

The Latest in Treating Depression and Anxiety in Primary Care

Wendy L. Wright
DNP, ANP-BC, FNP-BC, FAANP, FAAN, FNAP
Adult/Family Nurse Practitioner

Owner – Wright & Associates Family Healthcare @ Amherst and @ Concord
Owner – Partners in Healthcare Education

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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, Merck, Sanofi – Vaccines
 - GlaxoSmithKline – OA/Pain
 - Bayer – CKD
 - Idorsia – Sleep
 - Seqirus – Vaccines
 - Shield Therapeutics - IDA
- Speakers Bureau:
 - Pfizer, Merck, and Sanofi – Vaccines
 - AbbVie and Biohaven - Migraines

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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 IK. 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 RAs (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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USPSTF

- Recommends screening:
 - 12-18 years of age annually for MDD
 - 8 – 18 years of age annually for GAD

<https://consumer.healthday.com/uspstf-recommends-anxiety-depression-screening-for-children-teens-2657105443.html> accessed 04-23-2022

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Scoring of Tools

- PHQ 9:
 - 0-4: Normal or no appreciable depression
 - 5-9: Mild depression
 - 10-14: Moderate depression
 - 15-19: Moderate – severe depression
 - 20 and higher: Severe depression
 - Max score: 27
- GAD 7:
 - Score 0-4: Minimal Anxiety
 - Score 5-9: Mild Anxiety
 - Score 10-14: Moderate Anxiety
 - Score greater than 15: Severe Anxiety
 - Max score: 21

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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

Carlat 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 the following:
 - Restlessness or feeling keyed up or on edge
 - Being easily fatigued
 - Difficulty concentrating or mind going blank
 - Irritability
 - Muscle tension
 - Sleep disturbance

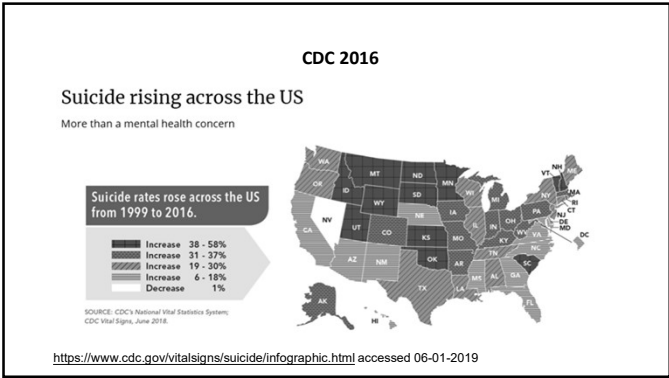
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Assessment of Suicidal Risk

- 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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U.S. Suicide Statistics
Breakdown by Gender/Ethnicity/Age Group
Source- www.cdc.gov/violenceprevention/pdf/Suicide-DataSheet-a.pdf

All Ages Combined			Elderly (65+ years)		Youth (15-24 years)	
Group	Number of Suicides	Rate of Suicide per 100,000	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

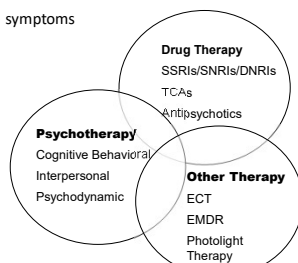
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Treatment of Depression

Goals of Treatment:

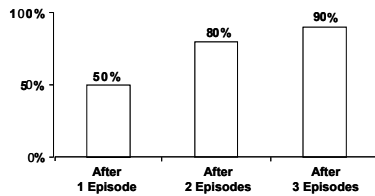
- Reduce/eliminate symptoms
- Restore function
- Prevent relapse and recurrence



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Depression Can Be a Chronic Illness



American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Text Revision - Fourth. Washington, DC: American Psychiatric Association; 2000.
Kupfer DJ, Frank E, Wamboldt J. Mood disorders: Update on prevention of recurrence. In: Mundy C, Goldstein MJ, editors. Interpersonal factors in the origin and course of affective disorders. London, England: Gaskell/Royal College of Psychiatrists; 1996. pp. 289-302.

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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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Management of Depression

- Latest APA guidelines state:
 - Psychotherapy
 - 2nd generation antidepressant
 - SSRI
 - SNRI

<https://www.apa.org/monitor/2019/09/ce-corner-depression> accessed 01-01-2021

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Pharmacologic Treatment Options

- | | |
|---|---|
| <ul style="list-style-type: none">• Selective Serotonin Reuptake Inhibitors (SSRIs)<ul style="list-style-type: none">• fluoxetine (Prozac)• sertraline (Zoloft)• paroxetine (Paxil)• fluvoxamine (Luvox)• citalopram (Celexa)• escitalopram (Lexapro)• Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)<ul style="list-style-type: none">• Tricyclic antidepressants (TCAs)• Venlafaxine (Effexor), desvenlafaxine (Pristiq)• Duloxetine (Cymbalta)• 5-HT Antagonists and Agonists<ul style="list-style-type: none">• levomilnacipran (Fetzima) | <ul style="list-style-type: none">• Mixed Serotonergic Medications (5-HT)<ul style="list-style-type: none">• vilazodone (Vibryd)• mirtazapine (Remeron)• vortioxetine (Trintellix)• Serotonin modulator<ul style="list-style-type: none">• trazodone• Monoamine Oxidase Inhibitors (MAOIs)• Augmentation<ul style="list-style-type: none">• <u>Antipsychotics</u>: aripiprazole (Abilify); olanzapine (Zyprexa); quetiapine (Seroquel); risperidone (Risperdal); ziprasidone (Geodon); brexpiprazole (Rexulti)• <u>Norepinephrine & Dopamine Reuptake Inhibitor</u>: 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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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
 - Zolpidem (Ambien/CR)
 - Zaleplon (Sonata)
 - Lorazepam (Ativan)
 - Ramelteon (Rozerem)
 - Eszopiclone (Lunesta)
 - Suvorexant (Belsomra)
 - Lemborexant (Dayvigo)
 - Daridorexant (May 2022)

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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

Product inserts accessed 06-17-2017
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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) • Quetiapine fumarate (Seroquel) • MDD, bipolar, schizophrenia

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Additional Treatments for Anxiety
• Gabapentin • Hydroxyzine • Buspirone • Beta blocker

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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. Adolesc 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
- 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
 - No longer have to document > 50% counseling but must recap what was done during this visit

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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

- For further information, contact:
Wendy Wright: wendyarnp@aol.com

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