Psicofarmaci e allattamento

Carlo Marchesi

Dipartimento di Medicina e Chirurgia
Sezione di Neuroscienze
Università degli Studi di Parma

carlo.marchesi@unipr.it

Benessere

materno ⟷ neonato

Conseguenze depressione:

- attaccamento insicuro
- compromissione linguaggio
- compromissione QI
- alterazioni comportamentali
- infanticidio

È compatibile con le condizioni materne:

- gravità
- insonnia

← Beneficio dell'allattamento →

Tutti gli psicofarmaci passano nel latte

Punti in discussione

Come garantire il benessere materno ?

Compromissione del benessere materno

Gravi Disturbi Psichici nel post-partum

1. I disturbi *più gravi* nel post-partum:
- Depressione Melanconica e/o Psicotica,
- Disturbo Bipolare,
- DOC,
- Psicosi Puerperale.

Postpartum depression: a disorder in search of a definition

Wisner et al, *Arch Womens Ment Health 2010: 13: 37-40*

The diagnostic entities most frequently observed after birth were major mood disorders, with a particular risk for bipolar disorder.

Bipolar Disorder relative risks of
- 23.3 in the first 30 days
- 6.3 in the 31–60 days after birth.

Admission with *psychosis* (primarily *bipolar disorder*)
- RR of 21.7 within 30 days of birth.

Compromissione del benessere materno

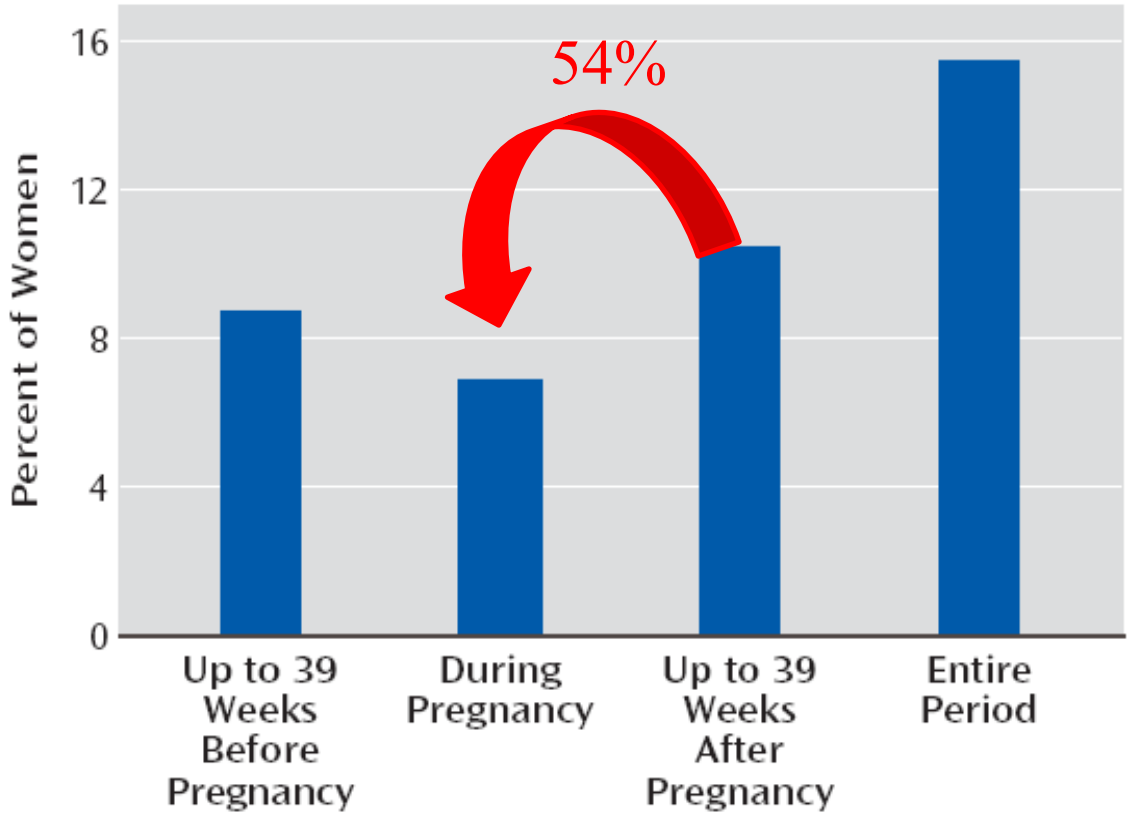
Gravi Disturbi Psichici nel post-partum

2. *Esordiscono più frequentemente in gravidanza (« nel postpartum raccogliamo ciò che abbiamo seminato in gravidanza »)*

Clinically Identified Maternal Depression Before, During, and After Pregnancies Ending in Live Births

Am J Psychiatry 2007; 164:1515–1520

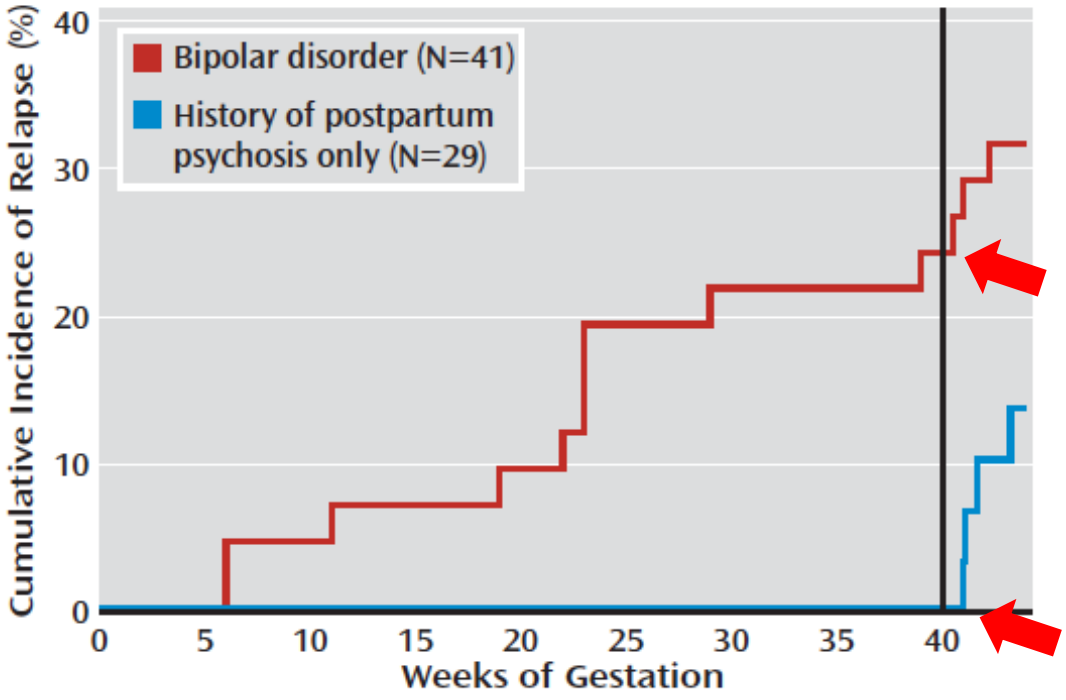
FIGURE 1. Percent of Women With Diagnosed Depression Before, During, and After Pregnancy

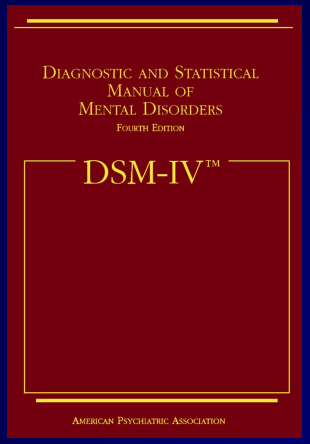


Prevention of Postpartum Psychosis and Mania in Women at High Risk

Bergink et al, *Am J Psychiatry 2012; 169: 609-615*

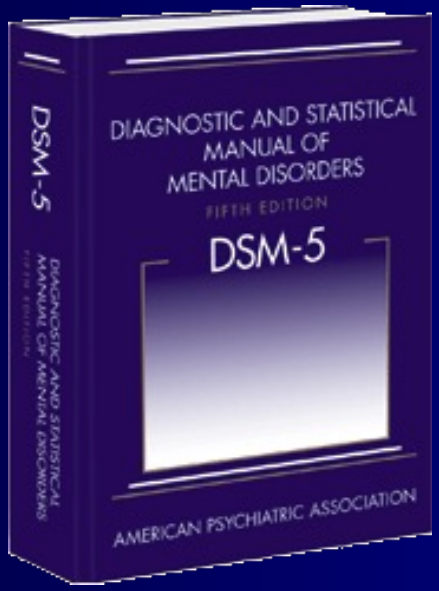
FIGURE 2. Cumulative Incidence of Relapse During Pregnancy and the Postpartum Period in Women With Bipolar Disorder or a History of Postpartum Psychosis Only





Depressive Disorders and Bipolar Disorders with postpartum onset

if onset of mood symptoms occurs in the 4 weeks following delivery.



Depressive Disorders and Bipolar Disorders with peripartum onset

if onset of mood symptoms occurs during pregnancy or in the 4 weeks following delivery.

Compromissione del benessere materno

Gravi Disturbi Psichici nel post-partum

3. E' possibile *prevenirli con un adeguato screening, monitoraggio e terapia prima e durante la gravidanza e dopo il parto, collaborando tra servizi*

ISSN 1591-223X
DOSSIER
Agenzia sanitaria e sociale regionale
RegioneEmilia-Romagna
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

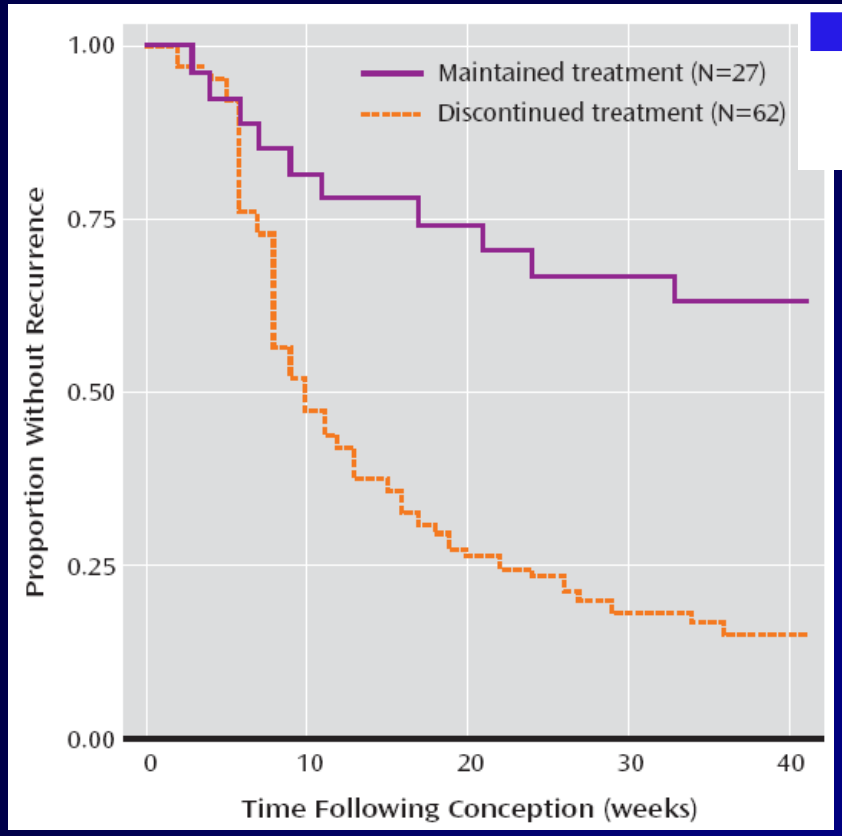
Mortalità e morbosità materna in Emilia-Romagna. Rapporto 2001-2007

97 casi di morti materne → 18 suicidi

Per i casi in cui è stata possibile una valutazione della qualità del percorso assistenziale, i fattori di ***substandard care*** rilevati sono stati:

- la mancata attivazione e presa in carico dei servizi territoriali psichiatrici alla dimissione di donne sintomatiche

- la sospensione inappropriata della terapia con psicofarmaci durante la gravidanza.



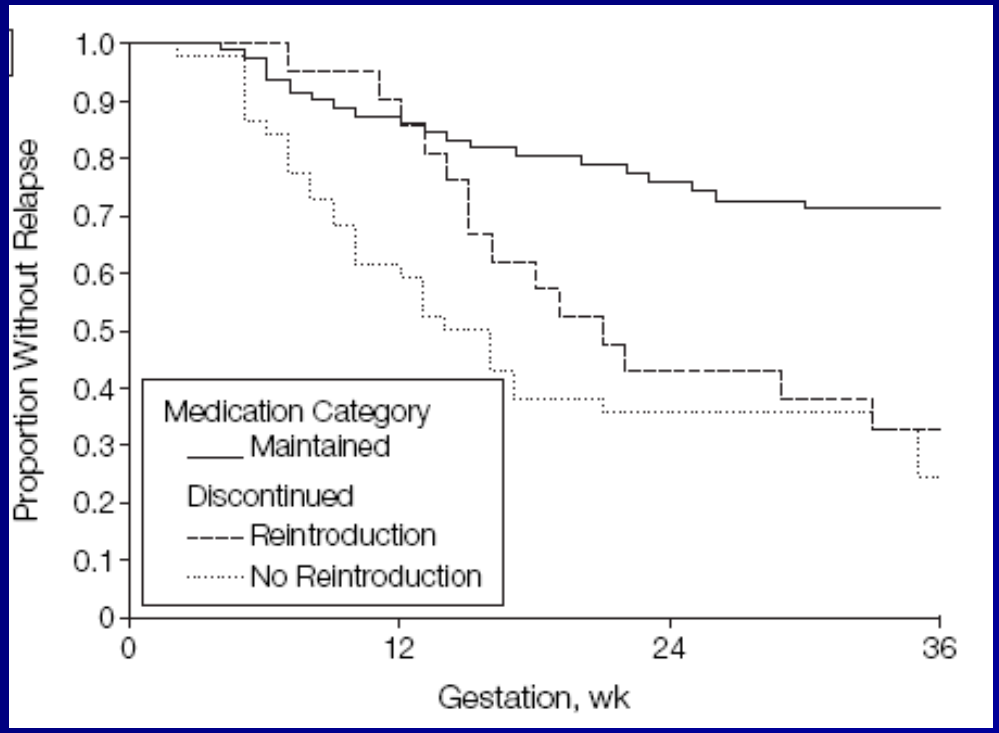
Article

Risk of Recurrence in Women With Bipolar Disorder During Pregnancy: Prospective Study of Mood Stabilizer Discontinuation

Viguera et al, *Am J Psychiatry 2007; 164: 1817-1824*

Relapse of Major Depression During Pregnancy in Women Who Maintain or Discontinue Antidepressant Treatment

Cohen et al, *JAMA 2006; 295: 499-507*



Come garantire il benessere materno ?

Benessere

madre ***assume*** farmaci

- stato di benessere in terapia di mantenimento;
- stato di malessere in trattamento

neonato

Beneficio dell'allattamento

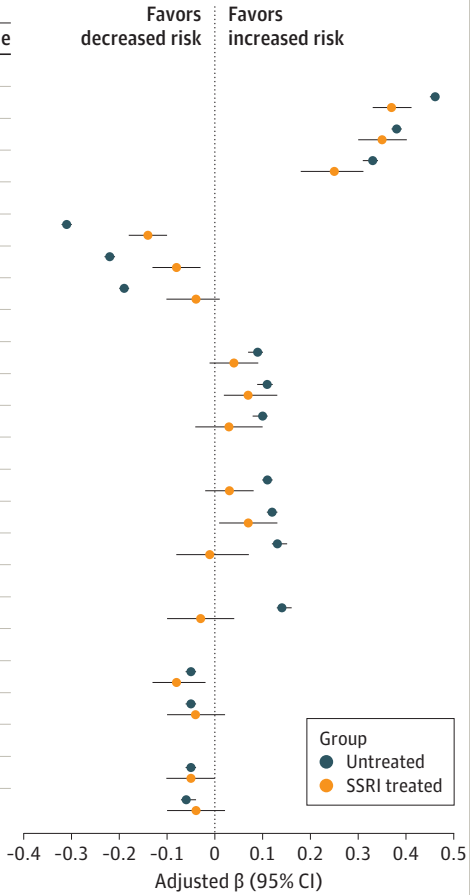
Tutti gli psicofarmaci passano nel latte

Long-Term Maternal and Child Outcomes Following Postnatal SSRI Treatment

Chaoyu et al *JAMA Network Open 2023; 6: e2331270*

Figure 1. Maternal and Child Outcomes and the Association Between Postnatal Maternal Depression, Selective Serotonin Reuptake Inhibitor (SSRI) Treatment, and the Study Outcomes in the Study Population

	PND		SSRI treatment for PND		Moderation of association between treatment and PND	
Outcomes	β (95% CI)	*P* value	β (95% CI)	*P* value	β (95% CI)	*P* value
Maternal depression						
1.5 y	0.46 (0.45 to 0.46)	<.001	0.37 (0.33 to 0.41)	<.001	-0.08 (-0.12 to -0.04)	<.001
3 y	0.38 (0.37 to 0.39)	<.001	0.35 (0.30 to 0.40)	<.001	-0.02 (-0.07 to 0.03)	.37
5 y	0.33 (0.31 to 0.34)	<.001	0.25 (0.18 to 0.31)	<.001	-0.08 (-0.14 to -0.02)	.01
Relationship satisfaction						
6 mo	-0.31 (-0.32 to -0.30)	<.001	-0.14 (-0.18 to -0.10)	<.001	0.17 (0.13 to 0.21)	<.001
1.5 y	-0.22 (-0.23 to -0.21)	<.001	-0.08 (-0.13 to -0.03)	<.001	0.14 (0.09 to 0.19)	<.001
3 y	-0.19 (-0.20 to -0.18)	<.001	-0.04 (-0.10 to 0.01)	.13	0.14 (0.08 to 0.20)	<.001
Internalizing problems						
1.5 y	0.09 (0.07 to 0.10)	<.001	0.04 (-0.01 to 0.09)	.10	-0.04 (-0.09 to 0.01)	.25
3 y	0.11 (0.09 to 0.12)	<.001	0.07 (0.02 to 0.13)	.007	-0.02 (-0.08 to 0.04)	.65
5 y	0.10 (0.08 to 0.11)	<.001	0.03 (-0.04 to 0.10)	.25	-0.06 (-0.13 to 0.02)	.25
Externalizing problems						
1.5 y	0.11 (0.10 to 0.12)	<.001	0.03 (-0.02 to 0.08)	.28	-0.08 (-0.14 to -0.03)	.006
3 y	0.12 (0.11 to 0.13)	<.001	0.07 (0.01 to 0.13)	.01	-0.05 (-0.10 to 0.01)	.25
5 y	0.13 (0.12 to 0.15)	<.001	-0.01 (-0.08 to 0.07)	.96	-0.13 (-0.21 to -0.06)	.002
ADHD						
5 y	0.14 (0.13 to 0.16)	<.001	-0.03 (-0.10 to 0.04)	.42	-0.17 (-0.24 to -0.10)	<.001
Motor development						
1.5 y	-0.05 (-0.06 to -0.04)	<.001	-0.08 (-0.13 to -0.02)	.009	-0.02 (-0.07 to 0.03)	.65
3 y	-0.05 (-0.06 to -0.04)	<.001	-0.04 (-0.10 to 0.02)	.13	0 (-0.06 to 0.06)	.91
Language development						
1.5 y	-0.05 (-0.06 to -0.04)	<.001	-0.05 (-0.10 to 0)	.10	0.01 (-0.05 to 0.06)	.91
3 y	-0.06 (-0.07 to -0.04)	<.001	-0.04 (-0.10 to 0.02)	.21	0.02 (-0.04 to 0.08)	.65



Una madre,
che assume psicofarmaci
per il suo benessere,
può allattare al seno il suo neonato ?

Benessere

madre ***assume*** farmaci

neonato

Beneficio dell'allattamento

Tutti gli psicofarmaci passano nel latte

Pharmacotherapy for depression and bipolar disorder during lactation: A framework to aid decision making

Sprague et al, *Semin Perinatol 2020; 44: 151224*

M/P ratio: milk to plasma ratio
TID: theoretic infant dose
RID: relative infant dose

M/P = [drug in milk] / [drug in maternal plasma]

TID (mg/kg/day) = [drug in milk] x daily milk volume (~150 ml/kg/day)

RID (%) = TID (mg/kg/day) / Mother's weight adjusted dose (mg/kg/day)

medications with a RID

- *< 10% relatively safe and acceptable*,
- 10-25% caution with consideration to alternative medications.
- > 25% potentially toxic.

Maternal Medication, Drug Use, and Breastfeeding

Antidepressivi

Rowe et al,
Child Adolesc Psychiatric Clin N Am 2015; 24:1-20

Table 1
Antidepressants and reported levels in breast milk

Antidepressant	Relative Infant Dose (RID) %	Comments
Selective Serotonin Reuptake Inhibitors (SSRIs)		
Citalopram	3.6[90]	Compatible: SSRIs are recommended first-line agents for depression and anxiety, and are suitable when breastfeeding. There have been 2 cases of excessive somnolence, decreased feeding, and weight loss with citalopram; however, most new data suggest these side effects are rare.[91,92] Fluoxetine has been reported to cause colic, fussiness, and crying[93,94]
Escitalopram	5.3[95]	
Fluvoxamine	1.6[8]	
Fluoxetine	5–9[93,94]	
Sertraline	0.54[7]	
Paroxetine	1.4[9]	
Serotonin Norepinephrine Reuptake Inhibitors		
Venlafaxine	8.1[96]	Compatible: No adverse events reported in breastfed infants with these 3 medications
Desvenlafaxine	6.8[97]	
Duloxetine	0.1[98]	

Sertralina: se la madre assume 100mg/die → neonato 0.03mg/die

A New Safety Scoring System for the Use of Psychotropic Drugs During Lactation

Uguz, *Am J Ther 2021; 28: e118-e126*

8.6–10.0 points: These drugs have a very good safety profile. The risk of adverse effects is very low. Their usage during lactation is highly acceptable.

7.1–8.5 points: These drugs have a good safety profile. The risk of adverse effects is low. Their usage during lactation is acceptable.

5.1–7.0 points: These drugs have a moderate safety profile. The risk of adverse effects is moderate but not expected life-threatening events. Their usage during lactation is possible.

3.1–5.0 points: These drugs have a low safety profile. The risk of adverse effects is relatively high or these drugs have limited data on their safety. Their usage during lactation is possible with caution. These drugs should be preferred only if safer drugs are ineffective or intolerable in lactating patients and their potential benefits are superior to potential risks.

≤3 points: These drugs have a very low safety profile. These drugs either lack data on their usage during lactation or have a poor safety data that indicate a high-level infant exposure and/or a high prevalence of adverse effects. Their usage during breastfeeding is not recommended.

A. Reported total sample: maximum score: 3
- 0: No data
- 0.5: N ≤ 5
- 1.0: N = 6–15
- 1.5: N = 16–50
- 2.0: N = 51–100
- 2.5: N = 101–200
- 3.0: N > 200

B. Reported maximum RID: maximum score: 2
- 0: No data or >25%
- 0.5: 10.1%–25.0%
- 1.0: 6.1%–10.0%
- 1.5: 2.1%–6.0%
- 2.0: 0%–2.0%

C. Reported sample size for RID: maximum score: 1
- 0: No data or N ≤ 5
- 0.5: N = 6–15
- 1.0: N ≥ 15

D. Infant plasma drug levels: maximum score: 1
- 0: No data or detectable in plasma of all reported infants
- 0.5: Below the detection limits in ≤50% of reported infants
- 1.0: Below the detection limits in >50% of reported infants

E. Prevalence of reported any adverse effect: maximum score: 2
- 0: No data or >25%
- 0.5: Limited data (reported total sample <10) but no report or 15.1%–25.0%
- 1.0: 5.1%–15.0%
- 1.5: 2.1%–5.0%
- 2.0: No report or ≤2%

F. Reported serious adverse effects: maximum score: 1
- 0: No data or reported serious effect(s)
- 0.5: Limited data (reported total sample <10) but no report
- 1.0: No report

A New Safety Scoring System for the Use of Psychotropic Drugs During Lactation

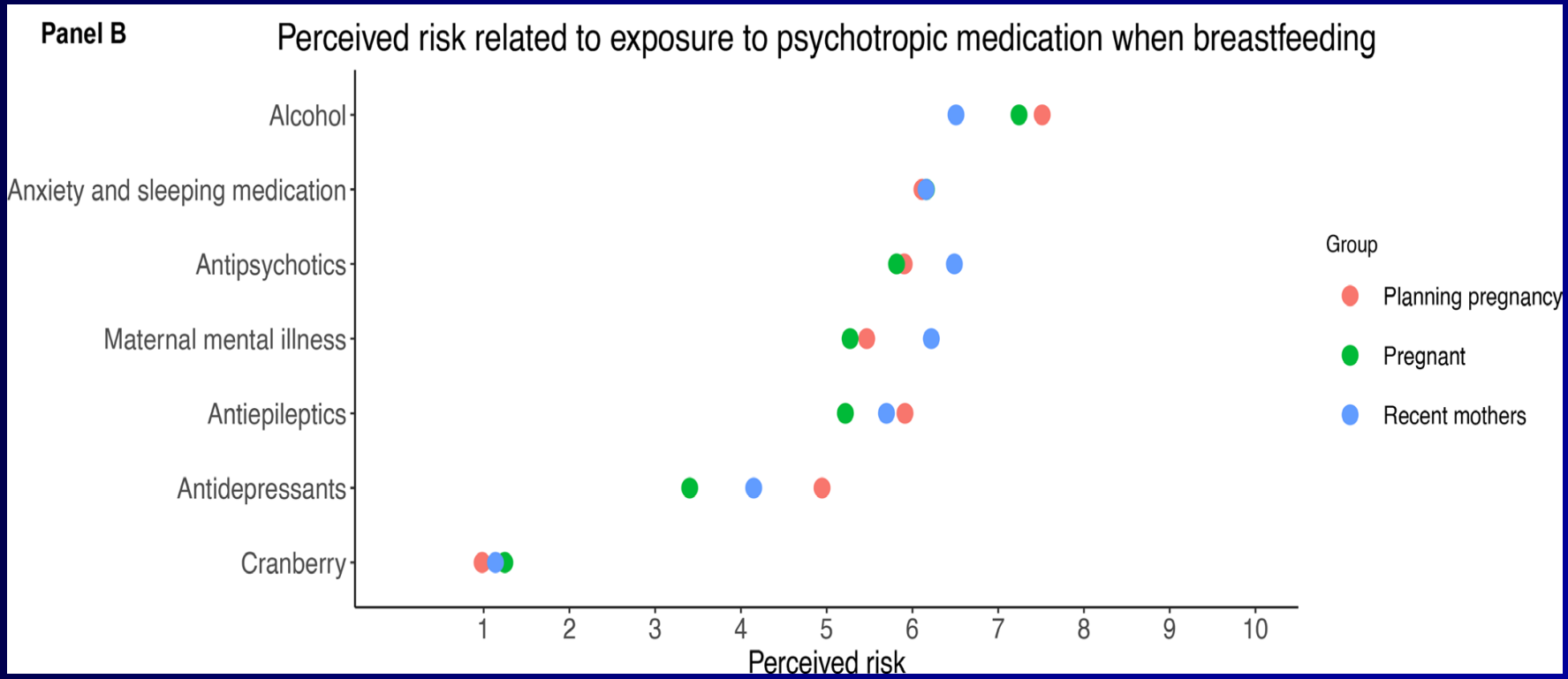
Uguz, *Am J Ther 2021; 28: e118-e126*

Table 3. Safety scores of psychotropic drugs used during the lactation period according to the present scoring system.

Drug	Item A	Item B	Item C	Item D	Item E	Item F	Total score	Safety profile	Comments on the usage
Antidepressants									
Fluoxetine	3.0	0.5	1.0	0.5	1.5	0	6.5	Moderate	Possible
Sertraline	3.0	1.5	1.0	1.0	2.0	1.0	9.5	Very good	Highly acceptable
Paroxetine	3.0	1.5	1.0	1.0	1.5	1.0	9.0	Very good	Highly acceptable
Citalopram	2.5	1.5	1.0	1.0	1.0	1.0	8.0	Good	Acceptable
Escitalopram	1.5	1.0	0.5	1.0	1.5	0	5.5	Moderate	Possible
Fluvoxamine	1.5	2.0	0.5	1.0	1.0	1.0	7.0	Moderate	Possible
Venlafaxine	1.5	1.0	1.0	0.5	2.0	1.0	7.0	Moderate	Possible
Mirtazapine	1.0	1.5	0.5	0.5	1.0	1.0	5.5	Moderate	Possible
Bupropion	1.5	0.5	0.5	0.5	1.0	0	4.0	Low	Possible with caution
Duloxetine	1.0	2.0	0.5	0.5	0.5	0.5	5.0	Low	Possible with caution
Amitriptyline/nortriptyline	1.5	2.0	0	1.0	1.5	1.0	7.0	Moderate	Possible
Imipramine/desipramine	1.5	1.5	0	1.0	2.0	1.0	7.0	Moderate	Possible
Doxepin	0.5	1.5	0	0.5	0	0	2.5	Very low	Not recommended
Clomipramine	1.0	1.5	0	1.0	0.5	0.5	4.5	Low	Possible with caution
Trazodone	1.0	2.0	0	0	0.5	0.5	4.0	Low	Possible with caution

Perceived risk of neurodevelopmental outcomes in offspring related to psychotropic and mental illness exposures in pregnancy and breastfeeding: a cross-sectional survey of women with past or current mental illness

Bjørndal et al. *BMJ Open 2022;12:e061159*



Perinatal antidepressant use and breastfeeding outcomes: Findings from the Norwegian Mother, Father and Child Cohort Study

Grzeskowiak et al, *Acta Obstet Gynecol Scand. 2022;101:344–354*

	Unexposed mental disorder comparison		Antidepressant use – continued from late gestation		Antidepressant use – new/restarted postpartum		Population comparison	
	n (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)	*n* (%)	aRR (95% CI)
Any breastfeeding until 6 months[a]	5768 (77.3)	Ref	141 (75.8)	0.99 (0.91–1.07)	137 (36.7)	**0.49 (0.42–0.56)**	61 671 (85.5)	**1.06 (1.05–1.07)**
Predominant breastfeeding until 6 months[a]	874 (11.7)	Ref	20 (10.8)	0.94 (0.60–1.48)	16 (4.3)	**0.37 (0.22–0.61)**	10 893 (15.1)	**1.14 (1.07–1.22)**
Abrupt breastfeeding discontinuation[a]	577 (7.3)	Ref	13 (7.0)	0.98 (0.56–1.71)	84 (22.5)	**2.64 (2.07–3.37)**	3301 (4.6)	**0.75 (0.68–0.82)**
Breastfeeding problems reported in first month postpartum								
Any breastfeeding problems[a]	1410 (18.9)	Ref	30 (16.1)	0.75 (0.53–1.07)	99 (26.5)	**1.37 (1.14–1.64)**	10 078 (14.0)	**0.75 (0.71–0.79)**
Sore nipples[a]	555 (7.4)	Ref	11 (5.9)	0.70 (0.38–1.30)	37 (9.9)	1.35 (0.97–1.87)	4030 (5.6)	**0.78 (0.71–0.85)**
Mastitis[a]	700 (9.4)	Ref	17 (9.1)	0.93 (0.58–1.49)	45 (12.1)	1.26 (0.94–1.69)	5565 (7.7)	**0.82 (0.76–0.89)**
Other breastfeeding problems[a]	737 (9.9)	Ref	12 (6.5)	0.54 (0.30–0.96)	62 (16.2)	**1.60 (1.25–2.07)**	3878 (5.4)	**0.56 (0.52–0.61)**

Antidepressant prescriptions, discontinuation, depression and perinatal outcomes, including breastfeeding: A population cohort analysis

Jordan et al, *PLOS ONE 2019; 14: e0225133*

Table 6. Breastfeeding at 6–8 weeks (n = 38725).

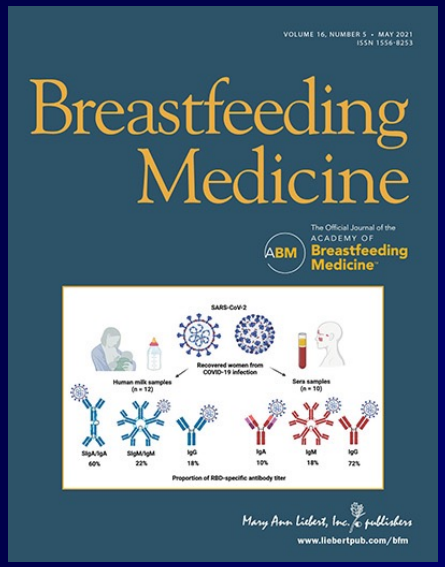
Exposures	Exposed n [%]	Unexposed [n [%]	Unadjusted OR [95% CI]	Adjusted* OR [95% CI]
SSRI [any N06AB] in trimesters 2 or 3	137/645 [21.24]	12,656/38,080 [33.24]	0.54 [0.45–0.66]	0.77 [0.62–0.95]
SSRI high dose in trimesters 2 or 3	47/214 [21.96]	12,746/38,511 [33.1]	0.57 [0.41–0.79]	0.45 [0.23–0.86]
Antidepressant [any N06A] in trimesters 2 or 3	179/806 [22.21]	12,614/37,919 [33.27]	0.57 [0.48–0.68]	0.81 [0.67–0.98]
SSRI in trimester 1 but not in trimesters 2 or 3	207/862 [24.02]	12,586/37,863 [33.24]	0.64 [0.54–0.74]	0.66 [0.51–0.87]
Antidepressant in trimester 1 but not in trimesters 2 or 3	376/1619 [23.22]	12,417/37,106 [33.46]	0.60 [0.54–0.68]	0.70 [0.57–0.85]
Depression diagnosed and unmedicated in t2 and t3	1365/5241 [25.87]	11,428/33,484 [34.13]	0.68 [0.67–0.73]	0.87 [0.82–0.92]
Depression medicated in t2 or t3	102/472 [21.62]	12,691/38,253 [33.18]	0.56 [0.45–0.69]	0.70 [0.58–0.85]
Depression diagnosed	1467/5713 [25.7]	11,346/33,012 [34.31]	0.66 [0.62–0.71]	0.76 [0.70–0.82]

Antidepressant prescriptions, discontinuation, depression and perinatal outcomes, including breastfeeding: A population cohort analysis

Jordan et al, *PLOS ONE 2019; 14: e0225133*

Women using prescription medicines are less likely to breastfeed, particularly if there is ***little information*** about the transfer of the medicine to breastfed infants.

Our findings suggest that successfully targeting women prescribed antidepressants or with a recorded diagnosis of depression would improve breastfeeding rates by ~10%, and protect (reduction) 1.3% of infants from obesity and 0.7% of women from breast cancer.



Calls to a Major Teratogen Information Service Regarding Exposures During Breastfeeding

Hegedus et al, *Breastfeeding Medicine 2019; 14: 674-679*

MotherSafe is a free telephone-based counseling service for ***Australian*** consumers and health care providers concerned about drug exposures during pregnancy and breastfeeding

- 315,158 calls received at MotherSafe between 2000 and 2018,
- 116,876 (***37.1%***) were regarding drug exposure via ***breastfeeding***;
- 30% of these calls related to nonsteroidal anti-inflammatory drugs, antihistamines, antidepressants, simple analgesics, and antibiotics,
- 5% were regarding an exposure specifically contraindicated when breastfeeding.

Pharmacotherapy for depression and bipolar disorder during lactation: A framework to aid decision making

Sprague et al, *Semin Perinatol 2020; 44: 151224.*

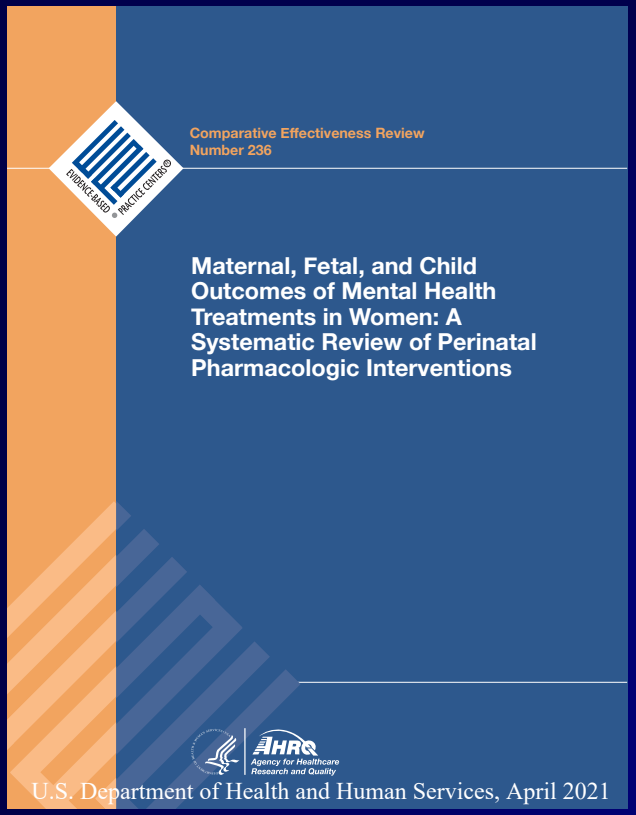
- Women who perceive their *physician* had a *neutral* attitude regarding breastfeeding are *less likely to breastfeed* beyond 6 weeks.

- Among those who perceived that their physician *favored* breastfeeding, the proportion of mothers intending to breastfeed for a *longer duration* was much higher

Use of Psychotropic Medication During Lactation in Postpartum Psychiatric Patients: Results from an 8-Year Clinical Sample

Uguz et al, *Breastfeeding Medicine 2020;15:535-537*

Methods:
Clinical data collated for a period of 8 years were retrospectively retrieved from patient registers.
The sample included a total of 263 postpartum patients who were followed up for at least 4 weeks.
Results: The most commonly administered psychotropic medications were ***paroxetine (43.3%), sertraline (31.9%)***, ***olanzapine (12.2%), quetiapine (6.1%).***
Of the ***242 patients*** who received psychotropic medication, 41 (***16.9%***) ***discontinued breastfeedin***g.
The discontinuation in most cases was not due to psychiatrist's recommendation or adverse events due to medications.



Perinatal Period	Depression[33]
During breastfeeding	Concordance • For new episodes, start with psychotherapy as initial treatment and consider antidepressants for severe cases • Continue antidepressants to avoid relapse • Sertraline preferred due to its favorable profile during lactation • Two guidelines also recommend citalopram • Avoid fluoxetine due to its long half-life and presence in breastmilk

Maternal Medication, Drug Use, and Breastfeeding

Antipsicotici

Rowe et al,
Child Adolesc Psychiatric Clin N Am 2015; 24:1-20

Three of the most commonly used 2° generation antipsychotics are

- risperidone RID 4.3%
- quetiapine RID 0.09%
- olanzapine RID 1.6%

these medications are thought to be more suitable in breastfeeding than the older antipsychotics (phenothiazines), which have been associated with drowsiness and lethargy.

A New Safety Scoring System for the Use of Psychotropic Drugs During Lactation

Uguz, *Am J Ther 2021; 28: e118-e126*

Table 3. Safety scores of psychotropic drugs used during the lactation period according to the present scoring system.

Drug	Item A	Item B	Item C	Item D	Item E	Item F	Total score	Safety profile	Comments on the usage
Antipsychotics									
Haloperidol	1.5	0.5	0	0.5	1.5	1.0	5.0	Low	Possible with caution
Chlorpromazine	1.5	2.0	0	0.5	1.0	1.0	6.0	Moderate	Possible
Chlorprothixene	0.5	2.0	0	0	0.5	0.5	3.5	Low	Possible with caution
Zuclopenthixol	1.0	2.0	0	0	0.5	0.5	4.0	Low	Possible with caution
Flupenthixol	0.5	2.0	0	0	0.5	0.5	3.5	Low	Possible with caution
Trifluoperazine	0.5	0	0	0	0.5	0.5	1.5	Very low	Not recommended
Olanzapine	2.5	1.5	0.5	1.0	1.0	1.0	7.5	Good	Acceptable
Quetiapine	1.0	2.0	0	0.5	1.0	1.0	5.5	Moderate	Possible
Risperidone/paliperidone	1.0	1.5	0	1.0	0.5	0.5	4.5	Low	Possible with caution
Aripiprazole	0.5	1.0	0	0	0.5	0.5	2.5	Very low	Not recommended
Amisulpride	0.5	0.5	0	0	0.5	0.5	2.0	Very low	Not recommended
Ziprasidone	0.5	2.0	0	0	0.5	0.5	3.5	Low	Possible with caution
Clozapine	1.0	0	0	0	0	0	1.0	Very low	Not recommended

Aripiprazole, brexpiprazole, and cariprazine can affect milk supply: Advice to breastfeeding mothers

Naughton et al, *Australasian Psychiatry 2023, 31: 201–204*

Women who intend to breastfeed and who are taking Dopamine Receptor Partial Agonists should be informed of the possibility that their medication may have unpredictable effects on milk supply.

The decision to use additional galactagogues such as metoclopramide and domperidone in women already taking an antipsychotic requires an understanding of physiology, pharmacodynamics, and drug interactions.

?

Stabilizzatori Umore

Maternal Medication, Drug Use, and Breastfeeding

Rowe et al,
Child Adolesc Psychiatric Clin N Am 2015; 24:1-20

Table 2
Seizure and mood stabilizer medications and reported levels in breast milk

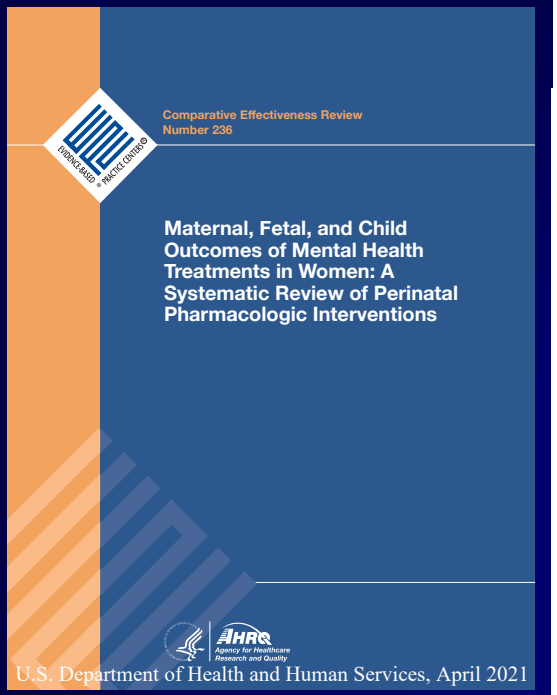
Drug	Relative Infant Dose (RID) %	Comments
Valproic acid	1.4–1.7[21]	Probably compatible: In a study of 16 patients receiving 300–2400 mg/d of valproic acid, breast milk concentrations ranged from 0.4 to 3.9 mg/L (mean = 1.9 mg/L)[21] One case report of a 3-mo-old breastfed infant who developed thrombocytopenia, petechiae, a minor hematoma, and anemia 6 wk after his mother's valproic acid dose was doubled. The investigators report the onset of symptoms occurred near a minor cold but believe the adverse events were not related to a viral illness[99] NEAD study demonstrated adverse cognitive effects from valproic acid exposure in utero. In a 3-year follow up study, 42% of children were breastfed; IQs for breastfed children did not differ from non-breastfed children. Although this study did not show adverse effects, there are many confounding variables; until further trials are published the long-term effects on cognitive development are unknown[100]
Carbamazepine	5.9[101]	Compatible: Levels in milk are reported to be low (2.8–4.5 mg/L), the estimated infant dose is <0.68 mg/kg/d. One report of elevated liver function tests occurred in a 9-d-old infant[101]
Lithium	30.1[102]	Compatible with close observation: Because the RID for lithium is variable, this medication should only be used if found to be the most suitable mood stabilizer for the mother and the infant is full term and healthy. Studies suggest monitoring serum creatinine, BUN, and thyroid function in the infant[102,103]
Lamotrigine	9.2[23]	Compatible: Reports of significant plasma levels have occurred in some breastfed infants, although none have been high enough to produce side effects. It may be helpful to monitor the infant's plasma levels[23,104]

A New Safety Scoring System for the Use of Psychotropic Drugs During Lactation

Uguz, *Am J Ther 2021; 28: e118-e126*

Table 3. Safety scores of psychotropic drugs used during the lactation period according to the present scoring system.

Drug	Item A	Item B	Item C	Item D	Item E	Item F	Total score	Safety profile	Comments on the usage
Mood stabilizers									
Lithium	1.5	0	0.5	0	1.0	1.0	4.0	Low	Possible with caution
Valproate	1.5	1.5	0	0.5	2.0	1.0	6.5	Moderate	Possible
Carbamazepine	2.5	1.5	0	0.5	1.0	0	5.5	Moderate	Possible
Lamotrigine	2.5	0.5	1.0	0.5	1.5	0	5.5	Moderate	Possible
Oxcarbazepine	0.5	2.0	0	0	0.5	0.5	3.5	Low	Possible with caution



Perinatal Period	Bipolar Disorder[37]
During breastfeeding	Concordance • Reintroduce lithium after delivery • Breastfeeding is not recommended with lithium due to a risk of toxicity for the baby Uncertainty • Lithium dose at reintroduction • Safety of breastfeeding with anticonvulsant mood stabilizers, including sodium valproate, carbamazepine, and lamotrigine, and second-generation antipsychotics • Safety of breastfeeding with antidepressants

U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Lithium. [Updated 2023 Dec 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Lithium

Revised: December 15, 2023.

Summary of Use during Lactation

Lithium ***excretion*** into breastmilk and ***concentrations*** in infant serum ***are highly variable***.

Although lithium appears on some lists of drugs contraindicated during breastfeeding, many sources ***do not*** consider it ***an absolute contraindication in healthy-full-term infants***.

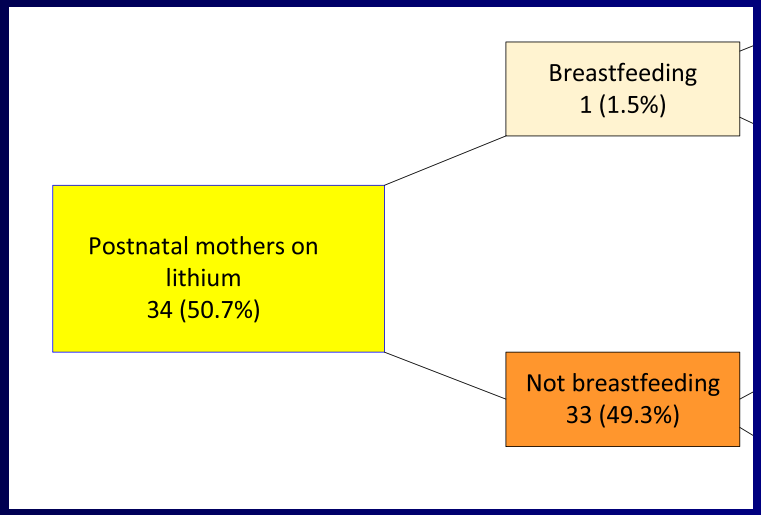
Numerous reports exist of infants who were breastfed during maternal lithium therapy ***without any signs of toxicity or developmental problems***.
Most were ***breastfed from birth*** and some continued to nurse ***for up to 1 year*** of maternal lithium therapy.

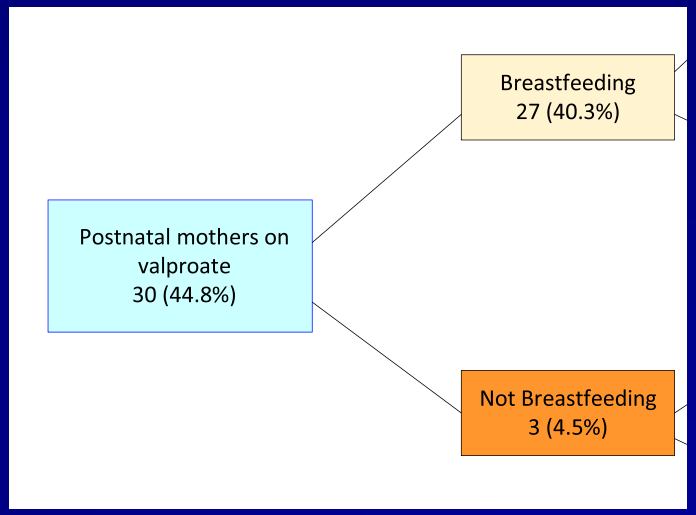
Some reports suggest that lithium in milk can ***adversely affect the infant acutely when its elimination is impaired***, as in dehydration or in newborn or premature infants.

The long-term effects of lithium on infants are not certain, but limited data indicate ***no*** obvious ***problems in growth and development***

Analysis of Perinatal Women Attending a Mother and Baby Unit Taking Sodium Valproate or Lithium with a Diagnosis of Bipolar Affective Disorder

Lebedevs et al, *Psychiatric Quarterly 2020; 91:695–701*





Lithium Use and Non-use for Pregnant and Postpartum Women with Bipolar Disorder

Hermann et al, *Curr Psychiatry Rep 2019; 21: 114*

Breastfeeding considerations for lactating women taking lithium

If a woman *wishes to breastfeed on lithium*, we would recommend:

1. Plan to minimize maternal interruptions in sleep overnight
2. Supplemental formula feeding, especially overnight, to maximize maternal sleep and reduce infant lithium exposure
3. Well informed parents and pediatrician who can collaborate effectively
4. Infant blood monitoring of TSH, renal function, and lithium level
5. Close monitoring for signs or symptoms of lithium toxicity in the breastfed infant

Maternal Medication, Drug Use, and Breastfeeding

Rowe et al,
Child Adolesc Psychiatric Clin N Am 2015; 24:1-20

Table 2
Seizure and mood stabilizer medications and reported levels in breast milk

Drug	Relative Infant Dose (RID) %	Comments
Valproic acid	1.4–1.7[21]	Probably compatible: In a study of 16 patients receiving 300–2400 mg/d of valproic acid, breast milk concentrations ranged from 0.4 to 3.9 mg/L (mean = 1.9 mg/L)[21] One case report of a 3-mo-old breastfed infant who developed thrombocytopenia, petechiae, a minor hematoma, and anemia 6 wk after his mother's valproic acid dose was doubled. The investigators report the onset of symptoms occurred near a minor cold but believe the adverse events were not related to a viral illness[99] NEAD study demonstrated adverse cognitive effects from valproic acid exposure in utero. In a 3-year follow up study, 42% of children were breastfed; IQs for breastfed children did not differ from non-breastfed children. Although this study did not show adverse effects, there are many confounding variables; until further trials are published the long-term effects on cognitive development are unknown[100]

Although it is generally agreed that the amount of valproic acid transferring to the infant via milk is low, the somewhat *high risk of pregnancy in women early postpartum* and the high risk of teratology of valproic acid suggest that *this drug should probably be avoided in women early postpartum*, and certainly in women at high risk of pregnancy.

U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Drugs and Lactation Database (LactMed®) [Internet]. Bethesda (MD): National Institute of Child Health and Human Development; 2006-. Valproic Acid. [Updated 2022 Nov 30].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Valproic Acid

Revised: November 30, 2022.

Summary of Use during Lactation

- Valproic acid levels in *breastmilk are low* and *infant serum* levels range *from undetectable to low*.
- *No definite adverse reactions to valproic acid in breastfed infants have been reported*
- Observe the infant for jaundice and unusual bruising or bleeding.
- Breastfeeding during valproic acid monotherapy *does not appear to adversely affect* infant growth or *development*.

Breastfeeding in Children of Women Taking Antiepileptic Drugs:

Cognitive Outcomes at Age 6 Years

Meador et al, *JAMA Pediatr 2014; 168: 729-736*

- Pregnant women with epilepsy receiving monotherapy (ie, carbamazepine, lamotrigine, phenytoin, or valproate).
- All mothers continued taking the drug after delivery.
- At age 6 years, 181 children were assessed (both breastfeeding and IQ data).
- 78 children (42.9%) were breastfed a mean of 7.2 months.

	IQ, Mean (95% CI)			
AED Group	**Breastfed**	**Nonbreastfed**	**Difference**	***P* Value**
All AEDs	108 (105 to 111) (n = 78)	104 (101 to 106) (n = 103)	4 (0 to 8)	.04
Carbamazepine	107 (101 to 113) (n = 23)	105 (99 to 110) (n = 24)	2 (–6 to 11)	.61
Lamotrigine	113 (110 to 117) (n = 27)	110 (107 to 113) (n = 34)	3 (2 to 8)	.23
Phenytoin	104 (99 to 110) (n = 17)	108 (103 to 113) (n = 20)	–4 (–12 to 4)	.23
Valproate	106 (97 to 115) (n = 11)	94 (88 to 100) (n = 25)	12 (1 to 24)	.04

Breastfeeding in Children of Women Taking Antiepileptic Drugs:

Cognitive Outcomes at Age 6 Years

Meador et al, *JAMA Pediatr 2014; 168: 729-736*

Conclusions

Our study does not provide a final answer, but *we recommend breastfeeding to mothers with epilepsy*, informing them of the strength of evidence for risks and benefits.

Our recommendation is based on the known positive effects of breastfeeding, the results of our study, an unsubstantiated speculative risk, and theoretical reasons why *breastfeeding when taking AEDs would not offer additional risk*.

Treatment and care of women with epilepsy before, during, and after pregnancy: a practical guide

Nucera et al, *Ther Adv Neurol Disord 2022; 15:1-31*

Many anti-seizure medication in monotherapy are (moderately) safe for breastfeeding and women *should be encouraged to do so*.

Ansiolitici / Ipnotici

A New Safety Scoring System for the Use of Psychotropic Drugs During Lactation

Uguz, *Am J Ther 2021; 28: e118-e126*

Table 3. Safety scores of psychotropic drugs used during the lactation period according to the present scoring system.

Drug	Item A	Item B	Item C	Item D	Item E	Item F	Total score	Safety profile	Comments on the usage
Benzodiazepines									
Lorazepam	2.0	1.0	0	0	2.0	1.0	6.0	Moderate	Possible
Diazepam	1.5	1.0	0	1.0	1.0	0	4.5	Low	Possible with caution
Clonazepam	1.5	1.5	0	1.0	0.5	0	4.5	Low	Possible with caution
Alprazolam	1.5	1.5	0.5	1.0	1.0	0	5.5	Moderate	Possible
Oxazepam	0.5	2.0	0	0	0.5	0.5	3.5	Low	Possible with caution
Midazolam	1.5	2.0	0	1.0	2.0	1.0	7.5	Good	Acceptable
Z-Drugs									
Zaleplon	0.5	2.0	0	0	0	0	2.5	Very low	Not recommended
Zopiclone	1.0	2.0	0	0	2.0	1.0	6.0	Moderate	Possible
Zolpidem	0.5	0	0	0	0	0	0.5	Very low	Not recommended

Una madre, che assume psicofarmaci per il suo benessere, può allattare al seno il suo neonato

- *Considera l'allattamento nel pianificare una gravidanza.*
- *Comunicazione univoca dal team alla madre e alla sua famiglia*
- *Sostieni la madre anche se non segue i consigli del team*

Benessere

materno ⟷ neonato

Buon lavoro, informato