MSO OF PUERTO RICO

DIAGNOSING AND MANAGING
MAJOR DEPRESSIVE DISORDER (MDD)

DSM-5 CRITERIA (MAJOR DEPRESSIVE EPISODE-MDE)

- **5 or more symptoms** during the same **2-week period (1 symptom must be depressed mood or diminished interest/pleasure):**
  - Depressed mood (For C&A can be irritable mood)
  - Diminished interest or loss of pleasure in almost all activities (anhedonia)
  - Significant weight change or appetite disturbance (increase or loss)
  - Sleep disturbance (insomnia or hypersomnia)
  - Psychomotor agitation or retardation
  - Fatigue or loss of energy
  - Feelings of worthlessness
  - Diminished concentration; indecisiveness
  - Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for committing suicide
- Impairment in social, occupational or other important areas of functioning.
- Symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
- The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorders.
- There has never been a manic episode or a hypomanic episode.

DIFFERENTIAL DIAGNOSIS

- **CNS diseases** (e.g. Parkinson disease, dementia, multiple sclerosis, neoplastic lesions) – Order dementia work-up if concentration is markedly affected – Vitamin B12, Folate & VDRL
- **Endocrine disorders** (e.g., hyperthyroidism, hypothyroidism) – order TSH on initial visit to R/O
- **Drug-related conditions** (e.g., cocaine abuse, side effects of some CNS depressants) – Order Toxicology Screen on initial visit to R/O
- **Infectious diseases** (e.g. mononucleosis, HIV)
- **Sleep-related disorders** (e,g. sleep apnea)

PHQ-9 SCREENING & MONITORING TOOL

- 9-item depression scale; each item is scored from 0-3 depending on frequency
- 0-27 severity score + functional impairment assessment

SYMPTOMS & IMPAIRMENT	SCORE	SYMPTOM SEVERITY	TREATMENT RECOMMENDATIONS	FOLLOW-UP
1-4 symptoms without functional impairment	0-4	Minimal or None	Watchful waiting Psychoeducation about Depression	At least annually
1-4 symptoms and positive response to questions 1 or 2 + functional impairment	5-9	Mild Depressive Symptoms	Supportive counseling Education to call if deteriorates	Every other month
2-4 symptoms and positive response to questions 1 or 2 + functional impairment	10-14	Moderate Depressive Symptoms	Psychotherapy If no improvement after one or more months, consider use of antidepressant	Monthly
5 symptoms and positive response to questions 1 or 2 + functional impairment	15-19	Moderately Severe Depressive Symptoms	Patient preference for antidepressant and/or psychotherapy	Every 2-4 weeks
5 symptoms and positive response to questions 1 or 2, functional impairment	≥20	Severe Depressive Symptoms	Antidepressant + Psychotherapy combination	Every 1-2 weeks until PHQ-9 improves ≥5 points or 50% reduction from baseline score

- **Basic recommended behavioral changes** Exercise, increased pleasurable activities, promote social interactions, motivate positive self-care, eliminate alcohol and other drugs of abuse, and encourage to postpone major life decisions
- **Referral or co-management with mental health clinician if:** patient has high suicide risk, bipolar disorder, inadequate treatment response, complex psychosocial needs and/or other active mental disorders.

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Should be taken daily and wait at least 2-4 weeks before initial improvement
Clinical response (50% reduction on PHQ-9 score from baseline) expected 2-12 weeks at a therapeutic dose
Full remission should be the goal (PHQ-9 score <5 sustained for 2 months) within 4-8 months from Tx start
Tx should continue for 6-9 months once full remission is achieved and before antidepressant tapering down is considered
If ≥2 MDEs within 5 years, long-term preventive treatment is suggested

CLASS	AGENT	INITIAL DOSE	TITRATION SCHEDULE*	MAXIMUM DOSE/DAY	GERIATRIC INITIAL DOSE	SIDE EFFECTS AND COMMENTS
SSRI's (First line of Tx due to safety)	**Citalopram** (Celexa)	20mg PO qd	20mg weekly	40mg; 20mg geriatric	10-20mg PO qd	■ Short-term: GI upset/nausea; jitteriness/restlessness/ insomnia; sedation/fatigue ■ Long-term: Sexual dysfunction in 25-33% of patients should consider lowering dose or changing to Bupropion or Mirtazapine ■ Weight gain in 5-10% of patients→ avoid Paroxetine ■ Dose-dependent QT prolongation with Citalopram ■ Paroxetine most anticholinergic; avoid in elderly ■ Paroxetine and fluoxetine CYP2D6 and CYP2B6 inhibitors ■ SSRI-discontinuation syndrome: GI upset, Flu-like symptoms, anxiety, dizziness, vivid dreams, and electric shock-like sensations throughout the body → more common with Paroxetine and less likely with Fluoxetine ■ Risk of Serotonin Syndrome if used with Triptan, Demerol, Dextromethorphan, St. John's Wort.
	Escitalopram (Lexapro)	10mg PO qd	10mg weekly	20mg	5-10mg PO qd	
	Sertraline (Zoloft)	50mg PO qd	50mg weekly	200mg	25mg PO qd	
	Fluoxetine (Prozac)	200mg PO qd	20mg every 2 weeks	80mg	10mg PO qd	
	Paroxetine (Paxil)	200mg PO qd	20mg weekly	50mg	10mg PO qd	
SNRI's	**Venlafaxine IR** (Effexor)	37.5mg PO bid	75mg weekly	375mg	25mg PO qd or bid	■ Sexual dysfunction common ■ Increase in blood pressure had been reported with Venlafaxine and Duloxetine ■ Venlafaxine NE activity dose-related ■ Fluid retention in geriatric patients ■ Desvenlafaxine active metabolite of Venlafaxine ■ Venlafaxine and Duloxetine may also present with discontinuation syndrome like that with SSRIs due to short half-life
	Venlafaxine XR (Effexor XR)	75mg PO qd	75mg weekly	225mg	37.5-75mg PO qd	
	Duloxetine (Cymbalta)	20-30mg PO qd	20-30mg weekly	120mg	20mg PO qd or bid	
	Desvenlafaxine (Pristiq)	50mg PO qd	Not necessary	100mg; no benefit at doses >50mg/day	If CrCl <30ml/min, 25mg PO qd	

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NDRI's	**Bupropion IR** (Wellbutrin)	100mg PO bid	100mg weekly	450mg	37.5mg PO bid	■ Risk of seizures is dose-related; avoid if seizure history, bulimia or eating disorder ■ Tremors CYP2D6 inhibitor
	Bupropion SR (Wellbutrin SR)	150mg PO qd	150mg weekly	200mg PO qd	100mg PO qd	
	Bupropion XR (Wellnutrin XL)	150mg PO qd	150mg weekly	450mg PO qd	150mg PO qd	
NE antagonist	**Mirtazapine** (Remeron)	15mg PO qhs	15mg weekly	45mg	7.5mg PO qhs	■ Very sedating & orthostatic hypotension → risk of falls ■ Doses >15 mg less sedating ■ May stimulate appetite
5-HT2 antagonist	**Trazodone (Desyrel)**	50mg PO tid	50mg weekly	400mg	25-50mg PO qhs	■ Very sedating & orthostatic hypotension → risk of falls ■ Priapism

- TCA's and MAOI's, even though effective, pose greater risk of serious side effects like cardiac arrythmias, seizures and hypertensive crisis.
- 50-70% of patients will require at least one change in antidepressant to achieve response or remission.
- Once clinically indicated, antidepressants should be tapered down the same way Tx is optimized to prevent discontinuation symptoms.

- Good reasons for considering stopping a medication include:
  - intolerable side effects, dangerous interactions with necessary medications,
  - the medication was not indicated to start with (e.g. bipolar depression);
  - and medication has been at maximum therapeutic dose (in an adherent patient) without improvement for 4-8 weeks

References:

2016 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder

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Diagnosis and Treatment of depression in adults: 2012 Clinical Practice Guideline – Kaiser Permanente Care Management Institute (https://www.guidelinecentral.com/share/summary/52d561eeef5ff#section-420)

APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition, October 2010.