MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Course and Treatment of Depression during Pregnancy and the Postpartum Period : Lessons Learned Across Two Decades

Lee S. Cohen, MD

Director, Ammon-Pinizzotto Center for Women's Mental Health

Massachusetts General Hospital

Edmund and Carroll Carpenter Professor of Psychiatry

Harvard Medical School

Disclosures

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

12-Month Disclosure

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Advisory/Consulting: Alkermes Biopharmaceuticals ,Praxis Precision Medicines, Inc.(through MGH Clinical Trials Network Initiative); **Honoraria:** None
Royalty/patent, other income: None

Reproductive Psychiatry and the COVID-19 Pandemic

- Family planning and the pandemic
- Telemedicine and implications for pregnancy and postpartum period
- Infertility treatment and the pandemic
- Perinatal anxiety during the COVID 19 crisis
- Importance of euthymia during pregnancy
- Reframing postpartum experience

JAMA Psychiatry. Published online July 15, 2020. doi:10.1001/jamapsychiatry.2020.1947
https://womensmentalhealth.org/obgyn/reproductive-psychiatry-during-the-covid-19-pandemic/

Virtual Rounds at CWMH during COVID : Wednesdays at 2 PM

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Resource: Join us for Virtual Rounds at the Center for Women's Mental Health on Wednesdays

By MGH Center for Women's Mental Health | April 3rd, 2020 | Resources | 0 Comments

As our faculty at the Center for Women's Mental Health (CWMH) have gone fully remote with respect to clinical and research activity, we have managed to stay connected these last three weeks with "virtual rounds". For over 25 years, our group has met on Wednesdays at midday to discuss clinical cases we have seen across the week and also to discuss recently published papers in reproductive psychiatry. We look forward to Wednesdays as we get to talk about how we think about treatment options with respect to presented cases and the decisions patients make about treatment before, during, and after pregnancy. Particular attention is given to the safest use of psychiatric medications during pregnancy, the postpartum period and lactation. Three decades after founding the Center, I still love Wednesday rounds and always learn something by listening to cases and hearing how my colleagues think about perinatal psychiatric disorders. We are continuing to round during the COVID19 epidemic and Zoom proves to be the next best thing to being there.

https://womensmentalhealth.org/posts/resource-join-us-for-virtual-rounds-at-the-center-for-womens-mental-health-on-wednesdays/

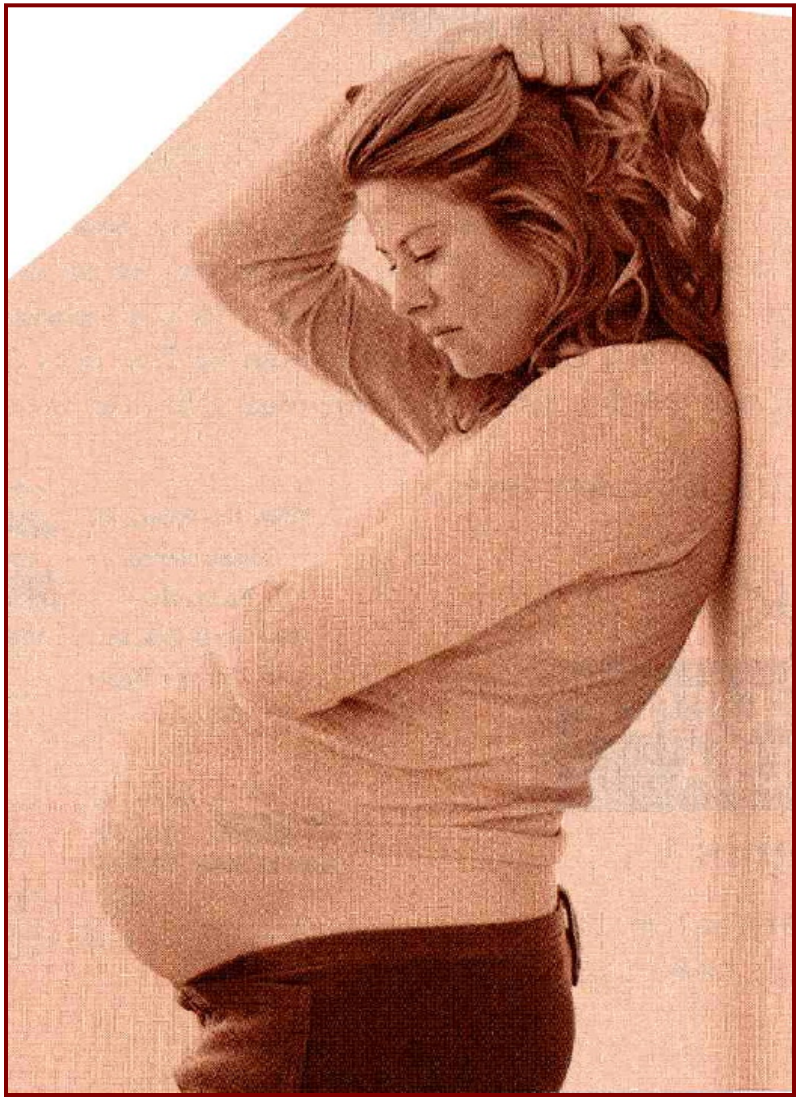
Treatment considerations for women with MDD in pregnancy and the postpartum period

- Depression during pregnancy is strongest predictor of postpartum depression
- **Nothing is more important maternal euthymia**

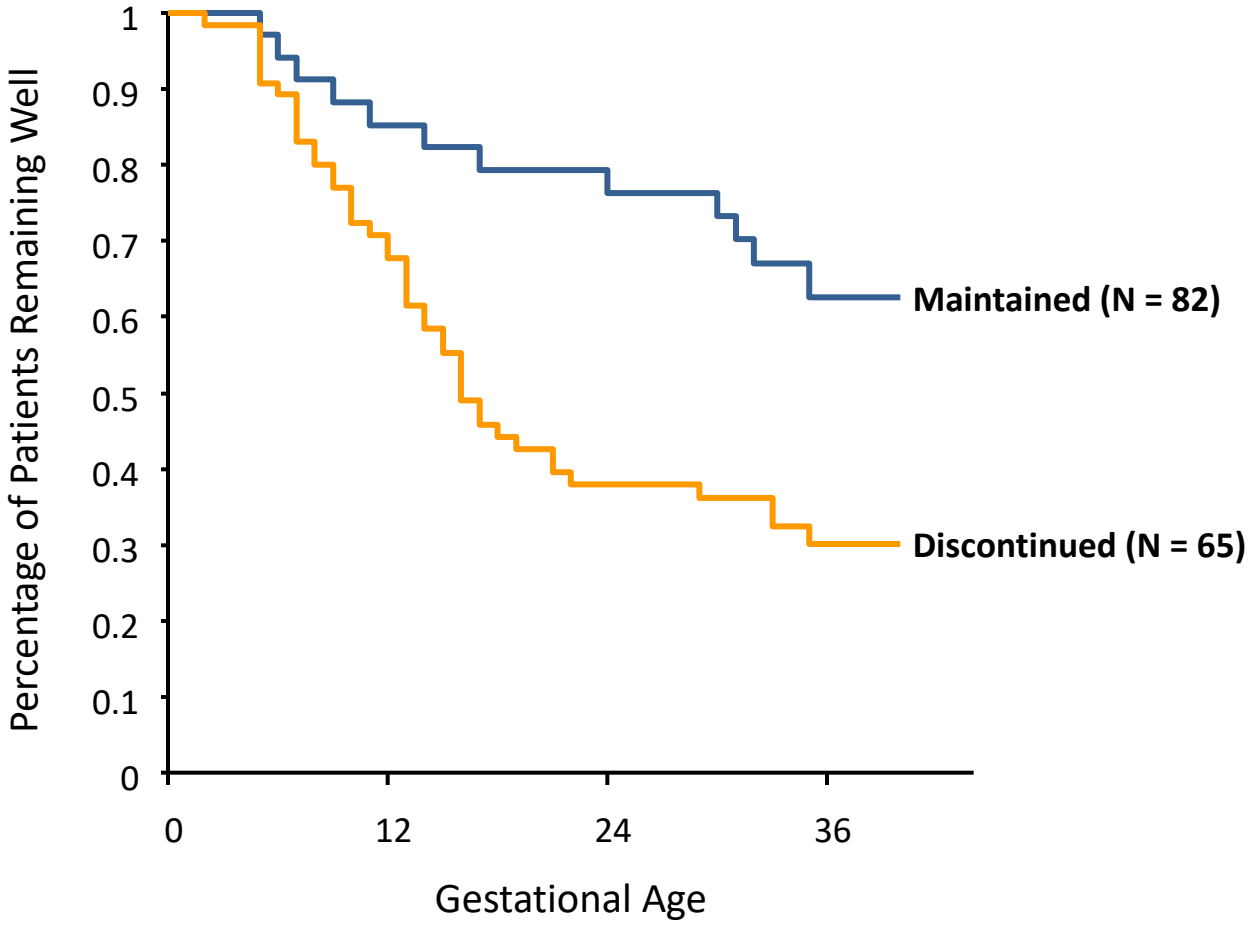
Major Depression During Pregnancy

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

O'Hara et al. *J Abnorm Psychol.* 1990
Evans et al. *BMJ.* 2001
Yonkers et al. *Epidemiology* 2011
Roca et al. *J Affective Disorders* 2013

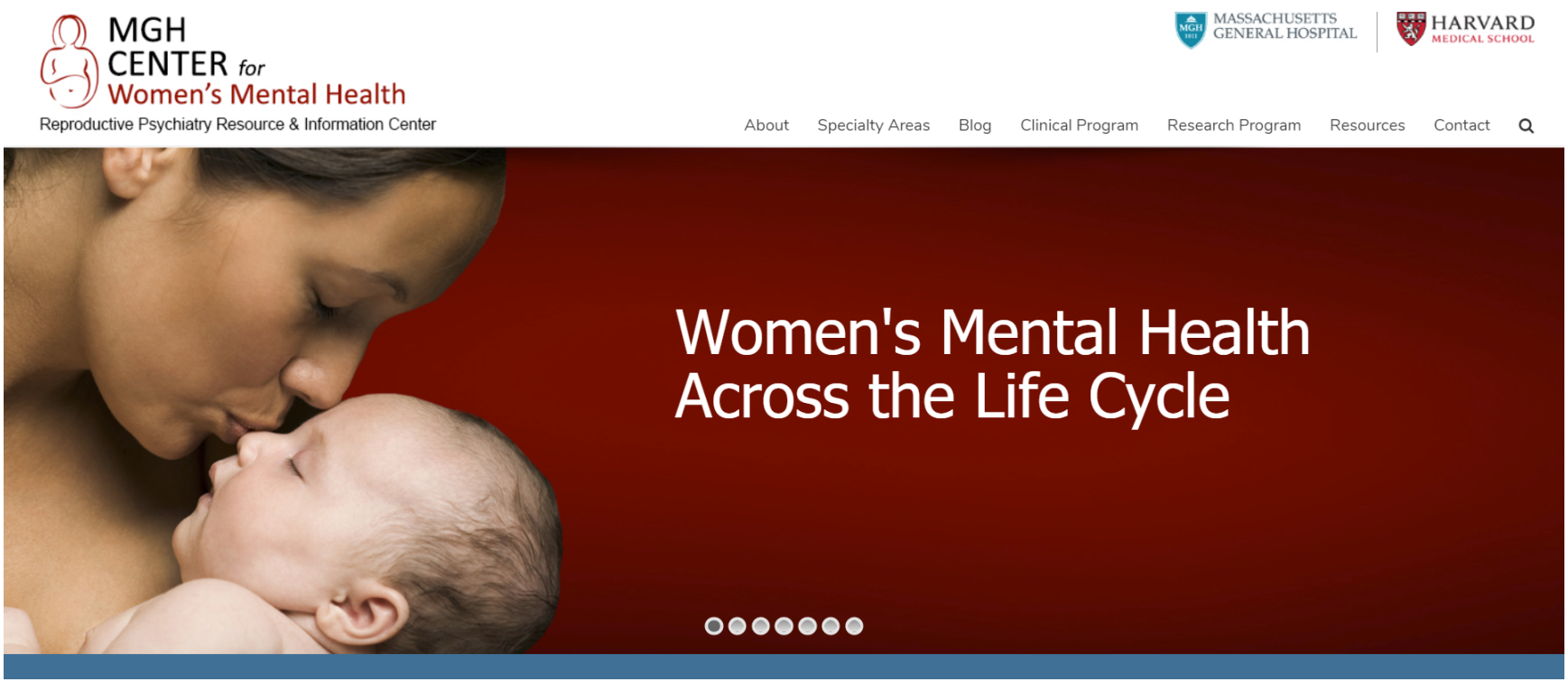


Time to Relapse in Patients Who Maintained or Discontinued Antidepressant



Cohen LS, et al. *JAMA*. 2006

Womensmentalhealth.org



Psychotropic Drug Use in Pregnancy

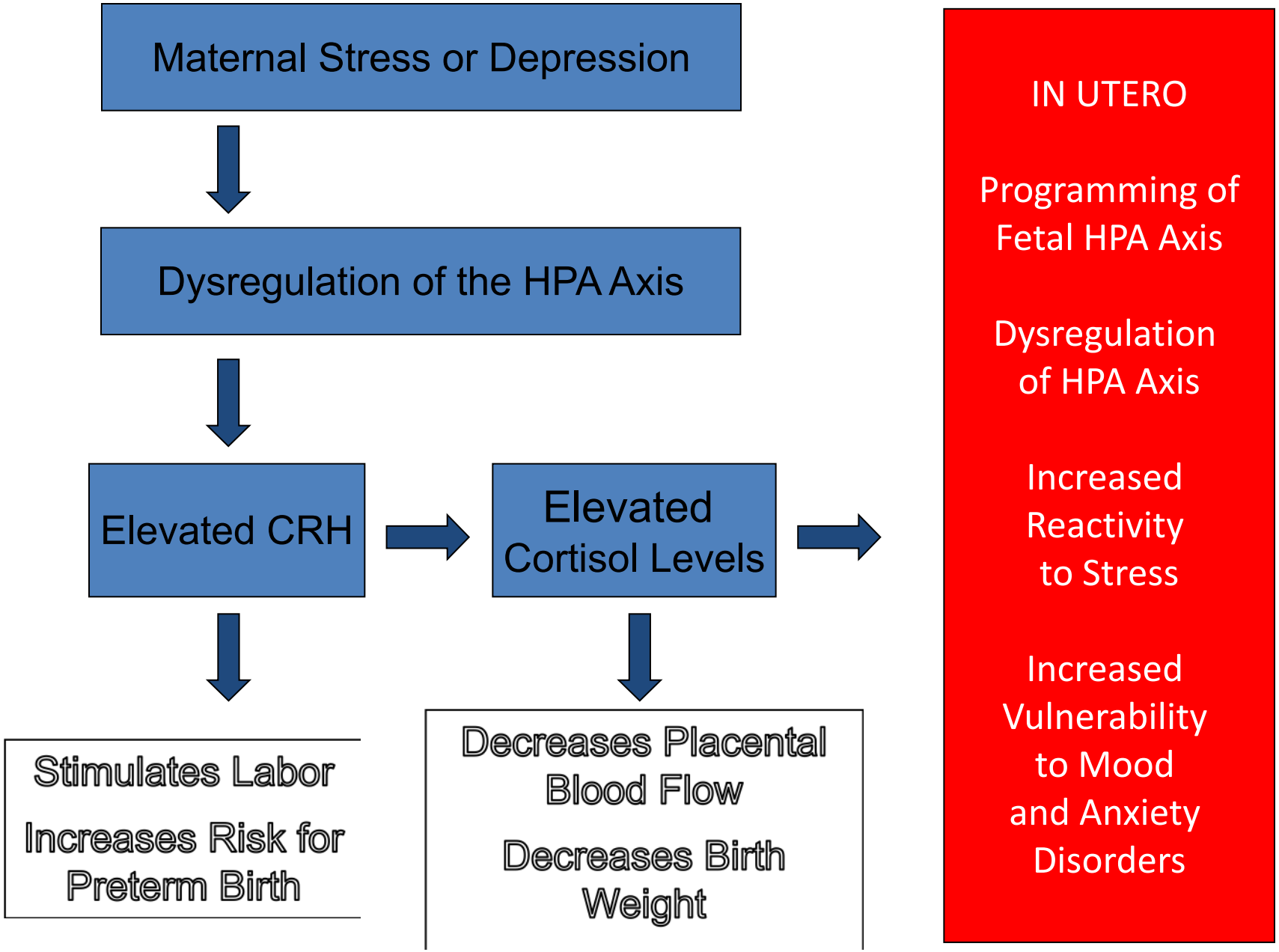
- Medications used when risk to mother and fetus from disorder outweighs risks of pharmacotherapy
- Optimum risk/benefit decision for psychiatrically ill pregnant women
- Patients with similar illness histories make different decisions regarding treatment during pregnancy
- No decision is risk-free
-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

Henshaw *Fam Plann Perspect*. 1998

Treatment of Depression During Pregnancy: Lessons Learned and New Directions

- 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

Research

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.

What is the Safest Antidepressant for Women of Childbearing Age?

Phasing Out: FDA Pregnancy Categories

- **Category A:**
  - Well controlled studies in human pregnancy show no increased risk to the fetus
- **Category B:**
  - Animal studies show no increased risk to the fetus OR
  - Animal studies show an increased risk to the fetus but well controlled human studies do not.
- **Category C:**
  - Animal studies show an increased risk to the fetus and there are no well controlled studies in human pregnancy OR
  - There aren't any animal studies or well controlled human studies.

U.S. Department of Health and Human Services

U.S. Food and Drug Administration
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FDA News Release

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

For Immediate Release December 3, 2014

Release

Español

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 drugs and biological

Inquiries

Media

Sandy Walsh
301-796-4669

Consumers

888-INFO-FDA

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http://womensmentalhealth.org/posts/fda-finalizes-guidelines-pregnancy-lactation-labeling-information/

Timeline to Changes in Product Labeling

	NDAs, BLA, ESs	Required Submission Date of PLLR Format
New Applications	Submitted on or after 6/30/2015	At time of submission
---------- PLLR Implementation Date (6/30/2015) ----------		
Older Approved Applications	Approved 6/30/2001 to 6/29/2002 Approved 6/30/2005 to 6/29/2007	6/30/2018
	Approved 6/30/2007 to 6/29/2015 Or pending on 6/30/2015	6/30/2019
	Approved 6/30/2002 to 6/29/2005	6/30/2020
	For applications approved prior to 6/30/2001 in old format labeling	Not required to be in PLLR format. However, must remove Pregnancy Category by 6/29/2018

SSRI Use During Pregnancy

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

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

[1] Louik C et al. *N Engl J Med* 2007; [2] Einarson TR, Einarson A. *Pharmacoepidemiol Drug Saf* 2005; [3] Einarson A, et al. *Am J Psychiatry* 2008; [4] Alwan S, et al. *N Engl J Med* 2007; [5] Greene MF. *N Engl J Med* 2007; [6] Hallberg P, Sjoblom V. *J Clin Psychopharmacol* 2005; [7]Wogelius P, et al. *Epidemiology* 2006; [8] www.gsk.ca/english/docs-pdf/PAXIL_PregnancyDHCPL_E-V4.pdf Dear Healthcare Professional (3/17/08); [9] www.fda.gov/medwatch/safety/2005/Paxil_dearhcp_letter.pdf Dear Healthcare Professional (3/17/08); Grigoriadis et al. *J Clin Psychiatry* 2013.

JAMA Psychiatry

Research

JAMA Psychiatry | Original Investigation

Maternal Use of Specific Antidepressant Medications During Early Pregnancy and the Risk of Selected Birth Defects

Kayla N. Anderson, PhD; Jennifer N. Lind, PharmD, MPH; Regina M. Simeone, MPH; William V. Bobo, MD, MPH; Allen A. Mitchell, MD; Tiffany Riehle-Colarusso, MD, MPH; Kara N. Polen, MPH; Jennita Reefhuis, PhD

IMPORTANCE Antidepressants are commonly used during pregnancy, but limited information is available about individual antidepressants and specific birth defect risks.

OBJECTIVE To examine associations between individual antidepressants and specific birth defects with and without attempts to partially account for potential confounding by underlying conditions.

DESIGN, SETTING, AND PARTICIPANTS The population-based, multicenter case-control National Birth Defects Prevention Study (October 1997–December 2011) included cases with selected birth defects who were identified from surveillance systems; controls were randomly sampled live-born infants without major birth defects. Mothers of cases and controls participated in an interview after the expected delivery date. The data were analyzed after the completion of the National Birth Defects Prevent Study's data collection.

EXPOSURES Self-reported antidepressant exposure was coded to indicate monotherapy exposure to antidepressants.

MAIN OUTCOMES AND MEASURES We used multivariable logistic regression to calculate adjusted odds ratios (aORs) and 95% confidence intervals for associations between maternal antidepressant use and birth defects. We compared early pregnancy antidepressant-exposed women with those without antidepressant exposure and, to partially account for confounding by underlying maternal conditions, those exposed to antidepressants outside of the birth defect development critical period.

Editorial

Supplemental c

EDITORIAL

The Association Between Antidepressant Exposure and Birth Defects—Are We There Yet?

Katherine L. Wisner, MD, MS; Tim F. Oberlander, MD, FRCPC; Krista F. Huybrechts, MS, PhD

Few moments are more concerning to parents than learning that their infant has a birth defect. Compounding this news is the possibility that the medication used to manage the mother's mood disorder may have increased the risk for her infant developing a birth defect. As health care professionals, we have an enormous obligation to get the science right. In 2007, an editorial was published in response to 2 large case-control studies, "Teratogenicity of SSRIs: Serious Concern or Much Ado about Little?"[1] What have we learned over the ensuing 13 years?

Related article

Anderson et al[2] aimed to determine which antidepressants are associated with birth defects. They state, "such analyses can support work to identify medications with the highest and lowest birth defect risks independent of the underlying condition."[2] This statement implies that the broad adverse effects of psychiatric illness can be distinguished from the effect of medications on the risk for birth defects, a formidable challenge in observational research.

Data from the National Birth Defects Prevention Study were used to compare the risks of congenital malformations in women exposed in early pregnancy to 2 reference groups: (1) unexposed women and (2) women treated with antidepressants 2 to 3 months before and/or after embryogenesis (months 4-9). The second group was included to account for confounding by indication, the major challenge plaguing observational studies. However, the National Birth Defects Prevention Study data set does not include psychiatric diagnosis, which is unlikely to change the effect estimate by at least 10%, several variables together might. Other principled approaches to confounder selection have been recommended over data-driven statistical methods.[4] Selective serotonin reuptake inhibitor exposure may be a proxy for unidentified environmental and/or genetic factors associated with maternal mental illness that are associated with birth defects. The absence of information on characteristics, such as socioeconomic disadvantage, toxin exposures, and substance use that often accompany poor mental health, renders the results challenging to interpret owing to concern about residual confounding.

The second comparison focused on women exposed to antidepressants during the first trimester vs exposed outside of the first trimester. The validity of this comparison depends on equivalence of the groups relative to the severity and functional sequelae of the underlying psychiatric disorder. Using the same 10% change-in-estimate approach, the authors adjusted only for maternal education. The set of characteristics presented in Table 2 are helpful but insufficient to demonstrate their comparability with respect to the psychiatric disorder, comorbid conditions (eg, diabetes and/or hypertension), or concomitant drug exposures (eg, anticonvulsants and/or antimanic agents) that may be associated with increased risk for fetal malformations. The authors highlighted the results for the serotonin-norepinephrine reuptake inhibitor venlafaxine, which is not a first-line drug for pregnant women, as indicated by the relatively low frequency of use

Read our blog post on this topic: https://womensmentalhealth.org/posts/antidepressant-birth-defects/

Anderson KN, Lind JN, Simeone RM, Bobo WV, Mitchell AA, Riehle-Colarusso T, Polen KN, Reefhuis J. Maternal Use of Specific Antidepressant Medications During Early Pregnancy and the Risk of Selected Birth Defects. JAMA Psychiatry. 2020 Aug 5:e202453.
Huybrechts KF, Palmsten K, Avorn J, Cohen LS, Holmes LB, Franklin JM, Mogun H, Levin R, Kowal M, Setoguchi S, Hernández-Díaz S. Antidepressant use in pregnancy and the risk of cardiac defects. N Engl J Med. 2014 Jun 19;370(25):2397-407.
Wisner KL, Oberlander TF, Huybrechts KF. The Association Between Antidepressant Exposure and Birth Defects-Are We There Yet? JAMA Psychiatry. 2020 Aug 5.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

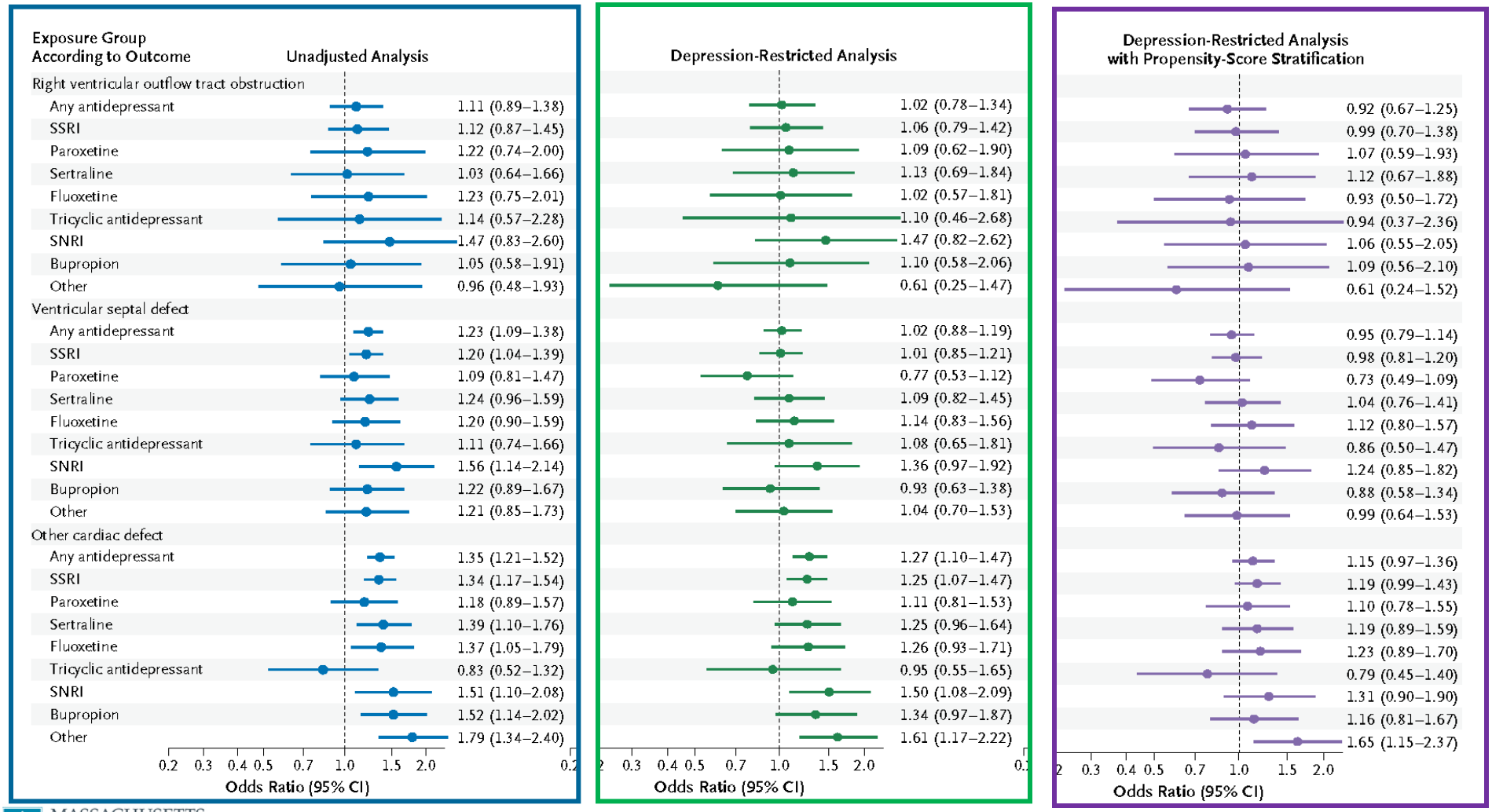
Antidepressant Use in Pregnancy and the Risk of Cardiac Defects

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.

N ENGL J MED 370;25 NEJM.ORG JUNE 19, 2014

- 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



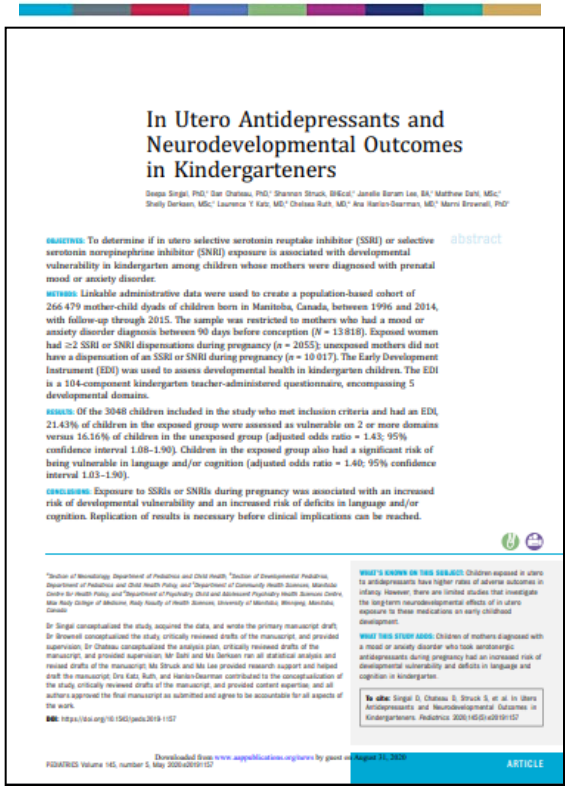
Huybrechts et al. *NEJM* 2014.

“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 ?

Levinson-Castiel R, et al. *Arch Pediatr Adolesc Med.* 2006
Chambers CD, et al. *N Engl J Med*. 2006
Chambers, *BMJ*, 2009
CWMH Blog, July 27 2005: http://womensmentalhealth.org/posts/neonatal-symptoms-after-in-utero-exposure-to-ssris/

What are the Long-term Neurobehavioral Effects of Prenatal Exposure to an Antidepressant?



Neurodevelopmental Outcomes in Kindergartners with Prenatal Exposure to Antidepressants

By MGH Center for Women's Mental Health | June 2nd, 2020 | Antidepressants and Pregnancy, Child Development, Psychiatric Disorders During Pregnancy | 0 Comments

While we have data to support the use of antidepressants, including the selective serotonin reuptake inhibitors (SSRIs) and the serotonin norepinephrine reuptake inhibitors (SNRIs), during pregnancy, most studies have focused on risk of congenital malformations, and we have less information on longer term neurodevelopmental outcomes. In a recent study, Singal and colleagues look at neurodevelopmental outcomes in kindergartners with prenatal exposure to

Full blog post: https://womensmentalhealth.org/posts/antidepressants-neurodevelopment/

Singal D, Chateau D, Struck S, Lee JB, Dahl M, Derksen S, Katz LY, Ruth C, Hanlon-Dearman A, Brownell M. In Utero Antidepressants and Neurodevelopmental Outcomes in Kindergarteners. Pediatrics. 2020 May;145(5).
Andrade C. Genes as Unmeasured and Unknown Confounds in Studies of Neurodevelopmental Outcomes After Antidepressant Prescription During Pregnancy. J Clin Psychiatry. 2020 May 26;81(3):20f13463. Free Article
Rommel AS, Bergink V, Liu X, Munk-Olsen T, Molenaar NM. Long-Term Effects of Intrauterine Exposure to Antidepressants on Physical, Neurodevelopmental, and Psychiatric Outcomes: A Systematic Review. J Clin Psychiatry. 2020 May 12;81(3):19r12965.
Andrade C. Offspring Outcomes in Studies of Antidepressant-Treated Pregnancies Depend on the Choice of Control Group. J Clin Psychiatry. 2017 Mar;78(3):e294-e297. Free Article

Research

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

JAMA Pediatr. 2017;171(6):555-563. doi:10.1001/jamapediatrics.2017.0124
Published online April 17, 2017.

Clinical and Practical **Psychopharmacology**

Antidepressant Exposure During Pregnancy and Risk of Autism in the Offspring, 1:

Meta-Review of Meta-Analyses

Chittaranjan Andrade, MD

Table 1. Important Findings From the Meta-Analysis of Kobayashi et al[9]

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, 1.28–1.88) 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.

Kobayashi et al[9]

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, 1.28–1.88) 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).

Table 3. Important Findings From the Meta-Analysis of Brown et al[11]

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 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.

Treatment Guidelines Depression : Does Severity Drive Treatment Recommendations (and Patient Choice)

- **Psychotherapy: First-line for mild to moderate MDD**
- Lifestyle components: Nutrition, weight management, prenatal care ; treatment for co-morbid substance abuse
- Evidence base for CBT , Behavioral Activation and MBCT (prevention)
- **Women trying to conceive who have histories of MDD:**
  - –Encourage period of euthymia
  - –Sustained remission: consider tapering and discontinuing ?
  - –More recently depressed or with symptoms: consider remaining on medication, optimizing medication
- **Pregnant women with severe MDD:** Medication is first-line
- **Pregnant women on antidepressants during pregnancy:** take into account patient preferences, previous course of illness
- Medication selection should be based on known safety information

MDD, major depressive disorder.

Yonkers KA et al. *Obstet Gynecol.* 2009;114(3):703-713.

Treatment of Depression During Pregnancy: Lessons Learned

- Treatment decisions are complex (maternal and fetal benefits and risks)
- Absolute quantification of risk associated with fetal exposure to medication or maternal disease is impossible
- No treatment decision is “perfect”

  - Each treatment decision should try to optimize pregnancy outcomes for the mother and her child

  - Consider the risks of untreated disease and the risks of medication treatment

  -wisdom of changing AD dose proximate to delivery is sparse

Kallen *Obstet Gynecol Int.* 2012
Palmsten and Hernandez-Diaz *Epidemiology* 2012

Summary of treatment considerations for women with MDD in pregnancy (cont.)

- Depression during pregnancy is strongest predictor of postpartum depression
- There are known and unknown risks associated with AD use during pregnancy
- Adverse effects of depression in pregnancy on patient, infant and families
- **Nothing trumps maternal euthymia**

Postpartum Depression (PPD)

- 10-15% of women experience PPD after delivery
- Similar to non-puerperal major depression
- Most common complication in modern obstetrics
- Impairment of functioning

Postpartum Depression: Non-Pharmacologic Strategies

- Maximize social supports – Postpartum Support International (https://www.postpartum.net/)
- Psychoeducation of patient and family members
- Group therapy and support groups
- Interpersonal therapy (IPT)
- Cognitive-behavioral therapy (CBT)
- Behavioral Activation – (BA)
- MBCT – relapse prevention ?

Cohen et al. *Psychiatr Clin North Am.* 2010; Perlstein et al. *Am J Obstet Gynecol* 2009; Appleby et al., 1997.
https://www.postpartum.net/ ;

Antidepressant Trials for the Treatment of PPD

Study	Design and Size	Medication studied, result
Appleby et al., 1997	Placebo-controlled, N=87 CBT studied in same trial	Fluoxetine - superior to placebo
Yonkers et al, 2008	placebo controlled, N=70	Paroxetine - not superior to placebo)
Wisner et al., 2006	RCT, Setraline vs. Nortriptyline, N=109	Sertraline vs. Nortriptyline - no significant difference
Hantsoo et al., 2013	Placebo-controlled RCT, N=36	Setraline- superior to placebo
Bloch et al., 2012	N=40, all received brief psychodynamic therapy, RCT to sertraline or placebo	Both groups improved – no significant difference for sertraline vs. placebo
Sharp et al., 2010	RCT, AD selected by general practitioner or counseling, N=254	Antidepressants- superior to placebo
Misri et al., 2012	Open trial, N=15	Citalopram – open study
Misri et al., 2004	N=35, all received parox, half randomized to CBT also	Paroxetine – no control group
Stowe et al., 1995	Open-label; N=21	Sertraline – open study
Cohen et al., 1997	Open-label; N=19	Venlafaxine- open study
Suri et al., 2001	Open-label; N=6	Fluvoxamine - open
Nonacs et al., 2005	Open-label; N=8	Bupropion- open

Brexanolone

- FDA approval in 2019
- IV delivered analogue of allopregnanolone
- Allosteric modulator of GABA receptors
- Two positive, controlled trials in postpartum depression (onset during late pregnancy or postpartum, presented within six months postpartum with MDD)
- Rapid onset of benefit, durable efficacy to 30 days
- Implementation challenges: cost, in hospital

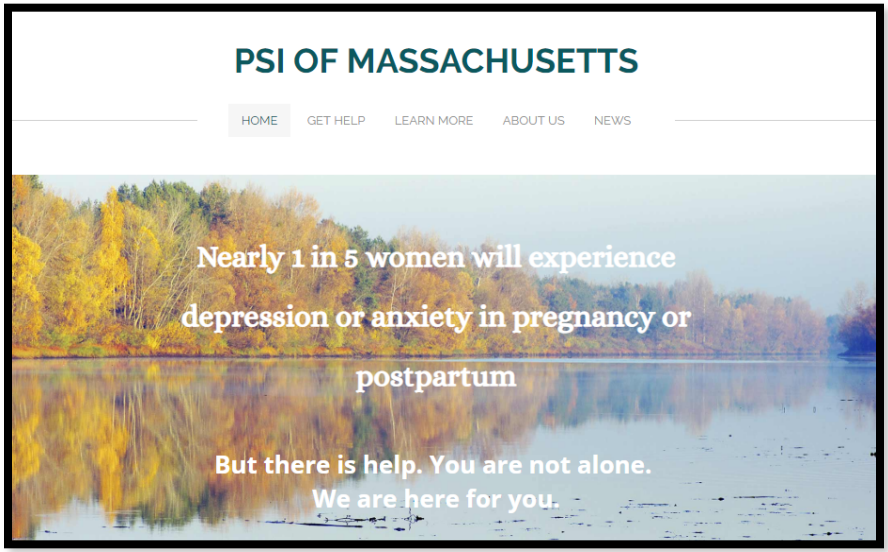
Meltzer-Brody et al., Lancet 2018; Wisner 2019, Cohen , 2019

SAGE 217 (Zuranolone)

- Neurosteroid with similar mechanism of action to brexanolone
- Data supporting efficacy in oral formulation for major depression mixed
- Studies underway for postpartum major depression

Deligiannidis et al , presented at annual meeting ASCP, Scottsdale , Arizona, June 2019

It Takes A Village



Womensmentalhealth.org

Postpartum Psychosis

Postpartum Psychosis

- 1 to 2 per 1000 pregnancies
- Rapid, dramatic onset within first 2 weeks
- **High risk of harm to self and infant**
- **Suspect Bipolar disorder**:
  - Underlying diagnosis: affective psychosis (bipolar disorder or schizoaffective disorder)
  - Family and genetic studies, index episode follow-up

Nonacs and Cohen, 1998; Jones & Craddock, 2001;
Spinelli, AJP, April 2009

Postpartum Psychosis

- Psychiatric emergency
- Estimated that 4% of women with postpartum psychosis commit infanticide
    - Actual rates of infanticide are difficult to estimate, as infanticide may be under-reported

- Spinelli, AJP 2004; Spinelli, AJP 2009

MGHP3 – The MGH Postpartum Psychosis Project

- **Specific aims:**
  - 1) Describe phenomenology of PPP with respect to time of onset, symptomology, and comorbidities
  - 2) Identify clinical and genomic predictors of this disorder

- **Eligibility:**
  - Women ages 18+
  - Experienced psychotic episode within 6 months of live birth, stillbirth, or intrauterine fetal demise
  - PPP episode occurred in the past 10 years
  - No prior diagnosis of schizophrenia, schizoaffective disorder, or psychosis NOS

Massachusetts General Hospital

Postpartum Psychosis Project

Researchers are interested in learning more about postpartum psychosis, a rare but serious complication of childbirth. If you gave birth within the past 10 years and had an episode of postpartum psychosis, we would like to ask about your experience.

MGHP3.o

Call 1-617-643-7205

Visit our website

MGHP3.org

Please call us today to enroll.

Interest

Screening for Postpartum Depression

Clinical Review & Education

Special Communication | USPSTF RECOMMENDATION STATEMENT

Screening for Depression in Adults
US Preventive Services Task Force Recommendation Statement

Albert L. Siu, MD, MSPH; and the US Preventive Services Task Force (USPSTF)

DESCRIPTION Update of the 2009 US Preventive Services Task Force (USPSTF) recommendation on screening for depression in adults.

METHODS The USPSTF reviewed the evidence on the benefits and harms of screening for depression in adult populations, including older adults and pregnant and postpartum women; the accuracy of depression screening instruments; and the benefits and harms of depression treatment in these populations.

POPULATION This recommendation applies to adults 18 years and older.

RECOMMENDATION The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation)

JAMA. 2016;315(4):380-387. doi:10.1001/jama.2015.18392

Editorial pages 349 and 351

Author Audio and Video Interviews and JAMA Report Video at jama.com

Related article page 388 and **JAMA Patient Page** page 428

CME Quiz at jamanetworkcme.com and **CME Questions** page 411

Related articles at jamapsychiatry.com, jamainternalmedicine.com, and jamaneurology.com

Author Affiliations: Author affiliations are listed at the end of this article.

Authors/Group Information: The USPSTF members are listed at the end of this article.

Corresponding Author: Albert L. Siu, MD, MSPH (albert.siu@mssm.edu).

PPD, Screening, and Large Scale Efforts

- Federal legislation includes provisions for postpartum depression
  - Language on screening for PPD and increased funding for its treatment and research
- Multiple states have implemented universal screening or are in the process of implementing screening
- Political impetus to screen for PPD

The Perinatal Depression Treatment Cascade:

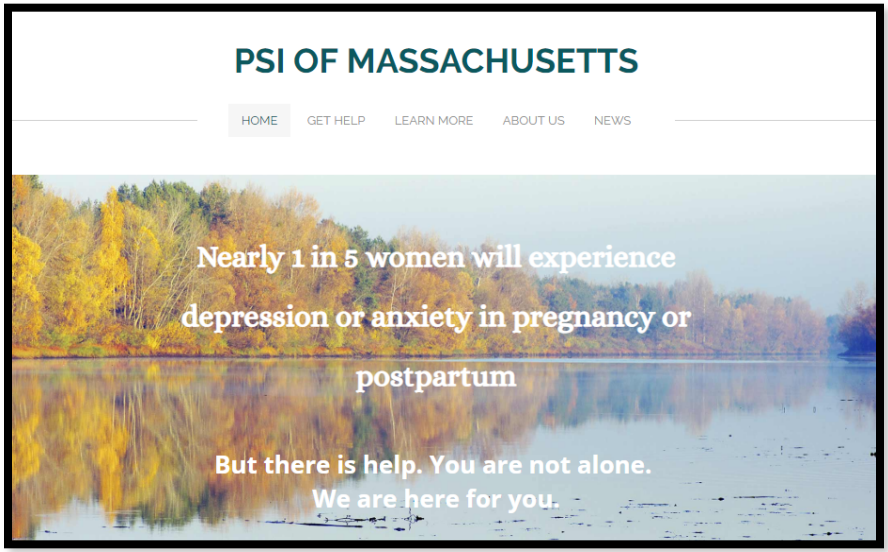
Baby Steps Toward Improving Outcomes

Elizabeth Q. Cox, MD[a,*]; Nathaniel A. Sowa, MD, PhD[a]; Samantha E. Meltzer-Brody, MD, MPH[a]; and Bradley N. Gaynes, MD, MPH[a]

J Clin Psychiatry 2016

MGH Perinatal Depression Scale

It Takes A Village



Womensmentalhealth.org

Cohen et al. *Psychosomatics* 1989

Treatment Guidelines for Psychotropic Drug Use in Pregnancy

LEE S. COHEN, M.D.
VICKI L. HELLER, M.D.
JERROLD F. ROSENBAUM, M.D.

Despite the apparent risks of psychotropic drug exposure in pregnancy, many pregnant women receive psychotropics. The major concerns associated with the use of antipsychotics, antidepressants, benzodiazepines, and lithium carbonate in pregnancy are reviewed, with clinical approaches for assessing the relative risks and benefits of treatment of psychiatrically ill pregnant patients and for choosing and instituting therapy with these agents.