Course and Treatment of Depression and Bipolar Illness during Pregnancy: Knowns and Unknowns

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My spouse/partner and I have the following relevant financial relationship with a commercial interest to disclose:

12-Month Disclosure

**Research Support for the National Pregnancy Registry for Atypical Antipsychotics**: Alkermes Biopharmaceuticals; Forest/Actavis Pharmaceuticals; Otsuka Pharmaceuticals; Sunovion Pharmaceuticals, Inc. Teva

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**Advisory/Consulting (through MGH Clinical Trials Network Initiative)**: Alkermes Biopharmaceuticals; Praxis Precision Medicines, Inc.

**Honoraria**: None

**Royalty/patent, other income**: None
Major Depression During Pregnancy

Are pregnant women protected against relapse or new onset of major depression?

Evans et al. *BMJ.* 2001
Yonkers et al. *Epidemiology* 2011
Roca et al. *J Affective Disorders* 2013
Time to Relapse in Patients Who Maintained or Discontinued Antidepressant

Relapse of Bipolar Disorder During Pregnancy

Psychotropic Drug Use in Pregnancy

• Medications used when risk to mother and fetus from disorder outweighs risks of pharmacotherapy
• Optimum risk/benefit decision for psychiatrically ill pregnant women
• Patients with similar illness histories make different decisions regarding treatment during pregnancy
• No decision is risk-free
• Collaborative, patient-centered approach required

Henshaw Fam Plann Perspect. 1998
Focus of concern regarding known and unknown risks of fetal exposure to psychiatric medications is increasingly balanced by data supporting risk of exposure to disorder, stress and HPA-axis dysregulation on fetoplacental unit

Enhanced appreciation for impact of disorder and chronic stress on long term behavioral outcomes
Maternal Stress or Depression

Dysregulation of the HPA Axis

Elevated CRH

Elevated Cortisol Levels

Stimulates Labor
Increases Risk for Preterm Birth

Decreases Placental Blood Flow
Decreases Birth Weight

IN UTERO Programming of Fetal HPA Axis
Dysregulation of HPA Axis
Increased Reactivity to Stress
Increased Vulnerability to Mood and Anxiety Disorders
Relative Impact of AD Exposure vs. Depression in Obstetrical and Neonatal Outcome

- Some data support increased rates of obstetrical complications and poor neonatal outcome in depressed or anxious pregnant women
  - Increased risk of preterm birth
  - Lower birth weight (LBW)
  - Small for gestational age (SGA)
- Depression and anxiety often comorbid
- Increased effort to distinguish impact of illness from medication exposure on obstetrical and neonatal outcome

Wisner Am J Psychiatry 2009
Warburton et al 2010
Original Investigation | META-ANALYSIS

Neonatal Outcomes in Women With Untreated Antenatal Depression Compared With Women Without Depression: A Systematic Review and Meta-analysis

Alexander Jarde, PhD; Michelle Morais, MD; Dawn Kingston, PhD; Rebecca Giallo, PhD; Glenda M. MacQueen, MD; Lucy Giglia, MD; Joseph Beyene, PhD; Yi Wang, BHSc; Sarah D. McDonald, MD

*JAMA Psychiatry.* doi:10.1001/jamapsychiatry.2016.0934
Published online June 8, 2016.
A Meta-analysis of Depression During Pregnancy and the Risk of Preterm Birth, Low Birth Weight, and Intrauterine Growth Restriction

Table 2

Effect of Antenatal Depression on Outcomes of PTB, LBW, and IUGR

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of Studies</th>
<th>Relative Risk (95% CI)</th>
<th>( P ) Value</th>
<th>( Q_d ) Within</th>
<th>( P ) Value</th>
<th>Variance Explained, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTB</td>
<td>20</td>
<td>1.13 (1.06–1.21)</td>
<td>&lt;.001</td>
<td>49.019</td>
<td>&lt;.001</td>
<td>61</td>
</tr>
<tr>
<td>LBW</td>
<td>11</td>
<td>1.18 (1.07–1.30)</td>
<td>.001</td>
<td>33.810</td>
<td>&lt;.001</td>
<td>70</td>
</tr>
<tr>
<td>IUGR</td>
<td>12</td>
<td>1.03 (0.99–1.08)</td>
<td>.14</td>
<td>22.411</td>
<td>.02</td>
<td>51</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IUGR, intrauterine growth restriction; LBW, low birth weight; PTB, preterm birth.

\(^a\)Pooled effect size was estimated using the random-effects model.

Grote et al. Arch Gen Psychiatry. 2010
Untreated Psychiatric Disorders During Pregnancy: Effects on Fetal Brain and HPA-Axis

Figure 1. The top and bottom rows, respectively, show the brain using the color map of diffusion tensor imaging and T2-weighted magnetic resonance imaging from one infant of our sample. The axial, coronal, and sagittal slices are respectively illustrated from left to right. The red contour indicates the amygdala on diffusion tensor imaging and T2-weighted magnetic resonance imaging.

What is the Safest Antidepressant for Women of Childbearing Age?
SEPTEMBER 11, 2014

DEPRESSION AND PREGNANCY: THE TERRIFYING DILEMMA

BY ANDREW SOLOMON
FDA issues final rule on changes to pregnancy and lactation labeling information for prescription drug and biological products

For Immediate Release
December 3, 2014

The U.S. Food and Drug Administration published a final rule today that sets standards for how information about using medicines during pregnancy and breastfeeding is presented in the labeling of prescription drug and biological products. The rule was required by the 21st Century Cures Act of 2016 and the Federal Food, Drug, and Cosmetic Act of 1938, as amended, which requires drug manufacturers to include pregnancy and breastfeeding information in the labeling of prescription drugs.

http://womensmentalhealth.org/posts/fda-finalizes-guidelines-pregnancy-lactation-labeling-information/
SSRI Use During Pregnancy

- Recent findings and more data inform the pharmacologic treatment of depression during pregnancy
  - Consistent conclusions that the \textit{absolute} risk of SSRI exposure in pregnancy is small\textsuperscript{1-3}
  - Consistent pattern of malformations with SSRI exposure is lacking
  - Case-control studies reveal inconsistent data regarding teratogenic risk of individual SSRIs\textsuperscript{4-9}

\textbf{Reproductive safety data on SSRIs exceed what is known about most other medicines used in pregnancy}

Antidepressant Use in Pregnancy and the Risk of Cardiac Defects

Krista F. Huybrechts, Ph.D., Kristin Palmsten, Sc.D., Jerry Avorn, M.D., Lee S. Cohen, M.D., Lewis B. Holmes, M.D., Jessica M. Franklin, Ph.D., Helen Mogun, M.S., Raisa Levin, M.S., Mary Kowal, B.A., Soko Setoguchi, M.D., Dr.P.H., and Sonia Hernández-Díaz, M.D., Dr.P.H.

• No evidence of increased risk for major malformations or cardiovascular malformations in children of pregnant women exposed to SSRIs
Cardiovascular Malformation and Fetal SSRI Exposure

Huybrechts et al. *NEJM* 2014.
“Poor Neonatal Adaptation” and SSRI Use During Pregnancy

• **Consistent data**: Late trimester exposure to SSRIs is associated with transient irritability, agitation, jitteriness, and tachypnea (25-30%)

• Overall studies do not adequately control for maternal mental health condition, adequate blinding of exposure in neonatal assessments

• **Clinical implication**: Should women be treated with antidepressants late in pregnancy and during labor and delivery (Warburton et al. 2010)

• Are any subgroups of newborns vulnerable to enduring symptoms beyond the first days of life?
Risk for PPHN Associated with Late Trimester Exposure to Antidepressant

JAMA Pediatrics | Original Investigation

Risk for Autism Spectrum Disorders According to Period of Prenatal Antidepressant Exposure
A Systematic Review and Meta-analysis

Antonia Mezzacappa, MD; Pierre-Alexandre Lasica; Francesco Gianfagna, MD, PhD; Odile Cazas, MD; Patrick Hardy, MD, PhD; Bruno Falissard, MD, PhD; Anne-Laure Sutter-Dallay, MD, PhD; Florence Gressier, MD, PhD

Published online April 17, 2017.
**Antidepressant Exposure During Pregnancy and Risk of Autism in the Offspring, 1:**

**Meta-Review of Meta-Analyses**

Chittaranjan Andrade, MD

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**Table 1. Important Findings From the Meta-Analysis of Kobayashi et al**

1. SSRI exposure during pregnancy was associated with an increased risk of ASD in the offspring in the case-control studies (5 studies; OR = 1.37; 95% CI, 1.08–1.74) and in one (2 studies; OR = 1.89; 95% CI, 1.28–2.18) but not the other (2 studies; OR = 1.69; 95% CI, 0.80–3.57) combination of the cohort studies.

2. There was no difference in ASD risk when exposure was compared between SSRIs and other antidepressant drugs in either case-control or cohort study analyses.

3. When analysis was restricted to datasets of mothers with psychiatric disorders, SSRIs were not associated with an increased risk of ASD in the case-control studies (1 study; OR = 1.86; 95% CI, 0.76–4.58) and in both sets of cohort studies (2 studies, each; OR = 0.79; 95% CI, 0.51–1.23 and OR = 1.03; 95% CI, 0.49–2.15).

**Abbreviations:** ASD = autism spectrum disorder, CI = confidence interval, OR = odds ratio, SSRI = selective serotonin reuptake inhibitor.

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**Table 2. Important Findings From the Case-Control Study Meta-Analysis of Kaplan et al**

1. SSRI (5 studies; OR = 1.66; 95% CI, 1.23–2.23) and non-SSRI (3 studies; OR = 2.05; 95% CI, 1.20–3.49) antidepressant exposure during pregnancy were both associated with an increased risk of ASD in the offspring.

2. Exclusive preconception exposure to SSRIs was associated with an increased risk of ASD in the offspring (3 studies; OR = 1.84; 95% CI, 1.48–2.28).

3. The ASD risk was also increased after first (4 studies; OR = 1.90; 95% CI, 1.28–2.83) and second (4 studies; OR = 1.73; 95% CI, 1.15–2.61) but not third (4 studies; OR = 1.64; 95% CI, 0.83–3.24) trimester exposure.

**Abbreviations:** ASD = autism spectrum disorder, CI = confidence interval, OR = odds ratio, SSRI = selective serotonin reuptake inhibitor.

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**Table 3. Important Findings From the Meta-Analysis of Brown et al**

1. In unadjusted analyses, exposure to SSRIs during pregnancy was associated with an increased risk of ASD in the offspring in both case-control (4 studies; OR = 1.7; 95% CI, 1.3–2.3) and cohort (2 studies; OR = 1.8; 95% CI, 1.3–2.6) studies.

2. In unadjusted analyses, exposure to SSRIs during the first trimester was associated with an increased risk of ASD in the offspring in both case-control (4 studies; OR = 2.0; 95% CI, 1.3–3.1) and cohort (2 studies; OR = 1.8; 95% CI, 1.3–2.6) studies.

3. After adjusting for potential confounders, exposure to SSRIs during pregnancy was associated with borderline significant risk of ASD in the offspring in the case-control studies (4 studies, OR = 1.4; 95% CI, 1.0–2.0) and with nonsignificant risk in the cohort studies (2 studies; OR = 1.5; 95% CI, 0.9–2.7).

4. After adjusting for potential confounders, exposure to SSRIs during the first trimester was associated with increased risk of ASD in the offspring in the case-control studies (4 studies, OR = 1.7; 95% CI, 1.1–2.6) and with nonsignificant risk in the cohort studies (1 study; OR = 1.4; 95% CI, 1.0–1.9).

5. In analyses restricted to datasets that controlled for maternal mental illness, SSRI exposure during pregnancy was not associated with an increased risk of ASD in the offspring in either case-control (3 studies; OR = 1.4; 95% CI, 0.9–2.2) or cohort (2 studies; OR = 1.5; 95% CI, 0.9–2.7) studies.

6. In analyses restricted to datasets that controlled for maternal mental illness, SSRI exposure during the first trimester was associated with an increased risk of ASD in the offspring in the case-control studies (3 studies; OR = 1.8; 95% CI, 1.1–3.1). In the cohort studies, the risk was not significant (1 study; OR = 1.4; 95% CI, 1.0–1.9).

**Abbreviations:** ASD = autism spectrum disorder, CI = confidence interval, OR = odds ratio, SSRI = selective serotonin reuptake inhibitor.
What are the Long-term Neurobehavioral Effects of Prenatal Exposure to an Antidepressant?
Recent review by Suri et al., J Clin Psychiatry 2014:

- 13 prospective studies have assessed neurobehavioral infant outcome after *in utero* antidepressant exposure
- N=721 children with antidepressant exposure and N=380 children without exposure
- The longest follow-up has been 4 to 5 years
- The majority do not suggest major long term adverse effects of prenatal antidepressant exposure on infant/child neurobehavioral development; no significant differences in neurobehavior/development
- Generally encouraging but sample sizes have been small, and there are reports of possible subtle effects on gross motor function and language development, as well as the potential for longer-term consequences following poor neonatal adaptation
- Most studies do not assess for nor quantify the severity of depressive symptoms in mothers across pregnancy
Associations Between Brain Structure and Connectivity in Infants and Exposure to Selective Serotonin Reuptake Inhibitors During Pregnancy

Claudia Lugo-Candelas, PhD; Jook Cha, PhD; Susie Hong, BS; Vanessa Bastidas, BS; Myrna Weissman, PhD; William P. Fifer, PhD; Michael Myers, PhD; Ardesheer Talati, PhD; Ravi Bansal, PhD; Bradley S. Peterson, MD; Catherine Monk, PhD; Jay A. Gingrich, MD, PhD; Jonathan Posner, MD

Published online April 9, 2018.
Figure 1. Brain Region Volumes in Infants With Prenatal Selective Serotonin Reuptake Inhibitor (SSRI) Exposure

A. Increase in GM volume in SSRI-exposed infants across the brain

- SSRI > PMO
- SSRI > HC
- SSRI > PMO + HC

1. Orbitofrontal c./insula
2. Amygdala/temporal pole
3. Caudate
4. Superior frontal g.
5. Precuneus
6. Occipital g.
7. Amygdala
8. Amygdala
9. Orbitofrontal c./insula
10. Caudate

B. Increase in GM volume in SSRI-exposed infants within amygdala and insula

- Right amygdala
- Right insula

A. Significant group volume differences in infant brains (mean, 4 weeks). Regression analyses were conducted on gray matter (GM) volume maps, estimated from T2-weighted magnetic resonance imaging and through voxel-based morphometry, using a whole brain corrected \( P < 0.05 \) (randomization permutation; cluster-antistat-based correction). The colored areas show an increase in volume in SSRI-exposed infants relative to prenatal maternal depression (PMD) without SSRI exposure (green), healthy controls (HC) (blue), and both groups combined (orange) (SSRI, \( n = 14 \); PMD, \( n = 19 \); HC, \( n = 47 \)). Compared with the PMD, HC, and both groups combined, the SSRI group showed significant expansion in volume in the right amygdala and insula compared with the PMD group and combined groups only in the superior frontal gyrus, and compared with combined groups only, the occipital gyrus.

B. Distribution (colored area), quartiles (thick bar), 95% CIs (thin line), and medians (white dots). Open triangles represent individual infant values. The significance of group differences was based on voxelwise analysis (whole-brain corrected using randomization permutation) from the 2 separate clusters in the right amygdala and the anterior insula. au indicates arbitrary unit; c, cortex; g, gyrus.

\( * P = 0.32 \) compared with both the PMD group, \( P = 0.22 \) compared with the HC group, and \( P = 0.14 \) compared with the PMD and HC groups combined, all significant results.

\( h P = 0.34 \) compared with the HC group.
Association of Selective Serotonin Reuptake Inhibitor Exposure During Pregnancy With Speech, Scholastic, and Motor Disorders in Offspring

Alan S. Brown, MD, MPH; David Gyllenberg, MD, PhD; Heli Malm, MD, PhD; Ian W. McKeague, PhD; Susanna Hinkka-Yli-Salomäki, Ph Lic; Milla Artama, PhD; Mika Gissler, PhD; Keely Cheslack-Postava, PhD; Myrna M. Weissman, PhD; Jay A. Gingrich, MD, PhD; Andre Sourander, MD, PhD

IMPORTANCE Speech/language, scholastic, and motor disorders are common in children. It is unknown whether exposure to selective serotonin reuptake inhibitors (SSRIs) during pregnancy influences susceptibility to these disorders.

OBJECTIVE To examine whether SSRI exposure during pregnancy is associated with speech/language, scholastic, and motor disorders in offspring up to early adolescence.

CONCLUSIONS AND RELEVANCE Exposure to SSRIs during pregnancy was associated with an increased risk of speech/language disorders. This finding may have implications for understanding associations between SSRIs and child development.
Neurodevelopmental Implications of Fetal Exposure to Selective Serotonin Reuptake Inhibitors and Untreated Maternal Depression Weighing Relative Risks

Lee S. Cohen, MD; Ruta Nonacs, MD, PhD
Study links antidepressants in pregnancy with language disorders

By Susan Scutti, CNN

Updated 11:08 AM ET, Wed October 12, 2016

http://www.cnn.com/2016/10/12/health/antidepressants-ssris-pregnancy-dyslexia/
Treatment of Bipolar Disorder During Pregnancy
Commonly employed antimanic agents are either known teratogens or have sparse available reproductive safety data.

Risks of untreated psychiatric illness

Risk of discontinuing maintenance psychotropic medications

Suppes T, et al. *Arch Gen Psychiatry*. 1991
Faedda GL, et al. *Arch Gen Psychiatry*. 1993
A **NEW** Research Study at the Massachusetts General Hospital Center for Women’s Mental Health

To determine the safety of atypical antipsychotics in pregnancy for women and their babies

Participation will involve **3** brief phone interviews over approximately **8** months

**Call Toll-Free:**

1-866-961-2388
• Primary aim: determine the risk of major malformations among infants exposed to second-generation antipsychotics
• Prospectively enrolled 487 women
• The odds ratio for major malformations comparing exposed and unexposed infants was 1.25 (95% CI=0.13-12.19)
• Current data indicate that second-generation antipsychotics are not major teratogens

Study is ongoing and continues to enroll women
• Prospective study
• As of April 23rd, 2018:
  – 1262 enrolled
  – 453 1st trimester exposures enrolled w/ evaluable data at time of analysis
  – Risk ratio = 3.22 (0.92, 11.3)
  – Quetiapine: 152 1st trimester exposures
    • Risk ratio = 0.90 (0.15, 5.46) AJP, (online, July 2018)
• Preliminary conclusions: **atypical antipsychotics are not major teratogens but more data are needed to narrow the confidence interval**

Presented at ASCP, Cohen et al., 2018
National Pregnancy Registry for Atypical Antipsychotics: Preliminary Findings

Table 4 – Pooled risk ratio of major malformations in babies exposed to quetiapine

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Risk Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habermann 2013*</td>
<td>1.46 (0.57-3.75)</td>
</tr>
<tr>
<td>Sadowski 2013*</td>
<td>2.49 (0.64-9.71)</td>
</tr>
<tr>
<td>Huybrechts 2016#</td>
<td>1.01 (0.88-1.17)</td>
</tr>
<tr>
<td>Cohen 2018 (current report)#</td>
<td>0.90 (0.15-5.46)</td>
</tr>
<tr>
<td><strong>Pooled risk ratio</strong></td>
<td><strong>1.03 (0.89-1.19)</strong></td>
</tr>
<tr>
<td>P-value to assess homogeneity of the data</td>
<td><em>P=0.526</em></td>
</tr>
</tbody>
</table>

*healthy control group

#comparison group, adjusted for underlying psychiatric disorder

**accumulated evidence suggests no meaningful increased risk with a pooled null risk ratio.

Presented at ASCP, Cohen et al., 2018; in press
Primary aim: determine the risk of major malformations among infants exposed to atypical antipsychotics

Examined Medicaid claim data from 1,341,715 pregnancies

After adjustment for confounding, the risk ratio for congenital malformation in exposed versus unexposed infants was 1.05 (95% CI=0.96-1.16)

A slightly increased risk in overall and cardiac malformations was noted for risperidone
Lithium and Pregnancy

- Lithium Register of Babies 1970s
- Ebstein’s Anomaly: 0.05 – 0.1% risk
- Recent analysis from Medicaid database shows dose-dependent increase in risk of cardiovascular anomalies

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>No. of Pregnancies</th>
<th>No. of Events</th>
<th>Prevalence per 100 Births</th>
<th>Propensity-Score-Adjusted Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No exposure</td>
<td>1,322,955</td>
<td>15,251</td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td>Exposure to lithium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤600 mg/day</td>
<td>305</td>
<td>&lt;11</td>
<td>1.64</td>
<td>1.11 (0.46–2.64)</td>
</tr>
<tr>
<td>601–900 mg/day</td>
<td>235</td>
<td>&lt;11</td>
<td>2.13</td>
<td>1.60 (0.67–3.80)</td>
</tr>
<tr>
<td>&gt;900 mg/day</td>
<td>123</td>
<td>&lt;11</td>
<td>4.88</td>
<td>3.22 (1.47–7.02)</td>
</tr>
<tr>
<td>Exposure to lamotrigine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤100 mg/day</td>
<td>904</td>
<td>&lt;11</td>
<td>1.11</td>
<td>0.70 (0.38–1.30)</td>
</tr>
<tr>
<td>101–200 mg/day</td>
<td>620</td>
<td>&lt;11</td>
<td>1.61</td>
<td>1.00 (0.54–1.86)</td>
</tr>
<tr>
<td>&gt;200 mg/day</td>
<td>421</td>
<td>&lt;11</td>
<td>1.66</td>
<td>1.02 (0.49–2.13)</td>
</tr>
</tbody>
</table>

Figure 2. Absolute and Relative Risk of Cardiac Malformations among Lithium-Exposed and Lamotrigine-Exposed Infants as Compared with Unexposed Infants, Stratified According to the Mother’s Dose of the Drug.

Stratification was according to thirds of the first prescribed daily dose that was filled during the first trimester. A separate exposure propensity score was estimated in each dose stratum as the predicted probability of receiving the treatment-dose range of interest versus no treatment, conditional on the covariates reported in Tables S6 through S9 in the Supplementary Appendix. For each estimated propensity score, the population in the nonoverlapping areas of the propensity-score distributions was trimmed, and 50 strata were created on the basis of the distribution of the treated women. Weights for the reference group were calculated according to the distribution of the exposed women among propensity-score strata and were used to estimate adjusted risk ratios and 95% confidence intervals.
Lithium Use in Pregnancy and the Risk of Cardiac Malformations

Elisabetta Patorno, M.D., Dr.P.H., Krista F. Huybrechts, Ph.D., Brian T. Bateman, M.D., Jacqueline M. Cohen, Ph.D., Rishi J. Desai, Ph.D., Helen Mogun, M.S., Lee S. Cohen, M.D., and Sonia Hernandez-Diaz, M.D., Dr.P.H.

https://womensmentalhealth.org/posts/12021/?doing_wp_cron=1506358912.7760159969329833984375
Valproic Acid and Pregnancy

• Overall risk of malformations elevated (6-10%): neural tube defects, cardiac anomalies, cleft lip/palate, limb abnormalities
• Dose dependent: Risk for major malformations highest (25.2%) in women on high dose valproate (above 1450 mg/day)
• Higher rates associated with polytherapy
• Neurodevelopmental sequelae: Increased risk of tauthism spectrum disorders, behavioral problems, lower IQ
• Folic acid appears to ameliorate risk of autism spectrum disorders but not risk of malformations
• UK and France have banned use of valproic acid in certain population s of reproductive age women
Other Antiepileptic Drugs and Pregnancy

Recent study from EUROCAT
• 107 of 1957 for carbamazepine = 5.5%
• 6 of 152 for topiramate = 3.9%, oral clefts
• 10 of 333 for oxcarbazepine = 3.0%
• 74 of 2514 for lamotrigine = 2.9%

• Inadequate data on the use of gabapentin, less than 350 exposures
Cognitive Function in 6 year olds Following Fetal Exposure to AED’s

Child IQ at 6 years, by exposure to maternal antiepileptic drug use and periconceptional folate

Cognitive Function in 6 year olds Following Fetal Exposure to AED’s

Child IQ at 6 years, by exposure to maternal antiepileptic drug use and periconceptional folate

Postpartum Prophylaxis in Bipolar Women

Significant difference between groups (Peto-Peto-Wilcoxon \( \chi^2 = 6.966, \text{df} = 1, p<0.01 \))

The Perinatal Depression Treatment Cascade:
Baby Steps Toward Improving Outcomes

Elizabeth Q. Cox, MD\textsuperscript{a,*}; Nathaniel A. Sowa, MD, PhD\textsuperscript{a}; Samantha E. Meltzer-Brody, MD, MPH\textsuperscript{a}; and Bradley N. Gaynes, MD, MPH\textsuperscript{a}

J Clin Psychiatry 2016
MGH Perinatal Depression Scale