



**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# TREATMENT OF DEPRESSION

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# GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.

# SPEAKER DISCLOSURES

✓ Any conflicts of interest? NO

# OBJECTIVES

1. Review commonly prescribed antidepressants
2. Review newer Antidepressants
3. Understand the basics of treatment selection
4. Discuss duration of treatment
5. Serotonin syndrome

# TREATMENT SELECTION

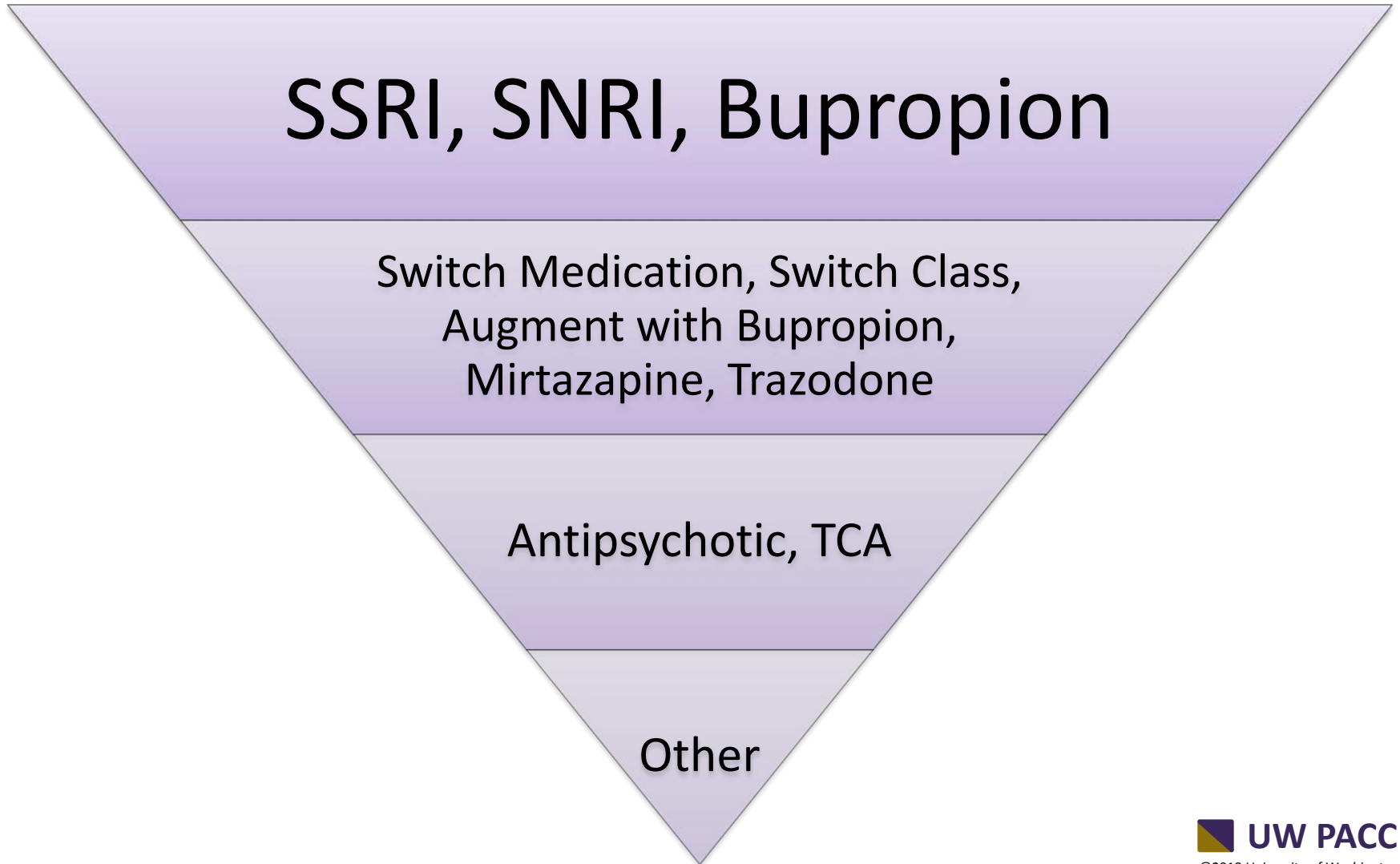
- **Mild depression:**
  - **Psychotherapy alone OR**
  - **Meds alone OR**
  - **Combination**
- **Moderate-Severe depression:**
  - **Meds alone OR**
  - **Meds with psychotherapy**
- **Psychotic depression**
  - **Antidepressant + Antipsychotics**
  - **ECT**

# ALL ANTIDEPRESSANTS HAVE FAIRLY SIMILAR EFFICACY...

## So what factors go into choosing the right antidepressant?

- patient tolerance
- Age, sex, cost
- dosing schedules (once daily, twice daily, three times daily?)
- possible drug interactions, side effects
- past response to med
- family member's response to med
- Comorbidities (medical/psychiatric)

# STEPPED DEPRESSION TREATMENT



# SSRI

- Block reuptake of serotonin
- Usually well tolerated
- Broad comorbidity coverage
- Comparatively safe (in overdose)



# COMMON SIDE EFFECTS

## Short term:

- GI upset / nausea
- Jitteriness / restlessness / insomnia
- Sedation / fatigue

## Long term:

- Sexual dysfunction (up to 33%)
- Weight gain (5 – 10%)

SSRIs	Pros	Cons
Citalopram (Celexa)	<p>Less drug interactions</p> <p>Possibly slightly lower rate of sexual dysfunction than other SSRIs</p> <p>May reduce agitation in demented elderly</p>	<p>QTc prolongation at doses &gt;40mg/day (20 mg for &gt;65 yrs)</p>
Escitalopram (Lexapro)	<p>Less drug interactions</p> <p>Starting dose usually = maintenance dose</p>	<p>Expensive</p>
Fluoxetine (Prozac)	<p>seems to cause least weight gain of SSRIs</p> <p>most studied in ESRD pts, no need to change dosing</p> <p>long half life so lower risk of discontinuation syndrome</p>	<p>strong 2D6 inhibitor!</p> <p>3A4, 2C19 inhibitor</p>

SSRIs	Pros	Cons
Sertraline(zoloft)	<p>Most studied in post-MI pts</p> <p>Safest in breastfeeding</p>	<p>Most GI sx of SSRIs</p> <p>2D6 inhibitor (higher doses)</p> <p>Discontinuation syndrome</p>
Paroxetine (Paxil)	<p>Least prone to cause GI side</p>	<p>Most anticholinergic</p> <p>Most weight gain</p> <p>Teratogenic</p> <p>Discontinuation syndrome</p>

# SNRI

- Dual reuptake inhibitors for serotonin and norepinephrine.
- Little or no effect on muscarinic, histaminic or adrenergic receptors
- Can act as TCAs without the side effects of TCAs

SNRIs	Pros	Cons
Venlafaxine (Effexor)	No sedation or weight gain Weak 2D6 inhibitor and less likely to interact Can be used for adult ADD	Increased HR and dose dep increase in BP, 100-225 mg (3-7%) , 300 mg (13%) Discontinuation syndrome: More fatal in OD than SSRI
Desvenlafaxine (Pristique)	Starting dose therapeutic No hepatotoxic side effects Less risk of increase in BP	Discontinuation syndrome
Duloxetine (Cymbalta)	Also used for pain No increase in BP, no weight gain, no effects on cardiac conduction Less risk of sexual side effects	2D6 inhibitor Hepatotoxic Mydriasis (avoid in glaucoma)



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# OTHER IMPORTANT ANTIDEPRESSANTS

Bupropion	<p>augment with SSRI</p> <p>ADHD</p> <p>Can counteract SSRI induced sexual side effects</p> <p>No weight gain</p> <p>Safe in depressed cardiac patients</p> <p>Used for smoking cessation</p>	<p>Can worsen anxiety</p> <p>Seizure risk</p> <p>2D6 inhibitor</p>
Mirtazapine	<p>Anti-nausea, stimulates appetite, sedating (upto 15 mg)</p> <p>Less sexual side effects</p> <p>augment with SSRI</p> <p>Minimal interaction</p>	<p>Weight gain, increase in cholesterol/ triglycerides</p> <p>Orthostatic hypotension and HTN</p> <p>Risk of neutropenia (1/1000)</p> <p>Anticholinergic side effects</p>
trazodone	<p>Used more often for sedation</p> <p>Not addictive</p> <p>Off label use for agitation in elderly</p>	<p>Orthostatic hypotension</p> <p>Priapism (1 in 20,000)</p>

# NEWER ANTIDEPRESSANTS

Med	Target Dose	Pros	Cons
Vilazodone (Viibryd)	20-40 mg with food	Less risk of sexual side effects Less risk of weight gain	GI side effects
Vortioxetine (Trintellix)	5-20 mg	Pro-cognitive effects Less risk of weight gain	GI side effects Sexual side effects



# NEWER SNRI

Levomilnacipran (Fetzima)	4-120 mg	Depression with fatigue and pain Less risk of weight gain	Urinary Retention Constipation Hyperhidrosis Expensive

# What You Should Know

## Sleep

## Weight Change

## Stopping Approach

### Will this medicine work for me?

- The antidepressants presented in this decision aid all work the same for treating depression.
- Most people with depression can find one that can make them feel better.
- 6 out of 10 people will feel better with the first antidepressant they try and the rest will have to try other antidepressants before they find the one that is right for them.

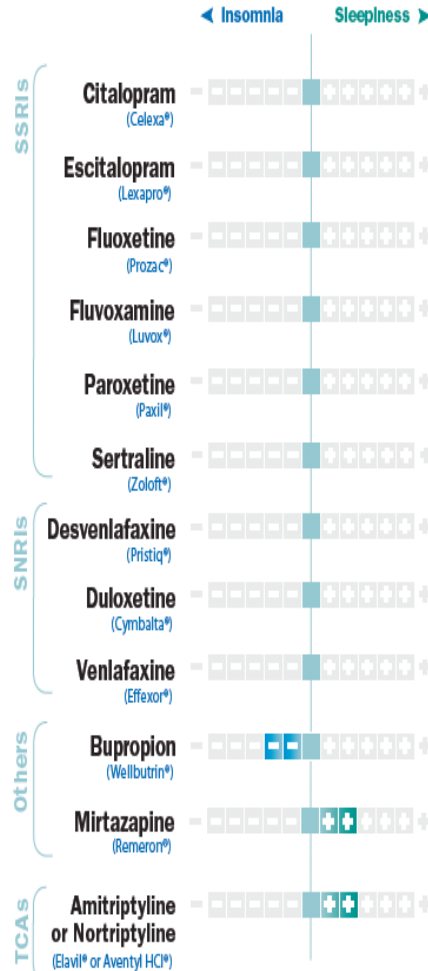
### How long before I feel better?

- Most people need to take an antidepressant regularly for at least 6 weeks to begin to get the full effect.

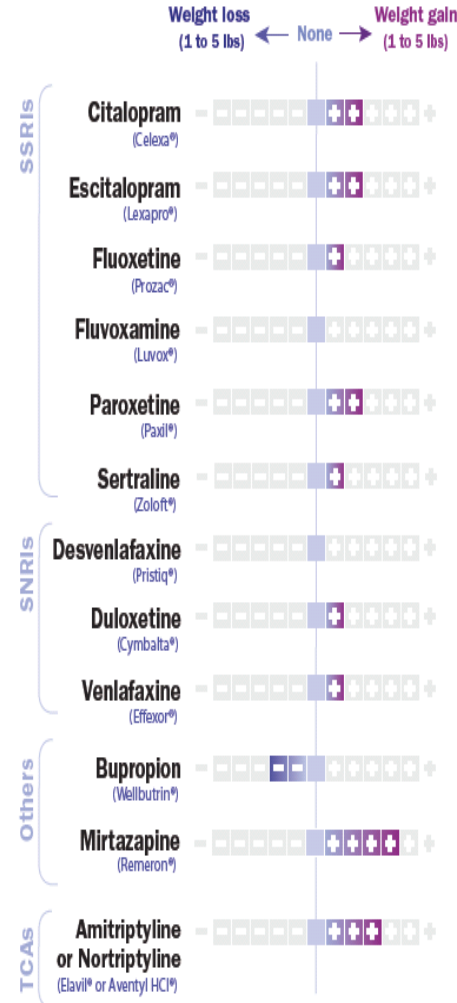
### Understanding side effects

- Most people taking antidepressants have at least one side effect.
- Many side effects go away after a few weeks, but some only go away after you stop the medicine.

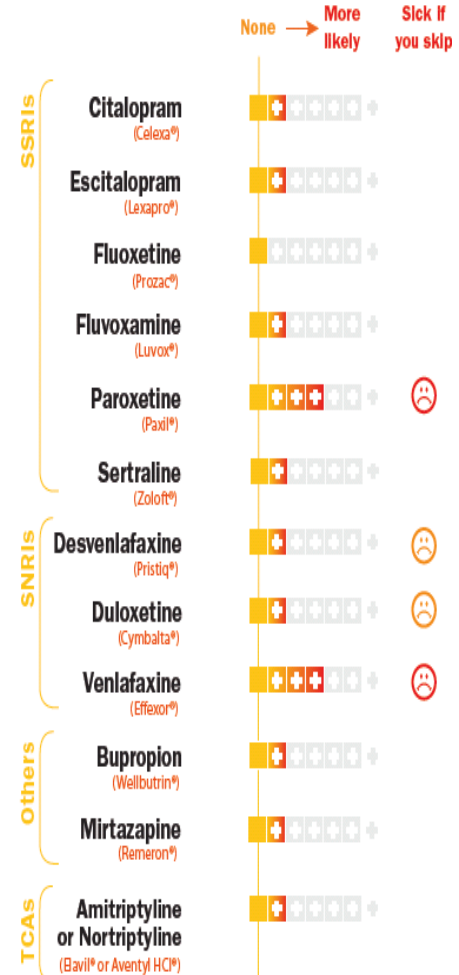
Some people may experience sleepiness or insomnia because of their antidepressant.



Some people may experience weight change. It is most likely to occur over six to twelve months and depends on your actual weight. The chart below is based on a 150 lb person.



Quitting your medicine all at once can make you feel sick, as if you had the flu (e.g. headache, dizziness, light-headedness, nausea or anxiety).



# Sexual Issues

# Cost

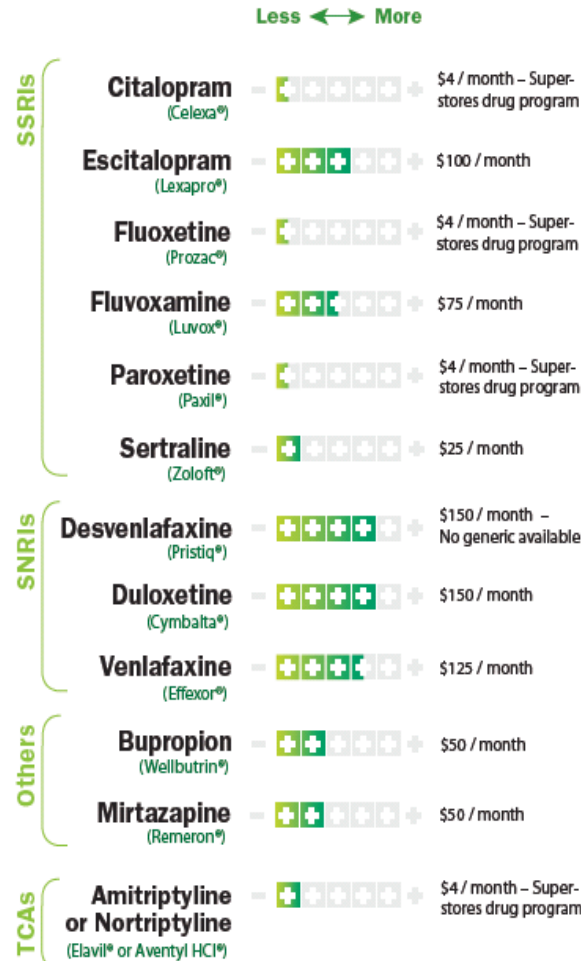
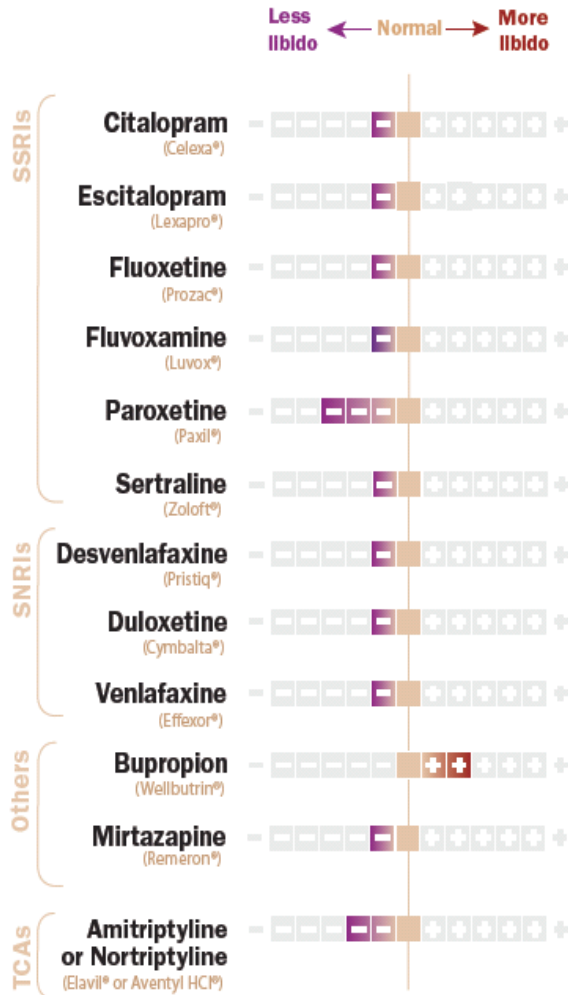
# Keep in Mind

Some people may experience loss of sexual desire (libido) or loss of ability to reach orgasm because of their antidepressant.

These figures are estimates and are for comparative reference only. Actual out-of-pocket costs vary over time, by pharmacy, insurance plan coverage, preparation and dosage.

Depression medicines may cause some:

- constipation, diarrhea and nausea
- increased risk of suicidal thoughts and behaviors (18- to 24-year-olds)
- harm to an unborn child
- risk of developing serotonin syndrome, a potentially life-threatening condition
- possible drug-drug interactions



## Additional considerations

Category	Medicine	Additional Considerations
SSRIs	Citalopram (Celexa®)	Can cause problems with your heart
	Escitalopram (Lexapro®)	Currently no other issues
	Fluoxetine (Prozac®)	More likely to interact with other drugs you are taking
	Fluvoxamine (Luvox®)	More likely to cause constipation, diarrhea or nausea Not officially recognized as a treatment for Major Depressive Disorder
	Paroxetine (Paxil®)	If you are pregnant, this medicine is more likely to cause problems with your unborn child
	Sertraline (Zoloft®)	More likely to cause diarrhea
SNRIs	Desvenlafaxine (Pristiq®)	Tell your doctor if you have high blood pressure
	Duloxetine (Cymbalta®)	Can help with pain Tell your doctor if you have high blood pressure
	Venlafaxine (Effexor®)	More likely to cause nausea and vomiting Can cause problems with your heart Tell your doctor if you have high blood pressure
Others	Bupropion (Wellbutrin®)	Higher risk of seizures
	Mirtazapine (Remeron®)	Starts to work more quickly
TCAs	Amitriptyline or Nortriptyline (Elavil® or Aventyl HCl®)	More likely to cause constipation, diarrhea or nausea Can help with pain If you are elderly, this medication may not be the best option

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# DURATION

## Adequate Trial

- 4-8 weeks on therapeutic dose
- If partial improvement in 6-12 weeks then increase the dose
- Continue for 6-12 months
- Long term use for second or third episode of depression

## Switch or Augment

# WITHDRAWALS

## Antidepressants

News about Antidepressants, including commentary and archival articles published in The New York Times.

Latest

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April 17, 2018

MIND

### Antidepressants and Withdrawal: Readers Tell Their Stories

Nearly 9,000 readers wrote to The Times to talk about their use of antidepressants. Here's what we learned.

By BENEDICT CAREY



April 9, 2018

LETTERS

### Withdrawing From Antidepressants

An article about antidepressant withdrawal set off a controversy in the mental health community. Psychiatrists and a patient urge caution.



April 7, 2018

### Many People Taking Antidepressants Discover They Cannot Quit

Long-term use of the medications is surging in the United States, according to an analysis by The Times. One reason: withdrawal symptoms that make it difficult to stop.

By BENEDICT CAREY and ROBERT GEBELOFF





# Psychiatric Times PsychiatricTimes.com

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## Weighing the Benefits of Genetic Information in Clinical Psychiatry

» Rebecca M. Allen, MD, MPH

*Dr. Allen is a Clinical Fellow in Neuropsychiatry, Brigham and Women's Hospital, Boston, MA.*

**G**enetic information is slowly working its way into psychiatric practice and our patients' daily lives. Pharmacogenomic panels can be ordered by psychiatrists, and genetic testing is being sold to the general public without any involvement of physicians or genetic counselors. The practicing psychiatrist needs to be informed about both of these types of services.

# ASSUREX EXAMPLE REPORT\*

\*Patient is 2D6 poor metabolizer & 2C19 ultra rapid metabolizer

**GeneSight® Psychotropic**  
COMBINATORIAL PHARMACOGENOMIC TEST



## Patient, Sample

DOB: 7/22/1984  
Order Number: 9904  
Report Date: 10/23/2015  
Clinician: Sample Clinician  
Reference: 1456CIP

Questions? Call 855.891.9415 or email [medinfo@assurexhealth.com](mailto:medinfo@assurexhealth.com)

## ANTIDEPRESSANTS

### USE AS DIRECTED

**desvenlafaxine** (Pristiq®)  
**levomilnacipran** (Fetzima®)  
**vilazodone** (Viibryd®)

### MODERATE GENE-DRUG INTERACTION

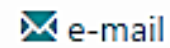
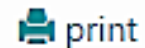
<b>trazodone</b> (Desyrel®)	1
<b>venlafaxine</b> (Effexor®)	1
<b>selegiline</b> (Emsam®)	2
<b>fluoxetine</b> (Prozac®)	1,4
<b>citalopram</b> (Celexa®)	3,4
<b>escitalopram</b> (Lexapro®)	3,4
<b>sertraline</b> (Zoloft®)	3,4

### SIGNIFICANT GENE-DRUG INTERACTION

<b>bupropion</b> (Wellbutrin®)	1,6
<b>mirtazapine</b> (Remeron®)	1,6
<b>amitriptyline</b> (Elavil®)	3,8
<b>clomipramine</b> (Anafranil®)	1,6,8
<b>desipramine</b> (Norpramin®)	1,6,8
<b>doxepin</b> (Sinequan®)	1,6,8
<b>duloxetine</b> (Cymbalta®)	1,6,8
<b>imipramine</b> (Tofranil®)	1,6,8
<b>nortriptyline</b> (Pamelor®)	1,6,8
<b>vortioxetine</b> (Brintellix®)	1,6,8
<b>fluvoxamine</b> (Luvox®)	1,4,6,8
<b>paroxetine</b> (Paxil®)	1,4,6,8



# Genelex Example Report



Known	Potential
3	3

Gene Only

All Drugs

Overall Impact <sup>i</sup>	Affected Drug <sup>i</sup>	Drug Exposure (PK) <sup>i</sup>	Clinical Effect (PD) <sup>i</sup>	Significant Cause(s) <sup>i</sup>
	<b>codeine</b> component of Tylenol 3 <a href="#">+ Expand Details</a>	Prodrug <sup>i</sup>	Major	2D6 Intermediate Metabolizer, Paxil
	<b>Lopressor</b>	>200%	Moderate	2D6 Intermediate Metabolizer, Paxil
	<b>Plavix</b> <a href="#">+ Expand Details</a>	Prodrug <sup>i</sup>	Major	2C19 Poor Metabolizer
	<b>acetaminophen</b> component of Tylenol 3 <a href="#">+ Expand Details</a>		Minor	
	<b>Paxil</b>	26-75%	Minor	2D6 Intermediate Metabolizer
	<b>Zocor</b> <a href="#">+ Expand Details</a>	Prodrug <sup>i</sup>		

# SEROTONIN SYNDROME

- Interaction between multiple meds that increase net serotonergic neurotransmission
- It can also occur after starting or increasing a single serotonergic medication
- Other non psychiatric meds which increase serotonin:
  - antiemetic (ondansetron, metoclopramide)
  - antimigraine (sumatriptans)
  - antibiotics (linezolid, ritonavir)
  - OTC (dextromethorphan)

# SEROTONIN SYNDROME

- **Mental status changes**

confusion  agitation  delirium

- **Neuromuscular changes**

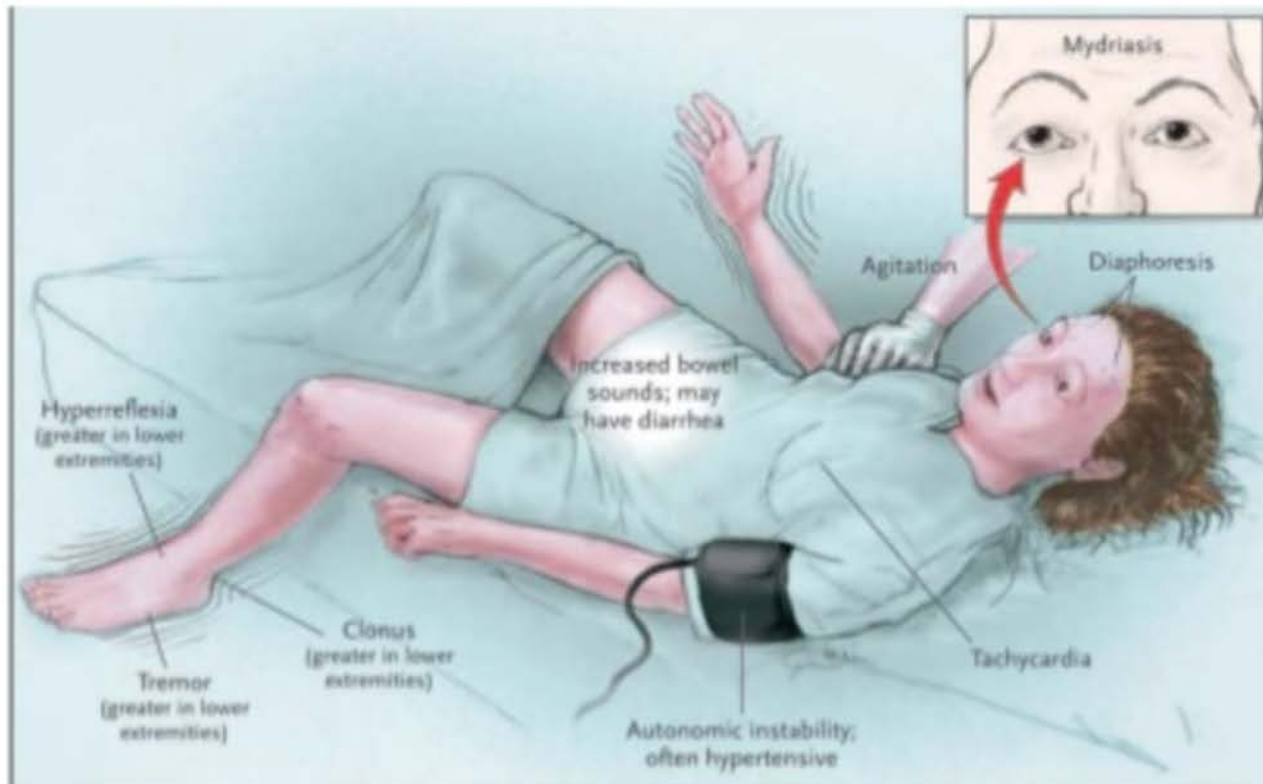
*hyperreflexia*, clonus, myoclonus, shivering, tremor

- **Autonomic instability**

tachycardia, diaphoresis, fever, diarrhea

# Serotonin Syndrome

- Cluster of autonomic, motor & mental status changes resulting from excess 5-HT (5-HT<sub>2A</sub>)



Agents  
MAO-Is  
TCA  
SSRIs  
opiate analgesics  
cough medicines (OTC)  
antibiotics  
triptans  
anti-nausea  
herbal products  
abused drugs

**THANK YOU!**