VA/DOD CLINICAL PRACTICE GUIDELINE

Management of Major Depressive Disorder (MDD)

KEY ELEMENTS OF THE MDD GUIDELINE

- Screen annually for Depression (PHQ-2)
- Assess for Suicide Risk
- Obtain Standardized Symptom Score (PHQ-9)
- Diagnose based on DSM IV-TR Criteria
- Evaluate For Alternative Diagnosis (Bipolar, PTSD, Other)
- Initialize Treatment Strategies based on Symptom Severity
  - » Mild: watchful waiting and counseling
  - » Moderate (or mild not improving): monotherapy psychotherapy or medication
  - » Moderate to Severe: may require combination of psychotherapy and medication
- Shared decision in selection of treatment option considering patient preference
- Address psychoeducation and self-management for all patients
- Consult/refer to specialty for incomplete response, complicated MDD or patient request
- Monitor and follow-up especially when beginning therapy and changing of medication
- Use PHQ-9 to assess treatment response
- Continue therapy (9-12 months) to prevent relapse
- Consider long-term maintenance to prevent reoccurrence

Access to full guideline and toolkit:
http://www.healthquality.va.gov or,
https://www.qmo.amedd.army.mil
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VA/DoD Evidence-Based Practice

Algorithm A: *Assessment and Diagnosis*

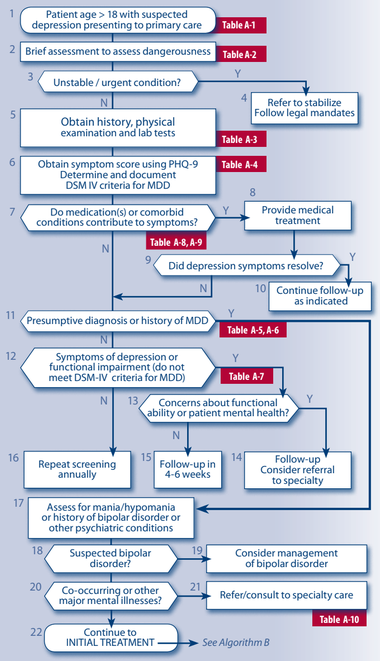


TABLE A-1 Screening for Depression (PHQ-2)

Over the last two weeks, have you been bothered by any of the following problems?	Yes	No
Little interest or pleasure in doing things?	✔	✔
Feeling down, depressed, or hopeless?	✔	✔

If the patient responded "yes" to either question, consider asking more detailed questions or using PHQ-9 patient questionnaire. (Table A-4)

If the patient's response to both questions is "no", the screen is negative.

TABLE A-2 Assessment for Dangerousness

1. Assess Threat to SELF

ASK THE QUESTIONS:
Are you feeling hopeless about the future/present?

IF YES ASK:
Have you had thoughts about taking your life?

IF YES ASK:
When did you have these thoughts and do you have a plan to take your life?
Have you ever had a suicide attempt?

2. Assess Threat to OTHERS

a. Assess whether the patient has an active plan and method/means (e.g., weapons in the home)
b. Assess whom the patient wishes to harm
c. Assess whether the patient has ever lost control and acted violently
d. Assess seriousness/severity of past violent behavior

3. If patient expresses dangerousness to self or others, take steps to ensure patient safety until consultation with a mental health professional has taken place

TABLE A-3 Clinical Assesment of the Patient with MDD

- Medical history
- Physical examination
- Mental status examination (MSE)
- Relevant laboratory tests
- Psychosocial history
- Drug inventory, including over-the-counter (OTC) drugs and herbals
- Comorbid conditions

TABLE A-4 Patient Health Questionnaire (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following?		*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
	Total Score ____		=	+	+

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

TABLE A-5 Symptom Severity Classification

Severity Level	*(PHQ-9) Total Score*	*Functional Impairment*
Mild	5-14	Mild
Moderate	15-19	Moderate
Severe	≥ 20	Severe
Modifiers		
Complications	Co-occurring post traumatic stress disorder (PTSD), substance use disorder (SUD), psychosis, suicide risk, mania, significant social stressors, war related conditions	
Chronicity	More than 2 years of symptoms despite treatment	

The PHQ-9 assessment tool combined with a clinical interview should be used to obtain the necessary information about symptoms, symptom severity, and effects on daily functioning that is required to diagnose MDD based on DSM-IV-TR criteria.

TABLE A-6 DSM-IV Diagnostic Criteria for MDD

MDD diagnosis is based on the following list of symptoms, and requires the presence of symptom 1, 2, or both; and at least 5 of 9 symptoms overall; these symptoms must persist for at least 2 weeks

1. Depressed mood nearly every day for most of the day, based on self-report or observation of others
2. Marked reduction or loss of interest or pleasure in all, or nearly all, activities for most of the day, nearly every day
3. Significant non-dieting weight loss or weight gain (> 5% change in body weight)
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation (should be observable by others)
6. Fatigue/loss of energy nearly every day
7. Feelings of worthlessness or excessive/inappropriate guilt (possibly delusional) nearly every day
8. Diminished cognitive function (reduced ability to think or concentrate, or indecisiveness) nearly every day
9. Recurrent thoughts of death and/or suicide, suicide planning, or a suicide attempt

TABLE A-7 Nomenclature for Clinical Depressive Conditions

DSM-IV-TR	*Diagnostic Criteria*	*Duration*
Major Depression	At least 5 depressive symptoms* (must include either depressed mood or anhedonia)	≥ 2 weeks
Dysthymia	3 or 4 dysthymic symptoms§ (must include depressed mood)	≥ 2 years
Depression NOS	***Variables:*** all included disorders must cause clinically significant impairment of daily functioning but fail to meet the classification for major depression or dysthymia. ***Example:*** minor depression with 2 to 4 depressive symptoms	≥ 2 weeks

** Depressive symptoms - See Table A-4*
§ Dysthymic symptoms are generally the same as major depressive symptoms, with the addition of feeling of hopelessness and the omission of suicidal ideation.

TABLE A-8 Pathobiologies Related to Depression

Pathology	*Disease*
Cardiovascular	Coronary artery disease; Congestive heart failure; Stroke; Vascular dementias
Chronic Pain	Fibromyalgia; Low back pain; Bone pain
Degenerative	Hearing loss; Neurodegenerative diseases (i.e. Alzheimer's, Parkinson's, Huntington's)
Immune	HIV; Multiple sclerosis; Systemic lupus erythematosis; Sarcoidosis
Metabolic/Endocrine (including renal and pulmonary)	Malnutrition; Vitamin deficiencies; Hypo/hyperthyroidism; Addison's disease; Diabetes Mellitus; Hepatic disease (cirrhosis); COPD; Asthma; Kidney disease
Neoplasms	Of any kind, especially pancreatic or CNS
Trauma	Traumatic Brain Injury; Amputation; Burn injuries

TABLE A-9 Medication Induced Depression

Class	*Association*	*Class*	*Association*
ACE-inhibitors	+/–	Lipid-lowering agents	+/–
Barbiturates	+	NSAIDs	+
Benzodiazepines	+	Progesterone implants	+/–
Beta-blockers	+/–	Reserpine, Clonidine, Methyldopa	+
Calcium channel blockers	+/–	Selective estrogen receptor modulators	+/–
Interferon-α	+/–	Topiramate	+
Interleukin-2	+	Vareniciline (Chantix)	+

TABLE A-10 Indications for Referral to Mental Health

- Evidence of psychotic features, past mania or hypomania
- History of/Potential for Suicide/Violence
- Unclear diagnosis (PTSD, SUD)
- Signs of comorbid psychiatric conditions
- Unable to treat patient in primary care
- Need for psychosocial interventions
- Patient preference

Algorithm B: *Treatment, Re-assessment and Follow-up*

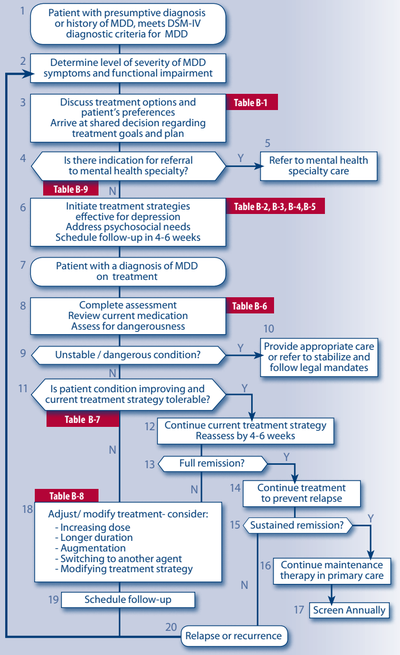


TABLE B-1 Shared Decision & Treatment Plan

Present Treatment Options	• Present feasible treatment options • Describe pros/cons of each approach
Discuss with Patient	• Side effect profiles for antidepressants • Availability of psychological counseling • Description of psychological counseling
Elicit Patient Preference	• Ask patient for their treatment preference

TABLE B-2 Treatment Strategies

Severity	*PHQ Score Functional Impairment*	*Initial Treatment Strategies*
Mild	5-14 Mild	• Watchful waiting • Supportive counseling • If no improvement after one month, consider antidepressant or brief psychotherapy counseling
Moderate	15-19 Moderate	• Start with monotherapy of either antidepressants or psychotherapy, or a combination of both
Severe	> 20 Severe	• May start with monotherapy of either antidepressants or psychotherapy; • Should emphasize combination of both or multiple drug therapy
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 (antidepressants or psychotherapy), or a combination of both • For Mod/Severe: combination or multiple drug therapy

Treatment Strategy Options Include:

1. Psychoeducation and self-management (provide to all MDD patients)
2. Watchful waiting
3. Monotherapy (psychotherapy or pharmacotherapy)
4. Combination psychotherapy and antidepressants
5. Treatment of complex patients
6. Somatic treatment
7. Inpatient and residential

TABLE B-3 Psychoeducation and Self-Management

Collaboratively choose one or two goals at a time.

Nutrition	Maintain a balanced diet.
Exercise	Strong evidence shows 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.

TABLE B-4 First-Line Treatment Options

Psychotherapies

- **Cognitive Behavioral Therapy (CBT)**
- **Interpersonal Therapy (IPT)**
- **Problem Solving Therapy (PST)**

Recommended for patients who:
- Prefer psychological counseling.
- Had a previous good response to psychological counseling.
- Cannot tolerate medications.
- Have a prior course of illness that is chronic or characterized by poor inter-episode recovery.

May be helpful for patients who:
- Have partial response to full dose of an antidepressant;
- Have personality disorders; and/or
- Have complex psychosocial problems.

Pharmacotherapy

Antidepressants

- **SSRIs**
- **SNRIs**
- **Bupropion**
- **Mirtazapine**

- No evidence that any one medication is better than another
- Select based on side effects, cost, and availability

TABLE B-5a Antidepressant Dosing and Monitoring

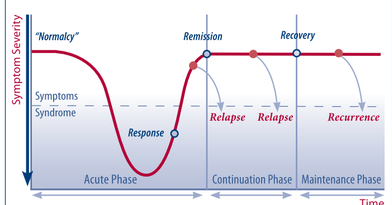
Class	*Agent*	*Initial Dose*	*Titration Schedule†*	*Maximum Dose/ Day*	*Initial Dose or Guidance: Special Populations*		
					Geriatric	*Renal*	*Hepatic*
SSRIs	Citalopram	20 mg once a day	weekly	60 mg	10-20 mg	Avoid: CrCl <20 ml/min	↓ dose
	Escitalopram	10 mg once a day	weekly	40 mg	5-10 mg	Avoid: CrCl <20 ml/min	10 mg
	Fluoxetine	20 mg once a day	every 2 weeks	80 mg	10 mg	No change	↓ dose 50%
	Fluoxetine Weekly	90 mg once a week	NA	90 mg	90 mg	Avoid	Avoid
	Paroxetine	20 mg once a day	weekly	50 mg	10 mg	10 mg	10 mg
	Paroxetine CR	25 mg once a day	weekly	62.5 mg	12.5 mg	12.5 mg	12.5 mg
	Sertraline	50 mg once a day	weekly	200 mg	25 mg	No change	↓ dose
SNRIs	Duloxetine	60 mg as a single or divided dose	NA	60 mg	20-40mg	Avoid if CrCl<30	Avoid
	Venlafaxine IR	37.5 mg twice a day	weekly	225-375 mg	25-50 mg	CrCl = 10-70, ↓ dose 50%	↓ dose 50%
	Venlafaxine XR	75 mg once a day	weekly	225 mg	37.5-75 mg	CrCl = 10-70, ↓ dose 50%	↓ dose 50%
DNRIs	Bupropion IR	100 mg twice a day	weekly	450 mg	37.5mg twice a day	Has not been studied	Severe:
	Bupropion SR	150 mg once a day	weekly	400 mg	100 mg once a day		75 mg/day
	Bupropion XR	150 mg once a day	weekly	450 mg	150 mg once a day		100mg QD or 150mg QOD
SARIs	Trazodone	50 mg three times a day	weekly	600 mg	25-50 mg	No change	Unknown
NaSSAs	Mirtazapine	15 mg daily at bedtime	weekly	45 mg	7.5 mg at bedtime	CrCl <40 mL/min	CI ↓ 30%
TCAs	Nortriptyline	25 mg three to four times a day	weekly	150 mg	10-25 mg at bedtime	No change	Lower dose and slower titration recommended
	Desipramine	75 mg once a day or clivided	weekly	300 mg	10-25 mg once a day	No change	

†Recommended minimum time between dose increases; Duloxetine, Escitalopram, Fluoxetine, Paroxetine CR, are not on the VA National Formulary.
All antidepressants listed are FDA Pregnancy Category C, except paroxetine which is Category D. Desipramine and Nortriptyline have not been assigned a pregnancy category by FDA.

TABLE B-5b Consider Medication Side Effects

Category	*Drug*	*Anticholinergic Activity (muscarinic)*	*Sedation (H1)*	*Orthostatic Hypotension (alpha1)*	*Cardiac Effects*	*GI Effects*	*Seizures*	*Weight Gain*	*Sexual Dysfunction*
SSRIs	Citalopram	0	0/+	0	0	+++	0	0	+++
	Escitalopram	0	0/+	0	0	+++	0	0	+++
	Fluoxetine	0	0/+	0	0/+	+++	0/+	0/+	+++
	Paroxetine	0/+	0/+	0	0	+++	0	0/+	+++
	Sertraline	0	0/+	0	0	+++	0	0	+++
SNRIs	Duloxetine	0	0/+	0/+	0/+	+++	0	0/+	+++
	Venlafaxine	0	0	0	0/+	+++	0	0	+++
NDRIs	Bupropion	0	0	0	0	++	+++	0	0
NaSSAs	Mirtazapine	0	+++	0/+	0	0/+	0	0/+	0

Phases of Treatment of Major Depression



Adapted from Kupfer. J Clin Psychiatry. 1991: 52 (suppl. 5) :28-34

TABLE B-6 Assessment of Treatment Response

- Symptom severity (PHQ-9) and risk for suicide
- Tolerability to treatment (Adverse effects)
- Adherence to treatment
- Medical problems influencing recovery
- Psychosocial barriers to therapy
- Revaluate diagnosis and appropriate treatment

TABLE B-7 Assess Treatment Response with PHQ-9*

Onset Response to Treatment	**Minimal clinically significant:** a change in PHQ-9 score of 25% **Response to treatment:** improvement in PHQ-9 score of 50% from baseline
Full Remission	PHQ-9 score of 4 or less, maintained for at least 1 month
Recovery	PHQ score of 4 or less, maintained for at least 6 months

**For other assessment tools see Full Guideline*

TABLE B-8 Treatment Response and Follow-up

Step	*Patient Condition*	*Options*	*Reassess†*
1	Initial Treatment	See Table B-2	2 weeks*
2	Non response to initial low dose*	• Increase dose • Consider longer duration • Switch • Consider referral to specialty care	4 to 6 weeks
3	Failed second trial of antidepressant	• Switch • Augment or combine • Consider referral to specialty care	8 to 12 weeks
4	Failed 3 trials including augmentation	• Re-evaluate diagnosis and treatment • Consider referral to specialty care	12 to 18 weeks

** If treatment is not tolerable, switch to another antidepressant.*
†Cumulative time from initial treatment.

TABLE B-9 Indications for Referral to Specialty

- Evidence of psychotic features, past mania or hypomania (Bipolar)
- Complicated depression with comorbidity (PTSD, SUD)
- Treatment resistance
- Primary care out of comfort zone
- Patient request