

**UW PACC** Psychiatry and Addictions Case Conference UW Medicine | Psychiatry and Behavioral Sciences

#### PRECONCEPTION COUNSELING FOR PATIENTS ON PSYCHIATRIC MEDICATIONS

#### DEB COWLEY MD UNIVERSITY OF WASHINGTON 5/7/20

UW Medicine





# **GENERAL DISCLOSURES**

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### **GENERAL DISCLOSURES**

# UW PACC is also supported by Coordinated Care of Washington



#### **SPEAKER DISCLOSURES**

#### Medical Director, PAL for Moms

#### Co-Director, UW Perinatal Psychiatry Clinic



### PAL FOR MOMS 877-725-4666 (PAL4MOM)



- Partnership Access Line (PAL) for Moms
- Perinatal psychiatry telephone consultation
- Free for any healthcare provider in Washington State
- Mon-Fri 9-5
- Funded by State of Washington Health Care Authority (HCA)



#### **PLANNER DISCLOSURES**

The following series planners have no relevant conflicts of interest to disclose:

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# **OBJECTIVES**

- Discuss general approach to risk-risk assessment involved in preconception counseling for patients on psychiatric medications
- 2. Apply this general approach to two specific case examples



# PRECONCEPTION COUNSELING: THINGS TO CONSIDER

#### • 50% of pregnancies are unplanned

 Consider medication effects in pregnancy and lactation in treating any woman of childbearing potential

#### Minimize exposures

- Medications, illness episodes/relapse, alcohol/drugs/nicotine
- Safety of current medication(s) vs. starting a new medication



#### **PRESCRIBING IN PREGNANCY**

#### RULE 6

#### Be supportive if the patient goes against your recommendations

There are many reasons why a woman might choose to go against her psychiatric treatment provider's advice, particularly regarding drug use during pregnancy.

It is important that the treatment provider continues to support the patient despite such disagreements.

Again, a team approach will often help avoid disagreements, and providing as much information as possible on the risks of untreated psychiatric disorders during pregnancy can also be helpful

#### RULE 5

#### Use a team approach

This includes family and other doctors involved in the patient's care.

To provide good care for mother and child it is essential to educate the family about the risks and benefits of treatment and no treatment, as well as signs and symptoms of relapse.

Similarly, communicating directly with the obstetrician and the pediatrician will minimize miscommunication and differences of opinion, and maximize the patient's treatment outcomes

#### RULE

#### Minimize the number of exposures for the baby

Try to minimize the number of drugs used but consider exposure to psychiatric illness an exposure.

Changing drugs once a woman is pregnant increases the number of exposures. One common scenario is for a woman on a newer psychotropic drug to become pregnant and be switched to an older drug that has more evidence for safety. This plan increases the exposures for the baby—first to the newer drug and secondly to the older drug.

In addition, it is highly likely that the mother would relapse after switching, and exposure to the psychiatric disorder would constitute a third exposure for the child

#### RULE 1

All changes to drugs should be carried out before pregnancy if possible

This minimizes the number of exposures to the baby and promotes mood stability for the mother

#### RULE 2

Ideally the patient should be stable psychiatrically for at least 3 months before trying to get pregnant

This is not always practical but should provide some evidence and reassurance that the patient's mood is stable before pregnancy begins

#### RULE 3

Use drugs that we know something about: fewer data are available for recently approved drugs

If a drug has been available for several years there is at least some evidence that it is unlikely to be associated with major organ malformations, for example



#### FDA CATEGORIES – A THING OF THE PAST





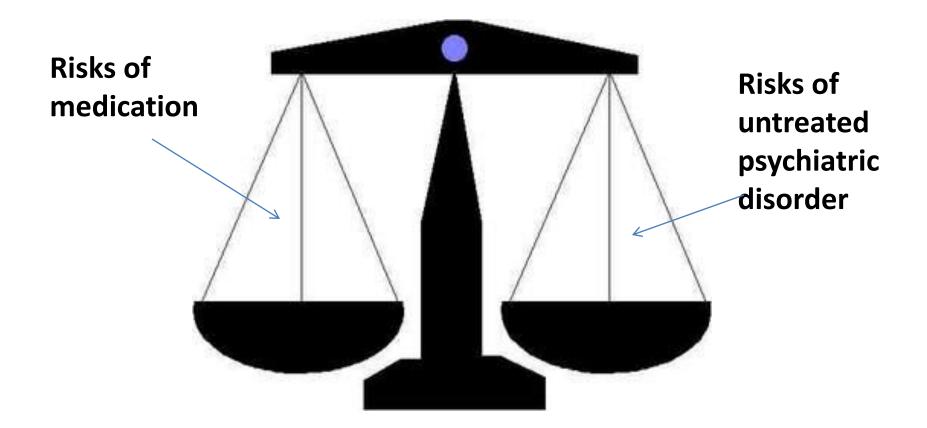


# **TYPES OF RISK**

- Malformations
  - Base rate 3%
- Adverse pregnancy outcomes
  - e.g. miscarriage, stillbirth, preterm birth, pre-eclampsia, gestational diabetes, postpartum hemorrhage
- Neonatal symptoms
- Long-term neurobehavioral effects



### **RISK-RISK ASSESSMENT**



#### \*Alternatives?



#### INFORMATION ABOUT MEDICATIONS IN PREGNANCY IS A CHANGING LANDSCAPE...



#### HOW TO KEEP UP?



### RESOURCES

Reprotox: <u>www.reprotox.org</u>

LactMed: <u>http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm</u>

Infant Risk Center (website and app): <a href="https://www.infantrisk.com">https://www.infantrisk.com</a>

MGH: <u>www.womensmentalhealth.org</u>

Perinatal Support Washington: <u>http://perinatalsupport.org/</u>

Parent Child Assistance Program: <u>https://depts.washington.edu/pcapuw/</u>

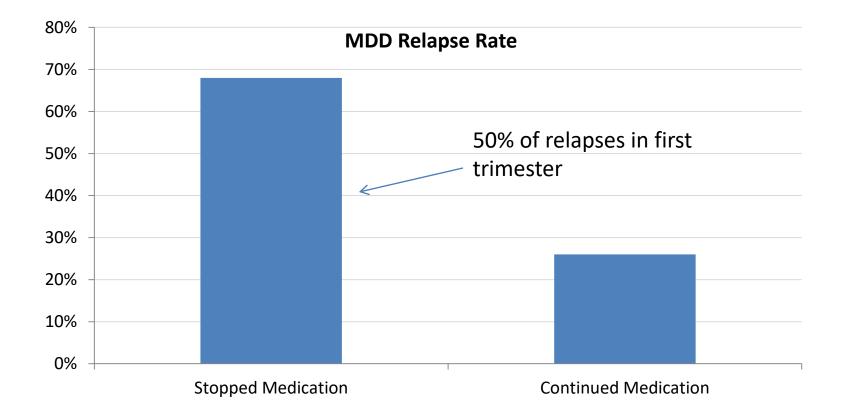


### **CASE #1**

- 27 yo woman wishes to conceive for the first time
- 4 past major depressive episodes
- 2 psychiatric hospitalizations
- Now doing well, PHQ-9 = 4
- No history of mania/psychosis
- On duloxetine (Cymbalta) 60 mg daily
- Multiple past antidepressant trials
- Duloxetine is helpful; therapy has helped at times
- She wants to know what to do about her depression treatment during pregnancy.



#### WHAT IF SHE STOPS HER ANTIDEPRESSANT?



Cohen et al., JAMA, 2006



#### RISKS OF UNTREATED DEPRESSION IN PREGNANCY AND POSTPARTUM



- Impaired functioning
- Suicide, hospitalization
- Poor prenatal care
- More substance use
- Preterm birth
- Postpartum depression
- Problems with attachment
- Behavioral problems and psychiatric disorders in children



# WHAT DO WE KNOW ABOUT DULOXETINE?

- Limited information
- 668 infants with first trimester exposure, 2.4% rate of malformations (Lassen, 2016)
- ? Gestational hypertension
- Neonatal adaptation syndrome (like SSRIs)
- Low transmission in breast milk (10 reported cases)





# SERTRALINE

- No consistent evidence for increased risk of malformations
- SSRI least often associated with persistent pulmonary hypertension of the newborn (PPHN)
  - Meta-analysis, 11 studies, 156,978 exposed women
  - PPHN 2.9/1000 with SSRI exposure vs. 1.8/1000 without
  - Lowest risk with sertraline

- Masarwa et al., AJOG, 2019

- Safest in breastfeeding
- Effective for anxiety as well as depression



### **ALTERNATIVES?**

- Evidence supports:
  - Psychotherapy
    - CBT
    - IPT
  - Bright light therapy
  - ECT
  - TMS
  - Exercise
  - Yoga



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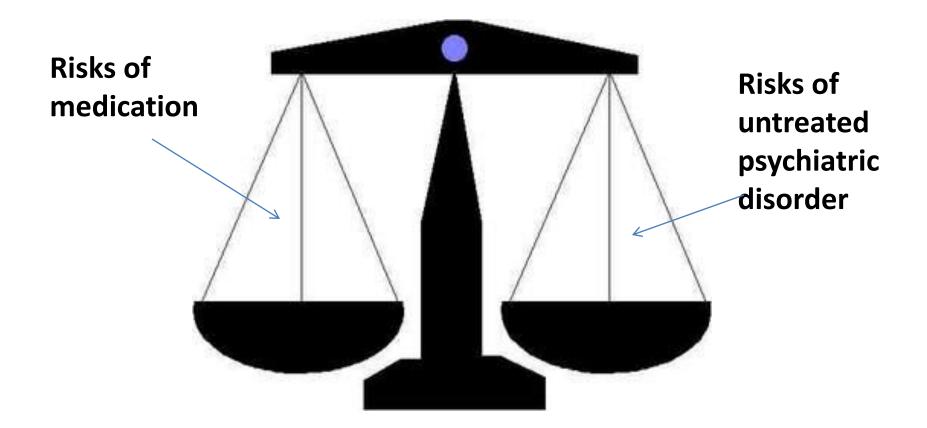


### **CASE #2**

- 35 yo woman with bipolar I disorder
- H/o multiple hospitalizations for mania
- Now stable on VPA 750 bid and quetiapine 150 mg qhs
- Desires pregnancy and not using birth control



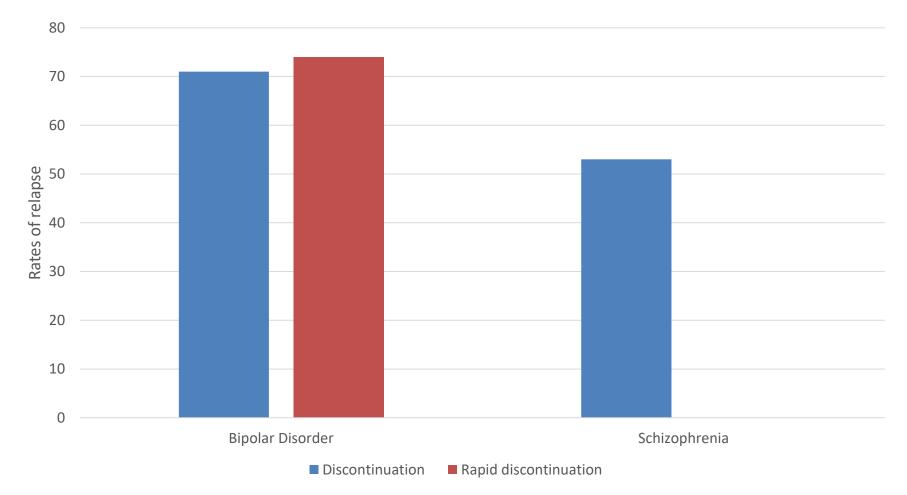
### **RISK-RISK ASSESSMENT**



#### \*Alternatives?



### RISKS OF RELAPSE WITH MEDICATION DISCONTINUATION





# **RISKS OF UNTREATED DISORDER**

- Risks to mother
  - Symptoms, impaired functioning
  - Hospitalization, suicide
- Risks to pregnancy
  - Poor prenatal care
  - Increased substance use
  - Preterm birth
- Risks postpartum/to child
  - Postpartum mood episode, psychosis
  - Problems with bonding, attachment
  - Behavioral problems in child



#### MALFORMATION RATES FOR AEDS IN PREGNANCY (EURAP, JULY 2011)

Valproate	< 700 mg/d	5.6%	
	700- <u>&lt;</u> 1500	10.4%	
	<u>&gt;</u> 1500 mg/d	24.2%	
Carbamazepine	< 400 mg/d	3.4%	
	400- <u>&lt;</u> 1000	5.3%	
	<u>&gt;</u> 1000 mg/d	8.7%	
Lamotrigine	< 300 mg/d	2.0%	
	<u>&gt;</u> 300 mg/d	4.5%	



#### **VALPROATE AND IQ AT AGE 6**

- 305 mothers, 311 children
- In utero valproate exposure
- Dose-dependent decreases in IQ (8-11 points) versus other anticonvulsants
- 8-fold increase in need for educational intervention
- Verbal>non-verbal cognitive effects
- IQ higher with periconception folate

» Meador et al., Lancet Neurol, 2013





# LITHIUM

- ? Ebstein's anomaly
  - Baseline 1 in 20,000; Lithium 1 in 1000
- Increase in cardiac malformations with first trimester exposure
  - RR of 1.65 (95% CI, 1.02-2.68); highest with > 900 mg/day (RR = 3.22)
- Higher rate of malformations overall
  - 7.2% versus 4.3% in mood disorder reference group
- No increase in adverse pregnancy or delivery outcomes
- Relative infant dose in breastfeeding about 50%



# LAMOTRIGINE IN PREGNANCY

- Prospective study from teratology service (median dose 200 mg/d): No increase in malformations (no oral clefts)
- No increase in rates of miscarriage, stillbirth, preterm birth, SGA babies
- May need dose increase during pregnancy
- Check pre-pregnancy euthymic level; monthly monitoring
- With breastfeeding, RID 6-50% maternal dose
- No neurodevelopmental disorders in children exposed to in utero lamotrigine (up to 6 years)



# **ANTIPSYCHOTICS**

- 23 studies, 14,382 pregnant women exposed to a SGA.
- Congenital malformations:
  - aripiprazole, olanzapine, quetiapine
  - ± risperidone, paliperidone
  - ? ziprasidone, clozapine, amisulpride, asenapine, lurasidone, sertindole
- Pregnancy outcomes: No class effect
- Neonatal adaptation / EPS (FDA warning)
- Gestational diabetes ± (olanzapine)
- Low infant doses with breastfeeding
- Child neurodevelopment?



# ALTERNATIVES

- Reduce/stop Depakote; add folate
- Atypical antipsychotic
  - Increased dose of quetiapine
  - Olanzapine, aripiprazole
- Change mood stabilizer
  Lamotrigine? Lithium?
- Therapy



Routine, optimize sleep, monitor for warning symptoms



### **QUESTIONS?**



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