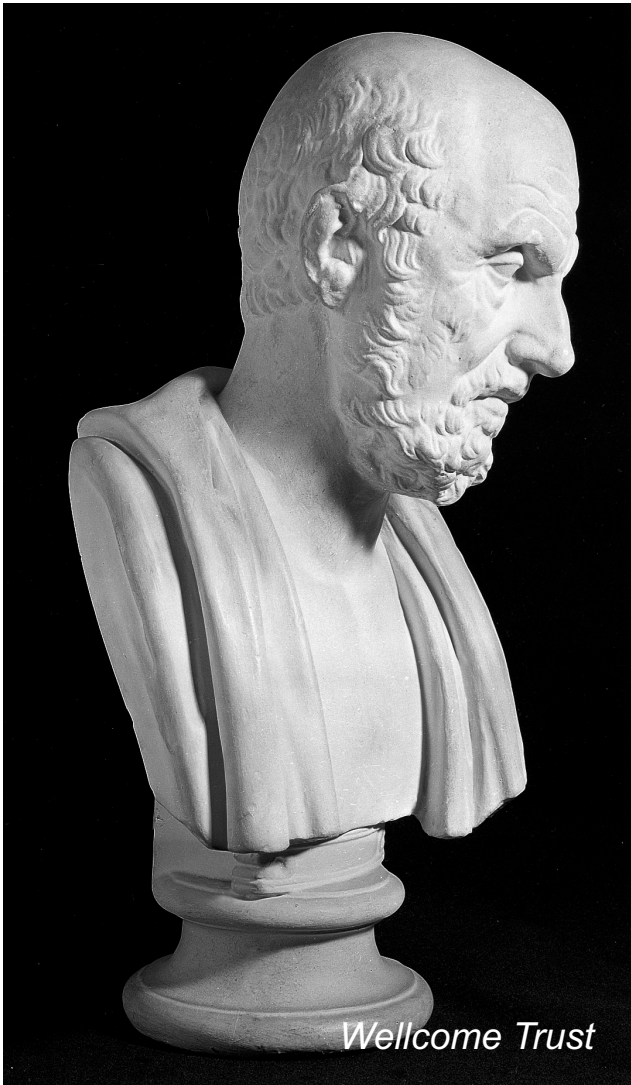


# Psychosis and Motherhood

Arianna Di Florio  
diflorioa@cf.ac.uk



**Hippocrates of Kos**  
(c. 460 – c. 370 BC)

SPRiG 2020



**Jean-Étienne Dominique Esquirol**  
(1772 –1840)

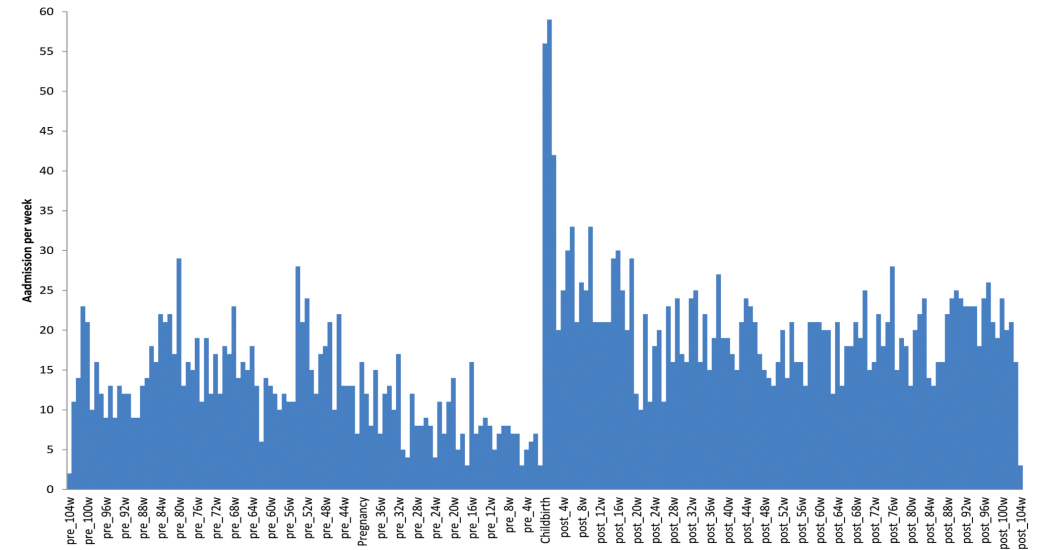
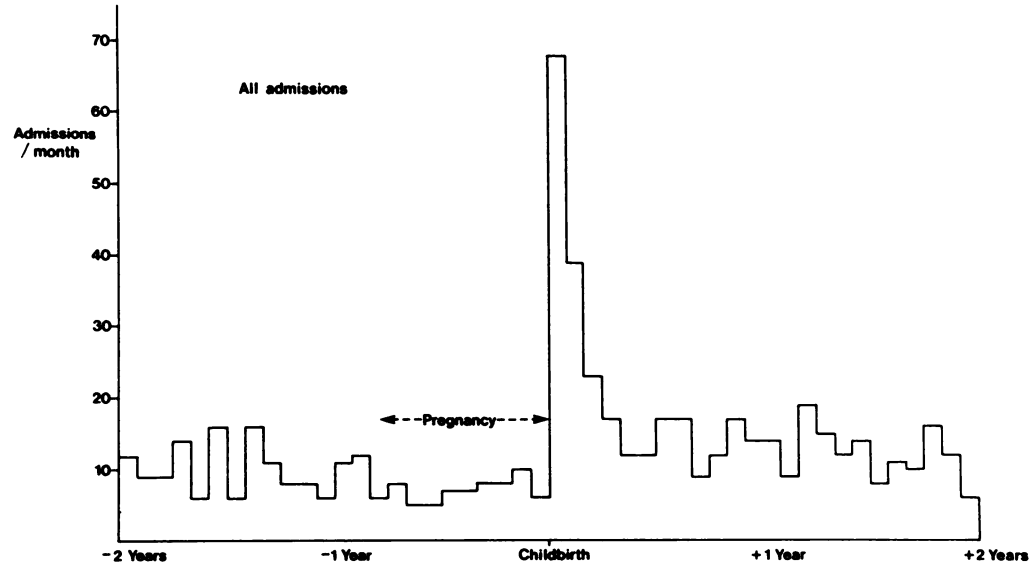
Arianna Di Florio



**Louis-Victor Marcé**  
(1828, 1864)



# The postpartum is a period of high risk



*British Journal of Psychiatry* (1987), 150, 662–673

## Epidemiology of Puerperal Psychoses

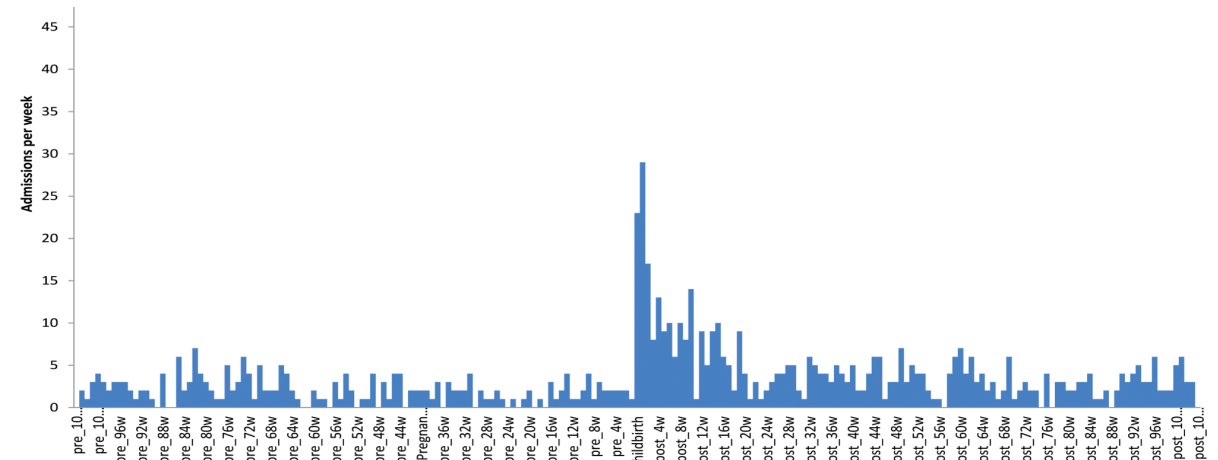
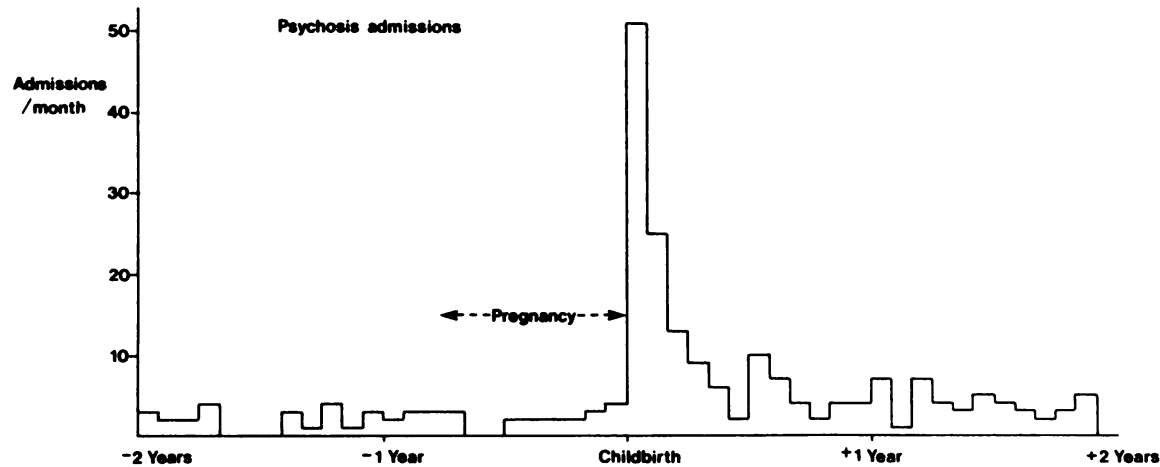
R. E. KENDELL, J. C. CHALMERS and C. PLATZ

## BMJ Open Admission to psychiatric hospital in the early and late postpartum periods: Scottish national linkage study

Julie Langan Martin,<sup>1</sup> Gary McLean,<sup>1</sup> Roch Cantwell,<sup>2</sup> Daniel J Smith<sup>1</sup>

2016;6:e008758. doi:10.1136/bmjopen-2015-008758

# The postpartum is a period of high risk of psychosis



*British Journal of Psychiatry* (1987), 150, 662–673

## Epidemiology of Puerperal Psychoses

R. E. KENDELL, J. C. CHALMERS and C. PLATZ

## BMJ Open Admission to psychiatric hospital in the early and late postpartum periods: Scottish national linkage study

Julie Langan Martin,<sup>1</sup> Gary McLean,<sup>1</sup> Roch Cantwell,<sup>2</sup> Daniel J Smith<sup>1</sup>

2016;6:e008758. doi:10.1136/bmjopen-2015-008758



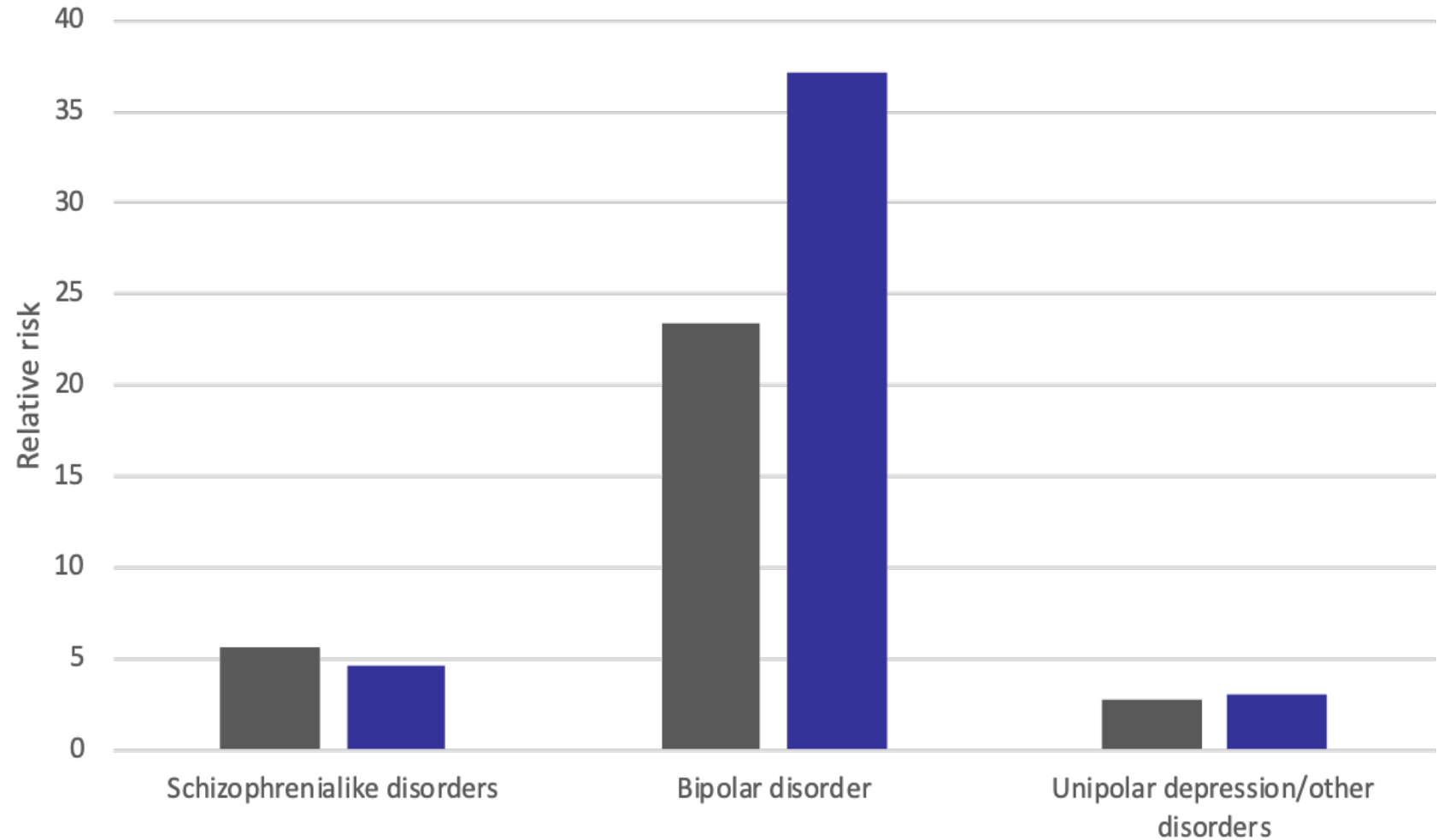
## New Parents and Mental Disorders

A Population-Based Register Study

*JAMA. 2006;296:2582-2589*

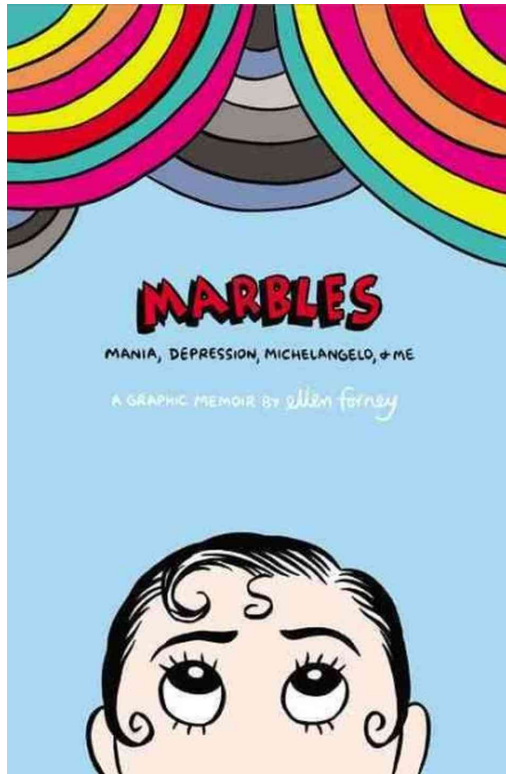
## Risks and Predictors of Readmission for a Mental Disorder During the Postpartum Period

*Arch Gen Psychiatry. 2009;66(2):189-195*

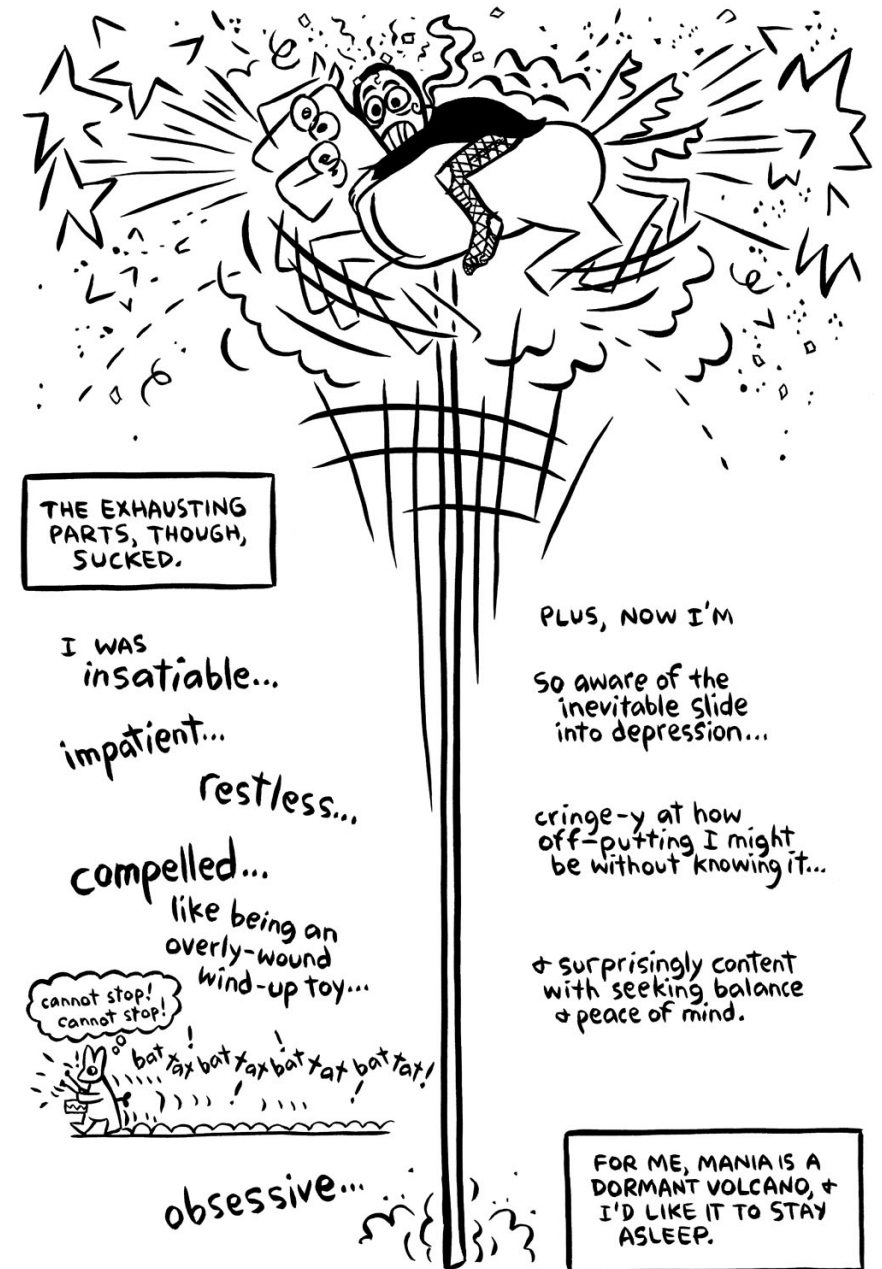


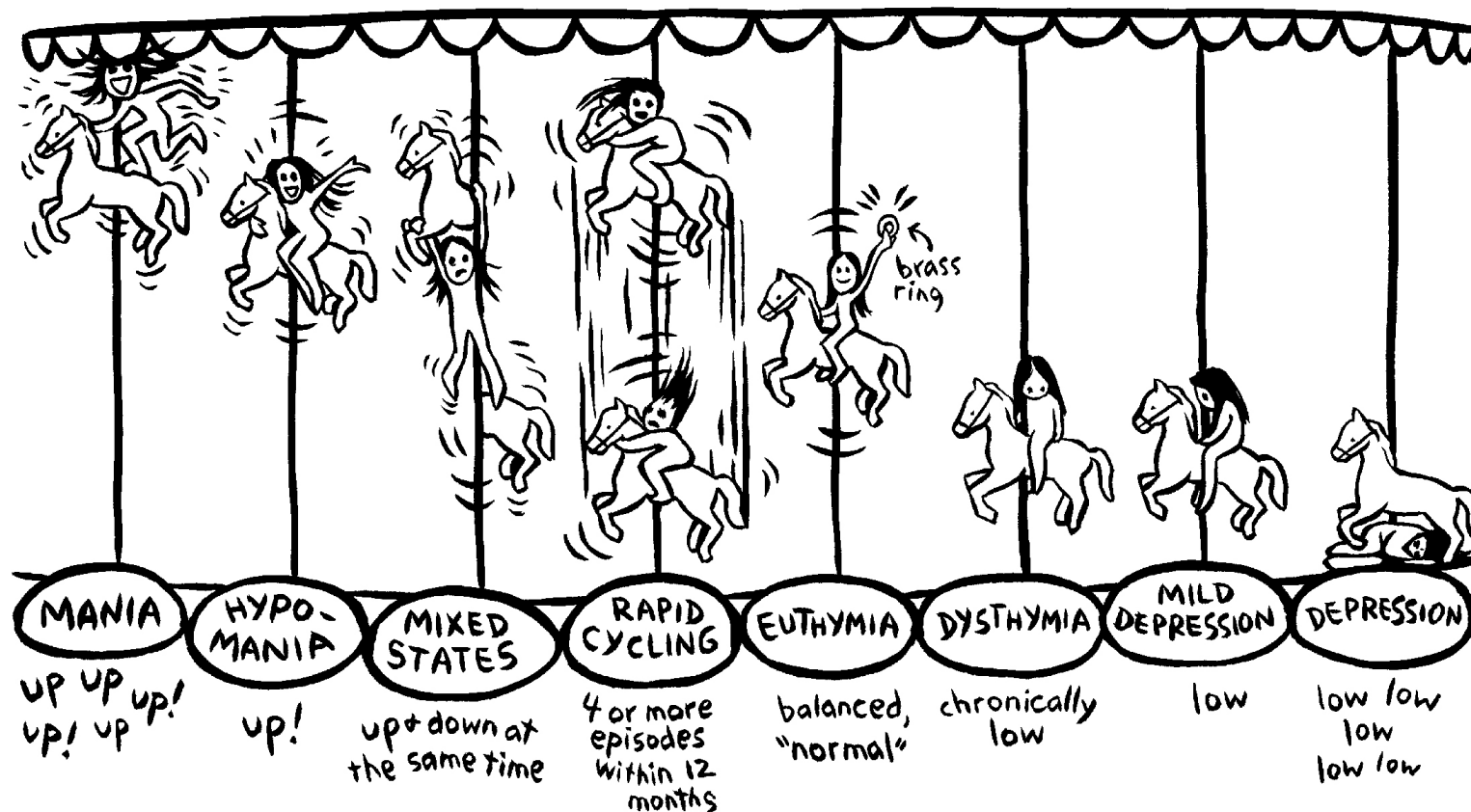
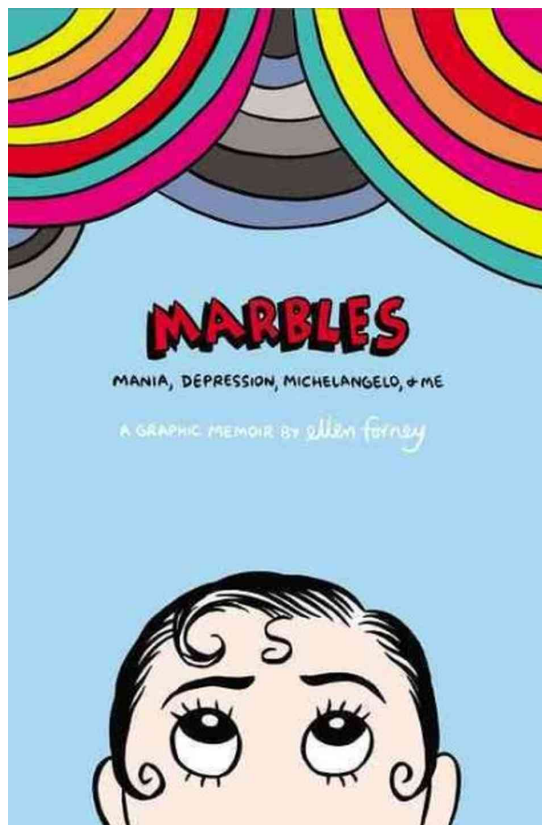


# Mania



Ellen Forney  
*Marbles: Mania, Depression, Michelangelo, and Me: A Graphic Memoir*  
Penguin, 2012





Ellen Forney  
*Marbles: Mania, Depression, Michelangelo, and Me: A Graphic Memoir*  
 Penguin, 2012

# Conclusion

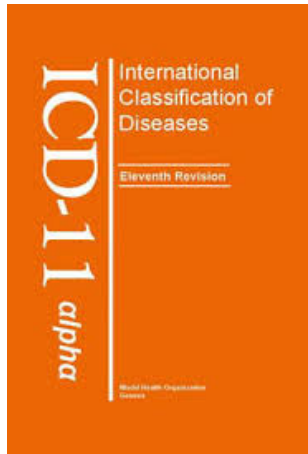
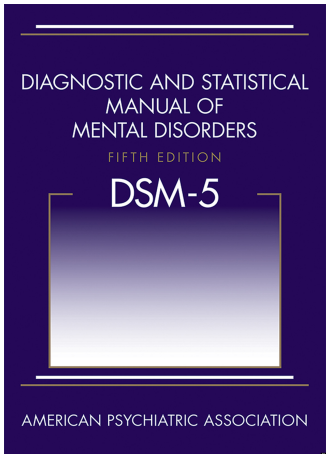
- Robust evidence for association between psychosis and childbirth
  - Specific for bipolar disorder



# Problems

- Nature of the association between postpartum psychosis and bipolar disorder
- Identification and clinical management of women at risk

# Nature of the association between postpartum psychosis and bipolar disorder



## THE LANCET Psychiatry

CORRESPONDENCE | [VOLUME 3, ISSUE 6, P502, JUNE 01, 2016](#)

### The birth of a psychiatric orphan disorder: postpartum psychosis

[Arianna Di Florio](#) ✉ • [Trine Munk-Olsen](#) • [Veerle Bergink](#)

## Postpartum psychosis

ORPHA:443173

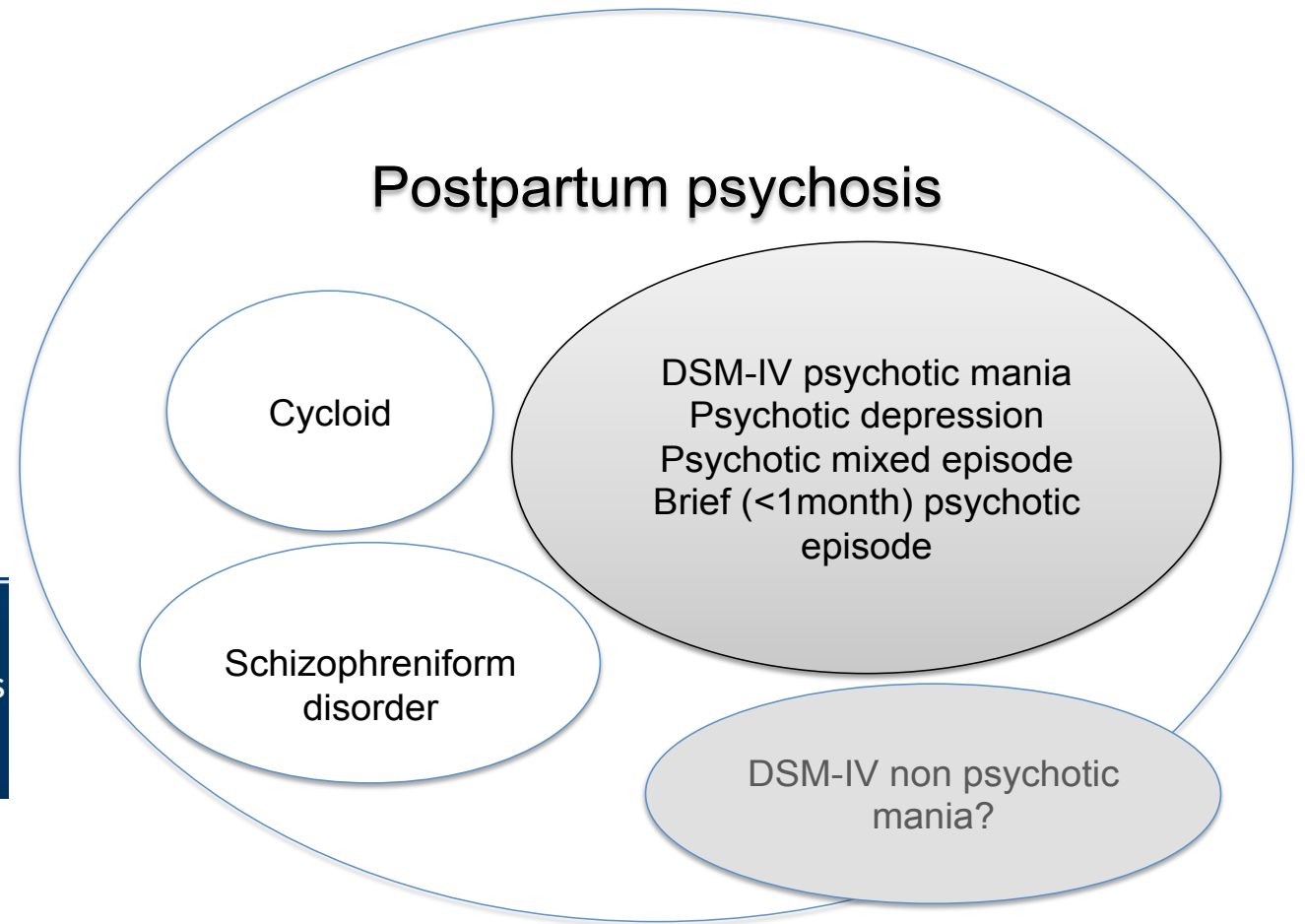
[Classification level: Disorder](#)

*Synonym(s):*

*Age of onset:* Adult

**Puerperal psychosis**

*ICD-10:* F53.1





# A case – control study of filicide in 90 mothers



30 committed filicide  
30 with psychopathology  
30 without psychopathology





Bipolar Disorder

**BDRN**

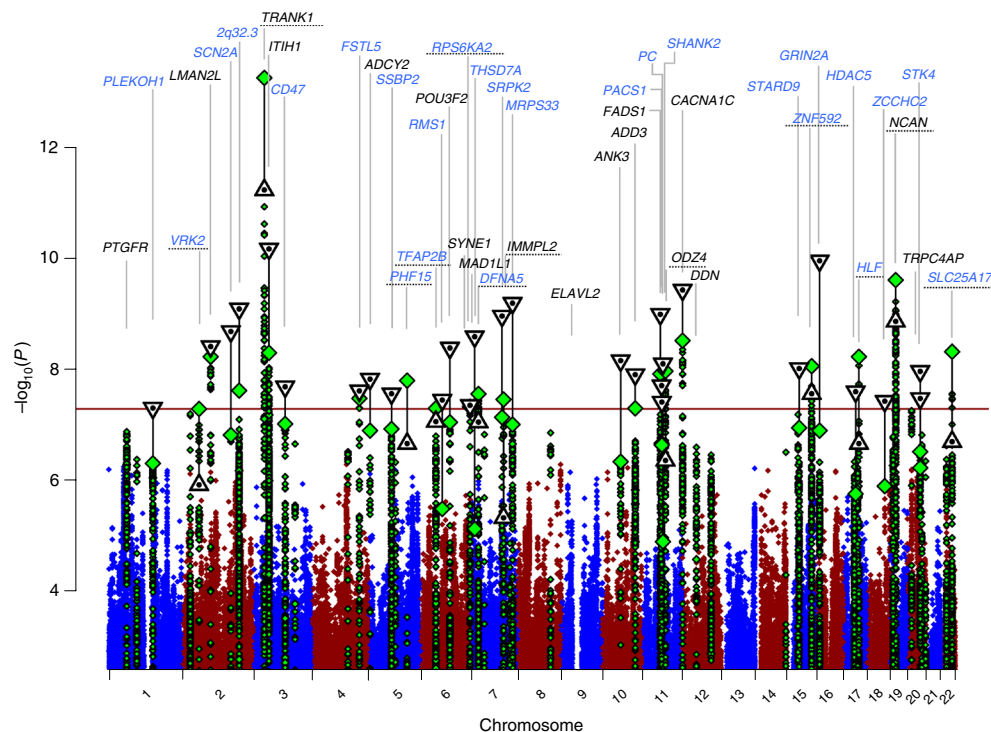
Arianna Di Florio Research Network



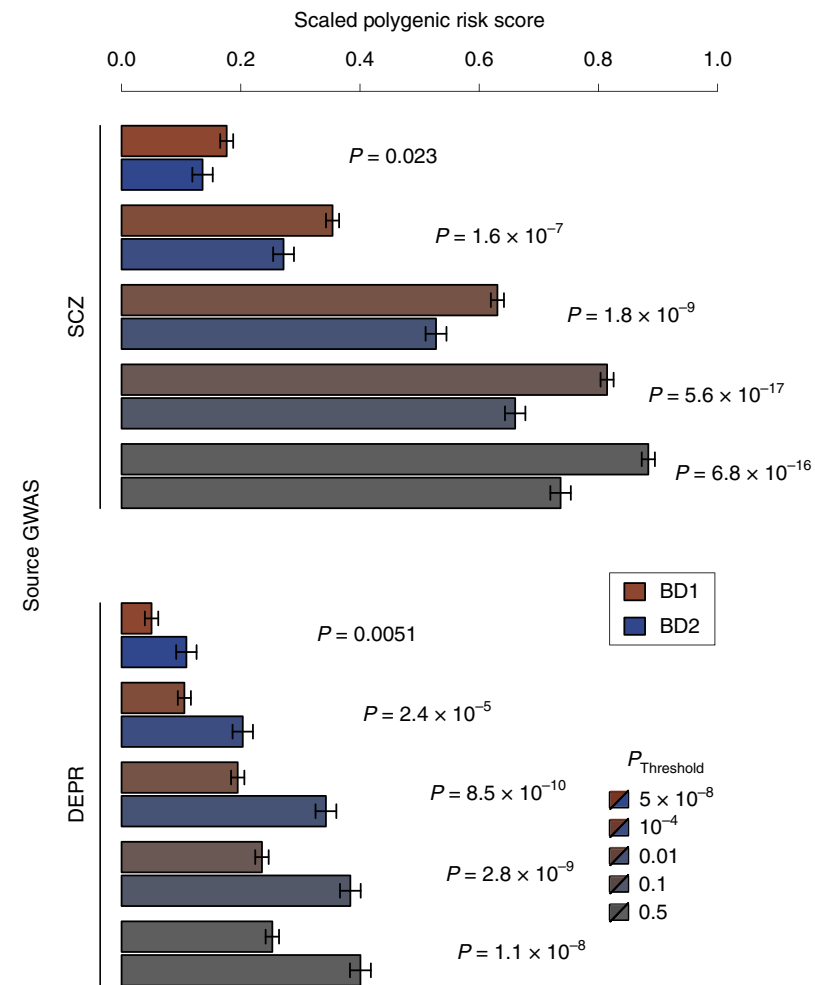
# Genomic evidence differentiates First Onset Postpartum Psychosis from Bipolar Disorder



## Genome-wide association study identifies 30 loci associated with bipolar disorder



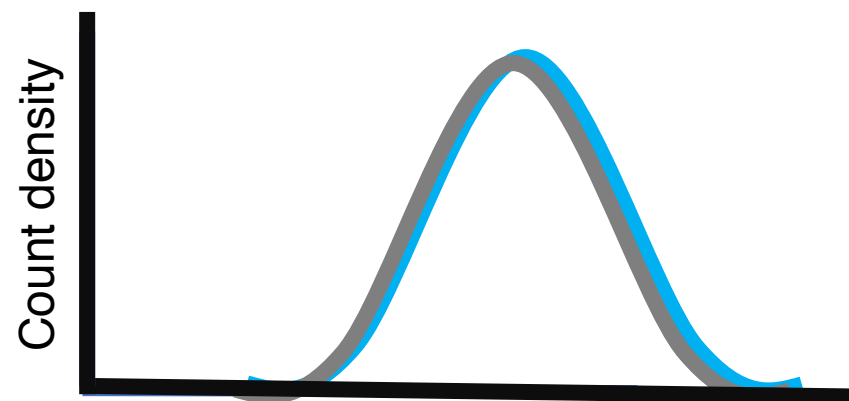
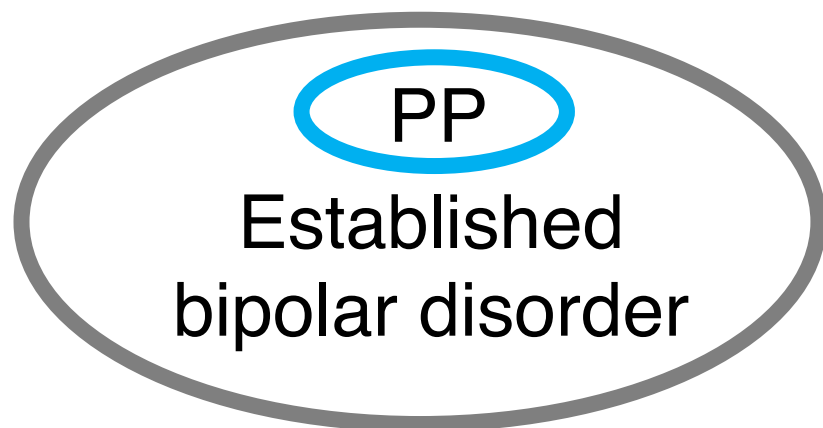
**Fig. 1 |** Manhattan plot for our primary genome-wide association analysis of 20,352 cases and 31,358 controls. GWAS  $-\log_{10}P$  values are plotted for all SNPs across chromosomes 1–22 (diamonds, green for loci with lead SNP GWAS  $P < 10^{-6}$ ). Combined GWAS + follow-up  $-\log_{10}P$  for lead SNPs reaching genome-wide significance in either GWAS or combined analysis (triangles, inverted if GWAS + follow-up  $-\log_{10}P > \text{GWAS } -\log_{10}P$ ). Labels correspond to gene symbols previously reported for published loci (black) and the nearest genes for newly identified loci (blue), at top if GWAS + follow-up  $P < 5 \times 10^{-8}$ . Loci with one-tailed follow-up  $P > 0.05$  (Table 1) have dotted underlined locus names.



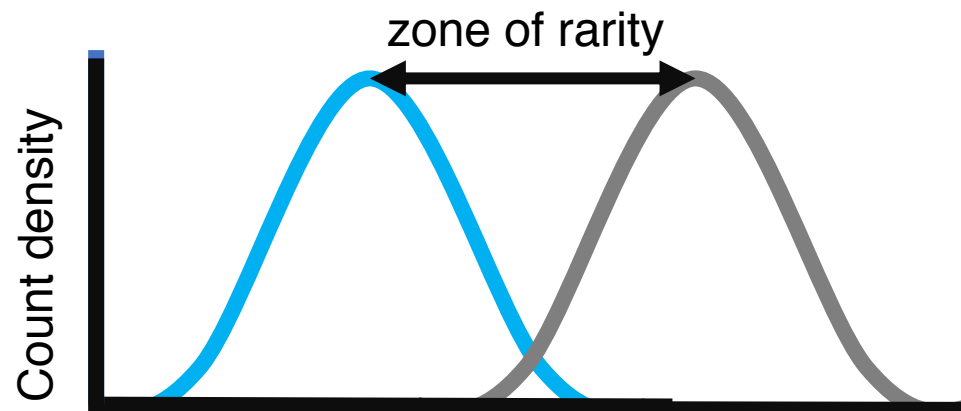
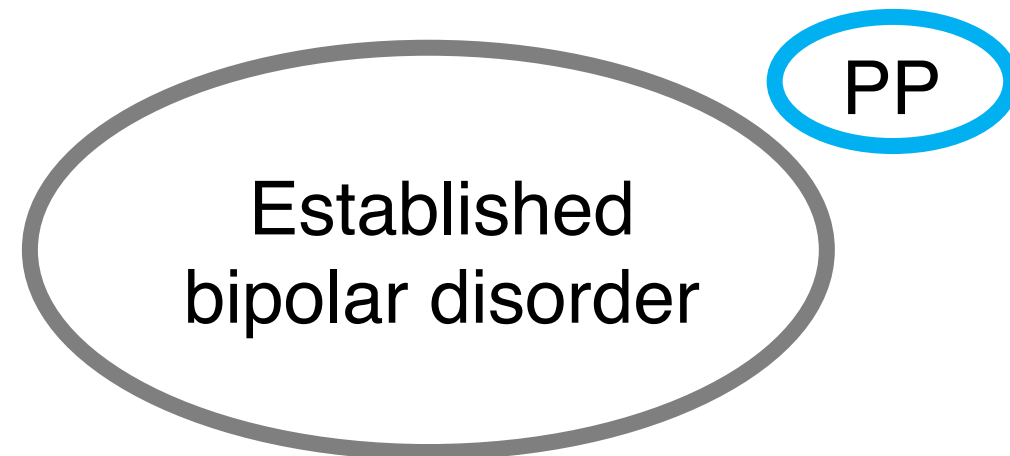
**Fig. 2 |** Association of BD1 and BD2 subtypes with SCZ and DEPR PRS.

The mean PRS values (1 s.e.m. error bars) are shown, adjusted for study and ancestry covariates and scaled to the PRS mean and s.d. in control subjects, in BD1 (red) and BD2 (blue) cases, for increasing source GWAS  $P$  value thresholds (increasing gray) as indicated.  $P$  values (italics) test BD1 versus BD2 mean PRS, in logistic regression of case subtype on PRS with covariates. Results are detailed in Supplementary Table 13.

# Heuristic model



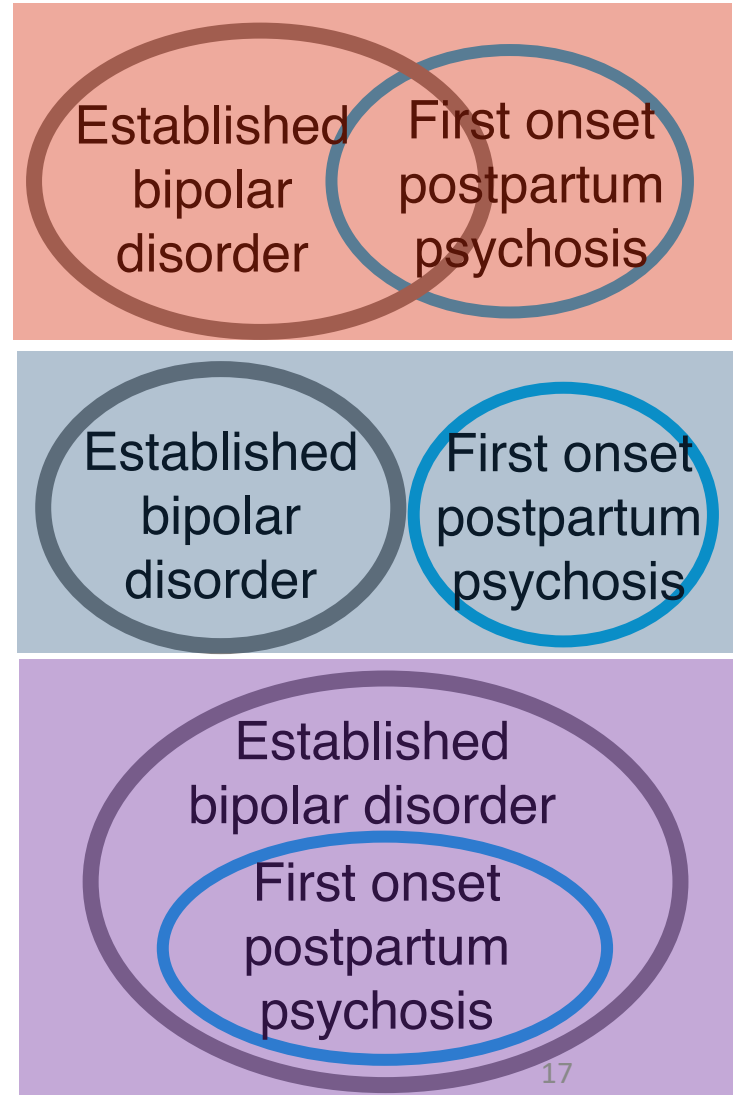
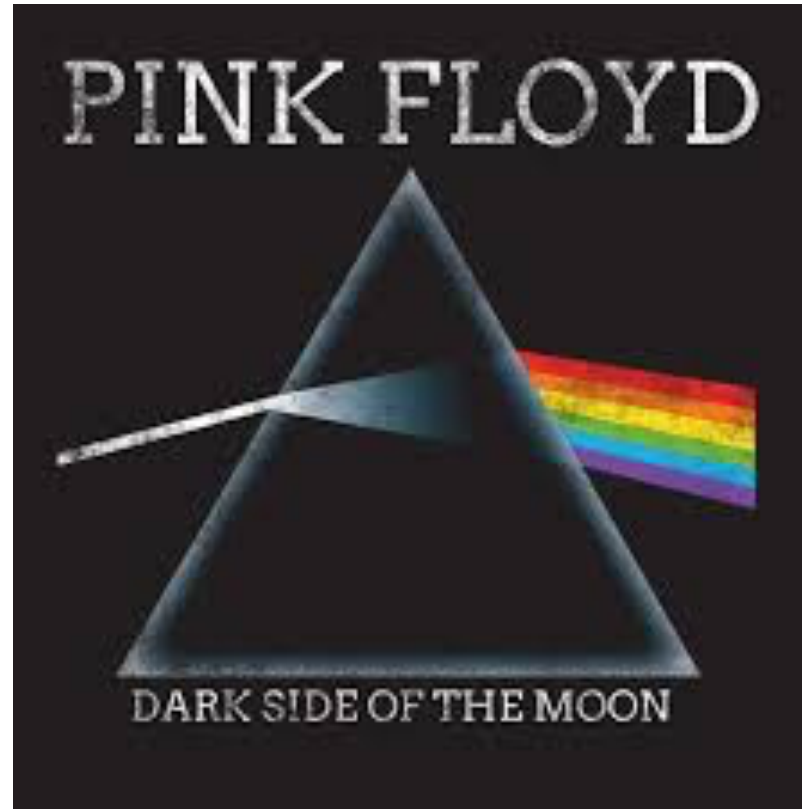
Genetic liability



Genetic liability

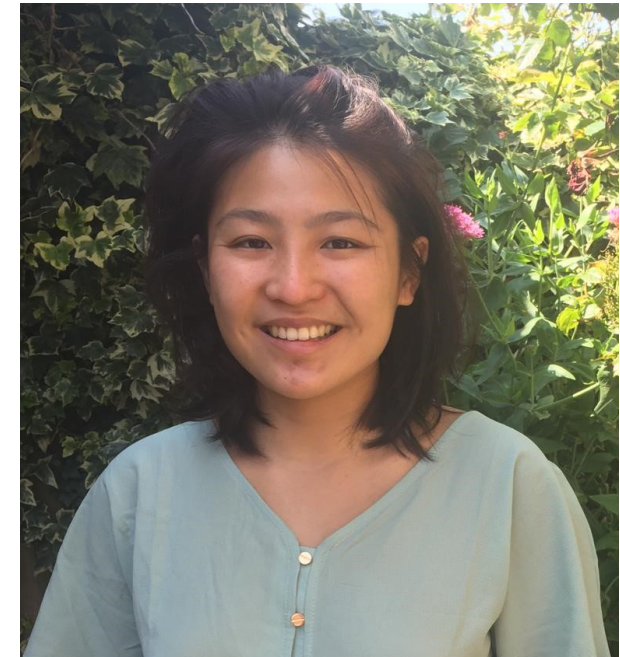
# Is postpartum psychosis a disorder in its own right?

*“Postpartum psychosis”*





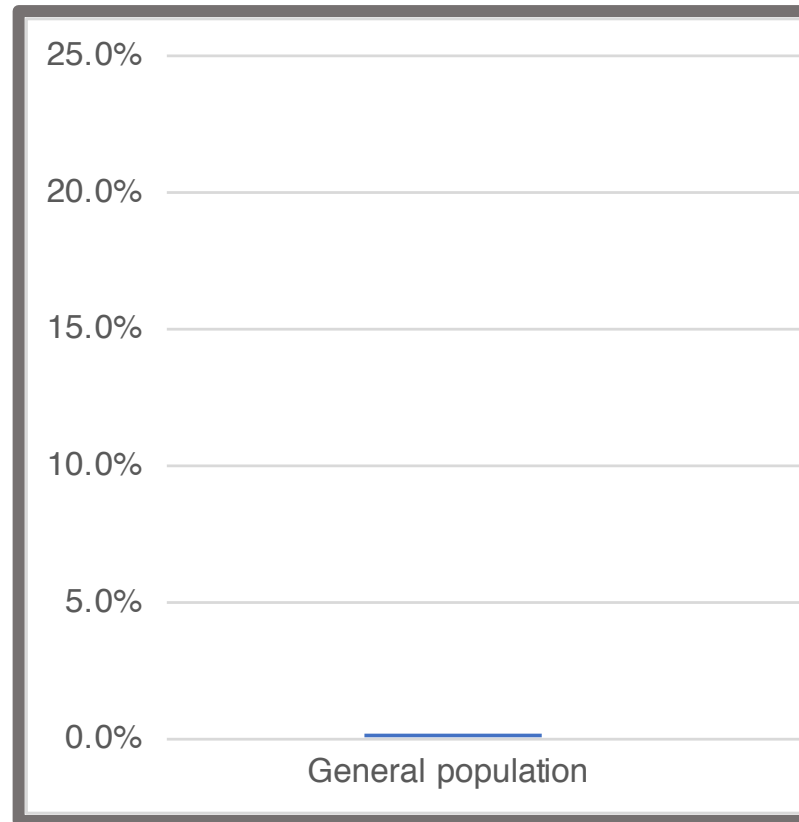
# Large-scale, international, clinical-genetic study of postpartum psychosis



*YangJM1@cardiff.ac.uk*



# Identification and clinical management of women at risk



# Recognising women at risk



# Perinatal Episodes Across the Mood Disorder Spectrum

Arianna Di Florio, MD; Liz Forty, PhD; Katherine Gordon-Smith, PhD; Jess Heron, PhD; Lisa Jones, PhD; Nicholas Craddock, FRCPsych, PhD; Ian Jones, MRCPsych, PhD

*JAMA Psychiatry*. 2013;70(2):168-175.  
Published online December 17, 2012.  
doi:10.1001/jamapsychiatry.2013.279



## INCLUSION CRITERIA

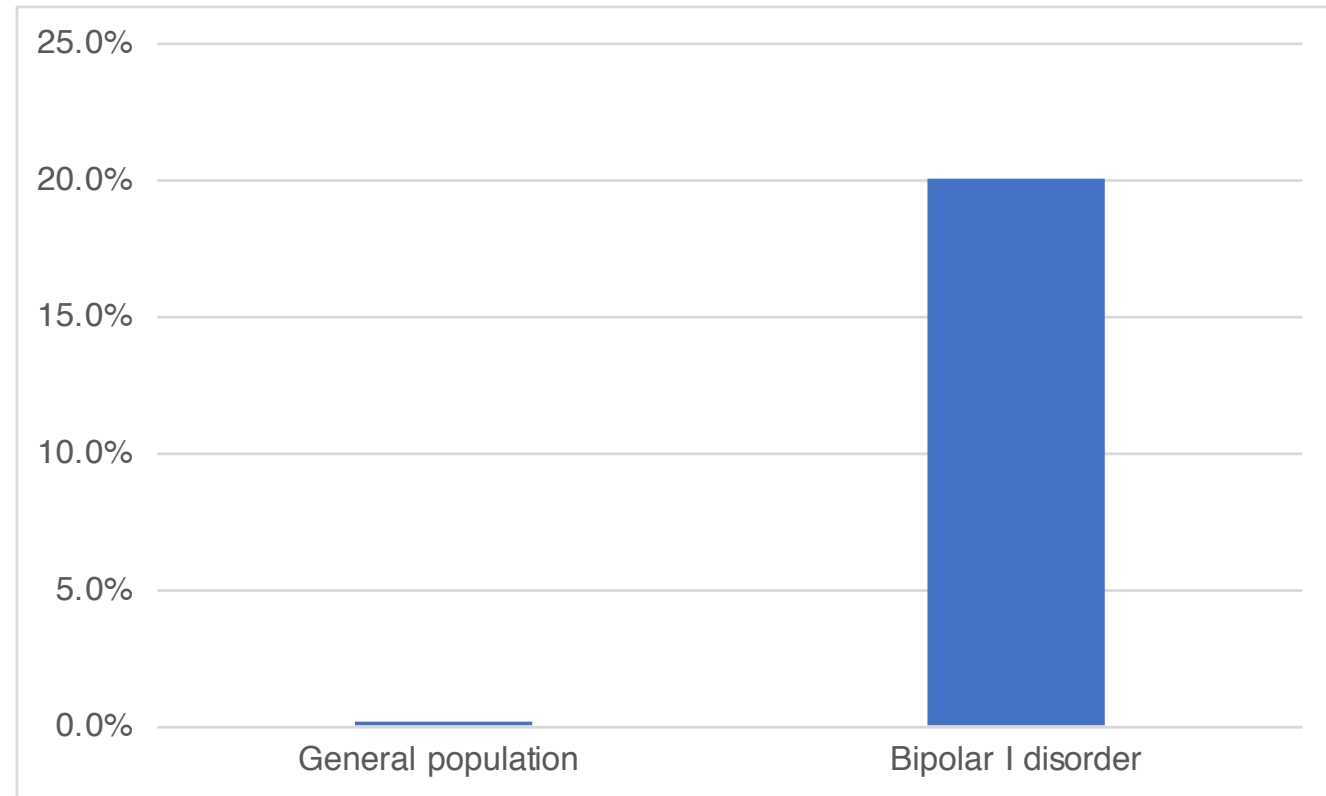
- Parous
- Primary mood disorder before 50
- Not recruited because PNE

## LIFETIME DIAGNOSIS

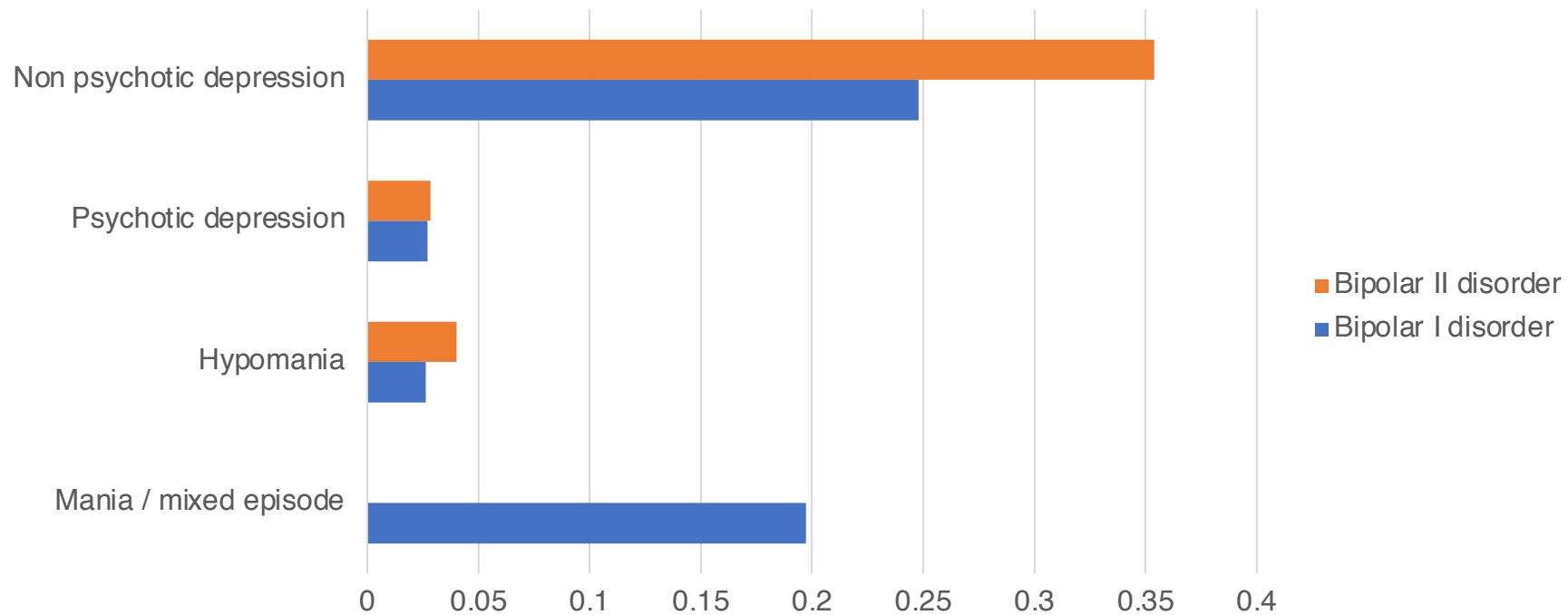
BD-I (N=980, 1,404 deliveries)

BD-II (N= 232, 424 deliveries)

# Rates of postpartum psychosis

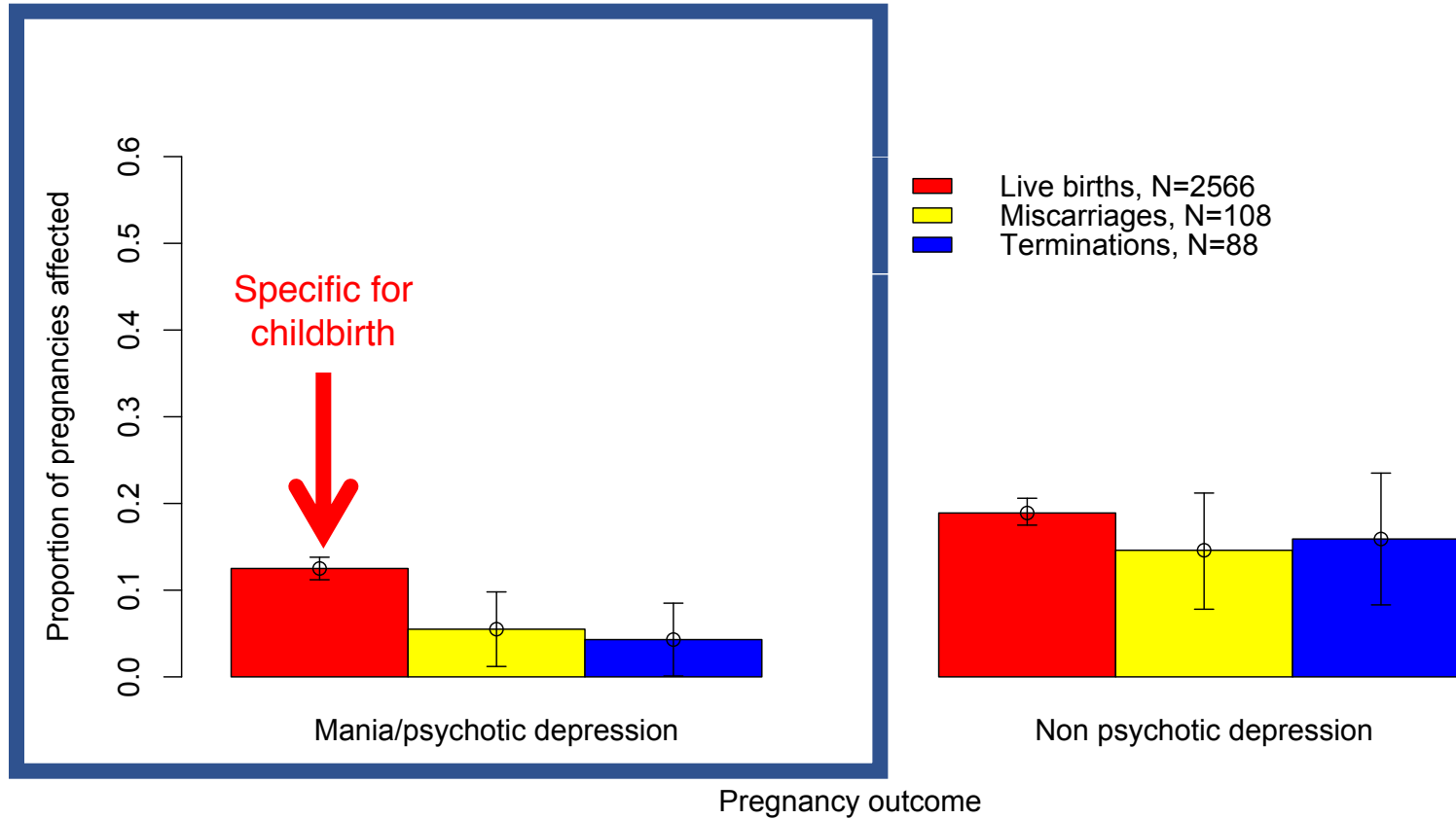


# Bipolar disorder in the perinatal period



*Di Florio et al, JAMA Psychiatry 2013*

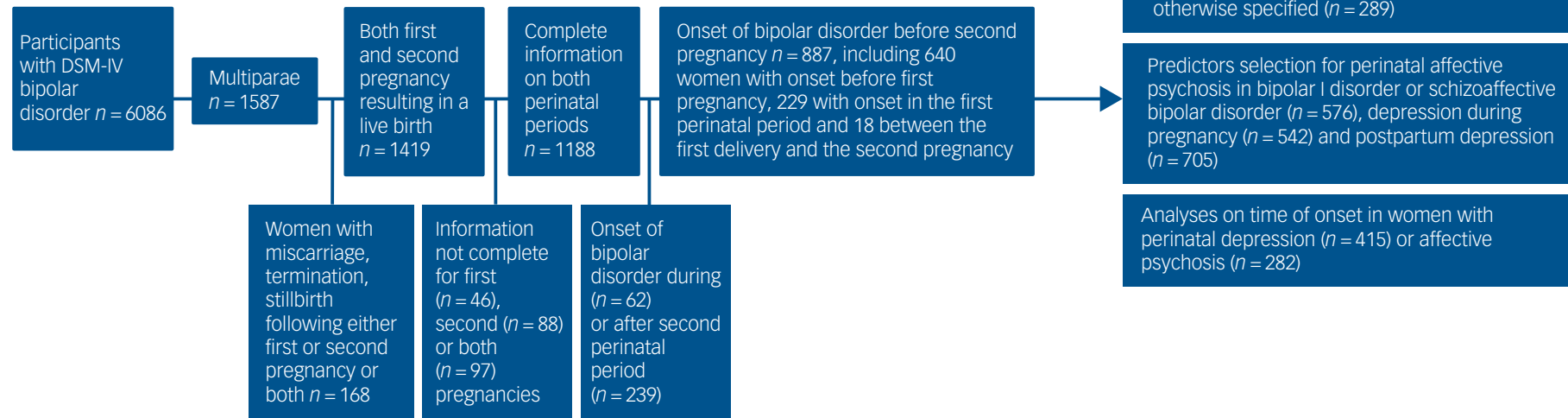
# Specificity of childbirth trigger in bipolar disorder



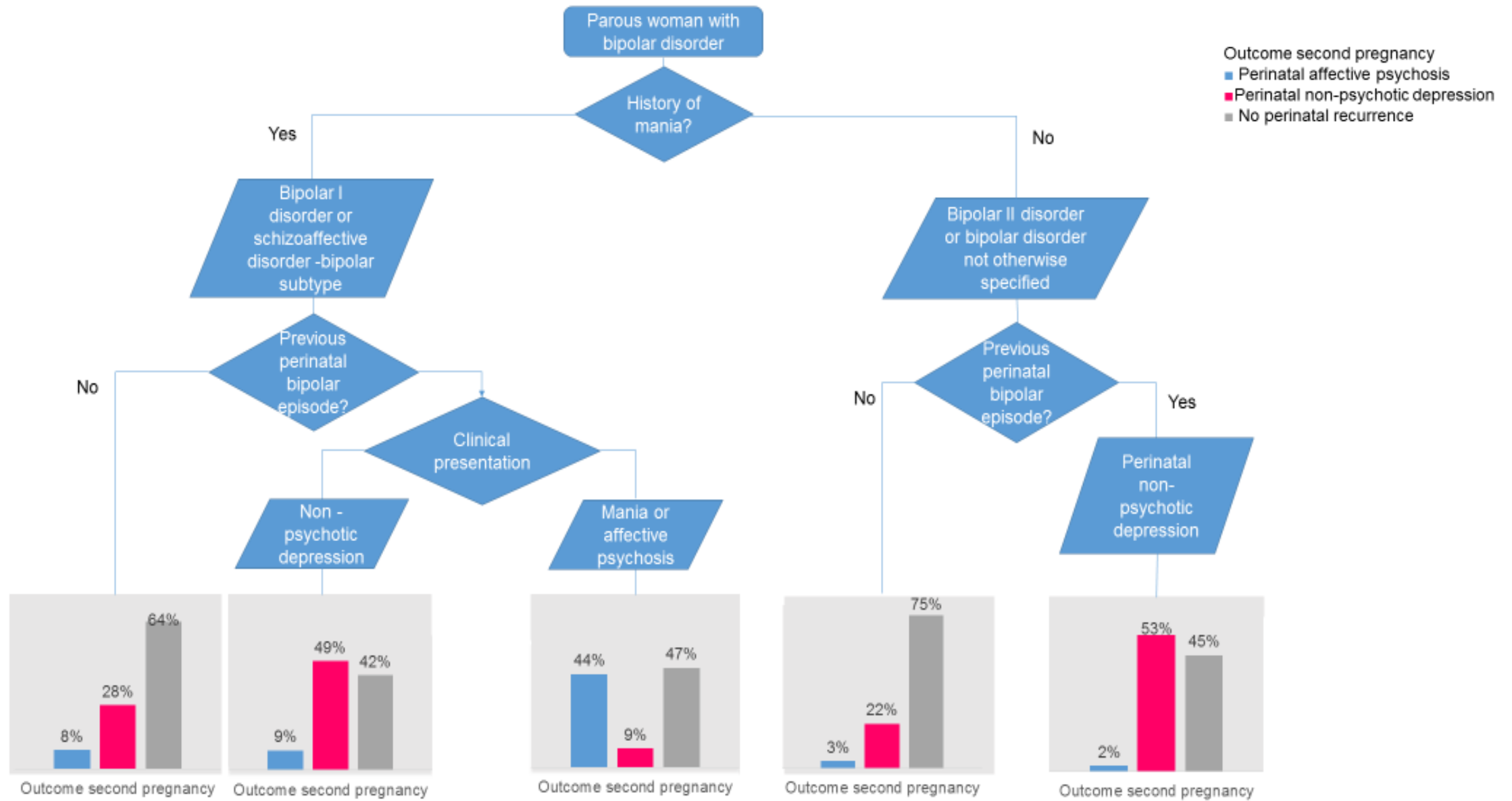
*Di Florio et al, Bipolar Disorders, 2014*

# Stratification of the risk of bipolar disorder recurrences in pregnancy and postpartum

Arianna Di Florio, Katherine Gordon-Smith, Liz Forty, Michael R. Kosorok, Christine Fraser, Amy Perry, Andrew Bethell, Nick Craddock, Lisa Jones and Ian Jones



**Fig. 1** Participant selection and analytic plan.



Di Florio et al, British J Psych 2018



# Conclusion

- Robust evidence for association between psychosis and childbirth
  - Specific for bipolar disorder
- Only a partial biological overlap between bipolar disorder and postpartum psychosis
- Not all women with bipolar disorder have the same perinatal risk profile

Bipolar Disorder

**BD RN**  
Research Network

**NCMH**  
National Centre for Mental Health

**MRC** | Centre for  
Neuropsychiatric Genetics  
and Genomics



 The  
Stanley  
Foundation

**W**  
wellcome

 **erc** | European  
Research  
Council

 **BRAIN &  
BEHAVIOR**  
RESEARCH FOUNDATION  
Awarding **NARSAD** Grants

**MRC** | Medical  
Research  
Council

 Ymchwil Iechyd  
a Gofal **Cymru**  
Health and Care  
Research **Wales**

 Ariennir gan  
**Lywodraeth Cymru**  
Funded by  
**Welsh Government**