

How to Evaluate and Treat Depression in Medical Settings

Learning Objectives:

- 1) Demonstrate knowledge of common etiologies and medical workup to evaluate depression symptoms in patients with medical illness.
- 2) Describe a treatment approach for the management of depressive disorders in patients with medical illness.

Step 1: Familiarize oneself with medical correlates, causes of, and contributors to depressive disorders

- Clinically significant depressive symptoms are common in patients with medical illnesses such as coronary artery disease, diabetes, hypothyroidism, HIV, cancer, stroke, epilepsy, multiple sclerosis, and Parkinson's disease.
- Differential diagnosis of depressive disorders in medical settings:
 - Anatomic or physiological effects of an illness (DSM 5 Diagnosis: Depression Due to Another Medical Condition)
 - Prescribed medications or recreational drugs (DSM 5 Diagnosis: Substance Induced Depressive Disorder).
 - A psychological reaction to having a serious medical illness. In such cases the patient may have an adjustment disorder (DSM 5 Diagnosis: Adjustment Disorder with Depressed Mood). An adjustment disorder may progress to major depressive disorder or a persistent depressive disorder.
 - A primary psychiatric disorder (e.g., major depressive disorder)

Step 2: Maintain vigilance for syndromes that are distinct from but may be mistaken for depression

- Hypoactive delirium presents with withdrawal, apathy, and psychomotor slowing. It can be distinguished from depression by sleep-wake disturbance, a sudden change in mental state, inattention, and other cognitive abnormalities.
- Demoralization is characterized by loss of meaning, disenchantment, helplessness, and feeling ineffective. In contrast to depression, patients with demoralization can experience pleasure.

Step 3: Evaluate and diagnose depressive disorders

- The diagnostic criteria for a major depressive episode include depressed mood or anhedonia and four additional symptoms including impaired sleep, feelings of guilt or worthlessness, low energy, impaired concentration, changes in appetite/weight, psychomotor agitation or slowing, or wish for death/suicidal thoughts/suicidal behaviors for a duration of 2 weeks.

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- Many of the physical symptoms of medical illnesses such as changes in sleep, appetite, energy, concentration, and psychomotor slowing overlap with the diagnostic criteria for major depressive disorder. An inclusive approach that includes physical symptoms is more sensitive at detecting depressive disorders.
- Alcohol, opioids, and benzodiazepines can cause or contribute to depression as can stimulant withdrawal.
- Certain prescribed medications can cause depressive symptoms. Angiotensin converting enzyme inhibitors, anticonvulsants, antihypertensives (e.g., clonidine, alpha-methyldopa, thiazide diuretics), antibiotics (e.g., metronidazole), antiretrovirals (e.g., efavirenz), L-dopa, antineoplastics (e.g., procarbazine, vincristine, vinblastine), propranolol, calcium channel blockers, statins, corticosteroids, estrogen, interferon-alpha, isotretinoin, and metoclopramide.
- Routine annual screening is recommended in primary care and in medical subpopulations when depression is highly prevalent, and there are measures in place to further evaluate the patient and treat accordingly.
- Validated screening tools in medical settings include the Patient Health Questionnaire-2 and the Patient Health Questionnaire-9 (PHQ-2 and PHQ-9), Hospital Anxiety Depression Scale (HADS), Center for Epidemiologic Studies Depression Scale - Revised (CESD-R), Brief Symptom Inventory, and the Distress Thermometer.
- Suicide risk assessment should be conducted during an evaluation on all patients who present with depression symptoms.
- A work-up for depression symptoms includes a complete blood count, basic metabolic panel, liver panel, thyroid stimulating hormone, vitamins B12 and D, and a urine toxicology screen.
- Neuroimaging is indicated when central nervous system pathology is suspected (e.g., mass lesion, stroke, multiple sclerosis plaques, or vasculitis).
- Electroencephalogram is useful in evaluation of depressive symptoms when the history is atypical and depressive symptoms are suspected to be due to seizures.

Step 4: Develop a treatment plan for depressive disorder

- Psychoeducation is the cornerstone of treatment.
- A supportive therapeutic relationship frames the care of individuals with depression. Providing hope, supporting the patient's self-esteem, and keeping nihilism at bay are essential tasks in caring for depressed patients
- Self-management strategies such as behavioral activation and mind-body interventions are simple and easily accessible first-line treatments for mild depression.
- Antidepressant medications can be the first-line treatment for major depressive disorder of mild severity and should be the first-line treatment in moderate or severe depression. Choice of antidepressant medication should be based on previous

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response to treatment, interaction with medical medications, vulnerability to adverse effects, and appreciation that specific side effects can be helpful in medical settings. Table 1 lists common antidepressants, benefits to specific populations, and adverse effects.

- Electroconvulsive therapy is a safe, effective, and fast-acting treatment for major depressive disorder. It should be considered when the patient's functioning is precarious, and in treatment resistant depression, depression during pregnancy, psychotic depression, catatonia, and depression in Parkinson disease.
- Cognitive behavior therapy, interpersonal psychotherapy, short-term psychodynamic psychotherapy, and mindfulness-based cognitive therapy are evidence-based psychotherapies to treat depression.
- Complementary and alternative treatments that are effective for mild moderate depression are yoga, exercise, light therapy, S-Adenyl methionine (SAM-e), Omega-3 fatty acids, and St. John's Wort.
- Collaboration and coordination with the patient's medical providers is an important feature of successful treatment. These principles are formalized in the collaborative care model, a fully integrated care delivery model.

Table 1: Antidepressants

Class/Mechanism	Examples	Benefits to specific populations	Side/adverse effects
SSRIs	Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram, Fluvoxamine	• Comorbid anxiety and trauma related disorders • Irritable bowel syndrome (constipation subtype)	• Sexual dysfunction • Nausea, vomiting, diarrhea • Headaches • Gastrointestinal bleeding • QTc prolongation with citalopram • Serotonin syndrome when used with other serotonergic agents* • SIADH, especially in elderly
SNRIs	Venlafaxine, Duloxetine, Desvenlafaxine, Levomilnacipran	• Comorbid anxiety and trauma related disorders • Comorbid chronic musculoskeletal and neuropathic pain syndromes	• Sexual dysfunction • Hypertension, especially with venlafaxine • Nausea and vomiting • Headaches • Hepatotoxicity with duloxetine • Serotonin syndrome when used with other serotonergic agents* • SIADH, especially in elderly

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Dopamine/ Norepinephrine reuptake inhibitor	Bupropion	• Help with weight loss, motivation, energy, and attention • Antidepressant of choice when sexual dysfunction present • Comorbid ADHD	Avoid with seizures and brain injury
Serotonin- histamine antagonist	Mirtazapine	• Appetite stimulation/weight gain • Sleep • Nausea	• Weight gain • Sedation
Serotonin reuptake inhibitor and serotonin partial agonist	Vilazodone	Unknown	• Nausea, vomiting • Headache • Dry mouth • Dizziness • Insomnia • Pancreatitis • Sleep paralysis • Serotonin syndrome when used with other serotonergic agents*
Tricyclic antidepressants	Amitriptyline, Nortriptyline, Imipramine, Desipramine, Clomipramine	• Chronic pain • Irritable bowel syndrome (diarrhea subtype) • Migraine prophylaxis	• Weight gain • Anticholinergic side effects (dry mouth, delirium, mydriasis, ileus, urinary retention) • Cardiac arrhythmias and conduction abnormalities • Orthostatic hypotension
MAO inhibitors (MAOIs)	Phenelzine, tranylcypromine, and isocarboxazid (MAO-A and MAO-Bi; irreversible), Selegiline (MAO- Bi only; irreversible), Moclobemide (MAO-Ai only, reversible)	Parkinson's disease (MAO-B inhibitors - selegiline)	• Weight gain • Nausea, vomiting, diarrhea • Headaches • Drug-food interactions: • Hypertensive crisis when foods rich in tyramine (aged cheeses, sauerkraut, cured meats, beer, wine, fermented soy products, avocado) are combined with nonselective and irreversible MAOIs. A hypertensive crisis is characterized by headache, nausea, vomiting, diaphoresis, palpitations, tachycardia and hypertension. • Drug-drug interactions:

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			• Serotonin syndrome when MAOIs used with other serotonergic agents* • Hypertensive crisis when MAOIs are used with adrenergic agents**
Stimulants	Methylphenidate Amphetamine/dextroamphetamine	• Fatigue • Consider in patients with HIV, cancer, hospitalized patients needing fast-acting depression treatment	• Weight loss • Tachycardia

*Serotonergic agents: SSRIs, SNRIs, tricyclic antidepressants, MAOIs, opioids, dextromethorphan, ondansetron, linezolid, ritonavir, LSD, and ecstasy. SSRIs: selective serotonin reuptake inhibitor; SNRI: serotonin norepinephrine reuptake inhibitor; SIADH: syndrome of inappropriate antidiuretic hormone; ADHD: attention deficit hyperactivity disorder

* Adrenergic agents: decongestants, methylphenidate, amphetamines, SNRIs, tricyclic antidepressants, bupropion, phentermine, guanethidine, methyl dopa, levodopa

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