

4 Pharmacotherapy (see 2009 MDD CPG p. 83)

- ▶ There is insufficient evidence to recommend one antidepressant medication over another for all patients.
- ▶ The choice of medication is based on side effect profiles, history of prior response, family history of response, type of depression, concurrent medical illnesses, concurrently prescribed medications, and cost of medication.
- ▶ Selective Serotonin Reuptake Inhibitors (SSRIs) along with Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion and Mirtazapine are considered a first-line treatment option for adults with MDD.
- ▶ Generally, SSRIs or Venlafaxine are first-line antidepressants for patients in the primary care setting because of their low toxicity and ease of administration relative to other antidepressants.
- ▶ Generally, initial doses used for the elderly should be lower than in healthy adults.
- ▶ Prior to discontinuing an antidepressant for nonresponse, providers should ensure that an appropriate dose titration and target dose range has been achieved and an adequate response period allowed (a minimum of four to six weeks).

Managing Medication Side Effects

- ▶ Insomnia – Confirm time of dosing is daytime hours, decrease dose, or change antidepressants.
- ▶ Sexual Dysfunction – Common with all SSRIs, SNRIs, and others.
- ▶ Change antidepressant to Bupropion or Mirtazapine since these two medications are considered an alternative for patients who have experienced sexual side effects with other antidepressants.

Psychotherapy (see 2009 MDD CPG pp.101–107)

Evidence-based psychotherapies and antidepressant medications are equally effective for most patients across the spectrum of depressive patients in outpatient settings. Generally, medication, an evidence-based psychotherapy, or combination of both should be considered first-line treatment in most cases. If patient is not engaged in therapy after six weeks or is worse, consider antidepressant medication in addition to/or if already receiving medications, adjust accordingly.

Evidence-Based Psychotherapies for depression:

- ▶ Brief (six to 12 sessions)
- ▶ Present focused
- ▶ Assist patient in altering thought patterns & behavior

5 Treatment Response and Follow-Up (see 2009 MDD CPG p. 80)

STEP	PATIENT CONDITION	OPTIONS	REASSESS AT:
1	Initial treatment	▶ Initiate low dose antidepressant	2 Weeks*
2	No response to initial low dose antidepressant	▶ Increase dose ▶ Consider longer duration ▶ Switch ▶ Consider referral to specialty card	4 to 6 Weeks
3	Failed 2nd trial of antidepressant	▶ Switch ▶ Augment or combine ▶ Consider referral to specialty care	8 to 12 Weeks
4	Failed 3rd trial, including augmentation	▶ Reevaluate diagnosis and treatment ▶ Consider referral to specialty care	12 to 18 Weeks

*If treatment is not tolerable, switch to another antidepressant.

6 Second Opinion or Referral

Consider for the following:

- ▶ Suicidal patients
- ▶ Patients who need hospitalization
- ▶ Patient request or need for psychotherapy
- ▶ Psychosis
- ▶ Bipolar disorder
- ▶ PTSD
- ▶ Somatoform disorder
- ▶ Patients who require specialized treatment (MAOIs, ECT, light therapy)
- ▶ Need for involuntary commitment
- ▶ Patient who is pregnant or wants to become pregnant
- ▶ Cases where there is difficulty ascertaining the diagnosis
- ▶ Patients who have severe psychosocial problems
- ▶ Depression accompanied by panic, generalized anxiety disorder or phobias
- ▶ Depression accompanied by obsessive compulsive D/O
- ▶ Depression accompanied by eating disorders
- ▶ Presence of complex general medical problems
- ▶ Treatment non-compliance

VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder (MDD) in Adults: Primary Care



1 Patient Age >18 with Suspected Depression: Screen for the Presence of Depression Using the PHQ-2

2 Brief Assessment for Dangerousness

Obtain Relevant Hx, Physical Exam, and Lab Tests

3 Obtain Symptom Score Using PHQ-9 Determine and Document DSM IV-TR Criteria for MDD

If Medications or Comorbid Medical Conditions: Provide Medical Tx, Follow-Up as Indicated, Reassess Depression Symptoms

Assess for Manic or Hypomanic Symptoms, Family History of Bipolar Disorder, or Other Psychiatric Comorbidities

Discuss Treatment Options and Patient's Preferences Arrive at Shared Decision Regarding Tx Goals and Plan

4 Initiate Treatment Strategies Address Psychosocial Needs

5 Assess Tx Response in Four to Six Weeks, Adjust Tx as Necessary

6 Reassess Tx Response in Four to Six Weeks

Consider Consultation/Referral for Incomplete Response

If Remission, Continue Tx and Maintenance; Screen Annually

Access to full guidelines:

http://www.healthquality.va.gov/Major_Depressive_Disorder_MDD_Clinical_Practice_Guideline.asp

QMO website: <https://www.qmo.amedd.army.mil/>

Department of Veteran Affairs: <http://www.healthquality.va.gov/>

09/14/10

1 Patient Health Questionnaire 2 (PHQ-2)

Over the past two weeks, how often have you been bothered by either of the following problems?

A) Little interest or pleasure in doing things (0-3)

B) Feeling down, depressed, or hopeless (0-3)

	Not at all	Several days	More than half the days	Nearly every day
	0	1	2	3

2 STEP 1. Assess Suicidal Ideation

Assess level of discouragement/sadness; feelings of life not worth living, whether or not a specific plan to end life is present, whether or not the means to complete plan is available, and history of suicidal gestures/attempts.

STEP 2. Assess Risk Factors

Family history suicidal behavior, substance use, psychiatric illness, serious medical illness, means for suicide available, psychosocial disruption, history of previous suicide attempts, impulsivity, male, elderly, and/or Caucasian.

STEP 3. Respond to Suicide Risk

Imminent Risk Indicators

- ▶ Patient endorses suicidal intent
- ▶ Organized plan present
- ▶ Has lethal means
- ▶ Signs of psychosis present
- ▶ Extreme pessimism expressed

If at imminent risk, IMMEDIATE action is required. DO NOT leave patient alone.

3 Patient Health Questionnaire 9 (PHQ-9)

Name: _____ Date: _____
 Over the last two weeks, how often have you been bothered by any of the following problems? (use “✓” to indicate your answer)

	Not at All	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

Add Columns: + +
 Total: _____

10. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?
 Not Difficult at All Somewhat Difficult Very Difficult Extremely Difficult

PHQ-9 Score	DSM-IV-TR Criterion Symptoms	Depression Severity	Proposed Treatment Action
1-4	Few	None	None
5-9	< 5	Mild Depressive Symptoms	Watchful waiting; repeat PHQ-9 at follow-up.
10-14	5-6	Mild Major Depression	Treatment plan: Consider counseling, follow-up, and/or pharmacotherapy.
15-19	6-7	Moderate Major Depression	Immediate initiation of pharmacotherapy and/or psychotherapy.
20-27	> 7	Severe Major Depression	Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management.

PHQ-9 is adapted from PRIME MD TODAY, developed by Drs Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke, and colleagues, with an educational grant from Pfizer Inc. For research information, contact Dr. Spitzer at rls8@columbia.edu. Use of the PHQ-9 may only be made in accordance with the Terms of Use available at <http://www.pfizer.com>. Copyright ©1999 Pfizer Inc. All rights reserved. PRIME MD TODAY is a trademark of Pfizer Inc.

4 Treatment Strategies (see 2009 MDD CPG p. 51–60)

	LEVEL	PHQ TOTAL SCORE	FUNCTIONAL IMPAIRMENT	INITIAL TREATMENT STRATEGIES*
Severity	Mild	5-14	Mild	Watchful waiting, supportive counseling, self-management (e.g., exercise – see self-management worksheet on cards 14 and 15); if no improvement after one or more months, consider use of an antidepressant or brief psychological counseling.
	Moderate	15-19	Moderate	Start with combination of medications and psychotherapy.
	Severe	≥20	Severe	Combination of antidepressants and psychotherapy, or multiple drug therapy.
Modifiers	Complicated	Co-occurring PTSD, SUD, mania, or significant social stressors		Start with combination of medications and somatic interventions.
	Chronicity	> 2 years of symptomatology despite treatment		For mild—start with monotherapy of either antidepressants or psychotherapy, or a combination of both. For mod/severe—combination of antidepressants and psychotherapy or multiple drug therapy.

- *Initial treatment strategy options include:
- Psychoeducation and self-management (provided to all MDD patients)
 - Watchful waiting
 - Monotherapy (psychotherapy or pharmacotherapy)
 - Combination psychotherapy and antidepressants
 - Treatment of complex patients
 - Somatic treatment
 - Inpatient and residential

Self Management (see 2009 MDD CPG pp. 53–55)

Self management strategies enhance the patient's active engagement in treatment. Choose one or two goals at a time collaboratively to pursue during treatment:	
Nutrition	Maintain a balanced diet.
Exercise	Strong evidence that exercise often has significant anti-depressant effects.
Bibliotherapy	Use of self-help texts.
Sleep hygiene	Education on sleep hygiene should be included for patients exhibiting sleep disturbance.
Tobacco use	Tobacco use has been demonstrated to impact the recovery of depression. Referral or treatment of nicotine dependence should be considered.
Caffeine use	Excessive caffeine use may exacerbate some symptoms of depression.
Alcohol use and abuse	Even low levels of alcohol use have been demonstrated to impact recovery of depression; patients should be advised to abstain until symptoms remit.
Pleasurable activities	Behavioral activation has been shown to have significant antidepressant effects.

Selective Serotonin Reuptake Inhibitors (SSRIs)			
Generic (Brand Name)	Adult Starting Dose and Max Dose Per Day	Advantages	Disadvantages
Citalopram (Celexa)	Initial adult dose = 20mg QD. Max dose/day = 60mg. Max geriatric dose/day = 40mg QD. ^{1,2,3}	May be used for diabetic neuropathy. ^{1,2} Generic. Possibly fewer cytochrome P450 (CYP450) interactions. ⁴ May be taken without regard to meals. ^{1,2,3} AM daily dosing.	No evidence of increased efficacy by dose escalation within the first four weeks. Dose escalation after six weeks appeared less effective than continuing the same dose.
Escitalopram (Lexipro)	Initial adult dose = 10mg QD. Max adult dose/day = 20mg. Initial geriatric dose = 10mg QD.	S-enantiomer more potent than racemic (Citalopram). ⁴ 10mg dose often effective. ⁴ Once daily dosing without regard to meals. ^{1,2,3} AM daily dosing.	No evidence of increased efficacy by dose escalation within the first four weeks. Dose escalation after six weeks appeared less effective than continuing the same dose.
Fluoxetine (Prozac)	Initial adult dose = 20mg QD. Max adult dose/day = 80mg QD. Initial geriatric dose = 10mg QD. User lower doses in the elderly. ^{1,2,3}	Long half-life good for poor adherence, missed doses. ⁴ Generic. May be taken with or without food. ^{1,2} FDA approved for OCD use in children =>7 and MDD in children =>8. ^{1,2,3} AM daily dosing.	Slower to reach steady state. ⁴ May be too stimulating and may have more CYP450 interactions. ⁴ Should not be taken at night in the elderly unless for sedation. ¹ Associated with rash and allergic events. ^{1,2,3}
Fluoxetine (Prozac) Weekly	90mg Q week.	Once weekly dosing in the maintenance therapy for patients who have responded to daily administration. ^{1,2,3}	If a satisfactory response is not maintained with once weekly dosing, consider re-establishing a daily dosing regimen. ^{1,2,3}
Paroxetine (Paxil)	Initial adult dose = 20mg QD. Max adult dose/day = 50mg QD. Initial geriatric dose = 10mg QD. Max geriatric dose = 40mg QD. ^{1,2,3}	May also be used for anxiety. ^{1,2,3} Can be used in adolescents. ^{1,2,3} Generic.	Of the SSRIs, highest reported dc rate, highest rate of sexual dysfunction and weight gain. Sometimes sedating and more anti-cholinergic symptoms. ⁴ Possibly more CYP450 interactions. ⁴ Avoid in pregnancy.
Paroxetine CR (Paxil CR)	Initial adult dose = 25mg QD. Max adult dose/day = 62.5mg QD. Initial geriatric dose = 12.5mg QD. Max geriatric dose = 50mg QD. ^{1,2,3}	Generic. May be taken with or without food. ^{1,2,3} AM daily dosing.	Of the SSRIs, highest reported dc rate, highest rate of sexual dysfunction and weight gain. Sometimes sedating and more anti-cholinergic symptoms. ⁴ Possibly more CYP450 interactions. ⁴ Avoid in pregnancy. Do not crush or chew CR tab.
Sertraline (Zoloft)	Initial adult dose = 50mg QD. Max dose/day = 200mg QD. Initial geriatric dose = 25mg QD.	Safety shown post-MI. ⁴ FDA approved for use in OCD in children =>6. ^{1,2,3} Generic. AM daily dosing.	Higher rate of diarrhea than other SSRIs. Monitor for weight and nutritional intake. ^{1,2}

First Line Antidepressant Medication
 Drugs of this class differ substantially in safety, tolerability and simplicity from other classes of antidepressants. Can work in Tricyclic Antidepressant (TCA) non-responders. Other possible uses are in anxiety disorders, Post-Traumatic Stress Disorder (PTSD), Obsessive Compulsive Disorder (OCD), panic disorder and Premenstrual Dysphoric Disorder (PMDD).^{1,2,3} SSRIs, Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion, Mirtazapine are first-line therapy for adults with Major Depressive Disorder (MDD). Reduce dose in the elderly. See specific literature for hepatic, renal dosing. Antidepressants may increase the risk of suicidal thinking in children, adolescents and young adults with MDD, monitor appropriately.^{1,2,3} Monitor patients for symptom resolution, depression, suicidal ideation, anxiety, panic attacks, and mania.^{1,2,3}

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)			
Generic (Brand Name)	Adult Starting Dose and Max Dose Per Day	Advantages	Disadvantages
Duloxetine (Cymbalta)	Initial adult dose = 20 – 30mg BID. Max adult dose/day = 60mg. Initial geriatric dose = 10-20mg BID.	Also used for anxiety, peripheral neuropathy, fibromyalgia or stress urinary incontinence. ^{1,2,3} May take without regards to meals. ^{1,2,3}	BID dosing. May increase BP. ⁴ Avoid in patients with substantial alcohol use or evidence of chronic liver disease. Avoid if CRCL < 30mL/min and in hepatic impairment. Monitor BUN, CR, glucose. ¹ Do not chew or crush capsules, swallow whole. ^{1,2,3}
Venlafaxine IR (Effexor IR)	Initial adult dose is 25mg TID or 37.5mg BID. ^{1,2,3} Max adult dose/day = 375mg. Initial geriatric dose = 25mg QD.	Also used in anxiety or panic disorder. ^{1,2,3} Possibly fewer CYP450 interactions. ⁴ Generic.	Take with food. May increase BP at higher doses. ^{1,2,4} More lethal in overdose (with other drugs & alcohol) than SSRIs but not TCAs. ⁴ Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 mL/min. Monitor height and weight in children. ^{1,2,3} Monitor cholesterol. ^{1,2,3}
Venlafaxine XR (Effexor XR)	Initial adult dose = 75mg QD. Max adult dose/day = 225mg. Initial geriatric dose = 37.5mg QD.	XR version administered QD. Used in anxiety or panic disorder. ^{1,2,3} Possibly fewer CYP450 interactions. ⁴ XR capsule dose may be swallowed whole or opened and sprinkled on apple sauce followed by a glass of water. ^{1,2,3}	Take with food. May increase BP at higher doses. ^{1,2,4} Expensive. ⁴ More lethal in overdose (with other drugs & alcohol) than SSRIs but not TCAs. ⁴ Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 mL/min. Monitor height and weight in children. ^{1,2,3} Monitor cholesterol. ^{1,2,3}

First-Line Antidepressant Medication
 Dual action drugs which are Serotonin and Norepinephrine Reuptake inhibitors. SSRIs, SNRIs, Bupropion, Mirtazapine are first-line therapy for adults with MDD. Possible efficacy in cases not responsive to TCAs or SSRIs. Reduce dose for the elderly. Monitor blood pressure regularly especially when initiating and titrating the dose.^{1,2,3} Antidepressants may increase the risk of suicidal thinking in children, adolescents and young adults with MDD, monitor appropriately.^{1,2,3} Monitor depression, suicidal ideation, anxiety, mania, and panic attacks.^{1,2,3}

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