

The Latest in Treating Depression and Anxiety in Primary Care

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Faculty Disclosure

Wendy L. Wright, DNP, ANP-BC, FNP-BC, FAANP, FAAN, FNAP, has the following relevant financial relationships with commercial interests to disclose:

- Consultant:
 - Pfizer – Vaccines
 - GlaxoSmithKline - NSAIDs
- Speakers Bureau:
 - Pfizer, Merck, and Sanofi – Vaccines

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Educational Objectives

- Upon completion of this program, the learner will be able to:
 - Discuss signs and symptoms of the patient with depression and anxiety
 - Discuss various pharmacologic treatments for the patient with depression and anxiety
 - Compare and contrast various pharmacologic agents currently available

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Pretest Question 1

Which of the following is the mechanism of action for vortioxetine?

- A. Serotonin modulator and stimulator
- B. SSRI and 5HT1A partial agonist
- C. Weak inhibitor of norepinephrine and dopamine
- D. Inhibitor of neuronal serotonin and norepinephrine reuptake

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Pretest Question 2

Which of the following is a depression assessment tool; available to providers to assist in screening?

- A. PHQ-15
- B. PHQ-6
- C. PHQ-2
- D. PHQ-11

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Pretest Question 3

Patient with MDD is currently managed on sertraline. She continues to experience significant anhedonia. Which of the following options could you employ to improve her depression?

- A. Add bupropion to her regimen
- B. Switch her to an SNRI
- C. Augment her treatment with nonpharmacologic options
- D. All of the above

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Case Study - Mary

- 42-year-old single female
- Presents with the following complaints:
 - Fatigue, insomnia, and inability to concentrate
 - Feeling overwhelmed
 - Palpitations and occasional racing heart
 - Agitated and easily frustrated with colleagues
- Difficulty functioning; doesn't want to go to work
- Doesn't enjoy running or spending time with friends like she used to

What is Mary's differential diagnosis and problem?
Could her depression and anxiety be related?

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Epidemiology of Depression

- Major depressive disorder
 - Leading cause of disability in the US for ages 15 to 44.3 years
 - More than 15 million American adults, or about 6.7% of the US population age 18 and older in a given year
 - Median age at onset is 32.5 years
 - More common in women than in men
 - At any given time, 3% to 5% of adults suffer from major depression

<https://www.adaa.org/understanding-anxiety/depression>, accessed 6-15-2017

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Impact of Anxiety as a Comorbidity

- Up to 85% of patients with major depressive disorder (MDD) also have an anxiety disorder
- Coexisting anxiety in depressed patients is associated with:
 - Increased severity of depression
 - More chronic course
 - Poorer outcome
 - Impaired psychosocial functioning
 - Increased risk of suicide

Gorman JM. Depression and Anxiety 1996;4:160-8.

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Importance of Early Diagnosis

- Failure to diagnose early can lead to:
 - More chronic course
 - Changes in the brain
- Primary care clinicians fail to diagnose depression in up to 50% of patients
- Once diagnosis is made, clinicians provide adequate treatment only 50% of the time
- Often too low dosage, too short duration

Lampe K. Am J Psychiatry 2003;160:2052-4.

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Causes of Depression and Anxiety

- Biochemical dysfunction
 - Neurotransmitters
 - Serotonin
 - Norepinephrine
 - Dopamine
 - Limbic system
 - Endocrine system
- Familial predisposition
- Environment
- Medical conditions/medications

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Common Medications That May Cause Depression

- | | |
|----------------------------------|--------------------|
| • Beta blockers | • Benzodiazepines |
| • Thiazide diuretics | • NSAIDs |
| • Digitalis | • Psychostimulants |
| • Oral contraceptives | • Interferon |
| • Steroids | • Clonidine |
| • H ₂ RA (cimetidine) | • L-dopa |
| • Corticosteroids | • Metoclopramide |

Patten SB. J Psychiatr Neurosci 1993;18:92-102
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1188504/pdf/jpn00050-0020.pdf> accessed 06-17-2017

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History, Physical Examination, and Laboratory Evaluations

- Complete history and physical examination should be conducted
 - Chemical abuse
 - Losses (relationships, death, job)
 - Hormonal changes
- Laboratory tests (based on presenting symptoms)
 - CBC with differential (anemia)
 - CMP (glucose, kidney, liver tests, electrolytes)
 - TSH (thyroid disorder)
 - Vitamin D
 - Lyme
- Office tests
 - 12-lead ECG (prior to prescribing tricyclic antidepressants, antipsychotics, certain QT prolonging medications)

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Tools Available for the Primary Care Provider

- **PHQ-2, PHQ-4, or PHQ-9**
http://www.cqaimh.org/pdf/tool_phq2.pdf
- **Beck Depression Inventory, Primary Care (BDI-PC)**
<http://harcourtassessment.com/haiweb/cultures/en-us/productdetail.htm?pid=015-8018-370>
- **Zung Depression Scale***
<http://www.neurotransmitter.net/depressionscales.html>
- **Hamilton Rating Scale for Depression* (HAM-D)**
<http://www.neurotransmitter.net/depressionscales.html>

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APA DSM V Criteria for Depression

For at least 2 weeks, five of the following symptoms with (A) at least one of the first two; and (B) significant impairment in functioning or distress

Depressed Mood

Loss of Interest or Pleasure in Almost All Activities

- Significant Weight Gain or Loss (~ >5%)
- Insomnia or Hypersomnia
- Increased Agitation or Sluggishness (Psychomotor Retardation)
- Fatigue or Loss of Energy
- Feelings of Worthlessness or Excessive/Inappropriate Guilt
- Diminished Concentration; Indecisiveness
- Recurrent thoughts of death; Suicidal ideation/attempt

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Pneumonic SIG E CAPS for the Diagnosis of MDD

- Sleep (or Sex)
- Interest
- Guilt
- Energy
- Concentration
- Appetite
- Psychomotor
- Suicidal thoughts

Carlatt DJ. Am Fam Physician 1998; 58:1617-24.

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APA DSM V Criteria for Generalized Anxiety Disorder

≥ 3 of the following, occurring on most days, for ≥ 6 months

Anxiety

- Excessive worry
- Anxiety (Mental and physical hypervigilance)
- Tension (muscular tension, GI upset)
- Difficulty concentrating
- Hyperarousal
- Energy loss
- Restlessness
- Sleep disturbance

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DSM – 5: Depression and Anxiety

DSM-5 Diagnostic Criteria for MDD

Depressed mood or anhedonia + 4 or more symptoms most of the day, nearly every day, during a 2 week period.

- Significant weight loss (when not dieting), or weight gain, or a marked increase or decrease in appetite nearly every day
- Excessive sleepiness or insomnia
- Agitation and restlessness
- Fatigue
- Feelings of worthlessness or excessive and inappropriate guilt nearly every day
- Diminished ability to think, concentrate, or make decisions
- Recurrent thoughts of death or suicide



DSM-5 Diagnostic Criteria for Generalized Anxiety Disorder (GAD)

- Excessive anxiety and worry
 - More days than not for at least 6 months; multiple topics
- Difficult to control
- Anxiety and worry are associated with ≥ 3 of following:
 - Restlessness or feeling keyed up or on edge
 - Being easily fatigued
 - Difficulty concentrating or mind going blank
 - Irritability
 - Muscle tension
 - Sleep disturbance

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Assessment of Suicidal Risk

- 1/2 to 2/3 of people who commit suicide have seen a health provider within the month
 - Eight out of 10 people considering suicide give some sign of their intentions
 - People who talk about suicide, threaten suicide, or call suicide crisis centers are 30 times more likely than average to kill themselves
 - Assessment focus and risk factors
 - Ideation
 - Plan
 - History of previous attempt (strongest factor)
 - History of family or friend's suicide
 - Support system
 - History of social embarrassment
- <http://www.mentalhealthamerica.net/suicide> accessed 06-17-2017

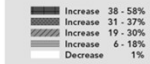
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CDC 2016

Suicide rising across the US

More than a mental health concern

Suicide rates rose across the US from 1999 to 2016.



SOURCE: CDC's National Vital Statistics System; CDC Vital Signs, June 2018.

<https://www.cdc.gov/vitalsigns/suicide/infographic.htm> accessed 06-01-2019

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U.S. Suicide Statistics

Breakdown by Gender/Ethnicity/Age Group

Source- www.cdc.gov/violenceprevention/pdf/Suicide-DataSheet-a.pdf

| Group | Number of Suicides | Rate of Suicide per 100,000 | Elderly (65+ years) | | Youth (15-24 years) | |
|----------------|--------------------|-----------------------------|---------------------|----------------------------------|---------------------|--------------------------------|
| | | | Elderly Suicides | Elderly Suicide Rate per 100,000 | Youth Suicide | Youth Suicide Rate per 100,000 |
| Nation | 32,439 | 11.1 | 5,198 | 14.3 | 4,316 | 10.4 |
| Men | 25,566 | 17.7 | 4,397 | 29.0 | 3,596 | 16.8 |
| Women | 6,873 | 4.6 | 801 | 3.8 | 720 | 3.6 |
| Whites | 29,251 | 12.3 | 4,924 | 15.4 | 3,610 | 11.0 |
| Nonwhites | 3,188 | 5.8 | 274 | 6.2 | 706 | 7.9 |
| Blacks | 2,019 | 5.2 | 148 | 4.8 | 465 | 7.2 |
| White Men | 23,081 | 19.6 | 4,180 | 31.1 | 3,016 | 17.9 |
| White Women | 6,170 | 5.1 | 744 | 4.0 | 594 | 3.8 |
| Nonwhite Men | 2,485 | 9.3 | 217 | 12.4 | 580 | 12.8 |
| Nonwhite Women | 703 | 2.4 | 57 | 2.2 | 126 | 2.8 |
| Black Men | 1,655 | 9.0 | 134 | 11.3 | 396 | 12.2 |
| Black Women | 364 | 1.8 | 14* | 0.7 | 69 | 2.2 |

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Differential Diagnoses to Consider

- Substance-induced mood disorder
- Bipolar disorder (often missed)
- Seasonal affective disorder (SAD)
- Premenstrual dysphoric disorder (PMDD)
- Dysthymia
- Panic disorder
- Schizophrenia
- Grief reaction
- Post-traumatic stress disorder
- Medical disorders
 - Hypothyroidism

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American Psychiatric Association Guidelines for Treating Depression

- Acute Phase
 - 1-8 weeks of treatment
 - Goal: Quick remission
 - Treatments: therapy, antidepressants
 - Light therapy, exercise, alternative therapies
- Continuation Phase
 - 8-20 weeks
 - Goal: Sustaining remission
 - Maintain same dose of medication as with the acute phase
 - Psychotherapy must be continued (enhances recovery); discontinued at end of phase
 - Note: Suicide rates increase here

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American Psychiatric Association Guidelines for Treating Depression (cont.)

- Maintenance Phase
 - Goal: Prevent relapse
 - This is often when the medications get discontinued (must taper off)
- Discontinuation of Active Treatment
 - Consider discontinuing medication if this is first episode
 - Decision to discontinue medication must be carefully considered and discussed with patient

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Treatment of Depression

Goals of Treatment:

- Reduce/eliminate symptoms
- Restore function
- Prevent relapse and recurrence

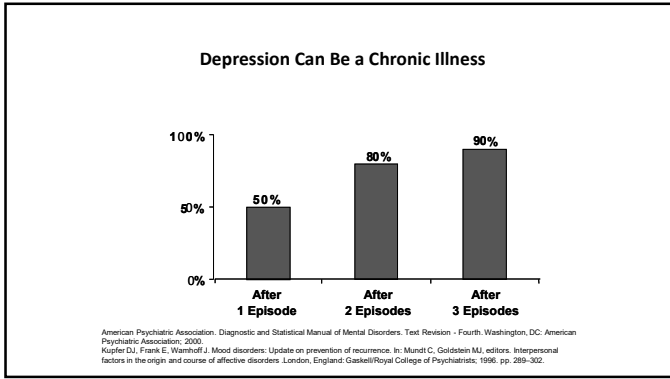
Psychotherapy
Cognitive Behavioral
Interpersonal
Psychodynamic

Drug Therapy
SSRIs/SNRIs/DNRIs
TCAs
Antipsychotics

Other Therapy
ECT
EMDR
Photolight
Therapy

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Nonpharmacologic Options

- Psychotherapy—use a familiar therapist
- EMDR (eye movement desensitization reprocessing)
 - PTSD
- ECT (electroconvulsive therapy)
 - Reduces cortisol levels
- Biofeedback/relaxation response
 - Reduces cortisol levels
- Massage therapy
 - Reduces cortisol levels
- Nutritional therapy
- Exercise
- Light box
- Community groups/support

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Psychotherapy

- Cognitive/behavioral—focus is on behaviors, thoughts, and emotions
- Psychodynamic/psychoanalytic—time limited, premise is that psychological events are not produced randomly but by causal forces operating in the individual
- Family therapy—family oriented, directed at the group system

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Pharmacologic Treatment Options

- **Selective Serotonin Reuptake Inhibitors (SSRIs)**
 - fluoxetine (Prozac)
 - sertraline (Zoloft)
 - paroxetine (Paxil)
 - fluvoxamine (Luvox)
 - citalopram (Celexa)
 - escitalopram (Lexapro)
- **Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)**
 - Tricyclic antidepressants (TCAs)
 - Venlafaxine (Effexor), desvenlafaxine (Pristiq)
 - Duloxetine (Cymbalta)
- **5-HT Antagonists and Agonists**
 - levomilnacipran (Fetzima)
- **Mixed Serotonergic Medications (5-HT)**
 - vilazodone (Viibryd)
 - mirtazapine (Remeron)
 - vortioxetine (Trintellix)
- **Serotonin modulator**
 - trazodone
- **Monoamine Oxidase Inhibitors (MAOIs)**
- **Augmentation**
 - **Antipsychotics:** aripiprazole (Abilify); olanzapine (Zyprexa); quetiapine (Seroquel); risperidone (Risperdal); ziprasidone (Geodon); brexpiprazole (Rexulti)
 - **Norepinephrine & Dopamine Reuptake Inhibitor:** bupropion (Wellbutrin)

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Choosing a Medication

- Use familiar medications
- Base medication choice on symptoms
- Check history of previous use
- Check history of family success w/ Rx
- Consider financial/insurance coverage
- Consider adherence
- Use evidence-based guidelines
- Beware of drug-drug interactions

APA. Practice Guideline for the Treatment of Patients with Major Depressive Disorder (3rd edition). Accessed June 17, 2017. American Psychiatric Association.

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Returning to Mary

- Early diagnosis and treatment are imperative
- The first few weeks of therapy are the most crucial
 - The educated patient is more likely to stay on a recommended treatment plan
 - Recognize the patient's cognitive level when discussing possible adverse effects
 - Be candid, yet give assurance that most of the adverse effects will begin to lessen or abate over the first week of therapy
 - Advise patient that mood changes will be subtle
 - Monitor daily (family) for signs of irritability, agitation, unusual behaviors, suicidality
- How would you treat Mary?

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Initial Treatment Options

Optimal initial therapy for most patients

- SSRIs
- SNRIs
- Bupropion
- Mirtazapine
- Trazodone

American Psychiatric Association, DSM V, 2013.

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SSRIs

- Considered one of initial treatment options for MDD
- Applies to all age groups
 - All antidepressants have black-box warning regarding use in children and adolescents
 - Most indicated for pediatric/adolescent depression, social anxiety, OCD
- Easy to use
- Well tolerated
 - As effective as TCAs
- Inhibit the reuptake of serotonin and/or enhance serotonergic neurotransmission
 - Possible weak effects on dopamine

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**SSRIs
Dosing and Time to Effect**

| | Citalopram | Escitalopram | Fluoxetine | Paroxetine | Sertraline |
|----------------------------|------------|--------------|------------|------------|------------|
| Start dose* | 20 mg | 10 mg | 10-20 mg | 20 mg | 25-50 mg |
| Max dose | 40 mg | 20 mg | 80 mg | 50 mg | 200 mg |
| Time to effect | 4-6 weeks | 4-6 weeks | 4-6 weeks | 4-6 weeks | 4-6 weeks |
| Titration increment | 1 week | 1 week | 3-4 weeks | 1 week | 1 week |

*In clinical practice, based on patient symptoms, starting doses are sometimes lower than that recommended by the drug manufacturer.

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SSRI Side Effects

| | Citalopram | Escitalopram | Fluoxetine | Paroxetine/CR | Sertraline |
|--------------|------------|--------------|------------|---------------|------------|
| Headache | | | +++ | ++ | ++++ |
| Insomnia | ++ | ++ | +++ | ++++ | +++ |
| Somnolence | +++ | +++ | ++ | ++++ | ++ |
| Nervousness | | | +++ | ++++ | ++ |
| Anxiety | +++ | +++ | ++++ | +++ | +++ |
| ↓ Libido | + | + | ++ | +++ | ++++ |
| Fatigue | +++ | +++ | | | ++++ |
| Constipation | | | ++ | ++++ | +++ |
| ↓ Appetite | | | | ++++ | +++ |

APA. Practice Guideline for the Treatment of Patients with Major Depressive Disorder (3rd edition). Accessed June 17, 2017. American Psychiatric Association.

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- Serotonin-Norepinephrine Reuptake Inhibitors**
- Venlafaxine and venlafaxine extended-release
 - Potent inhibitor of neuronal serotonin and norepinephrine reuptake and weak inhibitor of dopamine reuptake
 - Usual dosage: 150 mg/day
 - Start at 37.5 mg–75 mg/day
 - Titrate as high as 225 mg/day in 75-mg increments every 4 days
 - Adverse effects
 - Nausea
 - Dizziness
 - Nervousness
 - Hypertension
 - Sexual dysfunction
 - Contraindication: allergic to active ingredient
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Serotonin-Norepinephrine Reuptake Inhibitors

- Desvenlafaxine
- Potent inhibitor of neuronal serotonin and norepinephrine reuptake and weak inhibitor of dopamine reuptake
 - Usual dosage: 50 mg once daily
 - Start at 50 mg
 - Titrate as high as 100 mg once daily
 - Adverse effects
 - Nausea
 - Dizziness
 - Nervousness
 - Hypertension
 - Sexual dysfunction
 - Contraindication: allergic to active ingredient

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Serotonin-Norepinephrine Reuptake Inhibitors

- Duloxetine hydrochloride
- Inhibitor of neuronal serotonin and norepinephrine reuptake; less potent inhibitor of dopamine reuptake
 - Dose range: 120 mg/day
 - Adverse effects
 - Nausea
 - Dry mouth
 - Constipation
 - Insomnia
 - Sexual dysfunction
 - Contraindication: hepatic insufficiency

Cymbalta Prescribing Information.

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Dopamine-Norepinephrine Reuptake Inhibitors

- Bupropion
- Weak inhibitor of norepinephrine and dopamine; does not inhibit reuptake of serotonin
 - 150 mg once daily in AM; typical dosage: 300 mg/day; maximum: 400 mg-450 mg/day
 - Adverse effects
 - Seizures
 - Headaches
 - Agitation
 - Anxiety
 - Insomnia
 - Weight change
 - Contraindicated in patients with a history of seizures, significant head trauma, bulimia

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Norepinephrine-Serotonin Modulator

- Mirtazapine
- Enhances central noradrenergic and serotonergic activity
 - Potent H₁ receptor blocker
 - Dose range: 15-45 mg/day
- Adverse effects
 - Sedation
 - Increased appetite
 - Weight gain
 - Dizziness
 - Anticholinergic effects

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Mary: 2 Months Later

- **Scenario #1:** Mary had been given an SSRI
 - Titrated to maximum dose
 - Presents at 2-month visit without symptoms in remission
- What is the next step?
- **Scenario #2:** Mary had been given an SSRI
 - Titrated to maximum dose
 - Presents at 2-month visit with complaints of persistent symptoms
 - insomnia
 - sad mood
 - inability to concentrate
 - anhedonia
- What is the next step?

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Nonresponders: Next Steps

- 1) Optimize current therapy (use maximum dose)
- 2) Switch to a different SSRI
- 3) Augment with non-antidepressant medication
- 4) Change class of medication
- 5) Use a combination of therapies
- 6) Optimize nonpharmacologic therapies

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Fine-Tuning Treatment

- Additional options for depression treatment:
 - TCAs
 - Newer options:
 - Levomilnacipran
 - Vortioxetine
 - Vilazodone

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Fine-Tuning Treatment

- Augmenting for persistent insomnia
 - Trazodone (Desyrel)
 - Zolpidem (Ambien/CR)
 - Zaleplon (Sonata)
 - Lorazepam (Ativan)
 - Ramelteon (Rozerem)
 - Eszopiclone (Lunesta)
 - Suvorexant (Belsomra)

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Levomilnacipran

- Class: Extended-release selective norepinephrine and serotonin reuptake inhibitor (SNRI)
- Indication: MDD
- Dosage:
 - 40 mg to 120 mg once daily with or without food
 - Initiate dose at 20 mg once daily for 2 days
 - May increase by 20–40 mg every 2 days
 - The maximum recommended dose is 120 mg once daily
 - The capsules should be swallowed whole

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Levomilnacipran

- Contraindications:
 - Hypersensitivity to any components
 - Concomitant MAOI use
 - Uncontrolled narrow angle glaucoma
- Drug-drug Interactions:
 - Strong 3A4 inhibitors – increase exposure to levomilnacipran
 - ie, ketoconazole, clarithromycin, ritonavir
 - Do NOT exceed doses >80 mg
- Adverse effects levomilnacipran vs placebo:
 - Nausea: 17% vs 6%
 - Constipation: 9% vs 3%
 - Vomiting: 5% vs 1%

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Vilazodone hydrochloride

- Indications
 - MDD in adults
- Class: SSRI and 5HT1A partial agonist
- Dosage:
 - 10 mg once daily to start
 - Maximum: 40 mg once daily
 - Dosed with food (without food – decreased levels of medication)

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Vilazodone hydrochloride

- Contraindications: use with MOAIs
- Adverse effects:
 - Diarrhea 26-29%
 - Nausea 22-24%
 - Headache 14-15%
- Drug interactions:
 - CYP3A4 inhibitors
 - CYP3A4 inducers

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Vortioxetine

- Class: Serotonin modulator and stimulator
 - Novel class of medication
 - Enhances serotonergic activity by:
 - Inhibiting reuptake of 5HT, 5HT1A receptor agonist and antagonist of 5-HT3, 5HT1D, and 5HT7
- Indication: MDD
- Dosage:
 - 10 mg once daily; with or without food
 - Maximum dosage: 20 mg once daily
 - May use 5 mg for the individual experiencing adverse effects
 - 10 mg/day for individuals known to be 2D6 poor metabolizers

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Vortioxetine

- Drug-drug interactions:
 - Reduce dose by ½ for those on strong 2 D6 inhibitors such as:
 - Bupropion, fluoxetine, paroxetine, quinidine
 - Strong CYP inhibitors
 - Increase dose if on any of the following:
 - Rifampin, carbamazepine, phenytoin
- Adverse effects: (vortioxetine vs placebo)
 - Nausea: 21-32% vs 9%
 - Constipation: 7-10% vs 6%
 - Dizziness: 6-9% vs 6%
 - Remainder: similar to placebo
- Contraindications:
 - MAOIs within 21 days
 - Hypersensitivity to any components

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Serotonin Modulators

- Trazodone
- Dosage: Maximum 400 mg/d for outpatients
 - Initial dose: 150 mg/d increased by 50 mg every 4 days
 - Significant anticholinergic adverse effects
- Nefazodone (Serzone)
 - Maximum 600 mg as maintenance
 - Initial dose: 200 mg BID
- Adverse effects: headache, dry mouth, somnolence

Product insert, 2017

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Tricyclic Antidepressants

| | Amitriptyline (Elavil) | Desipramine (Norpramin) | Imipramine (Tofranil) | Nortriptyline (Pamelor) |
|------------|---------------------------|----------------------------|--------------------------|----------------------------|
| Start Dose | 50 mg hs | 25-50 mg | 75 mg | 10-25 mg |
| Max Dose | 300 mg hs | 300 mg | 300 mg | 150 mg |

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Product inserts accessed 06/19/2017

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Benzodiazepines

| | Alprazolam (Xanax/XR) | Clonazepam (Klonopin) | Diazepam (Valium) | Lorazepam (Ativan) |
|------------|--------------------------|--|-----------------------------|---|
| Start Dose | 0.25-0.5 3x/d | 0.25 mg - 0.5 mg | 2 mg 2-4x/d | 0.5 mg - 1.0 mg |
| Max Dose | 4 mg divided | 4 mg/day | 10 mg 2-4x/d | 10 mg |
| Half-life | ~11 hours | 30-40 hours | 20-100 hours | 12-18 hours |
| Onset | Intermediate-fast | Intermediate | Fast | Intermediate |
| Indication | GAD Panic disorder | Panic disorder Anxiety RLS Sleepwalking | Anxiety or anxiety disorder | Anxiety disorders/anxiety with depressive symptoms Insomnia (short term) |

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Product inserts, 2017

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Additional Medications

- Lamotrigine (Lamictal)
 - MDD, seizure disorder, bipolar (25 mg starting dose; 200 mg maintenance)
- Aripiprazole (Abilify)
 - MDD, bipolar, schizophrenia (2-5 mg once daily starting; 15 mg/day maximum)
- Lithium
 - Bipolar (300 mg once-twice daily; maximum 2400 mg/day)
- Ziprasidone (Geodon)
 - Bipolar, schizophrenia
- Quetiapine fumarate (Seroquel)
 - MDD, bipolar, schizophrenia

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Additional Treatments for Anxiety

- Gabapentin
- Hydroxyzine
- Buspirone

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Newer Agents: Promising Options

- Ketamine (anesthetic, centrally acting non-opioid)
 - Depression and anxiety
 - Reduction in suicidal ideations/suicidality
- Two types of ketamine
 - Racemic ketamine: IV infusion (off-label); most research
 - Esketamine (Spravato): Nasal spray and approved by FDA for depression which has failed to respond to two or more medications
- Believed to target the NMDA receptors in the brain, increasing glutamate – which then activate AMPA receptors to increase mood, thoughts and cognition
- Side effects: increased blood pressure, nausea, vomiting, perceptual disturbances, disassociation
- Schedule IV medication
- Generally given 8 treatments and then tapered
 - 56 mg day 1; then 56-84 mg intranasally 2x per week x 4 weeks; then 56 -84 mg every 1 -2 weeks
- Administered by an MD; 28 mg per device with each device delivering 2 sprays

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Common Reasons Why Patients Discontinue Medication Therapy

- Reasonable:
 - Sexual dysfunction
 - Weight gain
 - Sleep disturbance
 - Initial exacerbation of symptoms
- Unreasonable:
 - Altered personality
 - Organ damage

Ferguson JM. Prim Care Companion J Clin Psychiatry 2001;3:22-7
Stanton D. Address: Health Med Ther 2010;1:73-85.

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Documentation for Depression and Anxiety Visits

Documentation should include:

- Appearance and behavior
- Attitude (to examiner)
- Psychomotor activity: normal, slow, agitated
- Affect and mood
- Speech and thinking
- Perceptual disturbances
- Orientation
- Quotation of suicidal ideation denial
- Attention
 - Recall of three objects, serial sevens
- Comprehensive physical exam
- Time spent with patient

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**Patient Education:
Medications**

- Adverse effects
- Warnings found in the package inserts including suicidal thoughts, worsening depression, and allergic reactions
- Use of other drugs including alcohol
- Improvement of symptoms: expect 3-4 weeks
- Duration of treatment
- Frequent follow-up
- Discontinuation: Do not stop abruptly to avoid serotonin withdrawal symptoms
- Teach patient symptoms of serotonin syndrome and discontinuation syndrome

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When to Consult/Refer

- Patient is seen and therapies fail
 - 1 or 2 adequate trials of antidepressants
- Any suicidal/homicidal ideations
- Children with depression/anxiety
- Comorbidities
 - Psychotic depression
 - Bipolar disorder
 - Obsessive-compulsive disorder
 - Concomitant thought disorder (eg, schizophrenia)
 - Severe depression

American Psychiatric Association Practice Guideline for the Treatment of Patients with Major Depressive Disorder. http://www.psychiatryonline.com/pracGuide/pracGuideTopic_7.aspx.

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Using Pharmacogenomic/Pharmacogenetic Testing in Patients with Mood Disorders

- What is it?
 - Study of how a person's genes affect their metabolism of medications
- Numerous companies provide this service
- Covered by CMS (co-insurance) for most patients
- Can be really helpful in choosing medications or fine tuning therapy

<https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics> accessed 06-17-2017

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Reimbursement

- You may bill for the amount of time spent provided that the visit is predominantly counseling (>50%)
- If the nurse practitioner elects to choose the level of service based on counseling:
 - The total length of time of the encounter should be documented
 - The record should describe the amount of time spent in counseling

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Conclusion: Words of Wisdom

- Avoid using SSRIs and TCAs together
 - Increases the risk of serotonin syndrome
- In the elderly, start low, go slow
- Taper off medication slowly to avoid withdrawal symptoms
- Address weight gain and sexual dysfunction
- Be attentive to follow-up schedule
 - Weekly x 2-4 weeks (may be coordinated or augmented with therapist visits)
 - Every 2 weeks x 2-4 weeks

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Posttest Questions

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Posttest Question 1

Which of the following is the mechanism of action for vortioxetine?

- A. Serotonin modulator and stimulator
- B. SSRI and 5HT1A partial agonist
- C. Weak inhibitor of norepinephrine and dopamine
- D. Inhibitor of neuronal serotonin and norepinephrine reuptake

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Posttest Question 2

Which of the following is a depression assessment tool; available to providers to assist in screening?

- A. PHQ-15
- B. PHQ-6
- C. PHQ-2
- D. PHQ-11

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Pretest Question 3

Patient with MDD is currently managed on sertraline. She continues to experience significant anhedonia. Which of the following options could you employ to improve her depression?

- A. Add bupropion to her regimen
- B. Switch her to an SNRI
- C. Augment her treatment with nonpharmacologic options
- D. All of the above

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Summary and Questions

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