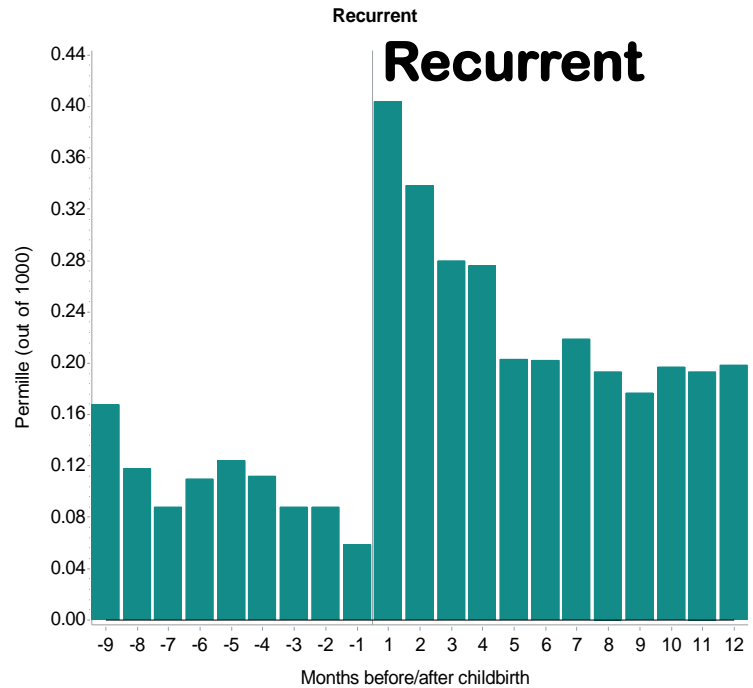
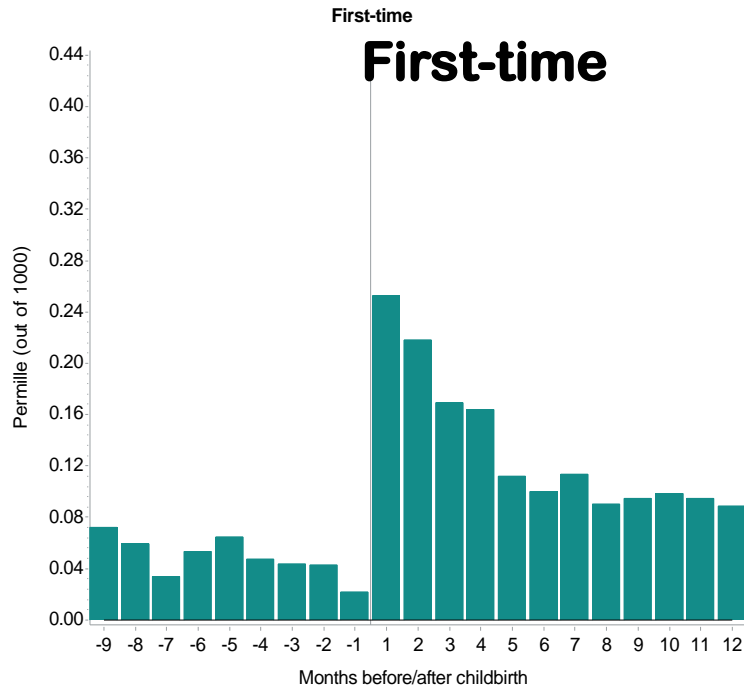


# **Manejo del Trastorno Bipolar en embarazo y postparto**

**Veerle Bergink, MD, PhD**

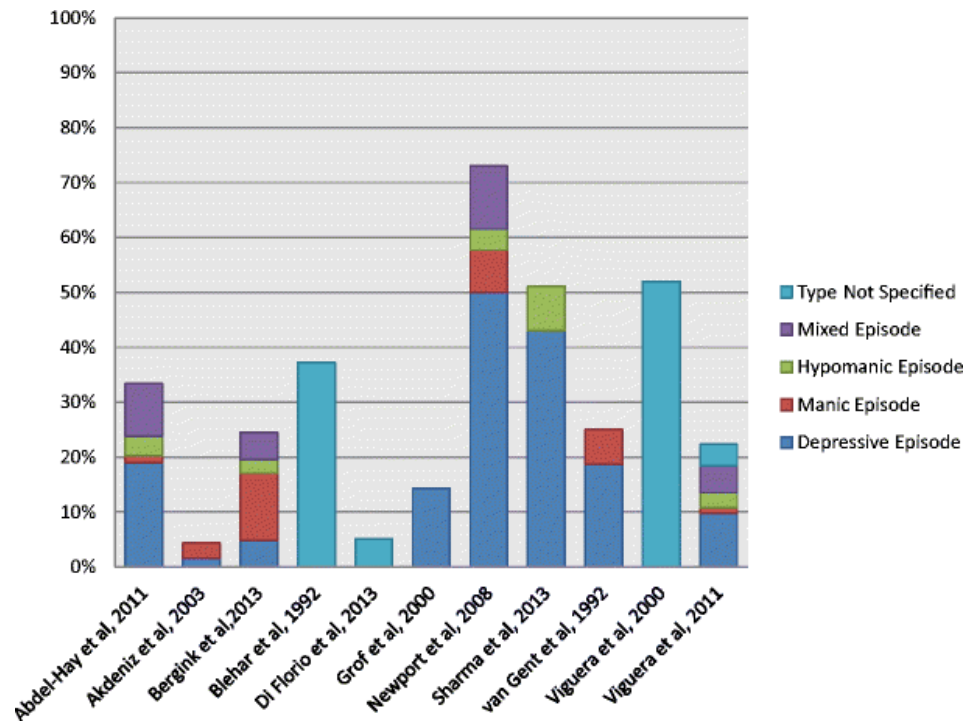
**Professor, Department of Psychiatry and  
Obstetrics**

# Pregnancy Embarazo



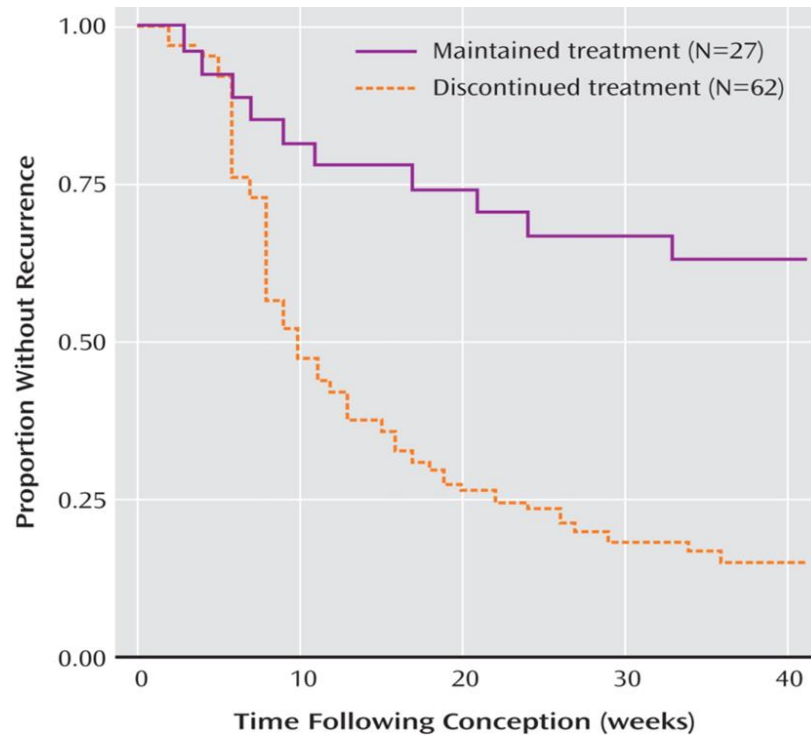
**Psychiatric Admissions during pregnancy and after delivery, all psychiatric disorders**

# Recurrence/relapse during pregnancy



Salim 2018, systematic review

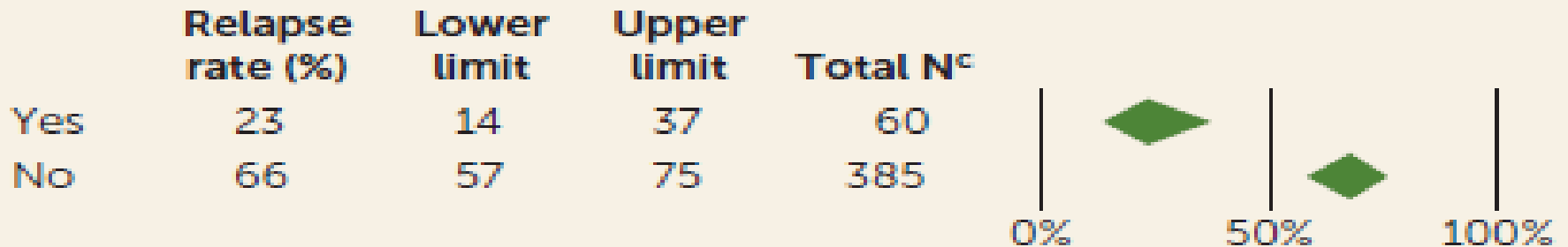
# Recurrence during pregnancy



- *Viguera 2007, Am J Psychiatry*

# Pharmacotherapy (lithium) during pregnancy and recurrence/relapse postpartum

## Prophylactic pharmacotherapy during pregnancy<sup>b</sup>



$I^2$  for yes=5%,  $I^2$  for no=36%, df=1, Q=22.92, p<0.001

# *Take home messages*

**In bipolar patients prophylaxis during pregnancy seems protective both for the pregnancy and the postpartum period.**

**Maternal and infant outcomes associated  
with lithium use in pregnancy: an  
international collaborative meta-analysis of  
six cohort studies**

**Trine Munk Olsen, Xiaoqin Liu, Veerle Bergink**



# Congenital malformations

Meta-analysis 6 studies

Lithium exposed = 727

Control group with unipolar and bipolar mood disorders = 21397

## Outcome:

- Increased risk **first trimester** exposure congenital malformations (pooled OR 1.71, 95% CI 1.07-2.72)
- Lithium group 7.4% , 4.3% in control group
- Not specific cardiac malformations
- No association with obstetric complications, preterm birth or birthweight

- Lithium exposure during the first trimester is associated with congenital malformations in, recent studies estimate the risk lower than previously reported. Tapering of lithium during the first trimester should be considered but weighed against the risks of relapse.
- Paterno NEJM 2017
- Munk-Olsen Lancet Psychiatry 2018

# Bipolar disorder, during pregnancy

Try to avoid polypharmacy and search for the lowest dose



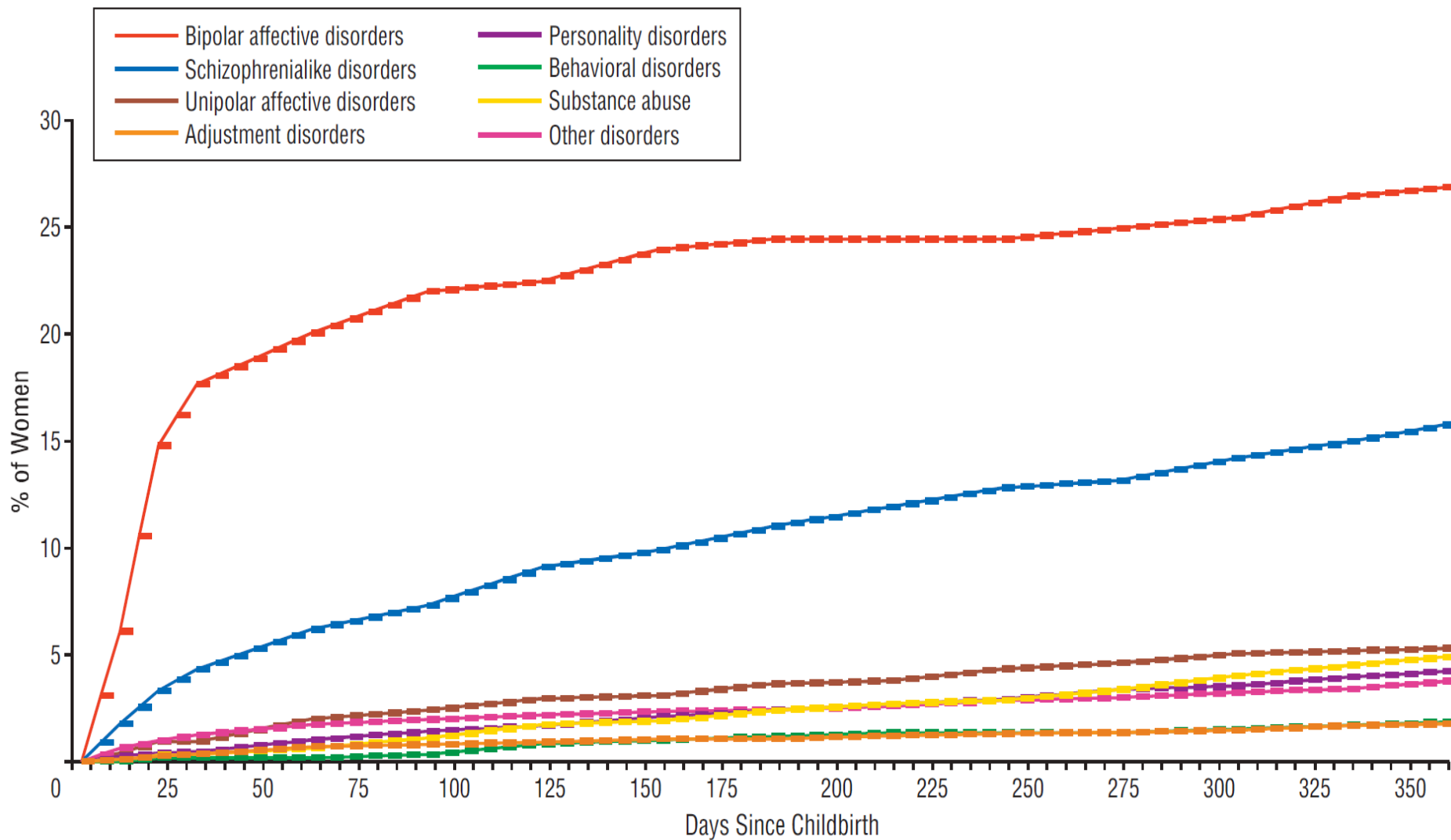
Valproate and to a lesser extent carbamazepine are known teratogenics, lamotrigine is not

Lithium: teratogenic but only during first trimester of pregnancy, the absolute risk is less than previous thought

Antipsychotics: increased risk gestational diabetes

Antipsychotics and antidepressants: some concerns long term outcome children

# Postparto



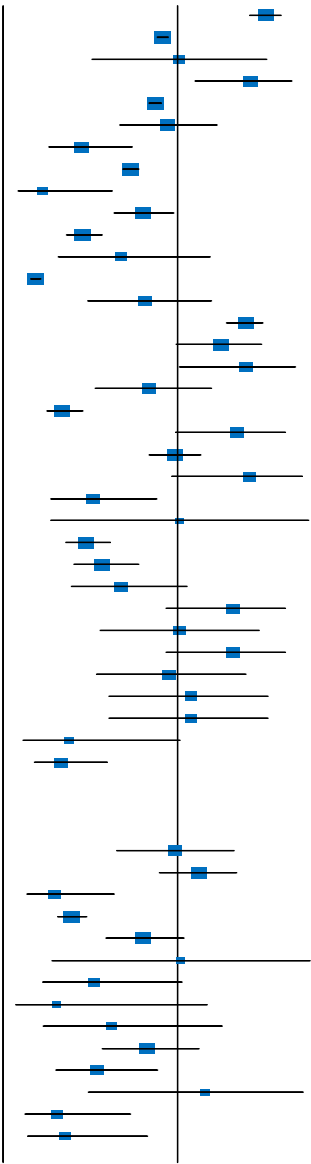
## *Postpartum psychiatric admissions*

# **Highest risk of relapse postpartum**

- **Women with bipolar disorder (BD)**
- **Women with a history of postpartum affective psychosis (PP)**
- **Women with BD + PP**

Postpartum relapse rate per study included in the qualitative and/or quantitative synthesis

	Relapse rate	Lower limit	Upper limit	n relapse / n total
<b>Bipolar disorder</b>				
<b>2014 Maina</b>	0.75	0.70	0.80	207 / 276
2014 Di Florio <sup>1</sup>	0.45	0.43	0.47	1052 / 2329
<b>2014 Arda</b>	0.50	0.24	0.76	6 / 12
<b>2013 Sharma</b>	0.70	0.54	0.83	26 / 37
<b>2013 Di Florio<sup>1</sup></b>	0.43	0.41	0.45	786 / 1828
2012 Doyle <sup>1</sup>	0.47	0.32	0.61	20 / 43
<b>2012 Bergink</b>	0.22	0.12	0.37	9 / 41
<b>2011 Viguera<sup>2</sup></b>	0.36	0.33	0.39	403 / 1120
<b>2010 Bilszta</b>	0.11	0.03	0.31	3 / 23
<b>2010 Colom</b>	0.39	0.31	0.49	43 / 109
<b>2009 Munk-Olsen</b>	0.22	0.17	0.28	46 / 208
<b>2008 Green</b>	0.33	0.15	0.59	5 / 15
<b>2007 Harlow</b>	0.09	0.07	0.11	67 / 786
<b>2006 Sharma</b>	0.40	0.23	0.60	10 / 25
2006 Blackmore <sup>1</sup>	0.69	0.63	0.75	167 / 242
2005 Robertson <sup>1</sup>	0.62	0.49	0.74	34 / 54
<b>2004 Wisner</b>	0.69	0.49	0.84	18 / 26
<b>2003 Kumar</b>	0.41	0.25	0.60	12 / 29
<b>2003 Akdeniz</b>	0.16	0.11	0.23	26 / 160
<b>2002 Freeman</b>	0.67	0.48	0.81	20 / 30
2001 Jones <sup>1</sup>	0.49	0.41	0.57	74 / 152
2000 Viguera <sup>2</sup>	0.70	0.47	0.86	14 / 20
<b>2000 Grof</b>	0.25	0.12	0.44	7 / 28
<b>1999 Pfuhlmann</b>	0.50	0.12	0.88	2 / 4
<b>1998 Blehar</b>	0.23	0.17	0.31	32 / 139
<b>1995 Hunt</b>	0.28	0.19	0.39	22 / 79
<b>1995 Cohen</b>	0.33	0.18	0.53	9 / 27
<b>1993 Kumar<sup>3</sup></b>	0.65	0.46	0.81	17 / 26
<b>1992 Van Gent</b>	0.50	0.27	0.73	8 / 16
1992 Marks <sup>3</sup>	0.65	0.46	0.81	17 / 26
<b>1992 Austin</b>	0.47	0.26	0.70	8 / 17
1991 Wieck <sup>3</sup>	0.53	0.29	0.76	8 / 15
1989 Wieck <sup>3</sup>	0.53	0.29	0.76	8 / 15
1988 Platz <sup>4</sup>	0.18	0.05	0.51	2 / 11
<b>1987 Kendell<sup>4</sup></b>	0.16	0.08	0.30	7 / 44
<b>History of postpartum psychosis</b>				
<b>2014 Kapfhammer</b>	0.48	0.31	0.66	14 / 29
<b>2013 Blackmore</b>	0.55	0.43	0.67	37 / 67
<b>2012 Bergink</b>	0.14	0.05	0.31	4 / 29
<b>1999 Terp<sup>5</sup></b>	0.18	0.14	0.24	49 / 266
<b>1999 Kirpinar</b>	0.39	0.28	0.51	25 / 64
<b>1998 Bagedahl</b>	0.50	0.12	0.88	2 / 4
1995 Videbech <sup>5</sup>	0.25	0.10	0.51	4 / 16
<b>1995 Sichel</b>	0.14	0.02	0.58	1 / 7
<b>1995 Meakin</b>	0.30	0.10	0.62	3 / 10
<b>1994 Schopf</b>	0.40	0.27	0.56	17 / 42
<b>1993 Rohde</b>	0.26	0.13	0.44	8 / 31
<b>1992 Benvenuti</b>	0.57	0.23	0.86	4 / 7
<b>1991 Stewart</b>	0.14	0.05	0.36	3 / 21
<b>1986 McNeil</b>	0.17	0.05	0.41	3 / 18



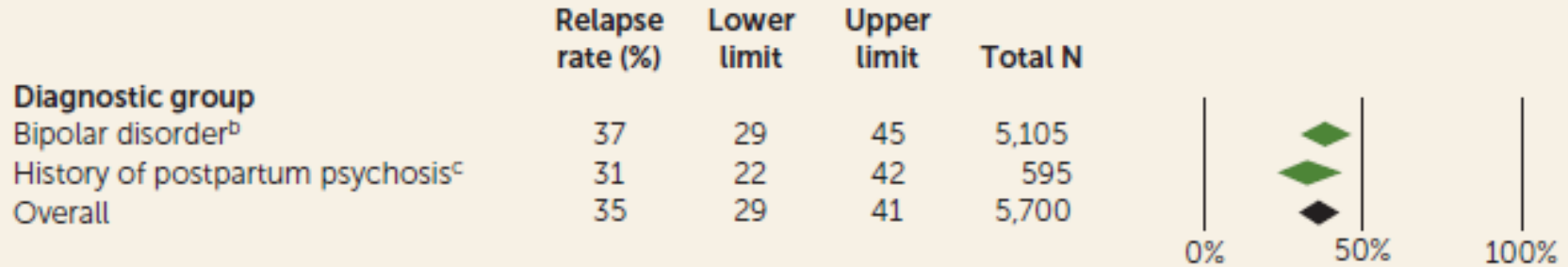
Postpartum relapse risk in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis.

Wesseloo et al, *Am J Psych* 2015

Studies included in the quantitative meta-analysis are shown in bold. If applicable, publications of a single diagnostic cohort are numbered identical.

# Postpartum relapse risk bipolar disorder

A. Overall relapse<sup>a</sup> rate postpartum per diagnostic group



$I^2$  for bipolar disorder=95%,  $I^2$  for postpartum psychosis=78%,  $df=1$ ,  $Q=0.71$ ,  $p=0.400$

**Risk is one out of three**

**There is an urgent need for:**

- Better data**
- Postpartum Relapse Prevention Plans**

R. Wesseloo et al. *Risk of postpartum relapse in bipolar disorder and postpartum psychosis: a systematic review and meta-analysis*. Am J Psychiatry 2015

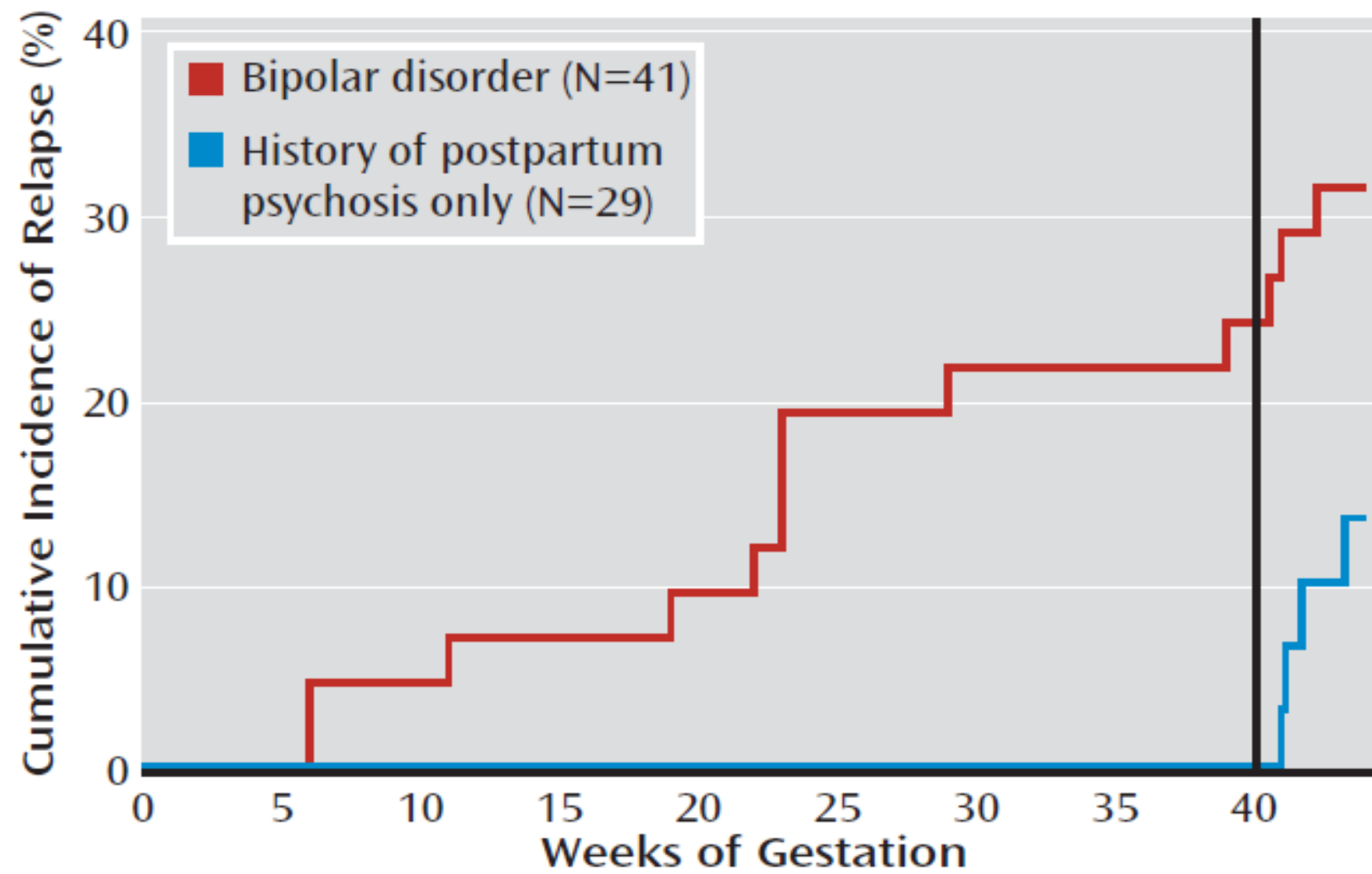


**We started medication after delivery in medication free women (lithium first choice).**



- **Sleep**
- **Regularity**

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



**Prophylaxis beginning postpartum is sufficient, in women with a history of postpartum psychosis only (psychosis or mania limited to the postpartum)**



***Selected as one of the top 10 clinically relevant publications in psychiatry for 2012 and 2015***



# Diagnostic recommendations, Treatment algorithm Prevention plans

## REVIEWS AND OVERVIEWS

Evidence-Based Psychiatric Treatment

### Postpartum Psychosis: Madness, Mania, and Melancholia in Motherhood

Veerle Bergink, M.D., Ph.D., Natalie Rasgon, M.D., Ph.D., Katherine L. Wisner, M.D., M.S.

**Objective:** Psychosis or mania after childbirth is a psychiatric emergency with risk for suicide and infanticide.

**Method:** The authors reviewed the epidemiologic and genetic research and physiological postpartum triggers (endocrine, immunological, circadian) of psychosis. They also summarized all systematic reviews and synthesized the sparse clinical studies to provide diagnostic recommendations, treatment options, and strategies for prevention.

**Results:** The incidence of first-lifetime onset postpartum psychosis/mania from population-based register studies of psychiatric admissions varies from 0.25 to 0.6 per 1,000 births. After an incipient episode, 20%–50% of women have isolated postpartum psychosis. The remaining women have episodes outside the perinatal period, usually within the bipolar spectrum. Presumably, the mechanism of onset is related to physiological changes after birth (e.g., hormonal, immunological, circadian), which precipitate disease in genetically vulnerable women. Some women have treatable

causes and comorbidities, such as autoimmune thyroiditis or infections. *N*-methyl-D-aspartate-encephalitis or inborn errors of metabolism may present after birth with psychosis. Fewer than 30 publications have focused on the treatment of postpartum psychosis. The largest study (N=64) provided evidence that lithium is highly efficacious for both acute and maintenance treatment. Another report (N=34) described successful ECT treatment. Inpatient care is usually required to ensure safety, complete the diagnostic evaluation, and initiate treatment. The relapse risk after a subsequent pregnancy for women with isolated postpartum psychoses is 31% (95% CI=22–42). Strategies for prevention of postpartum psychosis include lithium prophylaxis immediately postpartum and proactive safety monitoring.

**Conclusions:** Postpartum psychosis offers an intriguing model to explore etiologic contributions to the neurobiology of affective psychosis.

*AJP in Advance* (doi: 10.1176/appi.ajp.2016.16040454)

Bergink et al, Am J Psych 2016  
Bergink et al, Am J Psych 2015  
Bergink et al, Am J Psych 2012

# *Take home messages*

**Start in prophylaxis postpartum in women at high risk (PP in history, bipolar)!**

**Most evidence for lithium**

**Target dose  $> 0.8$**

# Thank you!

Trine Munk Olsen  
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