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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

TREATMENT OF DEPRESSION

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project ECHO

OBJECTIVES

1. Review commonly prescribed antidepressants
2. Understand the basics of treatment selection
3. Discuss duration of treatment

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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

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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)

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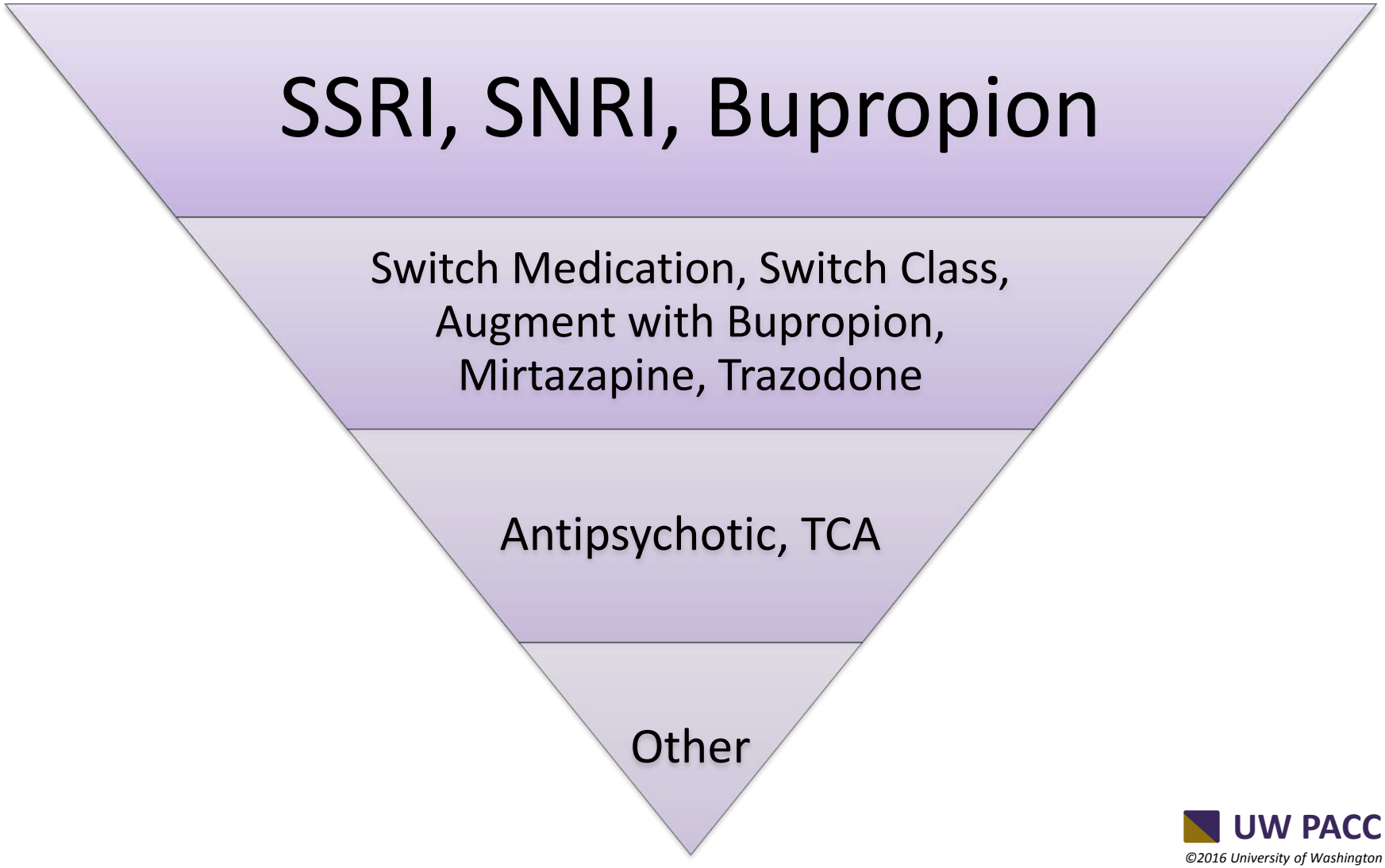
STEPPED DEPRESSION TREATMENT



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SSRI

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

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COMMON SIDE EFFECTS

Short term:

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

Long term:

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

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

SSRIs	Pros	Cons
Sertraline(zoloft)	Most studied in post-MI pts Safest in breastfeeding	Most GI sx of SSRIs 2D6 inhibitor (higher doses) Discontinuation syndrome
Paroxetine (Paxil)	Least prone to cause GI side	Most anticholinergic Most weight gain Teratogenic Discontinuation syndrome
Fluvoxamine (Luvox)	Approved for tx of OCD and not for depression	Strong 2D6, 3A4 inhibitor

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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)

OTHER IMPORTANT ANTIDEPRESSANTS

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

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:

- First recommend to switch to different antidepressant (SSRI/SNRI)
- After 3 trials can consider augmentation

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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)

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SEROTONIN SYNDROME

- **Mental status changes**

  confusion → agitation → delirium

- **Neuromuscular changes**

  hyperreflexia, clonus, myoclonus, shivering, tremor

- **Autonomic instability**

  tachycardia, diaphoresis, fever, diarrhea

DEPRESSION IN PREGNANCY

Untreated depression

For mother

- gain less weight, more likely to use drugs
- higher rates of miscarriage, premature delivery, pre-eclampsia

For newborn:

- smaller head circumference
- lower weight
- lower APGAR scores

Treated mothers

First trimester

- No increase risk of miscarriage
- No overall risk of birth defects (except paroxetine)

Later Pregnancy

- Increase risk of premature delivery (<37 wks)
- PPHN
- Neonatal distress syndrome

No long-term effects on development with SSRI/SNRI

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COMMONLY PRESCRIBED PSYCHOTROPIC MEDICATIONS

NAME Generic (Trade)	DOSAGE	KEY CLINICAL INFORMATION
Antidepressant Medications*		
Bupropion (Wellbutrin)	Start: IR-100 mg bid X 4d then ↑ to 100 mg tid; SR-150 mg qam X 4d then ↑ to 150 mg bid; XL-150 mg qam X 4d, then ↑ to 300 mg qam. Range: 300-450 mg/d.	**Contraindicated in seizure disorder** because it decreases seizure threshold; **stimulating; not good for treating anxiety disorders;** second line TX for ADHD; **abuse potential.** ¢ **(IR/SR), $ (XL)**
Citalopram (Celexa)	Start: 10-20 mg qday, ↑10-20 mg q4-7d to 30-40 mg qday. Range: 20-60 mg/d.	Best tolerated of SSRIs; very few and limited CYP 450 interactions; good choice for anxious pt. ¢
Duloxetine (Cymbalta)	Start: 30 mg qday X 1 wk, then ↑ to 60 mg qday. Range: 60-120 mg/d.	More GI side effects than SSRIs; tx neuropathic pain; **need to monitor BP**; 2nd line tx for ADHD. $
Escitalopram (Lexapro)	Start: 5 mg qday X 4-7d then ↑ to 10 mg qday. Range 10-30 mg/d (3X potent vs. Celexa).	Best tolerated of SSRIs, very few and limited CYP 450 interactions. Good choice for anxious pt. $
Fluoxetine (Prozac)	Start: 10 mg qam X 4-7d then ↑ to 20 mg qday. Range: 20-60 mg/d.	More activating than other SSRIs; long half-life reduces withdrawal (t ½ = 4-6 d). ¢
Mirtazapine (Remeron)	Start: 15 mg qhs. X 4-7d then ↑ to 30 mg qhs. Range: 30-60 mg/qhs.	Sedating and appetite promoting; Neutropenia risk (1 in 1000) so avoid in immunosupressed patients. ¢
Paroxetine (Paxil)	Start: 10 mg qhs X 4-7d then ↑ to 20 mg qday. Range: 20-60 mg/d.	Anticholinergic; sedating; **significant withdrawal syndrome.** ¢
Sertraline (Zoloft)	Start: 25 mg qam X 4-7d then ↑ to 50 mg qday. Range: 50-200 mg/d.	Few and limited CYP 450 interactions; mildly activating. ¢
Venlafaxine (Effexor)	Start: IR-37.5 mg bid X 4d then ↑ to 75 mg bid; XR-75 mg qam X 4d then ↑ to 150 qAM. Range: 150-375 mg/d.	More agitation & GI side effects than SSRIs; tx neuropathic pain above 150 mg qday; **need to monitor BP;** 2nd line tx for ADHD. **Significant withdrawal syndrome.** ¢ **(IR), $ (XR)**
*Warnings/precautions: 1) Potential increased suicidality in first few months, 2) Long term weight gain likely (except fluoxetine & bupropion), 3) Sexual side effects common (except bupropion & mirtazapine), 4) Withdrawal syndrome frequently occurs with abrupt cessation (especially with SSRIs and SNRIs), Increased risk of bleeding with SSRIs and SNRIs (especially in combo with NSAIDs), 5) Risk for Serotonin Syndrome (except bupropion), especially with combination of drugs effecting serotonin metabolism, 6) Hyponatremia sometimes seen with SSRIs and SNRIs.		
Antianxiety and Sleep (Hypnotic) Medications		
Alprazolam (Xanax)	Start: 0.25 mg – 0.5 mg tid. Usual MAX: 4 mg/d.	**Equiv. dose: 0.50 mg.** Onset: *intermediate* (1-2 hrs). T½: 11 hrs. More addictive than other benzos and has uniquely problematic withdrawal syndrome. **Try to avoid as 1st line tx.** ¢
Chlordiazepoxide (Librium)	Start: 10-20 mg 3-4X daily. Usual MAX: 200 mg/d	**Equiv. dose: 25 mg.** Onset: *intermediate* (0.5-2 hrs). T1/2: 10-48 hrs (parent compound), 14-95 hrs (metabolites). Useful for treating outpatient ETOH withdrawal because of long half-life. ¢
Clonazepam (Klonopin)	Start: 0.25 mg bid or tid. Usual MAX: 3 mg/d.	**Equiv. dose: 0.25 mg.** Onset: *intermediate* (1-4 hrs). T½: 40-50 hrs. Helpful in tx mania. ¢
Diazepam (Valium)	Start: 2–10 mg bid to qid with doses depending on symptoms severity. Usual MAX: 30-40 mg/d.	**Equiv. dose: 5 mg.** Onset: *immediate* (highly lipophilic). T½: 20-50 hrs. Note: the presence of liver disease will significantly lengthen half-life. ¢
Lorazepam (Ativan)	Start: 0.5-1 mg bid to tid. Usual MAX: 6 mg/d. Insomnia: 0.5-2 mg qhs.	**Equiv. dose: 1 mg.** Onset: *intermediate*. T½: 12 hrs. No active metabolites, so safer in liver dz. ¢
Buspirone (Buspar)	Start: 7.5 mg bid. Range: 10-30 mg bid.	Non-benzo SSRI-like drug FDA approved for anxiety. May take 4-6 weeks to become fully effective. ¢
Hydroxyzine (Vistaril)	Start: 25-100 mg 3-4 X per day. Usual MAX: 400 mg per day.	Antihistamine/antiemetic drug FDA approved for anxiety. Consider in pts w/ hx of substance abuse. ¢
Prazosin (Minipress)	Start: 1 mg qhs. Increase q 2-3 d until symptoms abate. Usual MAX: 10 mg qhs.	Old antihypertensive used to tx nightmares and night sweats d/t PTSD. Need to warn about orthostasis particularly in AM after first dose and after each new dosage change. ¢
Trazodone (Desyrel)	Start: 25-50 mg qhs. Range: 50-150 mg/qhs.	Commonly used as sleep aid; **inform about priapism risk in men.** ¢
Temazepam (Restoril)	Start: 15 mg at bedtime. MAX: 45 mg qhs.	**T½: 8.8 hrs.** Older benzo hypnotic. No P450 metabolism. More potential for physical dependence than Ambien/Sonata. ¢
Zolpidem (Ambien)	Start: 5-10 mg qhs. MAX: 20 mg qhs.	**T½: 2.6 hrs.** Potential for sleep-eating and sleep-driving. ¢ Available in longer acting form (CR $)
Mood Stabilizers		
Lithium	Start: 300 mg bid to tid. Target plasma level: acute mania & bipolar depression: **0.8-1.2 meq/L**; Maintenance: **0.6-0.8 meq/L**. Available in ER form dosed once daily (usually at HS, Lithobid & Eskalith). Plasma levels related to renal clearance.	**Black box warning for toxicity.** Teratogenic (cardiac malform.) and will **need to inform women of childbearing age of this risk.** Check TSH and BMP before starting and q 6-12 months thereafter. Advise pt about concurrent use of NSAIDS and HTN meds as can decrease renal clearance. Lithium strongly anti-suicidal. **¢, (lithium carbonate, citrate & SR), $ (Lithobid, Eskalith)**
Divalproex (Depakote)	Start: 750 mg daily (bid or tid, DR; qday, ER); increase dose as quickly as tolerated to clinical effect. Target plasma level: **75 to 100 mcg/mL (DR) & 85-125 mcg/ml (ER).**	**Multiple black box warnings** including for hepatotoxicity, pancreatitis, and teratogenicity (**need to inform women of childbearing age of this risk**). Need to monitor LFTs, platelet counts, and coags initially and q3-6 mo. Significant weight gain common. $
Lamotrigine (Lamictal)	Start: 25 mg daily for weeks 1 & 2, then 50 mg daily for weeks 3 & 4, then 100 mg qday for week 5, and finally 200 mg qday for week 6+ (usual target dose). Dosage will need to be adjusted for patients taking enzyme-inducing drugs or Depakote.	**Black box warning** for serious, life-threatening rashes requiring hospitalization and d/c of TX (Stevens Johnson syndrome @ approx. 1: 1-2000). No drug level monitoring typically required. Need to strictly follow published titration schedule. Fewer cognitive and appetite stimulating side effects. ¢
Antipsychotic/Mood Stabilizers**		
Aripiprazole (Abilify)	**Mania.** Start: 15 mg qday; Range: 15-30 mg/day. **MDD adj tx.** Start: 2-5 mg/day; adjust dose q 1+ weeks by 2-5 mg. Range: 5-10 mg/day. MAX: 15 mg qday. **Schizophrenia.** Start: 10-15 mg/day; ↑ at 2 week intervals; rec. dose: 10-15/day. MAX: 30 mg/day	EPS: moderate (especially akathisia); Metabolic side effects: low. Very long half-life: 75 hrs. Least amount of sexual side effects. FDA indication for adjunctive treatment of MDD. Potential increased suicidality in first few months. Need to screen glucose and lipids regularly. $
Olanzapine (Zyprexa)	Start: 5-10mg daily titrating to 15-30 mg daily once or divided bid.	EPS: Low; Metabolic side effects: high. Weight gain and sedation common. **Do not prescribe to diabetics.** Need to screen glucose and lipids regularly. $
Quetiapine (Seroquel)	**Bipolar Dep:** Start: 50 mg qhs; Initial target: 300 mg qhs; Range: 300-600 mg/d **Mania.** Start: 50 mg bid; Initial target: 200 mg bid. Range: 400-800 mg/d. **MDD adj tx.** Start: 50 mg qhs; Initial target: 150 mg qhs. Range: 150-300 mg/day. **Schizophrenia.** Start: 25 mg bid and increase by 50-100 mg/d (bid/tid). Initial target: 400 mg/d. Range: 400-800 mg/d	EPS: Lowest (except for Clozaril); Metabolic side effects: moderate. Highly sedating. FDA indication for bipolar depression and adjunctive treatment of MDD. Potential increased suicidality in first few months. Need to screen glucose and lipids regularly. **Abuse potential.** Available in an extended release form: Seroquel XR. **$ (IR & XR). Avoid or use alternative in combination with methadone due to QTc prolongation.$**
Risperidone (Risperdal)	Start: 0.5 – 1mg qhs or bid titrating to 4-6 mg daily or bid. Available as long-acting injectable given q 2 weeks called Risperdal Consta.	EPS: highest; Metabolic side effects: moderate. Hyperprolactinemia and sexual side effects common. Need to screen glucose and lipids regularly. ¢
Ziprasidone (Geodon)	Start: 40 mg bid titrating quickly to 60–80 mg bid. Needs to be taken w/ food (doubles absorption).	EPS: moderately high (especially akathisia); Metabolic side effects: lowest. Need to screen glucose and lipids regularly. Lower dosage can be more agitating than higher doses. **Contraindicated in combination with methadone due to QTc prolongation.$**
**Antipsychotic/mood stabilizer warnings/precautions: 1) Increased risk of death related to psychosis and behavioral problems in elderly patients with dementia, 2) Increased risk of QTc prolongation and risk of sudden death (especially in combination with other drugs that are known to prolong the QTc).		

po = by mouth; prn = as needed; qday = 1x/day; bid = 2x/day; tid = 3x/day; qid = 4x/day; qod = every other day; qhs = at bedtime; qac = before meals. ¢ = generic available. $ = Not available as generic or expensive. SSRI = Selective Serotonin Reuptake Inhibitor. SNRI = Serotonin Norepinephrine Reuptake Inhibitor. Developed by David A. Harrison, MD, PhD ©University of Washington V2.2 September 2010.