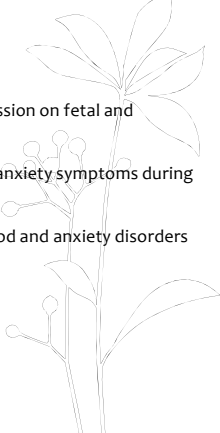
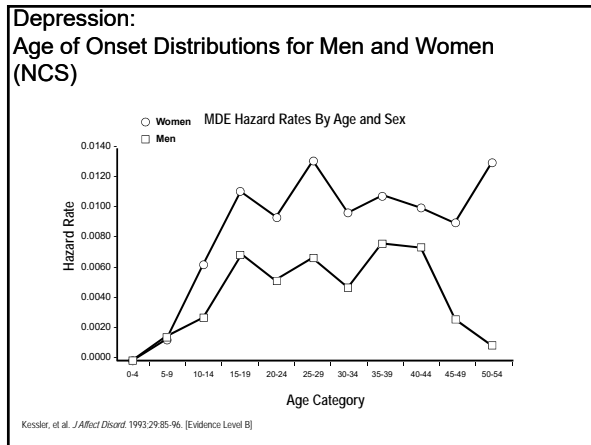


## MATERNAL DEPRESSION

Alison Reminick, MD  
 Director of Women's Reproductive Mental Health  
 University California, San Diego

### Objectives

- Describe the effects of maternal depression on fetal and neonatal health
- Describe normal changes in mood and anxiety symptoms during pregnancy and postpartum
- List and describe different types of mood and anxiety disorders in the postpartum

### Treating women of reproductive age

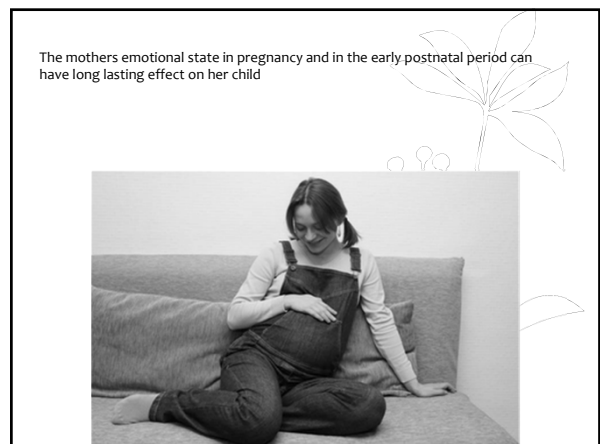
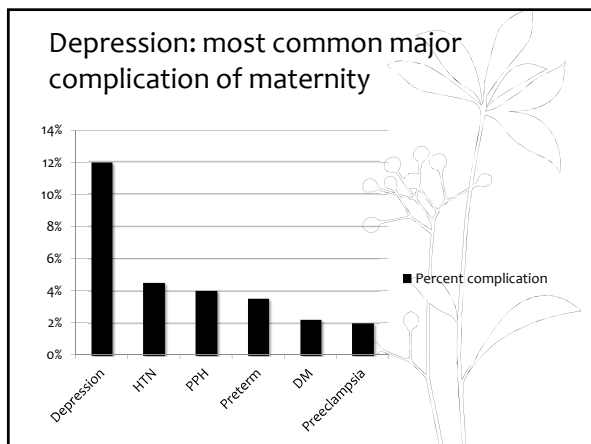
- 49% of pregnancies are unintended
- 82% of women have children
- Many clinicians do not discuss contraception/ family planning with their patients when prescribing medication

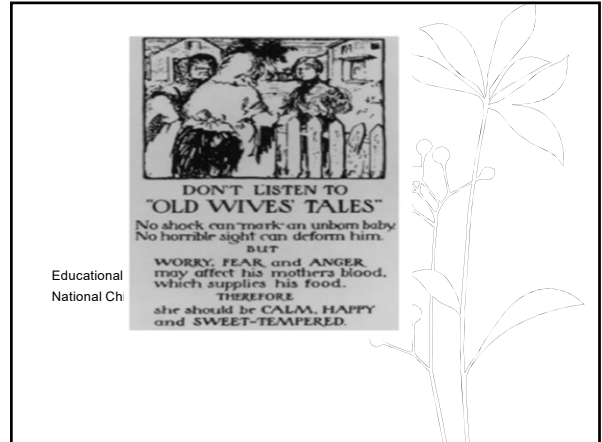
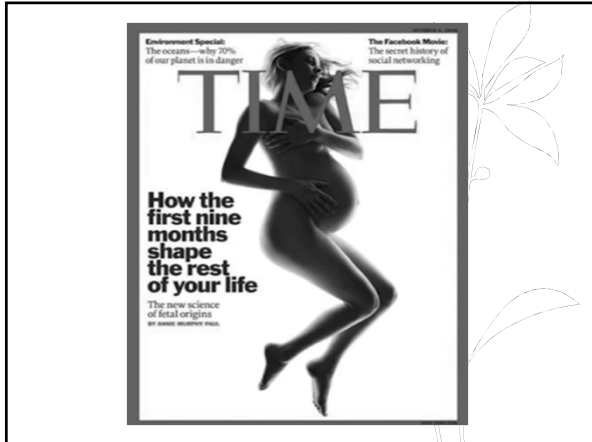
**FIGURE 1. Percentage distribution of pregnancies, by intendedness and outcome, 2001**

Category	Percentage
Unintended	49%
Intended	51%

N=6.4 million pregnancies

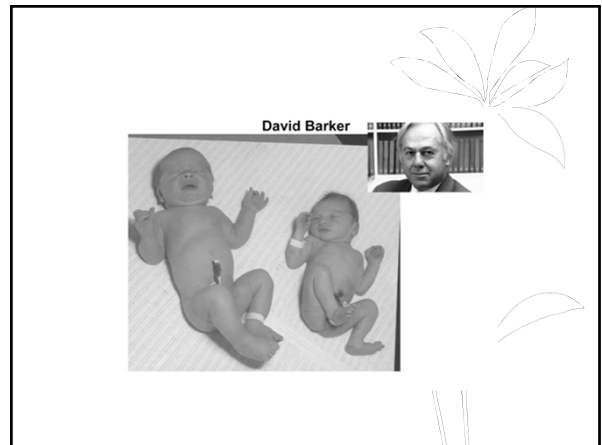
Finer, L and Henshaw K. Disparities in Rates of Unintended Pregnancy in the United States, 1994 and 2001. Perspectives on Sexual and Reproductive Health. Vol 38 (2), 90-96, 2006.





### Fetal Programming

The environment in the womb during different sensitive periods for specific outcomes can alter development of the fetus with long lasting effects on the child into adulthood



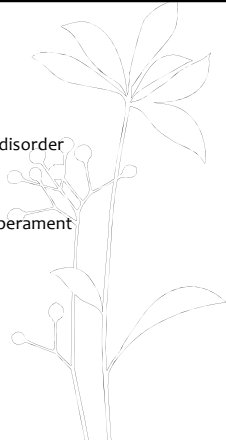
### National Institute of Child Health

The programming hypothesis brings a new perspective to public health. Diseases that were once thought to arise near the time of their manifestation are now known to have their roots in pre and early postnatal life

- ### Prenatal Stress in Humans
- Reduced birth weight
  - SGA
  - Asthma
  - Altered immune functioning
  - Decreased telomere length
  - Mixed handedness

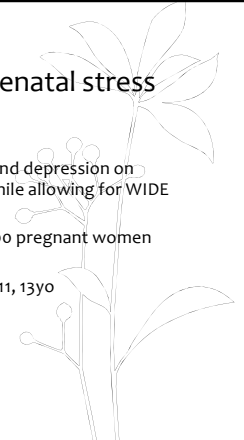
### Prenatal stress

- Increased anxiety and depression
- Behavioral problems, ADHD, conduct disorder
- Impaired cognitive development
- Sleep problems in infants
- Neonatal behavior/more difficult temperament
- Victimization in childhood
- Schizophrenia
- Autism



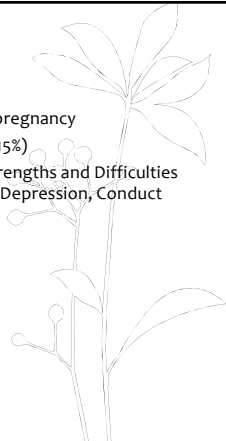
### ALSPAC Study: does antenatal stress affect child behavior

- Determine affects of antenatal stress and depression on behavioral development of the child while allowing for WIDE range of confounders
- Large prospective birth cohort N=14,000 pregnant women recruited in Bristol, UK 1990-1992
- Follow longitudinally children ages 4,7,11, 13yo



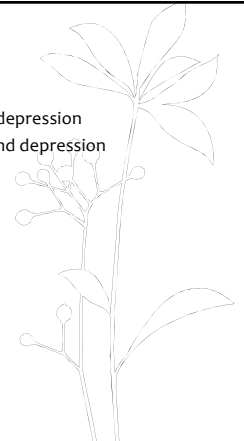
### ALSPAC Study

- Maternal anxiety at 18 and 32 wks of pregnancy
- Compared most anxious/depressed ( 15%)
- Child behavior: Report from 4-13yo Strengths and Difficulties Questionnaire (SDQ): ADHD, Anxiety, Depression, Conduct disorder

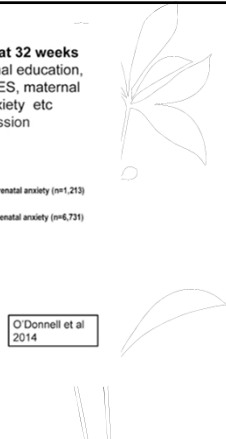
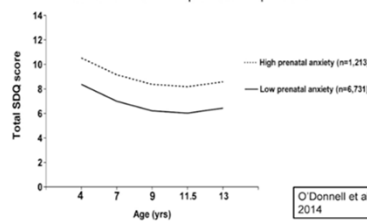


### Multivariate Analysis N=7,363

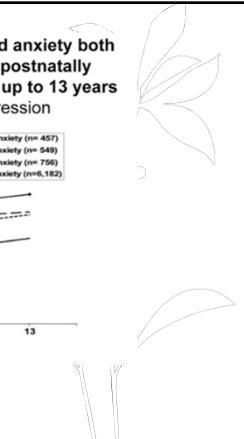
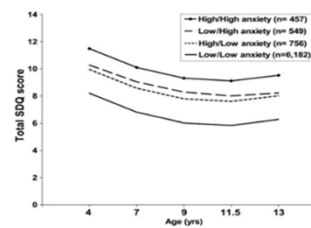
- Maternal and **Postnatal** anxiety and depression
- Paternal pre and postnatal anxiety and depression
- Parenting
- Maternal age
- Birth weight
- Gestational Age
- Smoking
- Alcohol
- SES
- Maternal education

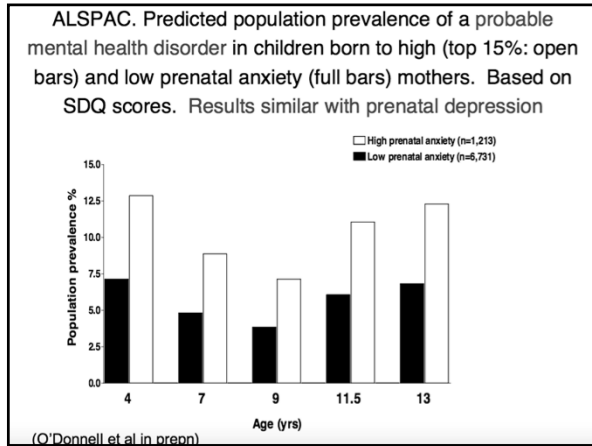


**Total SDQ scores and maternal anxiety at 32 weeks**  
 -allowing for BW, GA, maternal age, maternal education, postnatal depression, postnatal anxiety, SES, maternal substance use, parenting, paternal anxiety etc  
 Results similar with prenatal depression



**The combined effects of raised anxiety both antenatally (32 weeks) and postnatally (33months) on child outcome up to 13 years**  
 Similar results with depression

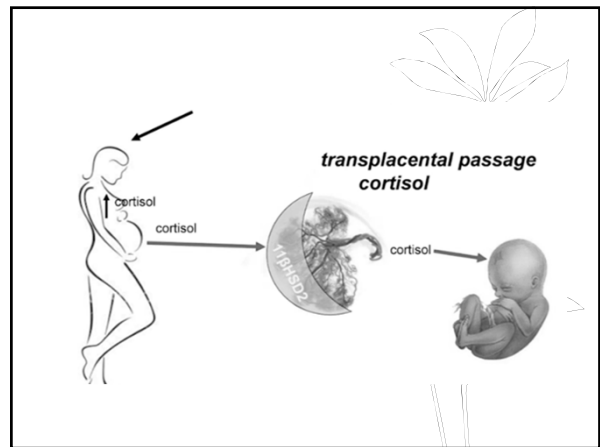
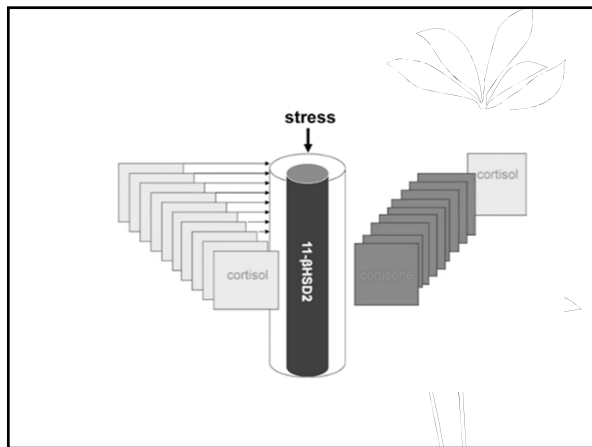
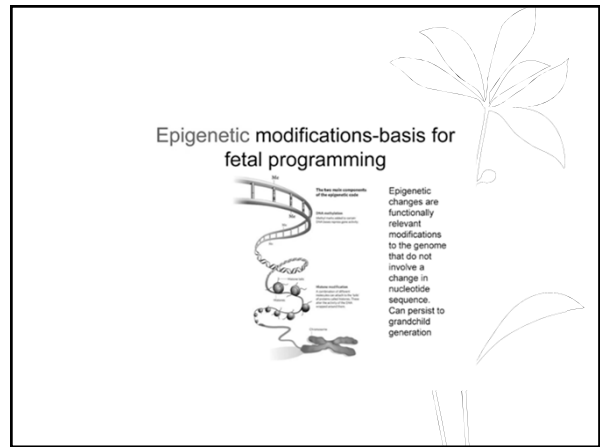


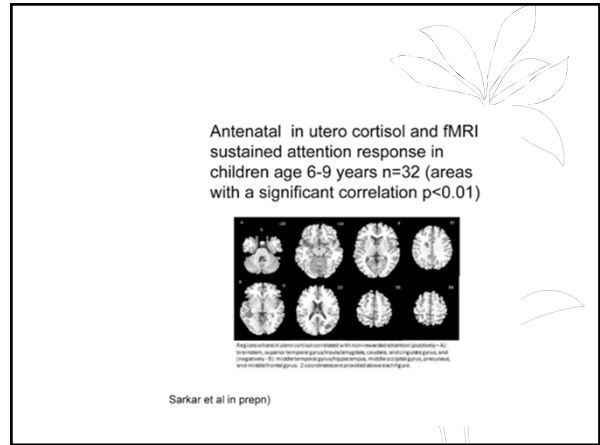
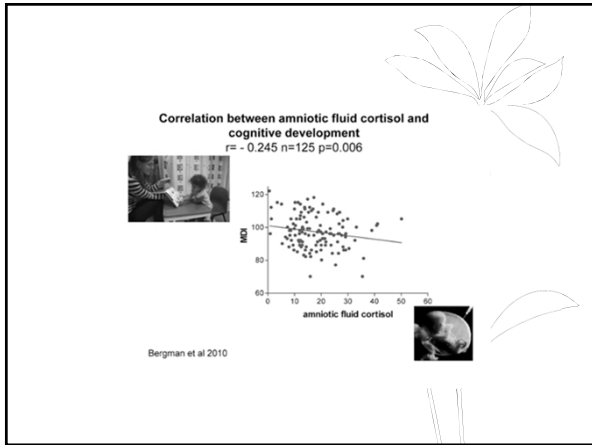
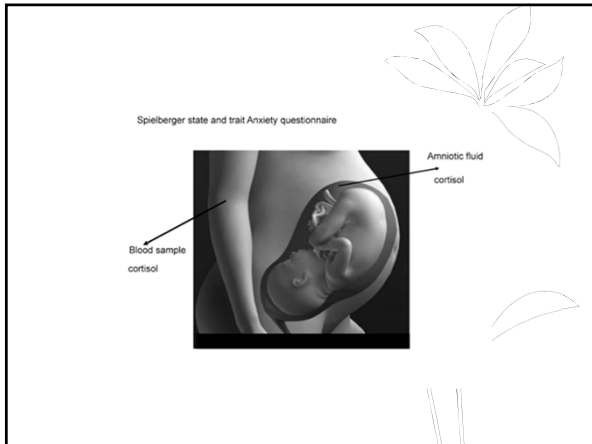


- Links are similar with prenatal anxiety at 18 wks gestation
- Similar with depression
- Not just first trimester

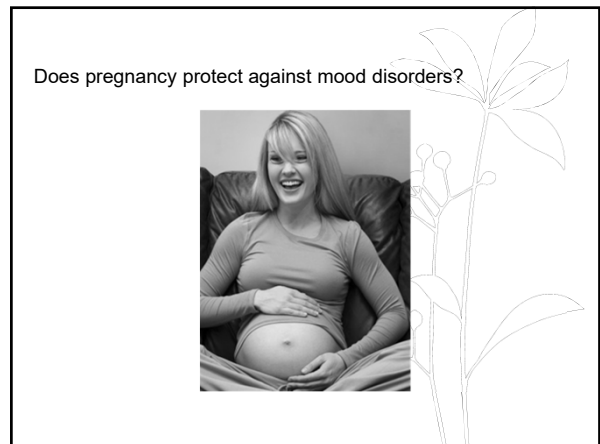
Summary of ALSPAC

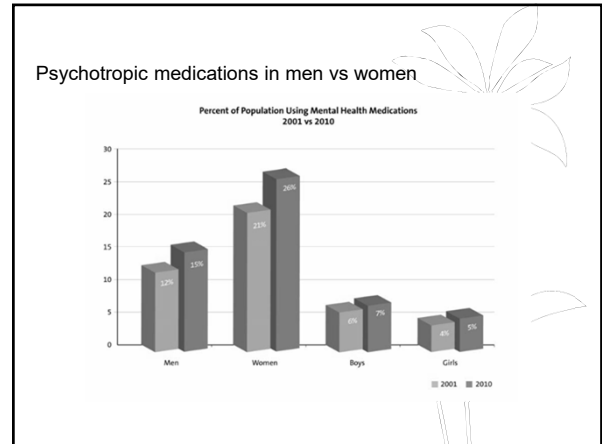
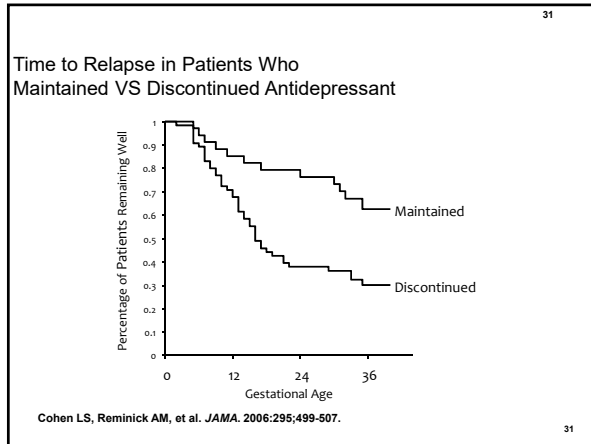
- For 15% most anxious/ depressed pregnant women the rate of mental illness in children doubled from 6 to 12% at age 13 after controlling for WIDE range of confounders
- Attributable load of prenatal anxiety and depression in association with a mental disorder is 10-15%





- Higher in utero exposure to cortisol is associated with lower cognitive function
- Sensitive early mothering can reverse the effects of high in utero exposure to cortisol





### Women: Psychotropic Medications

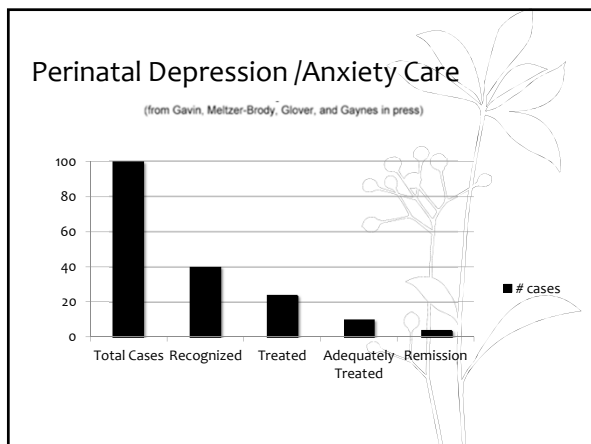
- Analysis from prescription claims data from 2.5 million Americans from 2001 to 2010
- 1 out of 4 women are dispensed medication for a mental health condition, compared to just 15 percent of men
- Antidepressant use among women is up 29 percent since 2001

### Suicide leading cause of maternal death

- Suicide and homicide are leading causes of maternal death

**EDITORIAL**

Suicide: the leading cause of maternal death  
 MARGARET OATES  
 The British Journal of Psychiatry Sep 2003, 183 (4) 279-281; DOI: 10.1192/bjp.183.4.279



### Summary of current knowledge about SSRI during pregnancy

- NO increase risk
  - Birth defects
  - IQ reduction or behavioral problems
  - Autism
- Increased risk
  - Neonatal side effects, esp tremor
  - Premature labor (as does untreated depression)
  - Neonatal persistent pulmonary hypertension (very, very rare)
- Might increase risk
  - Miscarriage (highest quality studies do not show increased risk)
  - Low birth weight (not clinically significant)

### Long term sequelae OF AD EXPOSURE

- Fluoxetine (prozac) (n=135) vs. vs TCA non-exposed
- No significant differences up to age 7 : IQ, language, temperament, behavior, mood, distractibility, or activity level
- Delayed language maturation associated with maternal depressive symptoms, not with SSRIs
- Autism: initial study found small increased risk. Subsequent studies have ruled out after controlling for confounders
  - Same level of risk for non-exposed sibling

Nulman et al. N Engl Med 1997  
Nulman et al. Am J Psychiatry 2003

### Why do we care?

How does depression affect mom, fetus and neonate?

### Depression Risks

#### Risk to mother:

- worsened depression
- preeclampsia (2.3-3.2 RR)
- increased risk of postpartum depression and somatic symptoms PP (HA, fatigue)
- possible increased risk SAB

Ansara et al. Journal of Psychosomatic Obstetrics & Gynecology, 26(2), 115 - 125  
Qiu, et al. BMC Women's Health, 2007, 7:15

### Depression Risks in Pregnancy

#### Risk to baby:

- Poor maternal self-care during pregnancy
- Pre-term birth (RR 2.0-2.2)
- Lower birth weight (180-200gms)
- Poor bonding postpartum
- Incr infant neg reactivity (esp >30wks)
- Infant sleep disturbance
- Child anxiety, language delay, ADHD, conduct disorder
- Incr adolescent depressive sx's

Davis et al. J Am Academy of Child and Adolescent Psychiatry, 2007, 46(6): 737-746  
Hollins, Current Opin Obstet and Gyn, 2007, 19:568-572  
Li et al. Human Reproduction, Vol.24, No.1 pp. 146-153, 2009

### Depression Risks Postpartum

#### Maternal depression and anxiety linked to:

- Withdrawn mother: fussy baby
- Anxious, intrusive mother: detached baby
- Lower IQ
- Delayed language development
- Poor infant growth and incr diarrheal episodes
- Higher rates of anxiety and depressive sx's, and behavioral problems in toddlers, preadolescents and adults

Edhborg, Arch Women's Mental Health 2003; 6(3): 211-6  
Hollins, Current Opinions in Obstetrics and Gynecology, 2007, 19:568-572  
Rahman et al, Acta Psychiatr Scand, 2007; 115:481-486  
Weinberg, Pediatrics 1998; 101(5): 1298-1304

### Depression Risks Postpartum

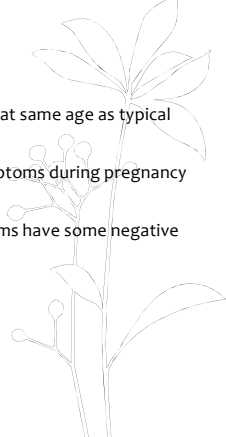
#### Remission of maternal depression benefits children:

- 151 mother-child pairs in STAR\*D study
- Remission of maternal depression after 3 mos of treatment associated with significant reductions in children's depressive, anxiety and disruptive behavior disorders and symptoms

Weissman, JAMA 2006; 295(12): 1389-98

## Major Depression

- Women in reproductive age group are at same age as typical onset of MDD
- 10-15% of women have depressive symptoms during pregnancy and postpartum
- Many women with depressive symptoms have some negative impact on function as a result



## Behavioral Effects?

### SSRIS AND AUTISTIC SPECTRUM DISORDERS:

Is there evidence of risk?

Caveat: Read each study very carefully before coming to conclusions...

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## Kaiser Permanente Medical Care Program: Croen Article 2011

- Population based case-control study
- Based on pharmacy and medical records
- 298 case children and mothers, arbitrary exclusion criteria based on date of study
- 1507 control children and mothers
- 20 case (6.7%) children and 50 control (3.3%) children exposed to SSRIs
- 2 fold increase risk of ASD with SSRI exposure
- Particularly with 1st trimester exposure

Croen La et al: Arch Gen Psychiatry. 2011 Nov;68(11):1104-12.

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## SSRIs and Autism:

### Case study in how the media can mislead

- Problems with Croen study:
  - based on only 20 exposures (actually only 15 after exclusions)
  - Family genetic risk not reported
  - Did not report underlying medical illness, smoking, EtOH use, substance abuse, other prescription or OTC medications
  - Psychiatric illness in mother not accounted for as risk factor for autism
- Result: many women stopped medication, and became ill

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## SSRIs and Autism

- Compared sibling pairs (exposed and unexposed)
- Conclusion: **No evidence that SSRIs are neurotoxic**
- **Maternal depression CAN be neurotoxic**  
(Nulman et al. J Clin Psychiatry. 2015 Jul;76(7))
- Data were drawn from three large Boston-based health systems and state birth certificates.
- For both ASD and ADHD, no significant increase in risk associated with prenatal antidepressant exposure (Castro VM, Translational Psychiatry (2016) 6, e708)

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## Summary of VPA Findings Across Pregnancy Registries

- Valproic acid (VPA) is associated with highest risk for all major malformations >20%
- Spina bifida risk 1-5% (15-30 days postfertilization)
- Craniofacial defects [incl. oral clefts], heart defects, polydactyly, hypospadias, LBW
- Cognitive developmental delay

Wyszynski DF et al. Neurology 2005;64:961-5  
Morrow J et al. J Neurolog Neurosurg Psychiatr 2006;77:193-8  
Cunnington M et al. Epilepsia. 2007;48:1207-10  
Meador KJ et al. Neurology. 2006;67:407-12  
Holmes LB et al. Arch Neurol 2004;61:673-8



### Valproate

- “Fetal valproate syndrome”
- Organ dysgenesis: NTD 5-9%
  - Risk dose dependent
  - related to use 17-30 days postconception
- Intrauterine growth: part of “fetal valproate syndrome”
- Neurobehavioral: data not definitive, MR?
- Neonatal toxicity: HR decelerations, irritability, feeding difficulties, abnormal tone
- Use during pregnancy:
  - switch to another mood stabilizer before conception

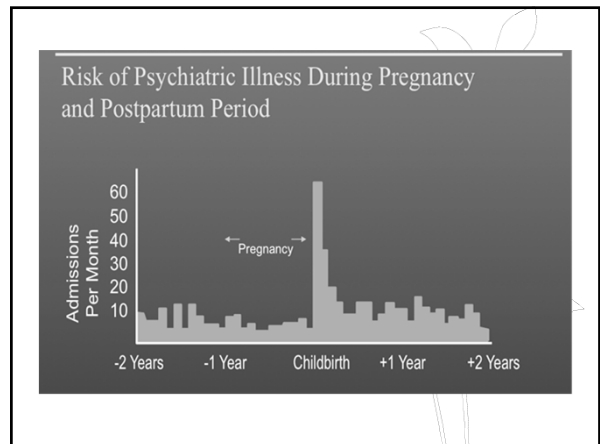
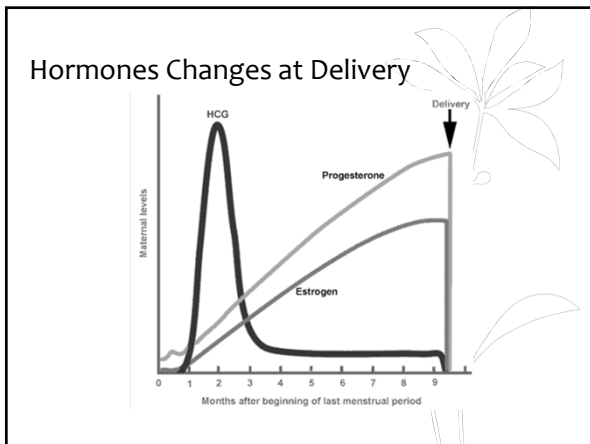
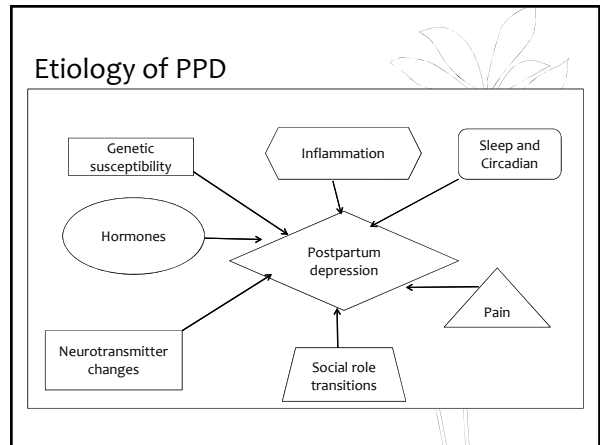
### Valproate (VPA) teratogenicity

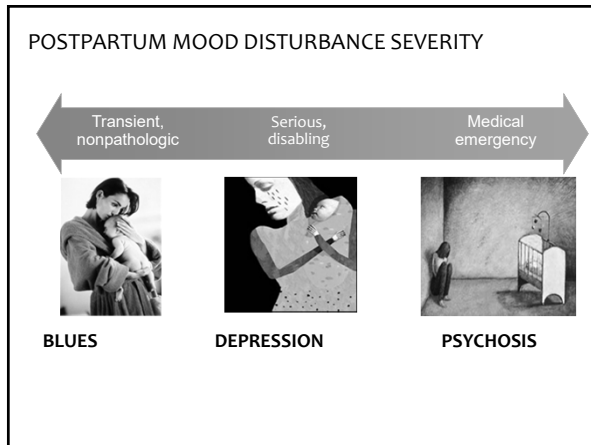
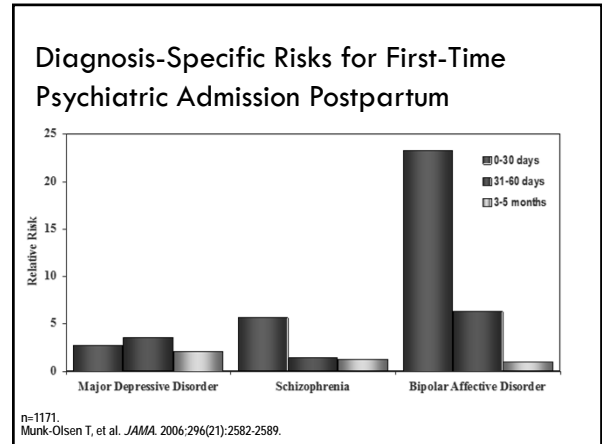
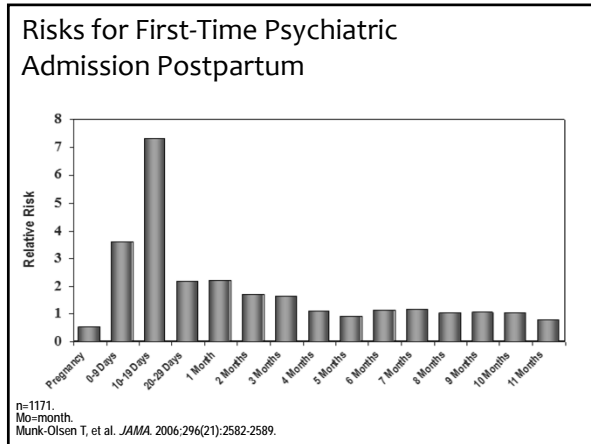
- Increased risk of neural tube defects
  - Risk increased by obesity and low folate
- Increased risk of other anomalies
- Increased risk of developmental delay, lower IQ
- Possible increased risk of autism
- Higher teratogenicity risks than other mood stabilizing medications
- Risks may be dose dependent, significantly greater with doses of >1000mg

### Long-term Effects of Li

- Observational retrospective study of 15 children investigated at 3-15 years of age
- 1 child had signs of minor neurological dysfunction but without further clinical implications
- Cognitive, behavioral and general development not affected

Van der Lugt, M. et al. Fetal, Neonatal and Developmental Outcomes of Lithium-exposed Pregnancies. Early Human Development 2012; 88:375-375.





### Postpartum Mood Disorders

Disorder	Incidence (%)
Postpartum blues	80%
Postpartum depression	10-22%
Postpartum psychosis	0.1%

Suri and Burt, 1997

- ### Impact of PPD on infant
- Poor maternal child bonding / attachment disorders
  - Less likely to breastfeed
  - Failure to thrive
  - Lower global IQ / poor language/ cognitive and social delay
  - Developmental delay on Bayley Scale at 1 year
  - Behavioral problems / emotional dysregulation
  - Early onset of ADHD, mood, anxiety conduct disorders, autism
  - Suicide/infanticide
- McLearn, Minkovitz, Siroshio, et al., 2006  
 Beck, 1998  
 Sola-Preston 2006

### UCSD Maternal Mental Health IOP

Postpartum Health Alliance : [postpartumhealthalliance.org](http://postpartumhealthalliance.org)

Postpartum Support International

Apps: PPD Gone (Shoshanna Bennett, PhD)

## Resources for Medications in Pregnancy and Breastfeeding

- **Reprotox:** [www.reprotox.org](http://www.reprotox.org)
- **Motherisk.org** [www.motherisk.org](http://www.motherisk.org) 1-877-439-2744
- **Infantrisk.com** (806)-352-2519 also phone app available
- **MothertoBaby:** [www.mothertobaby.org](http://www.mothertobaby.org) Good Handouts
- **MGH women's mental health program:**  
[www.womensmentalhealth.org](http://www.womensmentalhealth.org)
- **LactMed:** [www.lactmed.nlm.nih.gov](http://www.lactmed.nlm.nih.gov)
- **E-Lactania:** <http://www.e-lactancia.org/ingles/inicio.asp>
- **toxnet.nlm.nih.gov**

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*"Your wife's on the phone. She wants to know if you can watch the baby later so she can get in her daily 4 hours of sleep."*

Healthy mom = healthy baby

