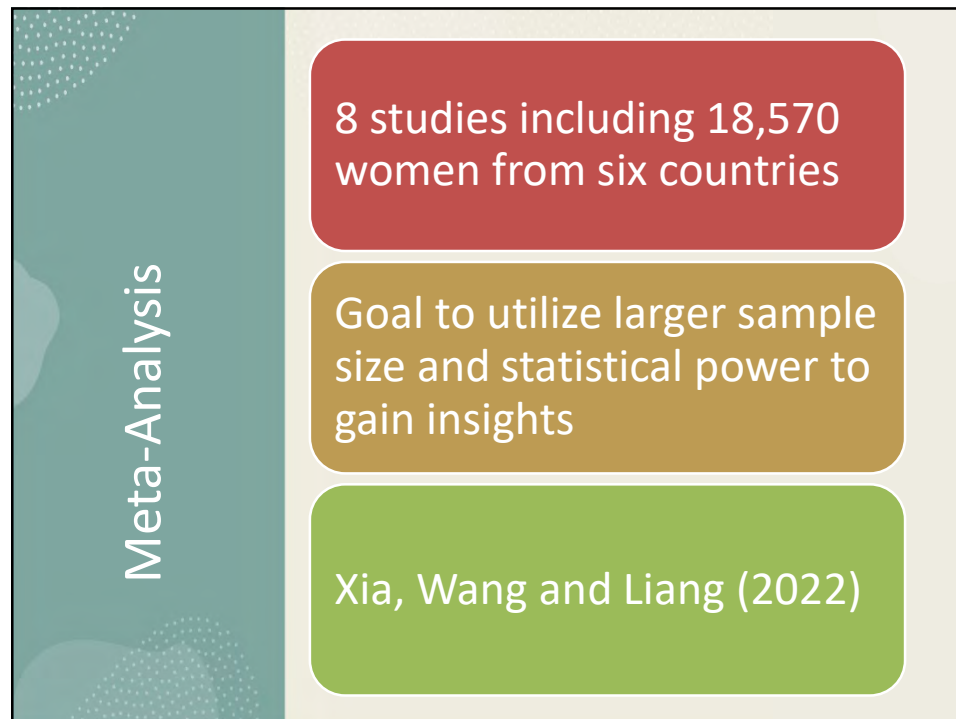
Does increased amount (frequency) of breastfeeding at 3 months postpartum result in additive effects of hormone exposures that have a downstream effect on reducing a mother's risk of developing PPD?

Does increased time breastfeeding promote more maternal bonding that makes a mother less susceptible to PPD?

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Are women who breastfeed more frequently at 3 months fundamentally different from mothers who breastfeed less frequently? i.e. could less frequent breastfeeding be an early “marker” of increased risk of developing PPD?

45



The graphic features a vertical teal bar on the left with the text 'Meta-Analysis' written vertically. To the right, three rounded rectangular boxes are stacked vertically: a red box at the top, a gold box in the middle, and a green box at the bottom. The background is a light beige color with decorative dotted patterns in the top-left and bottom-left corners.

Meta-Analysis

8 studies including 18,570 women from six countries

Goal to utilize larger sample size and statistical power to gain insights

Xia, Wang and Liang (2022)

46

Results

Inverse association between BF and PPD, OR 0.86, EBF 14% lower odds of PPD vs non or partial BF

Residual confounding factors as some studies did not adjust for SES, social supports

47

Results (cont)

4 strongest studies showed 8% reduction in PPD from BF

Consistent with beneficial effect

Improved separation when comparing exclusive breast feeding vs non breastfeeding

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Results (cont)

Limited cross study comparison but one study demonstrated partial breast feeding had similar risk for PPD as those not breastfeeding

(Raheem, 2019)

NOTE: This does not diminish other potential benefits of partial breastfeeding.

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Discussion

This study suggests BF may help reduce incidence of PPD and being able to BF may be emotionally beneficial

More research needed

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Objective 3:
Examine the impact of
antidepressant use on
breastfeeding

51

**Effects of maternal antidepressant-
use on breastfeeding**



52

168 women with and without depression were prospectively through pregnancy and postpartum.

Examined factor associated with choice of feeding in the women with depression.

J Clinical Psych, Bogen, 2010;Aug 71(8)

53

Results

Women with depressive symptoms were just as likely as non-depressed to breastfeed but women who were taking antidepressant medication during pregnancy were less likely to breastfeed, either exclusively or in combination with formula.

Strongest predictor for exclusive breastfeeding was a *women's intention to do so during her pregnancy*.

54

Take Aways

An interpretation of the results is that women who are taking antidepressants during pregnancy believe that breastfeeding is incompatible with their treatment and decide early not to breastfeed.

Women on antidepressant medication need additional support to initiate breastfeeding and discussion should be done as early as possible during pregnancy or the postpartum.

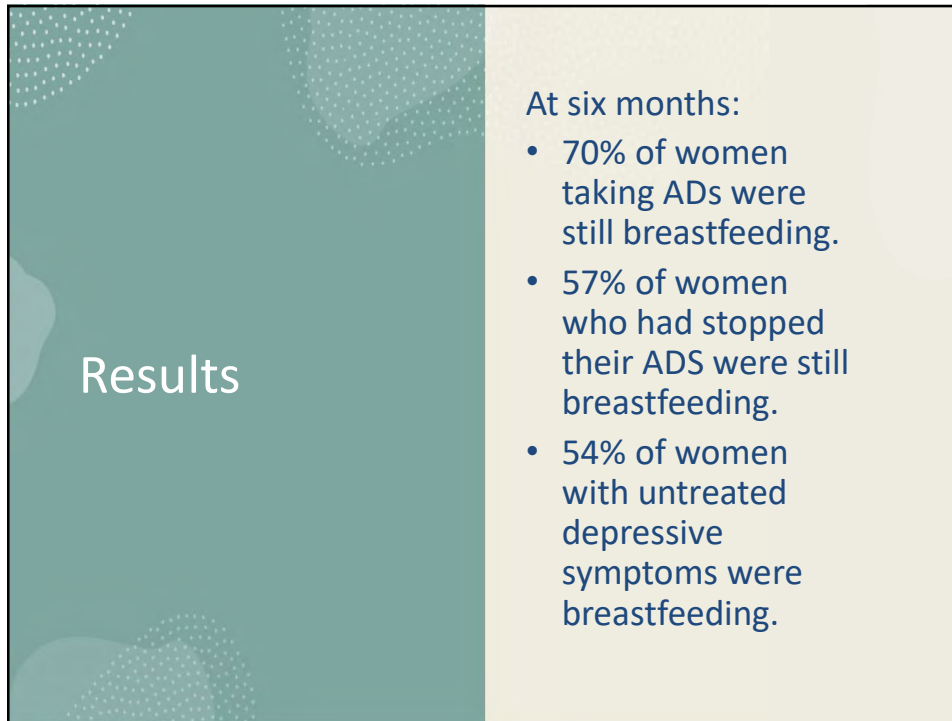
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Researchers compared 6-month breastfeeding outcomes in postpartum Danish women who used antidepressants through pregnancy and postpartum versus women with depression symptoms who were not taking medication.

18th Perinatal Society of Australia Conference, Grzeskowiak,

56



Results

At six months:

- 70% of women taking ADs were still breastfeeding.
- 57% of women who had stopped their ADS were still breastfeeding.
- 54% of women with untreated depressive symptoms were breastfeeding.

57



Proposed factors affecting these outcomes:

- Lack of standardized approach among OB-GYNs for discussing antidepressant use during lactation.

• Global Motherhood Huff Post, Almendrala, Apr 2014

58



American Academy of Pediatrics 2013 report: Many women are 'inappropriately' counseled to discontinue certain medications or stop breastfeeding altogether.

59

- The lack of consistency with information given from various sources can cause women to decide not to breastfeed while taking antidepressants.
- Researchers in the Danish study concluded that family members, friends and healthcare professionals all much support breastfeeding mothers with depression if she chooses to continue her medications for the best breastfeeding outcomes.

Grzeskowiak, press release, 2014

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Objective 4:
Evaluate safety data on
Psychotropic use during
lactation

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Assessment of
Antidepressant
Safety During
Breastfeeding



The image displays three pairs of ZOLOFT antidepressant tablets. Each pair consists of two tablets: one with the brand name 'ZOLOFT' and the other with the dosage strength. The top pair is light green and labeled '25 | MG'. The middle pair is light blue and labeled '50 | MG'. The bottom pair is light yellow and labeled '100 | MG'.

62

How Do We Assess Antidepressant Safety in Breastfeeding?

1. Studies that measure the medication levels in mother's serum, breast milk and/or infant's serum.
2. Case reports

63

Factors Affecting Infant Drug Exposure

- There is significant complexity and individual variability when trying to determine exposure.
- Breast milk drug levels vary based on pH, protein-binding of drugs and lipid content. Drug levels vary significantly at different times during the same feeding.
- Infant GI absorption.

64

Newborns metabolize drugs differently:

The hepatic P-450 system in a full-term infant is about half that of an adult and each enzyme system develops at a different rate. More pronounced in preterm infants.

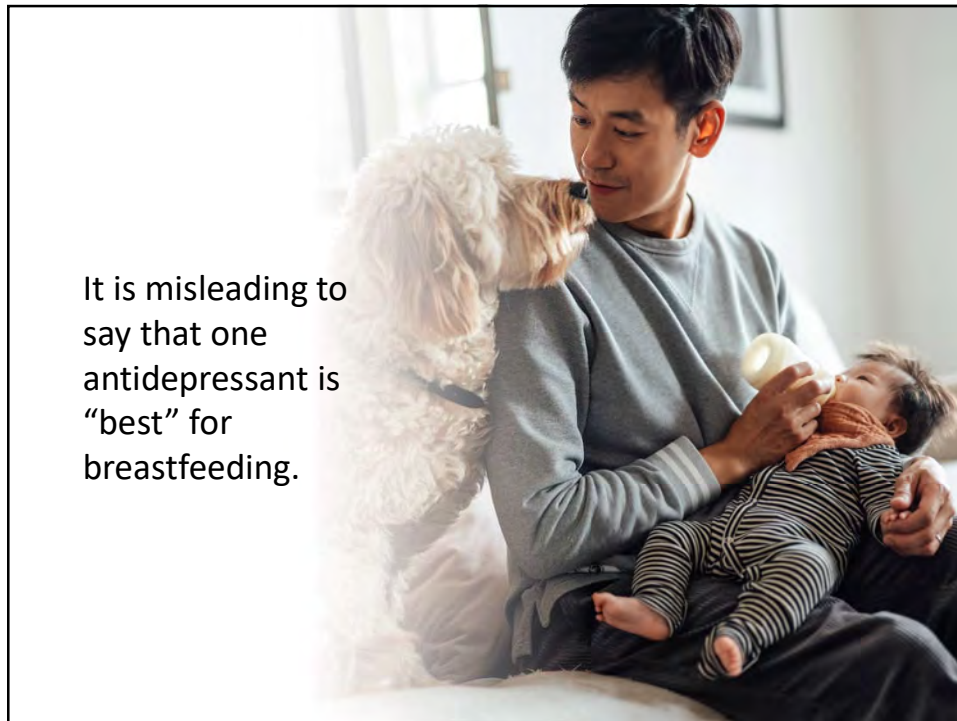
By two months of age, infant hepatic metabolism is 2 to 3-times faster than that of adults.

65

Infants have immature kidney function with glomerular filtration rates about 35% that of adults. An infant achieves adult GFR by 3 to 5 months of age.

Newborn's blood-brain barrier is immature and more permeable and they have less body fat so lipid-soluble agents can be significantly more concentrated in the CSF than occurs in adults.

66




It is misleading to say that one antidepressant is “best” for breastfeeding.

67



Most available breastfeeding information is on:
fluoxetine
sertraline
paroxetine
Tricyclic antidepressants

68



There is more information on some antidepressants than others, but the amount of data is simply too small to compare between drugs to determine the “safest” drug.

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Antidepressants and Breastfeeding

All antidepressants are transmitted into breast milk.

Infant exposure is evaluated by:

- **Calculations of the relative infant dose. (RID)**
- **Measurements of infant serum levels.**
- **Case reports of adverse symptoms/behaviors** in breastfed infants which may or may not be related to the drug involved unless feeding is stopped and then reinitiated.

70

Relative Infant Dose (RID)

- Standard in determining safety of drugs in breastfeeding
- Calculation based on amount of drug found in breast milk samples.
- Calculation assumes an infant consumes 150 ml of milk per kg per day and determines infant's total daily dose based on amount of drug per ml in breast milk samples.
- Compares that to mother's actual mg/kg/day dose.
- RID < 10% of maternal daily dose is considered "safe."

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RID limitations:

- Assumes the amount of breast milk an infant consumes per day.
- Does not take into account the variability of drug concentrations in milk that the infant is actually exposed to during a single feeding. Assumes "flat exposure" that matches the assay samples.
- Does not take into account factors in infant metabolism.
- Does not use infant serum levels which is the most accurate measure of infant exposure.

72



Let's take a look at some data

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“Pooled Analysis of Antidepressant Levels in Lactating Mothers, Breast Milk and Nursing Infants”

Most comprehensive review of antidepressant levels in breast milk - evaluated all studies to-date in which maternal serum levels, breast milk levels and infant serum levels were measured.

Authors found 15 studies with 337 mother-baby pairs involving 15 different antidepressants.

American J Psych, Weissman, June 2004;161(6)

74



Study published largest number of cases for individual antidepressants comparing the level of a drug in *mother's serum* with the level of that drug in the *infant's serum*.

Although total numbers are small, these studies are a more accurate measure of exposure than breast milk levels or RID.

75

<u>AD</u>	Mean Infant Serum <u>Level (ng/ml)</u>	Percent of Maternal <u>Serum Level</u>
sertraline (60)	.02	6%
paroxetine (47)	.01	<1%
Fluoxetine (36)	.06	18%
citalopram (12)	.03	20%
venlafaxine (5)		7%
bupropion(2)	.00	<1%

Wellbutrin data from J Clin Psych, Baab (63) 2002

76

Most of the infants exposed to sertraline and paroxetine had no measurable serum drug levels. (The drug levels were below the minimum level that the assays could detect.)

Citalopram and fluoxetine produced the highest infant serum levels.

Fluoxetine and its metabolite have very long half-lives.

Citalopram has low protein binding, which is associated with increased drug transmission into breast milk.

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Maternal Drug Dose and Infant Levels: Key Findings

Maternal drug doses were correlated with infant plasma levels for only one drug - Citalopram.

Maternal drug doses did not predict infant serum levels for fluoxetine, paroxetine, or sertraline

Infant age was not correlated with infant serum levels for any of the drugs.

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- Sertraline was the only antidepressant that showed a clear time course between ingestion and peak breast milk level.
- Peak breast milk level occurred 7 to 10 hours after the maternal sertraline dose.

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Dumping breast milk 8-hours after taking sertraline reduced infants overall exposure by 20% **but** pump-and-dump is not recommended.

- Difficult to properly time and accurately accomplish.
- the 20% decrease in exposure is of no known benefit.
- Gives mothers a concerning, mixed message.
- Stresses mothers and wastes breast milk.

80

Case Reports of Adverse Effects in Breastfed Infants:

- There have been a handful of case reports of adverse symptoms in breastfed infants: irritability, decreased feeding, sleep disturbances.
- *Well-documented* cases of adverse events are exceedingly rare.

81



- fluoxetine has the most adverse case reports – due to more use of fluoxetine over the years or to higher infant serum levels seen in studies (?)
- In one case report, a fluoxetine-exposed nursing infants with adverse symptoms had a serum level of 340 ng/ml which indicates accumulation.

82

- Routine monitoring of infant serum levels is not recommended.
- *Clinical monitoring* is the only recommended infant assessment method and is achieved by observation of infant behaviors in conjunction with the infant's pediatrician.
- Serum levels are not meaningful unless there are concerning signs in the infant combined with high serum levels in the infant.
- Breastfeeding may be suspended and reinitiated in rare cases of suspected adverse effects.

83

- Data on SRIs applies to healthy, full-term infants.
- Premature infants and those with medical complications need decision-making and monitoring in conjunction with neonatologist .
- fluoxetine and citalopram *may* be used in breastfeeding if they are the medications that a woman has historically responded to and *should* be used if they were used throughout pregnancy.

84




Long-term Effects on Breastfed Infants

Limited data from small controlled and uncontrolled studies is reassuring.

Stowe, Am J Psychiatry, 1997; 154
Yoshida, Br J Psychiatry, 1998; 172

85



Study of infants breastfed and exposed to sertraline failed to show decreased platelet serotonin uptake which is an indirect indication that serotonin metabolism in the infant brain is not affected by exposure.

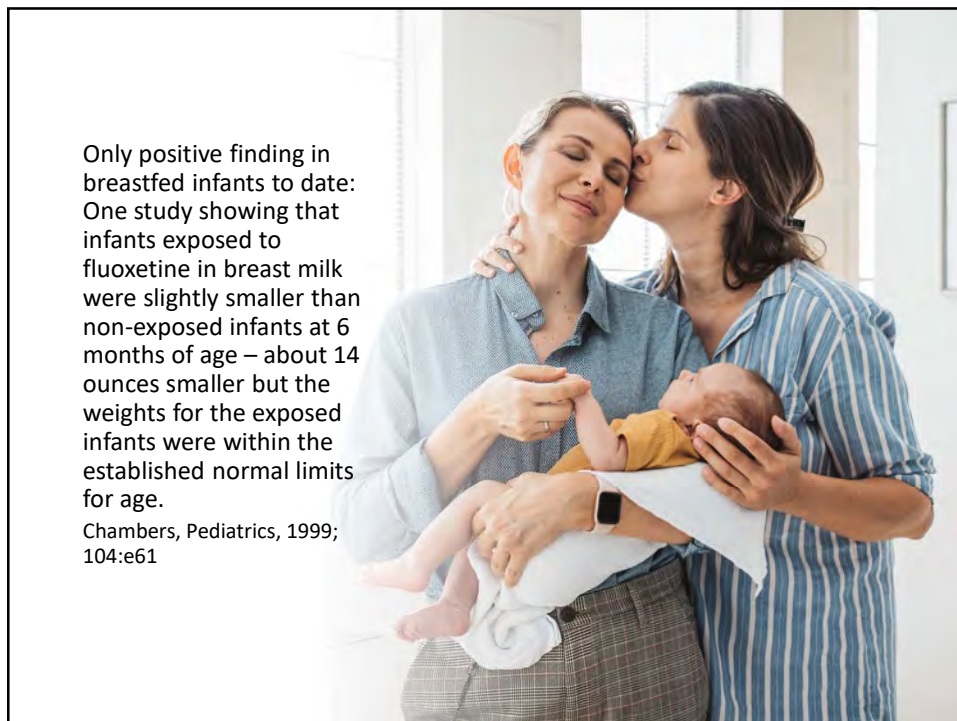
Epperson, Am J Psychiatry, 2001; 158

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There are several long-term studies showing no adverse effects of SRIs on infants who are exposed in-utero where the level of fetal drug-exposure far exceeds that due to breastfeeding.

87



Only positive finding in breastfed infants to date: One study showing that infants exposed to fluoxetine in breast milk were slightly smaller than non-exposed infants at 6 months of age – about 14 ounces smaller but the weights for the exposed infants were within the established normal limits for age.

Chambers, Pediatrics, 1999; 104:e61

88

Ketamine and Breastfeeding

- Ketamine rapidly metabolized and cleared from bloodstream
- Study of 4 lactating women:
 - Peak levels 3-4 hour after IV infusion
 - Breastmilk levels tend to parallel blood levels
 - Relative infant dose calculated at 0.650% at 0.5 mg/kg and 0.766% at 1 mg/kg per day dosing
- No studies have assessed ketamine blood levels in nursing infants

89

-
- 298 breastfeeding infants with mom receiving ketamine for tubal ligation surgery
 - Noted no weight loss in infants

90

Take Aways

- Data limited
- Given the limited data, ketamine should be used with careful infant monitoring for sedation and poor feeding.
- Avoiding breastfeeding for 6 to 12 hours after a single dose will markedly decrease infant exposure to the drug in milk.

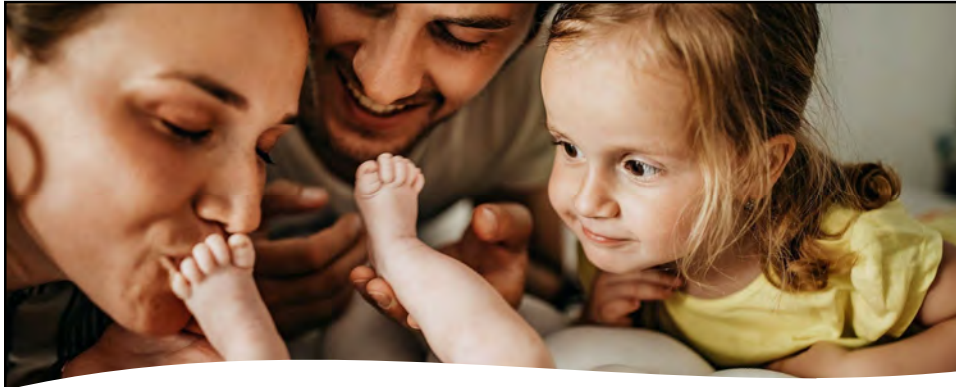
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**2022 American
Academy of
Pediatrics
Statement on
Breastfeeding**

“Most medications that women who are breastfeeding might take are compatible with breastfeeding.”

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**Mass General
Center for
Women's
Mental Health**

New mothers with depression “are an extremely vulnerable” breastfeeding population who need additional nursing support and information and “the benefits of breastfeeding outweigh the risk of exposure to most therapeutic agents via human milk.”
Cohen, Jan 27, 2014

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Resources:

- [Womensmentalhealth.org](https://www.womensmentalhealth.org)
- [Mothertobaby.org/fact-sheets/](https://www.mothertobaby.org/fact-sheets/)
- [Marcesociety.com](https://www.marcesociety.com)
- [Reprotox.org](https://www.reprotox.org)
- [Nrcptraining.org](https://www.nrcptraining.org)
- Infant Risk app
- Postpartum Support International Helpline: 1-800-944-4773
- Note: Lact Med no longer up to date

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Questions or Comments?



Email dana.bell@unmc.edu

