Psychiatric Illness in Childbearing Women

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Disclosures

I have no actual or potential conflicts of interest in relation to this presentation.

Recent History of Perinatal Psychiatry

1990: Prevalence and Risk Factors for PPD (O'Hara)
2001: Depression During Pregnancy (Evans)

1980: Marce Society

2015: ACOG Screening for PMAD

1868: Victor Louis Marce

1987: Prozac

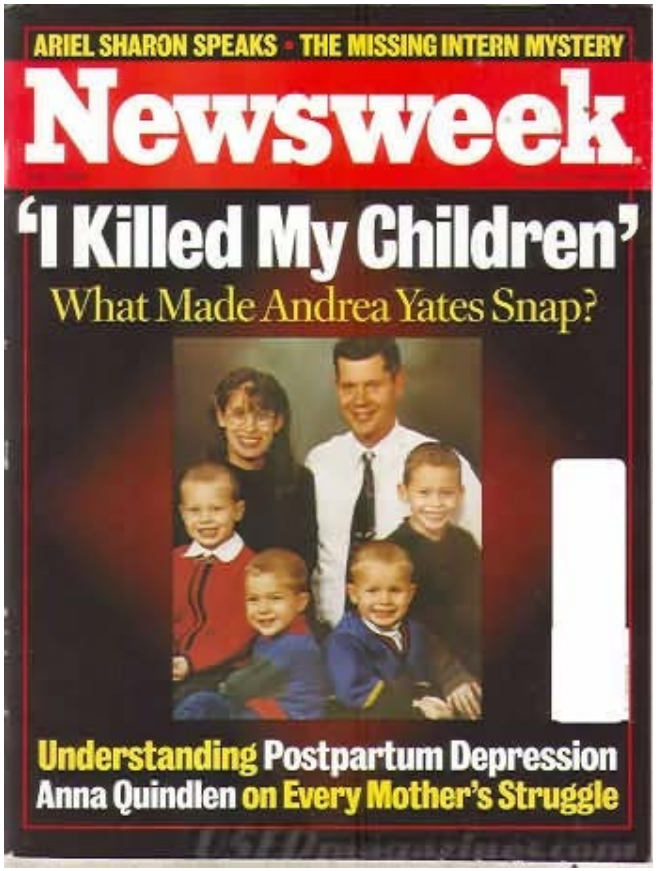
2001: Andrea Yates

1987: Postpartum Support International

2005: Brooke Shields

2007: MOTHERS Act

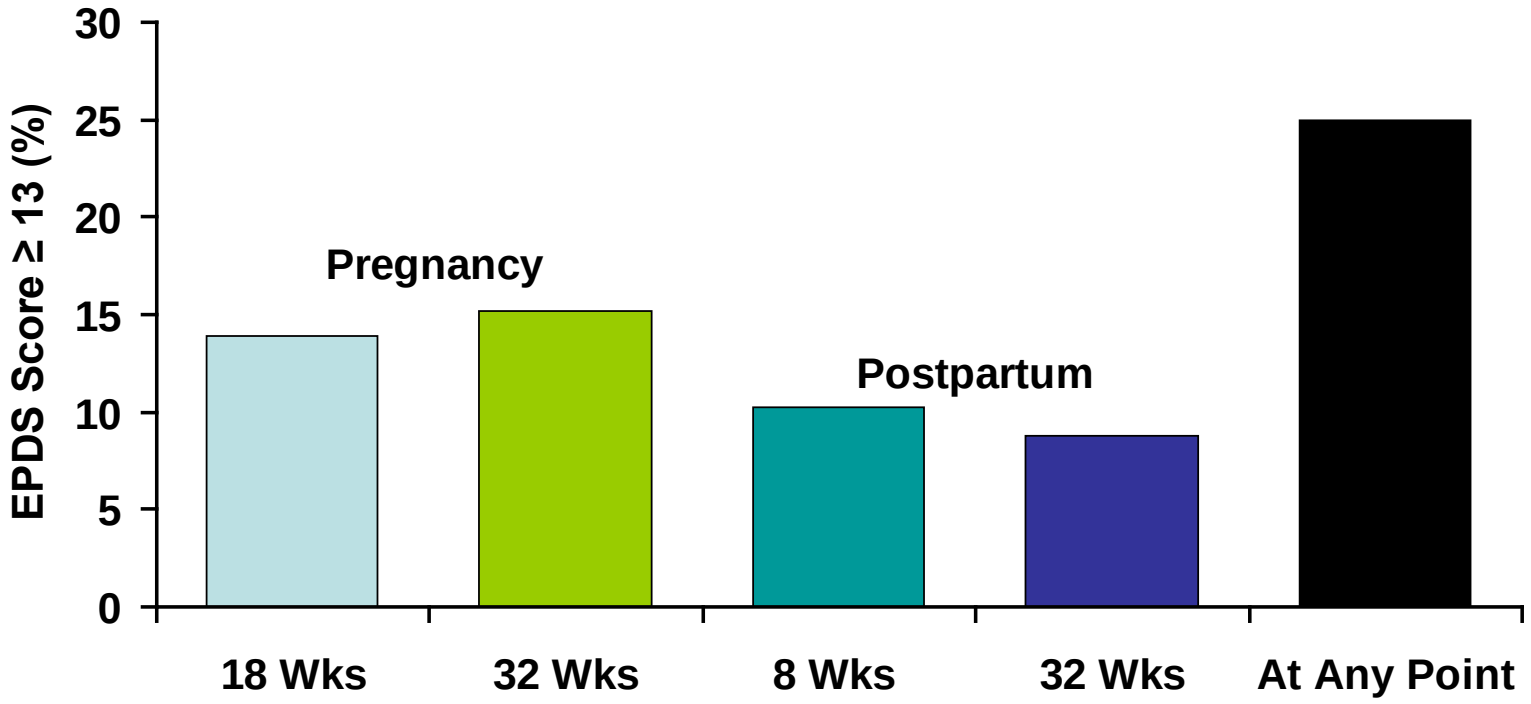
Perinatal Psychiatric Illness in the Media



2001

2017

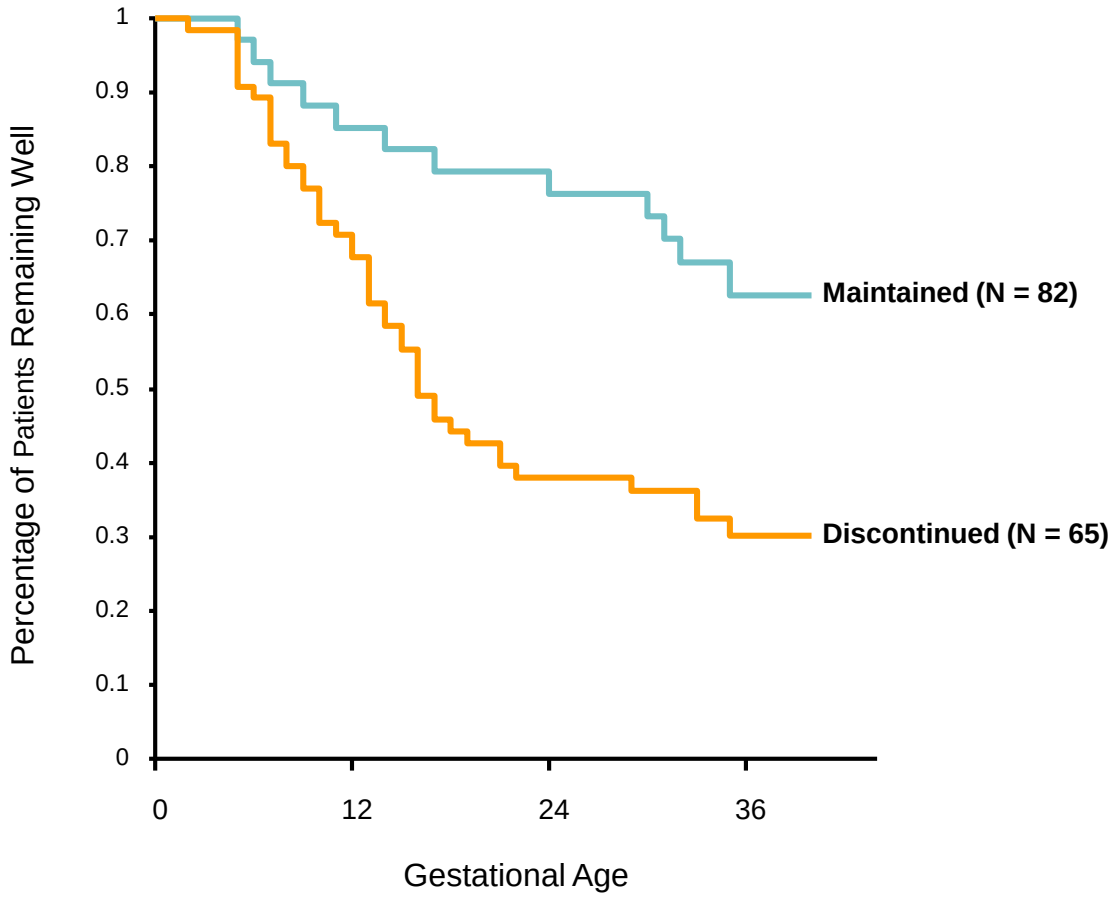
Depression During Pregnancy and the Postpartum Period



Results from 12,059 women screened with the Edinburgh Postnatal Depression Scale (EPDS) during pregnancy and postpartum period.

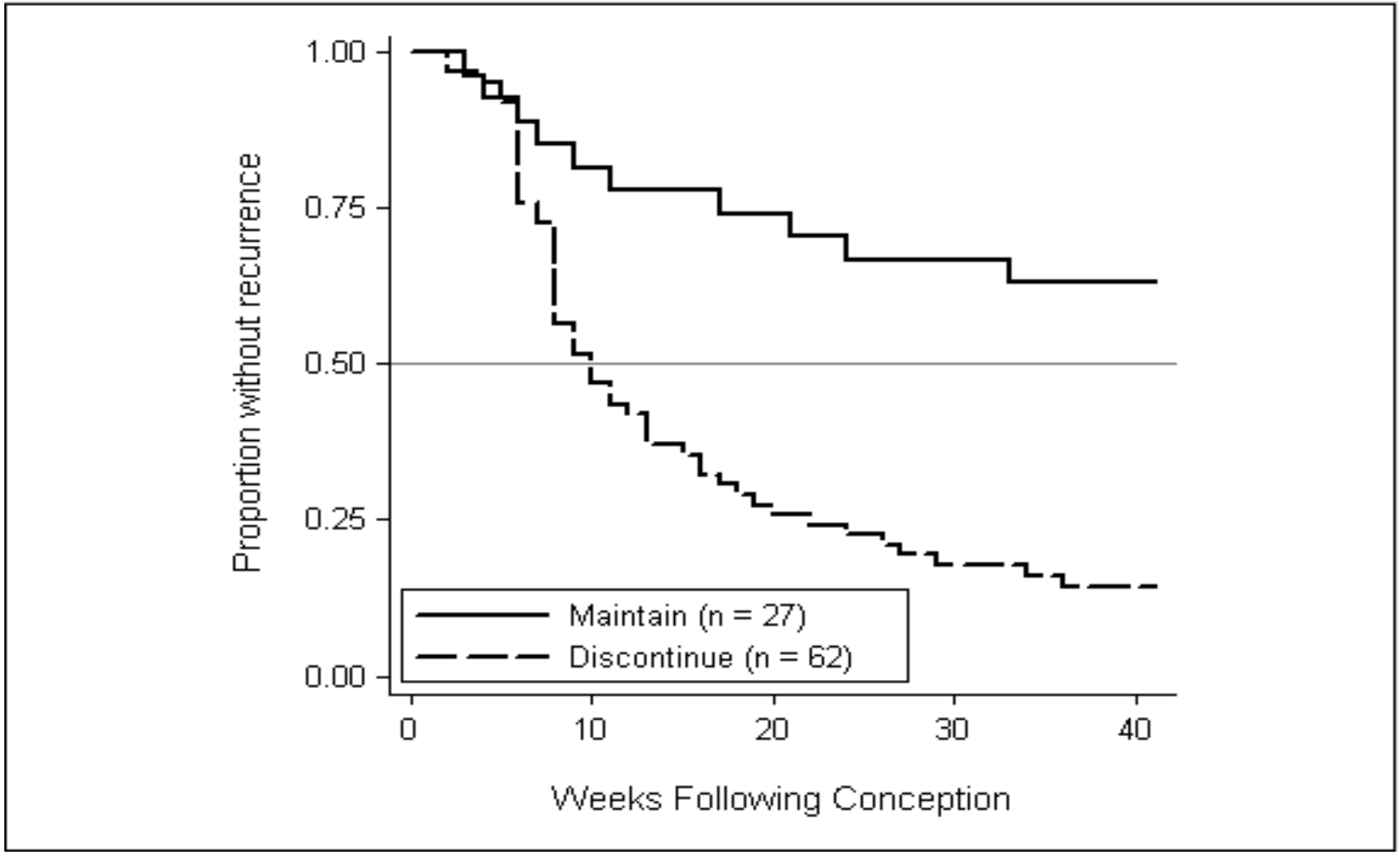
Evans J et al. *BMJ.* 2001;323:257-260.

Time to Relapse in Pregnant Women with MDD Who Maintain or Discontinue Antidepressant



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

Time to Relapse in Pregnant Women with Bipolar Disorder Who Maintain or Discontinue Mood Stabilizer



Viguera, et al , Am J Psychiatry, 2007

Perinatal Anxiety Disorders

- Inconsistent data on the prevalence and course of anxiety disorders during pregnancy
- About 15% of women report clinically significant anxiety symptoms
- Postpartum period associated with emergence or worsening of anxiety disorders
- Comorbidity: PPD commonly occurs with generalized anxiety, panic, OC symptoms

Goodman JH, et al. J Clin Psychiatry. 2014 Oct;75(10):1153-84.
Russell EJ, et al. J Clin Psychiatry. 2013 Apr;74(4):377-85.

How to Predict Which Women are at Greatest Risk?

History of psychiatric illness is most robust predictor of perinatal psychiatric illness

- Associated with previous pregnancy
- History of mood or anxiety disorder, PTSD

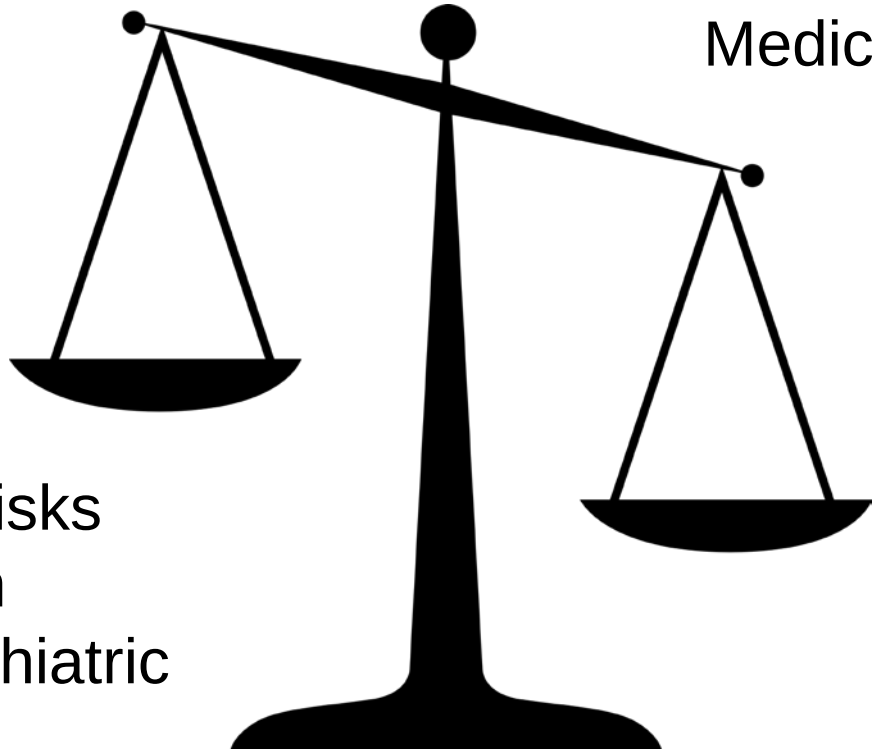
What drives this risk? Duration of illness? Stopping medication? Comorbidity? Stressful life events?

Which women can safely stop medications?

Which interventions reduce risk? Medication? Therapy? What kind of therapy?

Risk-Benefit Analysis

What are the Risks Associated with Medication Exposure?



What are the Risks Associated with Untreated Psychiatric Illness?

Published Data on Reproductive Safety

	1998	2018
Antidepressants	Fluoxetine Some tricyclics	Fluoxetine Sertraline Citalopram/Escitalopram Paroxetine Venlafaxine Duloxetine
Mood Stabilizers	Lithium Valproic Acid Carbamazepine	Lithium Valproic acid Carbamzeepine Lamotrigine Topiramate Levicetram
Anti-Anxiety Agents	Benzodiazepines	Benzodiazepines
Antipsychotic Agents	Haloperidol	Haloperidol Risperidone Olanzapine Quetiapine Aripiprazole

INFORMATION ON REPRODUCTIVE SAFETY

- Newer medications – insufficient data
  - Atypical antipsychotic medications
  - Newer antidepressants (e.g., esketamine)
- FDA does not require data on reproductive safety
- FDA labeling is in transition, confusing to prescribers
- Few registries to collect/aggregate data prospectively

National Pregnancy Registry for Atypical Antipsychotics

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

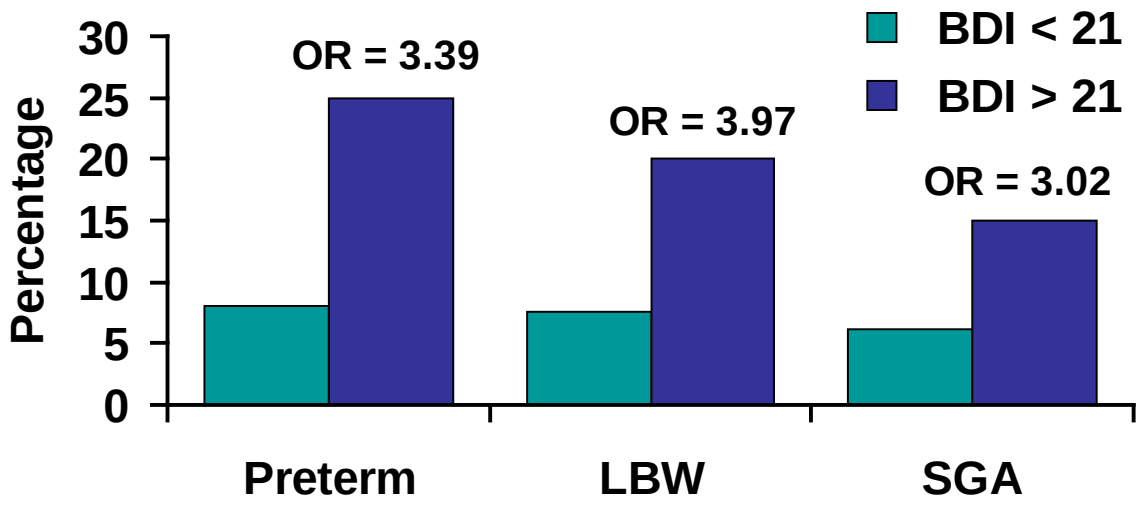
Depression During Pregnancy
What Are the Consequences?

- Poor compliance with prenatal care
- Risk of self-injurious or suicidal behaviors
- Increased use of tobacco, alcohol, and other substances
- Worse outcomes (e.g., shorter gestation, lower birth weight, small for gestational age)
- Increased risk of complications (e.g. HTN, pre-eclampsia, increased use of analgesia)

Kurki T et al. *Obstet Gynecol.* 2000;95:487-490.
Orr ST, Miller CA. *Epidemiol Rev.* 1995;17:165-171.
Zuckerman B et al. *Am J Obstet Gynecol.* 1989;160:1107-1111.
Bonari L et al. *Can J Psychiatry*. 2004;49:726-735.

Maternal Depression in Pregnancy
Obstetric Outcomes

389 Pregnant Women Screened with Beck Depression Inventory (BDI)



Preterm birth = < 37 wks; LBW = low birthweight (< 2500 g); SGA = small for gestational age.

Steer RA et al. *J Clin Epidemiol*. 1992;45:1093-1099.

Impact of Antenatal Depression on Infant Development

- Effect on fetal brain development and architecture
  - Amygdala – Increase in volume, changes in microarchitecture, connectivity
  - Right frontal EEG asymmetry (predicts negative affect and depressed mood in adults)
- Higher stress reactivity – Higher cortisol levels at baseline and in response to stress

- Soe NN, et al. PLoS One. 2016 Apr 13;11(4):
- Buss C, et al. Proc Natl Acad Sci USA 2012; 109: E1312–E1319.
- Rifkin-Graboi A, et al. Biol Psychiatry. 2013 Dec 1; 74(11):837-44.

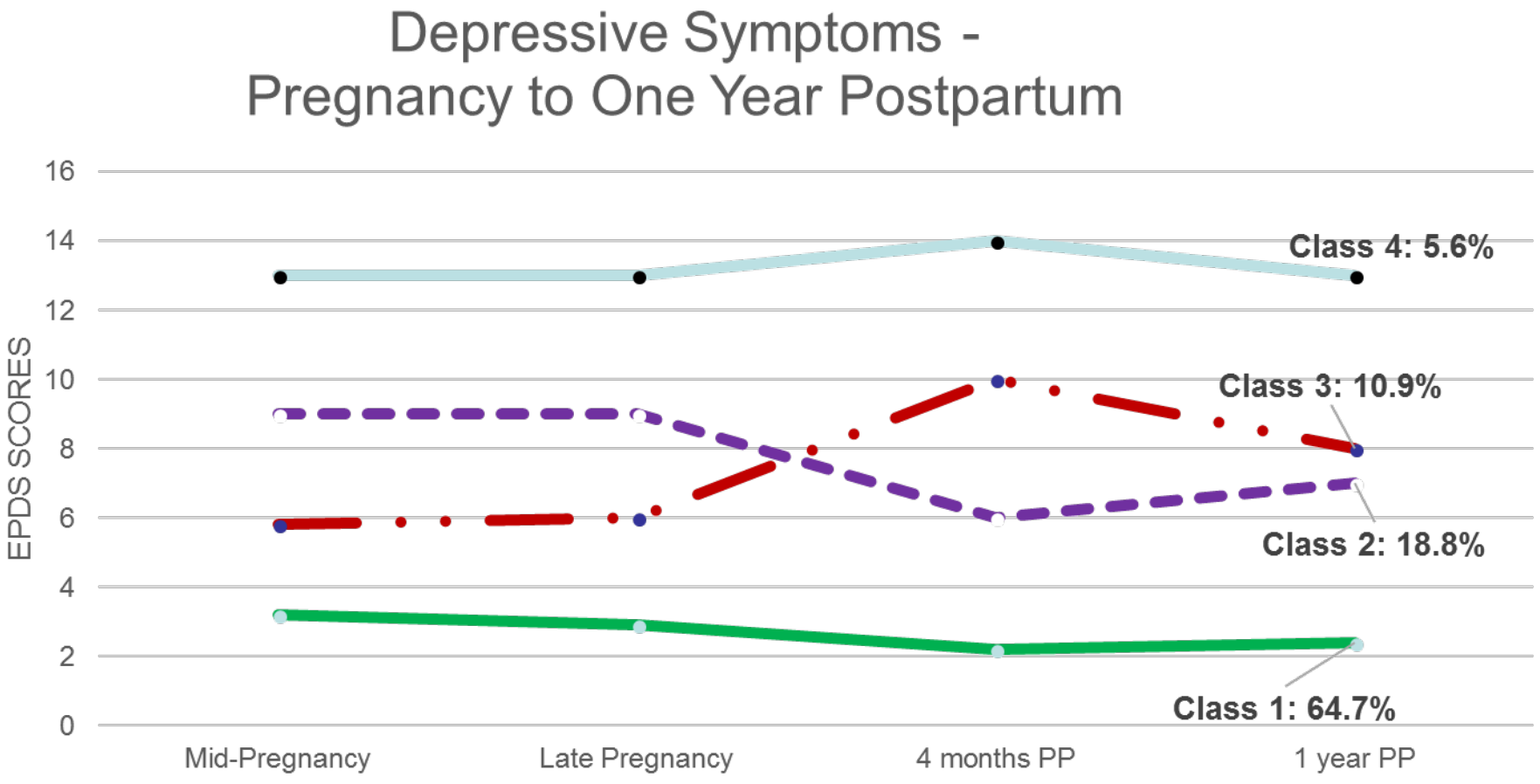
Antenatal Depression
Increased Risk of Psychiatric Illness in Children

- Avon Longitudinal Study of Parents and Children (ALSPAC)
- Community-based prospective study following mothers during pregnancy and children from birth to adulthood
- 3374 children
- 11.6% exposed to depression during pregnancy
- 7.4% exposed to postpartum depression
- Antenatal and postpartum depression act as independent risk factors for MDD in exposed adolescents
- Dose effect: Higher scores of both antenatal and postpartum depression associated with a higher risk of depression in the child

Pearson RM, Evans J, Kounali D, et al. JAMA Psychiatry. 2013 Oct 9.

Impact of Maternal Depression

Trajectory of Maternal Depression



All Our Families (AOF) in Alberta, Canada.
Maternal depressive symptoms assessed using EPDS
Kingston D, et al. PLoS One 2018.

Depression in Mothers of Younger Children

- 5303 mothers assessed
  - 28% with CES-D > 16 at 1.5 years
  - 20% with CES-D > 16 at 3 years
- Maternal depression associated with being unmarried, unemployed, health problems (in child or mother), low income
- Rates of depression 40%-50% in lower income populations

Civic D, Holt VL. *Matern Child Health J.* 2000;4:215-221.
McLennan JD et al. *J Am Acad Child Adolesc Psychiatry*. 2001;40:1316-1323.
Hall LA. *Public Health Nurs*. 1990;7:71-79.

Impact of Maternal Depression on Child Well-Being

- First year is time of increased vulnerability
- More likely to have insecure attachment
- Increased risk of behavioral problems
- Deficits in cognitive development
  - At ages 11 and 16: Lower IQ, attention (esp. in boys)
  - More prominent in moms with recurrent MDD
- HPA dysregulation: strongest predictor of cortisol levels in children (up to 16 yrs) is exposure to MDD (or stress) during first year of life

Atkinson L et al. *Clin Psychol Rev*. 2000;20:1019-1040.
Murray L, Cooper PJ. *Arch Dis Child.* 1997;77:99-101.
Hay D, et al. J Child Psychol Psychiatry 2008 Oct;49(10):1079-88.

Risk of Psychiatric Illness in Children Exposed to Parental Depression

- 78% of children had some psychiatric disorder
- Compared to children with nondepressed parents, children with a depressed parent have
  - 3-fold increased risk of depression, anxiety disorder
  - 5-fold increased risk of alcohol dependence
- Earlier onset of illness
  - Depression: 15-20 years
  - Anxiety disorders: 5-10 years
- Maternal remission was associated with a decrease in the child's symptoms
- Mother's relapse associated with an increase in the child's symptoms

Weissman MM et al. *Arch Gen Psychiatry.* 1997;54:932-940
Weissman MM et al, *Psychol Med*, 2014.

Public Awareness and Screening for Perinatal Mood and Anxiety Disorders

ACOG Recommends Universal Screening for Perinatal Mood and Anxiety Disorders

WHO?	• All women • Women with Hx of psychiatric illness at higher risk
WHY?	• Maternal psychiatric illness - worse pregnancy outcomes • Worse outcomes in children
HOW?	• Use of standardized assessments • How to screen for bipolar disorder? • How to screen for anxiety disorders?
WHEN?	• During pregnancy and the postpartum period • % of women do not return for PP visit • Last PP visit may occur at 6 weeks

Does screening for depression ensure treatment?

- 17 studies: Women screened for perinatal depression, assessed levels of subsequent treatment
- On average, 22% (13.8-33.0%) of women who screened positive for depression received >1 mental health visit
- Use of mental health services increased 2 to 4-fold when screening was combined with additional interventions geared to decrease potential barriers to treatment.

- Perinatal Depression Management Program multidisciplinary approach combining on-site screening and same-day evaluation by a perinatal care provider, training and support of perinatal healthcare providers: 90% entered into treatment

Obstacles to Treatment

- Stigma associated with psychiatric illness
- Cost of treatment
- Lack of insurance coverage
- Childcare issues
- Shortage of treaters with expertise in this area
- Misinformation

Media Coverage of SSRI Use and Risk for Autism

SUBSCRIBE

SCIENTIFIC AMERICAN

THE SCIENCES MIND HEALTH TECH SUSTAINABILITY EDUCATION VIDEO PODCASTS BLOGS STORE

REUTERS

HEALTH

Antidepressants in Pregnancy Tied to Autism

The new findings do not prove SSRIs cause autism, but they raise more questions about taking such medications late in pregnancy

December 14, 2015

SCIENTIFIC BLOGGING
SCIENCE 2.0

Taking Antidepressants During Pregnancy Increases Risk Of Autism By 87 Percent

By News Staff | December 19th 2015 10:58 AM | 1 comment | Print | E-mail | Track Comments

2K

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Major Study Links Autism To Antidepressant Use During Pregnancy

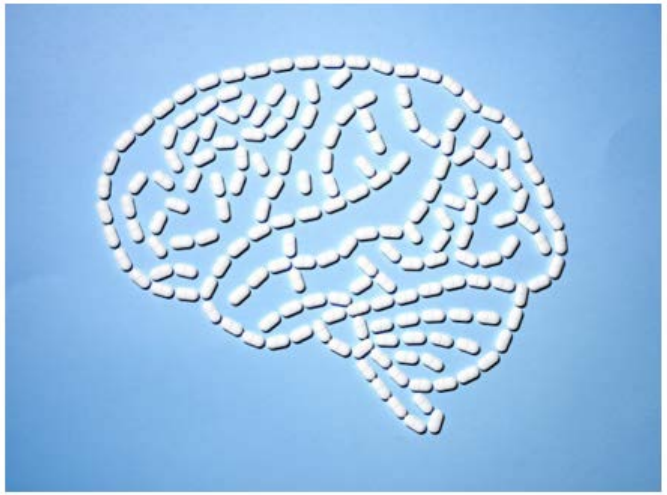
But this study doesn't necessarily mean you should quit your meds.

12/15/2015 05:33 pm ET

Anna Almendrala
Healthy Living Senior Editor, Huffington Post

SARAH ZHANG SCIENCE 12.14.15 11:00 AM

TAKING ANTIDEPRESSANTS WHILE PREGNANT MAY RAISE AUTISM RISKS, BUT IT'S COMPLICATED



OB/Gyn CME/CE

Antidepressant Birth Defect Risk Limited to Paxil and Prozac

— Researchers say other SSRIs are safe

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Fluoxetine, Paroxetine Linked to Increased Birth Defect Risks

Study Didn't Find Similar Risks for Other SSRIs

Depression >

Report: Prozac in Pregnancy Toxic to Fetus

Expert Panel Says Prozac Affects Fetus -- and Adult Sex

TODAY ON WEBMD

What Is Depression?

Differences between feeling depressed and feeling blue.

Celebrities With Depression

Antidepressants Side Effects to Birth Defects

Antidepressant drugs taken by women during pregnancy, have been linked to serious birth defects such as heart valve problems, cleft lip and palate, genital deformities and autism among others. Selective serotonin reuptake inhibitors, or SSRIs, first entered the US market in 1987 with the approval of Prozac. In many countries, SSRIs are the most widely prescribed antidepressants.

Side Effects:

Excessive Drowsiness
Excessive Diarrhea
Anhedonia

Dangerous Potential Birth Defects:

Pulmonary Valve Stenosis
Neural Tube Defects
Cleft Lip and Palate
Atrial Septal Defect

Antidepressant Drug Brands:

Celexa
Effexor
Lexapro
Paxil
Pristiq
Prosac
Wellbutrin
Zoloft

Antidepressants and Birth Defects Medical Studies:

The FDA in 2006, warned about the risk of neonatal persistent pulmonary hypertension. According to the FDA warning, physicians should be aware of the risks involved with prescribing Zoloft to pregnant women, and should never treat women with SSRIs late in pregnancy.

Other SSRI birth defects that have been linked to this class of drugs include seizures, cardiac malformations, cardiovascular malformations, omphalocele, and craniosynostosis.

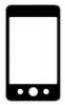
Antidepressants and Birth Defects Lawsuits:

GlaxoSmithKline (GSK), the drug company that has produced one of many SSRI drugs settled some 800 claims for an estimated $1 billion. This is in addition to other monetary settlements for an additional 200 antidepressant birth defect claims from June 2010.

800 Claims and $1 Billion

Antidepressants and Autism:

A recent study found that the use of SSRI antidepressants such as Celexa, Lexapro, Paxil, Prozac, or Zoloft during pregnancy doubled the chance that the child would develop an autism spectrum disorder. Individuals with autism often have difficulty regulating their levels of serotonin and evidence suggests that SSRI antidepressants' increase of serotonin in the brain of the mother could affect the development of the unborn child.



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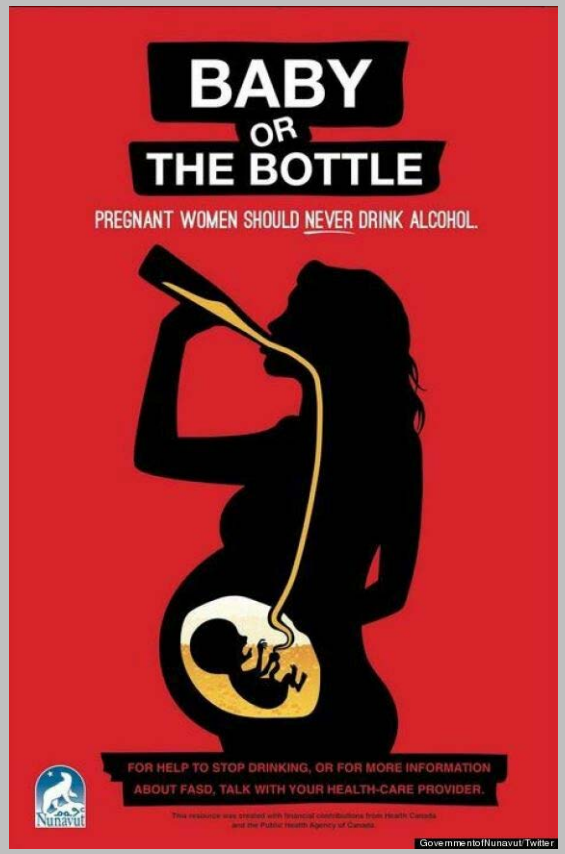
There is no "safe" level of smoking while pregnant.
Smoking during pregnancy affects you and yourbaby's health before, during, and after your baby is born.
Child's Voice Child's Voice CHILD'S VOICE


BABY OR THE BOTTLE
PREGNANT WOMEN SHOULD NEVER DRINK ALCOHOL.
FOR HELP TO STOP DRINKING, OR FOR MORE INFORMATION ABOUT FASD, TALK WITH YOUR HEALTH-CARE PROVIDER.
Nunavut
GovernmentofNunavut/Twitter

Summary

- About 20-25% of women suffer from clinically significant depression and/or anxiety during pregnancy and/or the postpartum period
- Women with histories of psychiatric illness are particularly vulnerable during pregnancy and the postpartum period
- More reproductive age women are stable on psychotropic medications; more women with psychiatric illness are planning to have children.
- Maternal psychiatric illness has a negative impact on child cognitive and emotional development and is associated with worse pregnancy outcomes.
- Growing body of regarding the safety of medications during pregnancy and lactation.

Moving Forward

- How do we identify reproductive age women at greatest risk for perinatal psychiatric illness
- What interventions decrease risk?
- How do we ensure women have access to treatment?
- How to ensure emotional well-being beyond the perinatal period?
- How to minimize impact of maternal depression on children

Thank You!!