



Prescribing for Pregnant Patients: Pause/Ponder/Proceed?

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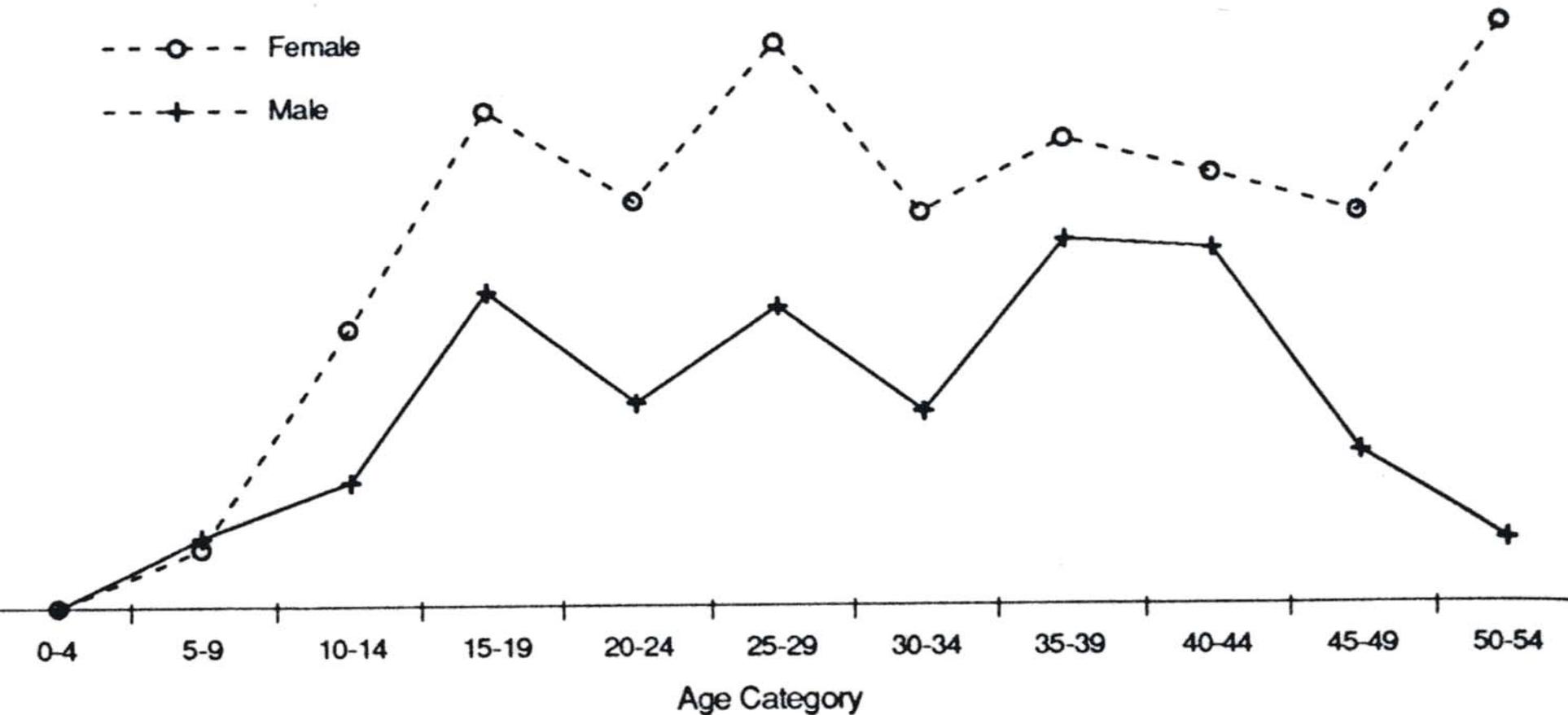
Maternal Disease Burden: Depression

You say that I'm depressed
I wonder if you understand
You've never lived, I think
In this God-forsaken land
I always fight to function
I'm fighting to survive
I'm trying desperately to remember
What it's like to feel alive
You say I'm carrying life inside
How can that really be?
How could life possibly survive
In a non-existent me?



Prevalence of Depression in Men and Women Across the Life Cycle

Lifetime-- 21% women; 12% men





Major Depression Recurrence during Pregnancy

- Recurrence risk for women who either maintained or discontinued antidepressants proximal to conception (*Cohen et al, JAMA 295:499-507, 2006*)
- Significantly more women who discontinued (44/65, 68%) compared to women who maintained (21/82, 26%) treatment suffered recurrent depression.
- Most recurrences emerged rapidly (50% in the first trimester, and 90% by the end of second trimester).

Risk-Benefit Decision-Making for Depression during Pregnancy: A Framework

- Wisner et al: Risk-benefit decision-making for treatment of depression during pregnancy. *Am J Psych* 157: 1933-1940, 2000
- Healthy outcomes for mother and baby are the rule rather than the exception!

Initial Structure to Consultation

- Woman (partner) expectations of consultation, primary concerns
- Knowledge of pregnancy physiology
- Knowledge of risk concepts
- Awareness of birth outcome information (defects 3%, no guarantee of normally formed child even without exposures)
- Understanding of disease and treatment exposures during pregnancy
- Decision process preferences (*Patel and Wisner, Depression and Anxiety 28:589-95, 2011*)

Approach-Data Collection

- Diagnostic Assessment
- History: Medical, Treatment, Substance Use, Reproductive
- Current - Standardized Measure of Symptom severity/type and Function
- Exposures since conception (smoking, alcohol, other drugs, environmental)
- Disease exposure (hyperglycemia/diabetes, obesity, hypothyroidism, other)
- Pregnancy Course, Testing

Approach –Data Analysis

- Evidence-based treatment for individual situation
- Discussions of modifications of above due to pregnancy (if appropriate)
- Non-drug interventions to augment impact of drug treatment/improve pregnancy outcome
- Document the woman's questions/ feedback/ rationale for decision

PHYSICIAN:

STRUCTURE OF PROBLEM

- Diagnostic Formulation
- Treatment Options for disorder
 - Somatic:
 - Antidepressants
 - ECT
 - Other
 - Psychotherapy
 - No Treatment

PHYSICIAN:

LIKELIHOOD OF OUTCOMES

- Fetal Toxicity
 - None
 - Intrauterine Death
 - Physical Malformations
 - Growth Impairment
 - Behavioral Teratogenicity
 - Neonatal Toxicity
- Depression Outcomes
 - Full Remission
 - Partial remission
 - No Improvement
 - Worsening

PATIENT:

VALUES OF OUTCOMES

- Evidence of Competency to Consent

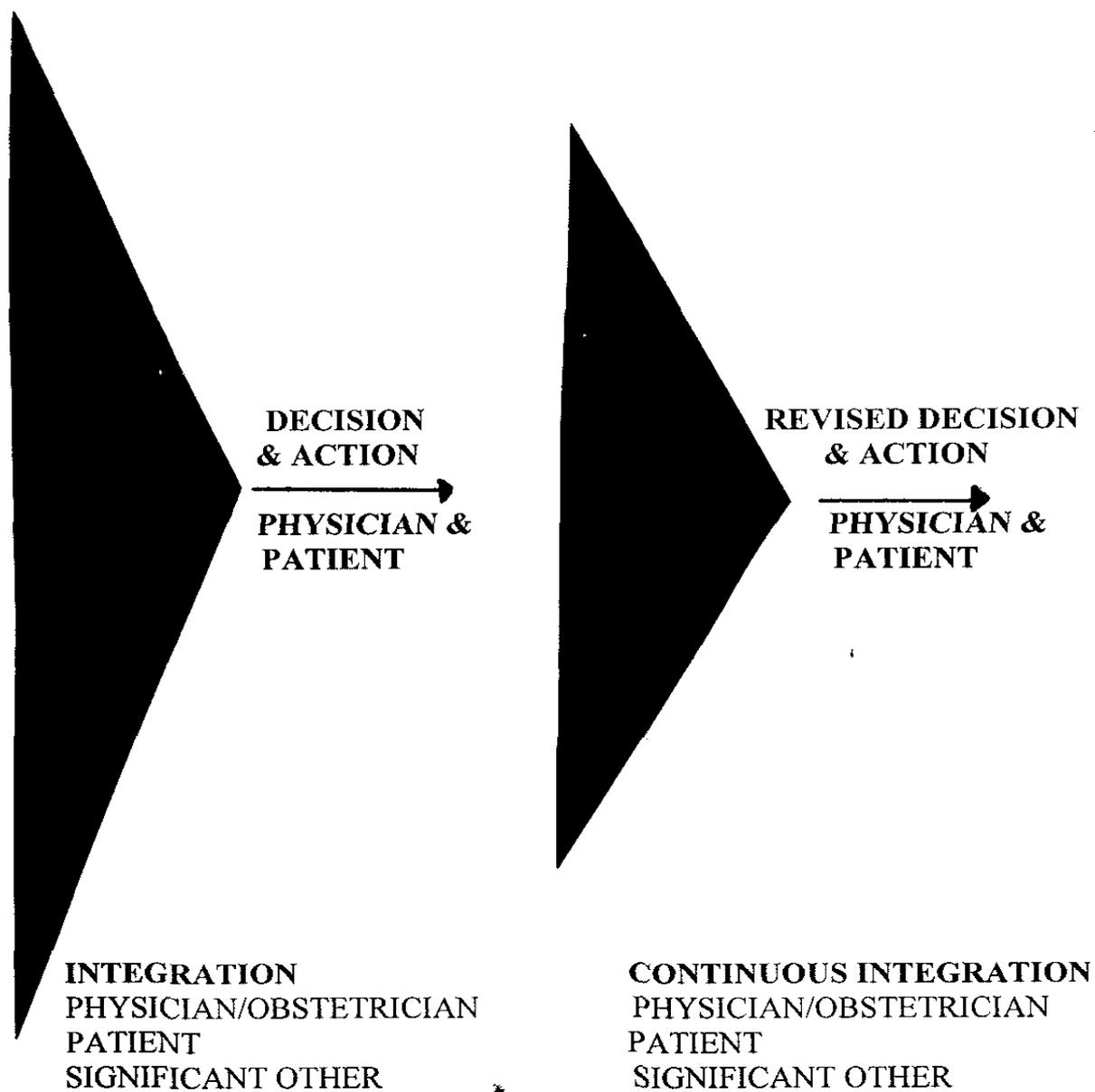


FIGURE 1 MODEL FOR DECISION-MAKING: DEPRESSION DURING PREGNANCY

Risks are More Heavily Weighted Than Benefits



**Antidepressant treatment during pregnancy:
Are we asking the right questions?**

Wisner, Depression and Anxiety: 27:695-698, 2010

Summary Points

- **Intrauterine Fetal Death-** No conclusive evidence; women with SSRI antidepressants and/or major depressive disorder (MDD) exposure have higher risk for miscarriage
- **Physical Malformations-** Specific defects (if any) are rare and absolute risks are small. *Greene, M. F. (2007). Teratogenicity of SSRIs -- Serious Concern or Much Ado about Little? NEJM 356: 2732-2733*
- **Growth- Maternal Weight Gain, Pregnancy duration, Birth weight-** Small for Gestational Age (SGA) inconsistently reported with SSRI exposure. Preterm Birth (PTB)--a converging finding for SSRI exposure-- MDD associated with a similar level of risk for PTB (*Wisner et al, Am J Psychiatry 166:557-566, 2009*). SGA and PTB associated with MDD (*Grote et al, Arch Gen Psychiatry 67(10):1012-1024, 2010*)

Summary Points

- **Behavioral Teratogenicity-** Offspring exposed to antidepressants similar to controls in cognitive function, expressive language, mood, activity levels, distractibility, behavior problems, temperament (*Nulman et al, NEJM 336:258-262, 1997*)

Casper et al (*J Pediatr 142:402-408, 2003*) found less favorable motor (not mental) development in SSRI vs. depression exposed in toddlers.

No difference in neuromotor function at 6 months in SSRI exposed vs. controls (*Johnson et al, Arch Gen Psych 69:787-794, 2012*).

Pedersen et al (*Pediatrics, Feb, 2010*) normal milestone development in SSRI exposed vs. depressed and controls.

Prenatal antidepressant exposure not associated with behavioral or emotional problems. (*Pedersen, Acta Psychiatrica Scand, Nov, 2012*).

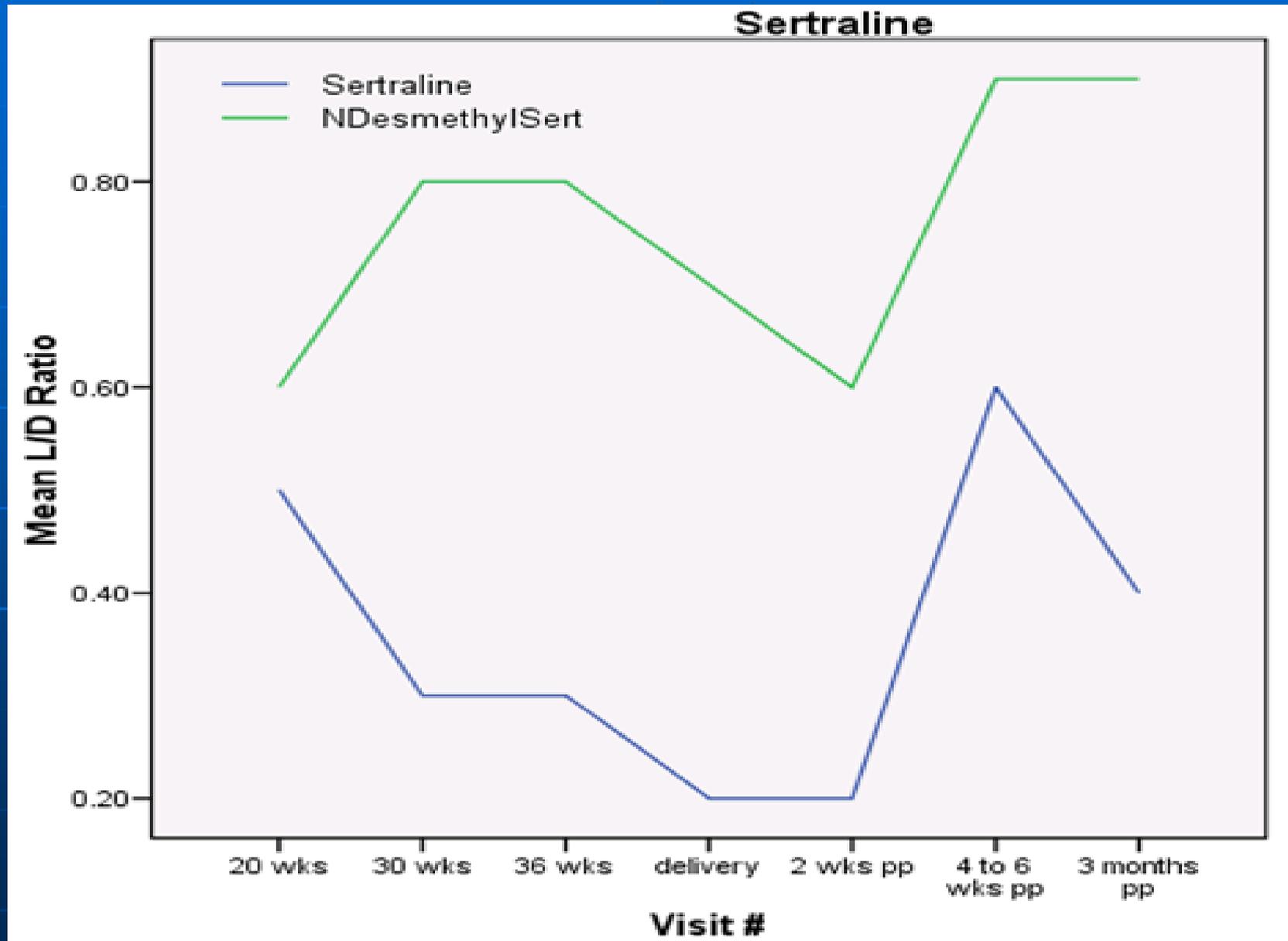
Summary Points

- **Neonatal Syndrome**- Time-limited < 2 weeks, rarely requires medical intervention; most commonly associated agents are paroxetine>fluoxetine>sertraline> fluvoxamine=citalopram= escitalopram (*Moses-Kolko et al, JAMA 294:2299-2300, 2005*)
- **PPHN**- Risk increased from 1-2/1000 to 6-12/1000 with exposure to SSRI after 20 weeks gestation (*Occhiogrosso et al, Am J Psych 169:134-140, 2012*); subsequent studies have not consistently replicated this finding

Optimize Maternal Treatment

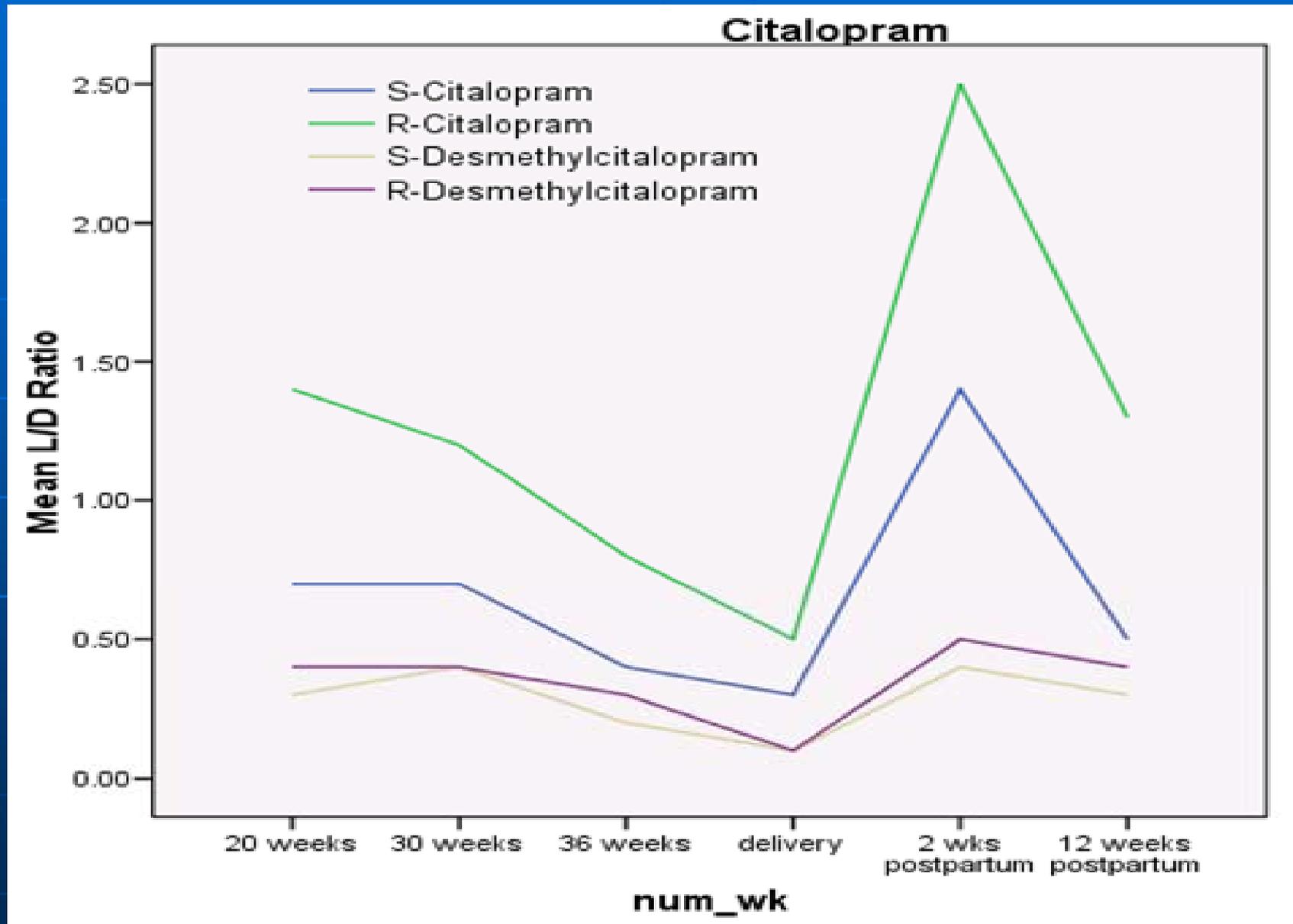
- Minimum **effective** dose through pregnancy!
- Standardized measure throughout pregnancy to monitor for symptom change
- Pharmacokinetic changes due to pregnancy, an evolving literature
- Postpartum management of dosing
- Breastfeeding (Surgeon General's report; excess risks with not breastfeeding
<http://www.ncbi.nlm.nih.gov/books/NBK52680/>)

SSRI Antidepressant Serum Levels Decline Across Pregnancy



Sit et al, J Clin Psych 69:652-8, 2008.

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What's the Practitioner to do?

- One source for clinically relevant information immediately available at the time of the encounter with the pregnant woman
- Consultation on application of this information to clinical practice (such as Organization of Teratology Information Specialists, OTIS, fact sheets for patients, *www.otispregnancy.org*)

REMS and ETASU

- Medication Guides
- Communication Plans (through professional societies, *Yonkers et al, Obstet Gynecol. 114: 703–713, 2009*)
- Evidence of special safe-use conditions (eg, documented negative pregnancy test)
- Registries to monitor pregnancy outcomes for drugs prescribed to pregnant women
- Defined responsibilities for sponsors
- Special training, certifications for prescribers or limitation of healthcare settings may further decrease accessibility of treatments

Pregnant Women are A Disadvantaged Population for Mental Health Utilization

Table 4. Prevalence and ORs of Mental Health Service Utilization Among Nonpregnant, Past-Year Pregnant, and Postpartum Women With 12-Month and Lifetime *DSM-IV* Disorders

	% (SE)		OR (95% CI)	AOR ^b (95% CI)	Postpartum Women, ^c % (SE) (n=994)	OR (95% CI)	AOR ^b (95% CI)
	Nonpregnant Women (n=13 025)	Past-Year Pregnant Women ^a (n=1524)					
Treatment seeking for any disorder^d							
Past 12 mo	16.5 (0.8)	10.5 (1.8)	0.59 (0.40-0.88)	0.68 (0.44-1.04)	11.1 (2.3)	0.63 (0.39-1.02)	0.64 (0.39-1.05)
Lifetime	41.0 (0.8)	35.8 (2.3)	0.80 (0.65-0.98)	0.88 (0.70-1.09)	40.7 (2.9)	0.99 (0.78-1.25)	1.03 (0.80-1.33)
Treatment seeking for alcohol use disorder							
Past 12 mo	6.0 (0.9)	9.9 (4.6)	1.70 (0.54-5.37)	1.79 (0.44-7.29)	8.3 (5.9)	1.40 (0.28-7.09)	1.06 (0.15-7.41)
Lifetime	41.0 (0.8)	7.6 (1.6)	0.67 (0.43-1.05)	0.69 (0.43-1.13)	9.1 (2.1)	0.81 (0.49-1.35)	0.75 (0.43-1.33)
Treatment seeking for drug use disorder							
Past 12 mo	17.0 (3.0)	30.3 (11.0)	2.13 (0.68-6.67)	2.56 (0.59-11.09)	34.6 (16.2)	2.59 (0.59-11.40)	2.43 (0.46-12.95)
Lifetime	15.3 (1.2)	18.0 (3.4)	1.22 (0.74-1.99)	1.18 (0.71-1.95)	21.0 (4.5)	1.46 (0.85-2.03)	1.36 (0.79-2.36)
Treatment seeking for mood disorder							
Past 12 mo	25.5 (1.4)	14.3 (2.7)	0.49 (0.31-0.77)	0.57 (0.34-0.93)	15.0 (3.3)	0.52 (0.30-0.88)	0.55 (0.31-0.96)
Lifetime	61.1 (1.1)	56.1 (3.2)	0.76 (0.53-1.07)	0.86 (0.58-1.27)	58.6 (3.7)	0.73 (0.48-1.10)	0.76 (0.48-1.19)
Treatment seeking for anxiety disorder							
Past 12 mo	11.6 (1.0)	6.1 (1.9)	0.50 (0.25-0.97)	0.62 (0.31-1.24)	7.5 (2.6)	0.62 (0.29-1.32)	0.72 (0.33-1.57)
Lifetime	29.0 (1.1)	23.2 (2.9)	0.74 (0.52-1.05)	0.92 (0.65-1.30)	27.9 (4.3)	0.95 (0.61-1.47)	1.10 (0.71-1.73)

FDA--Proposed Rule on Pregnancy and Lactation Labeling

- Standard format and content requirements
- Standard statement about population risk of fetal abnormalities
- Require updating for new information
- Pregnancy registry information
- Three main parts
 - Fetal risk summary
 - Prescribing Decisions for Pregnant Women
 - Data quality
 - www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093310.htm



Mental Health is Fundamental to Health

David Satcher, M.D.

**We must prioritize
the mental health
of the mothers of
our next generation!**

