TERMINOLOGY

CLINICAL CLARIFICATION

- Major depressive disorder is a chronic and relapsing disease, characterized by a pervasive sad mood and the loss of pleasure in most activities (anhedonia) persisting for at least 2 weeks [1]

CLASSIFICATION

- *DSM-5* diagnostic classification states that major depressive disorder presents with at least 5 of the following 9 symptoms: [2]
  - Depressed mood or anhedonia (patient must have at least 1; present most of the day nearly every day for a minimum of 2 consecutive weeks)
  - Sleep disturbance
  - Change in appetite or weight
  - Psychomotor problems
  - Lack of energy
  - Poor concentration
  - Feelings of worthlessness or guilt
  - Suicidal ideation
- Symptoms cause clinically significant distress or impairment in social, work, or other areas of functioning
- Episode is not attributable to the physiologic effects of a substance or other medical disorder

DIAGNOSIS

CLINICAL PRESENTATION

- History
  - Patients do not always present with a straightforward complaint of feeling depressed [3]
  - Vague somatic complaints or numerous complaints that do not fit any clear clinical pattern often occur, particularly in elderly patients and in patients for whom psychological symptoms are stigmatized [3]
    - Fatigue
    - Poor concentration
    - Memory impairment
    - Difficulty making day-to-day decisions
    - Decline in school or work performance
    - Decreased sexual interest
    - Sleep disturbance
    - Appetite changes
    - Weight changes (gain or loss)
    - Headache
    - Nausea
    - Pain
    - Change in bowel habits (constipation or diarrhea)
  - Depressive symptoms [3]
    - Loss of interest or pleasure in previously enjoyable things
    - Disproportionate feelings of guilt or thoughts of worthlessness
    - Suicidal thoughts or thoughts about dying
    - Psychotic symptoms (particularly in elderly patients)
    - Anxiety and worry
    - Preoccupation with physical complaints
- Physical examination
  - Psychological findings [3]
    - Depressed or flat affect
    - Appears withdrawn, with poor eye contact
    - Psychomotor agitation or retardation
    - Crying
    - Anxious behavior
    - Irritability
    - Evidence of self-neglect with poor personal hygiene
  - Dermatologic findings [3]
    - Evidence of self-harm (eg, healed lacerations, scars on body or extremities)

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- Weight loss, weight gain, or evidence of poor nutrition [3]

CAUSES AND RISK FACTORS

- Causes
  - Unknown
- Risk factors and/or associations
  - Age [1]
    - Median age of onset is 32 years
    - Overall prevalence is low until early adolescence
  - Sex [1]
    - Women are twice as likely as men to experience major depressive disorder, regardless of racial background, ethnic background, or socioeconomic status
      - Times of hormonal fluctuation convey the greatest risk
  - Genetics [1]
    - Major depressive disorder is a multifactorial disorder with genetic susceptibility
      - Greatest risk for major depressive disorder is observed in families with early age at onset [4]
  - Ethnicity/race [1]
    - Higher incidence in black and Hispanic populations compared with white populations
  - Other risk factors/associations [1]
    - History of childhood maltreatment in any form
    - Early parental loss (for women)

DIAGNOSTIC PROCEDURES

- Primary diagnostic tools
  - Depression screening tools (eg, Beck Depression Inventory, Patient Health Questionnaire-9) can be used initially to identify patients requiring full diagnostic interviews using standard diagnostic criteria [5, 6, 7, 8]
  - History and physical examination provide definitive diagnosis
  - Laboratory analyses (eg, hypothyroidism testing [TSH], urine or serum drug screen) can be used to exclude medical disorders that produce or exacerbate mood symptoms or screen for substance-induced mood symptoms [9]
- Other diagnostic tools
  - Standardized depression inventory tests
    - United States Preventive Services Task Force recommends the following: "All positive screening results should lead to additional assessment that considers severity of depression and comorbid psychological problems (eg, anxiety, panic attacks, or substance abuse), alternate diagnoses, and medical conditions" [5]
    - Beck Depression Inventory [8]
      - Self-rated questionnaire
      - Measures the intensity, severity, and depth of common depression symptoms
      - Standard test has 21 questions; a shorter 7-question version is optimized for screening use in the office setting
    - Hamilton Depression Rating Scale [8]
      - Observer-rated scale designed to be administered by the health care professional
    - Major Depression Inventory [7]
      - Self-rated questionnaire
      - Incorporates both the ICD10 symptoms of depression and the *DSM-IV* symptoms of major depression
    - Patient Health Questionnaire-9 [10, 6]
      - Self-rated questionnaire with 9 items

DIFFERENTIAL DIAGNOSIS

- Most common [11]
  - Persistent depressive disorder (dysthymia)
    - Characterized by:
      - Changes in eating
      - Altered sleeping pattern (eg, insomnia, hypersomnia)
      - Low energy
      - Low self-esteem
      - Inability to concentrate or make decisions
      - Feelings of hopelessness or pessimism
    - Fewer symptoms than major depressive disorder
    - Involves feeling depressed for periods of variable duration, but without meeting *DSM-5* criteria for major depressive disorder
    - Such patients often have major depressive disorder interspersed throughout their lifetime

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- Differentiated based on history and physical examination
- Bipolar disorder[12]
  - Mood disorder characterized by episodes of mania or hypomania
  - Carefully screen patients with major depression for bipolar disorder
    - 15% of patients with major depression have bipolar disorder[13]
    - Patients with bipolar disorder do not respond to antidepressants; therefore, differentiation is crucial
  - Presence of mania or hypomania is the cardinal feature that distinguishes bipolar disorder from major depressive disorder
    - Mania
      - A period of mood change (happy, excited, or irritable) that causes impairment and is distinct and noted by others
      - At least 4 of the following symptoms are present:
        - Inflated self-esteem or grandiosity
        - Little need for sleep (without the development of fatigue)
        - Pressured or overly verbose speech
        - Racing thoughts
        - Distractibility
        - Irritability or agitation
        - Reckless or high-risk behavior
  - Differentiated based on history and physical examination
- Adjustment disorder[14]
  - Temporary, short-term, nonpsychotic response to an event or situation, such as a divorce, death in the family, a disappointment, or a failure
  - Symptoms can include sadness, anxiety, insomnia, poor concentration, poor performance in school
  - Symptoms persist for no longer than 6 months after termination of the stressor
  - Does not meet criteria for another mental disorder
  - Differentiated based on history and physical examination
- Dementia[15]
  - Especially in elderly patients, may be mistaken for major depressive disorder during early stages of the illness
  - The following features are more closely associated with dementia:
    - Impaired, inconsistent, and fluctuating orientation, mood, and behavior
    - Cognitive impairment that worsens over time
    - Neurologic deficits often present (eg, dysphasia, apraxia)
    - Disabilities concealed by the patient
    - Inability to remember recent events; often unaware of memory loss
    - Onset of memory loss occurs before mood change
    - Frequently uncooperative, confused, or disoriented
    - Demonstrated lack of concern about cognitive deficit
  - Differentiated based on history and physical examination
- Parkinson disease[16]
  - Progressive disorder of the central nervous system that often coexists with depression
  - Associated with symptoms of major depressive disorder, in addition to:
    - Increased muscle tone with cogwheel rigidity
    - Coarse resting tremor
    - Akinesia
    - Loss of facial expression
    - Shuffling gait
    - Flexed posture
  - Differentiated based on history and physical examination
- Schizophrenia
  - Disorder that affects thoughts, feelings, and perceptions; primary symptom is psychosis with auditory hallucinations and delusions
  - Schizophrenic patients may develop secondary major depression[17]
  - Distinguished from major depressive disorder by the following:[17]
    - Severe personality deterioration
    - Thought disorder, including loose associations
    - Grandiose delusions

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- Hallucinations, which are typically auditory
- Bizarre behavior

– Differentiated based on history and physical examination

- Hypothyroidism [18]
  - Patients with hypothyroidism may have symptoms of major depressive disorder, in addition to signs and symptoms of slow metabolism (eg, dry skin, brittle hair, weight gain)
  - Differentiated by laboratory testing for hypothyroidism
- Substance use disorders
  - May cause symptoms of depression with chronic use or from withdrawal
  - Causative substances include:
    - Alcohol
    - Stimulants (eg, amphetamine, cocaine)
    - Cannabis (with chronic use)
    - Opiates
    - Anabolic steroids
  - Differentiated from major depressive disorder by:
    - Positive result from urine or serum drug screen for the substance, if available
    - History of mood disorder that occurs temporally with substance use or withdrawal
- Medication causes [10]
  - Drug classes that are known to produce symptoms similar to depression include:
    - Benzodiazepines
    - Steroids
    - Levodopa
    - Oral contraceptives
    - Interferon
  - Differentiated based on history and physical examination

TREATMENT

GOALS [10]

- Assess the patient for suicidality and take steps to protect the patient as needed
- Reduce signs and symptoms, including residual symptoms [19, 20, 21]
- Relieve any complications, such as malnutrition and substance abuse
- Restore prior level of psychosocial and occupational function
- Prevent relapse and recurrence

DISPOSITION

- Admission criteria [21]
  - Patients unable to take care of themselves at home
  - Patients undergoing electroconvulsive therapy
  - Suicidal/homicidal ideation with intention or overt suicide/homicide attempts
  - Psychosis
- Recommendations for specialist referral
  - Consult psychiatrist if the patient exhibits any of the following:
    - Suicidal or homicidal ideation or attempts
    - Severe confusion, raising the question of dementia or delirium
    - Delusions or hallucinations
    - Substance abuse or dependence
    - Suspected bipolar disorder
    - Depression that has not responded to appropriate drug therapy

TREATMENT OPTIONS

- Mild to moderate disease [22]
  - Psychotherapy is often adequate as initial therapy early in the disease course [23]
  - Use antidepressant medications for more severe or chronic disease
    - Antidepressant medications are first line treatment for depression of any severity that has persisted for 2 years or more [24]
    - First line options include: [25, 23, 26]
      - Selective serotonin reuptake inhibitors [27]
      - Serotonin-norepinephrine reuptake inhibitors

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        - Noradrenergic and specific serotonin antidepressants
        - Noradrenergic and dopaminergic antidepressants
      - Second line options include:[24]
        - Tricyclic antidepressants
        - MAOIs
    - Consider combination therapy (ie, psychotherapy and medication) when the response to a single therapy is inadequate
      - For most patients, combination therapy is more effective than either psychotherapy or antidepressant medication alone; particularly for chronic or moderate to severe disease
      - Also consider for recurrent disease (with 3 or more episodes)[25]
- Severe disease[22]
  - Drug therapy is required
  - For most patients, combination therapy (psychotherapy and medication) is more effective than either psychotherapy or antidepressant medication alone[25]
  - If patient has a high risk of suicide or if welfare is threatened (eg, lack or nutrition or fluid intake), electroconvulsive therapy will be necessary
  - Electroconvulsive therapy may be used as first line therapy for patients who have psychotic depression or catatonia and patients who have previously responded to this treatment method
- Relapse prevention[24]
  - Medication-responsive patients: continue medication at acute treatment dose after remission; use relapse risk to determine medication duration
    - Patients at lower risk of relapse (eg, experiencing first episode without other risk factors): continue medication at least 6 to 9 months after full remission[24,25]
    - Other patients: tailor medication duration to individual relapse risk
      - Patients with any increased risk of relapse: continue medication at least 1 year after full remission[25]
      - Higher risk patients (eg, having more than 5 lifetime episodes and/or 2 episodes in the past few years): continue medication for a minimum of 2 years; most will require long-term treatment
  - Patients with residual symptoms or at high risk of relapse: consider adding cognitive behavioral therapy to medication
  - Patients who respond well to acute-phase cognitive behavioral therapy: it is not routinely recommended to continue medication
  - Patients who are unstable or partial remitters (ie, patients in partial remission): continue cognitive behavioral therapy or antidepressants
  - Patients who respond to acute-phase electroconvulsive therapy: continue or initiate prophylactic medication; consider continuing electroconvulsive therapy in patients with frequent relapses who do not respond to prophylactic medication
- Esketamine nasal spray—the first NMDA (N-methyl-D-aspartate) receptor antagonist to receive FDA approval for major depression—can be used as an adjunct to an oral antidepressant for treatment-resistant depression (those whose condition has failed to respond to 2 or more standard antidepressant treatments)[28]
- Drug therapy
  - Selective serotonin reuptake inhibitors[29]
    - Citalopram
      - Citalopram Hydrobromide Oral tablet; Children and Adolescents 7 to 17 years: 10 mg PO once daily initially. Some experts recommend initial doses of 20 mg/day PO in those 12 years and older. Clinical guidelines recommend to start with a low dose and titrate gradually, in 10 mg/day increments at 4-week intervals until clinical response is achieved. Some studies titrate as often as every week. A dose of 20 mg/day PO is considered effective. Max: 40 mg/day in the general population and 20 mg/day in poor metabolizers of CYP2C19 due to the potential for QT prolongation. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.
      - Citalopram Hydrobromide Oral tablet; Adults 60 years and younger: Initially, 20 mg PO once daily; may increase to 40 mg PO once daily after 1 week if clinically indicated. Max: 40 mg/day in the general population and 20 mg/day in poor metabolizers of CYP2C19 due to the potential for QT prolongation. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.
      - Citalopram Hydrobromide Oral tablet; Adults older than 60 years: 20 mg PO once daily is the recommended and maximum daily dosage. Coadministration of certain drugs may need to be avoided or dosage adjustments may be necessary; review drug interactions.
    - Escitalopram[30,31]
      - Escitalopram Oral tablet; Children and Adolescents 12 to 17 years: The initial and recommended dose is 10 mg PO once daily. If needed, may increase to 20 mg/day after a minimum of 3 weeks, but a trial in adults suggested no additional benefit. Max: 20 mg/day PO. Periodically reassess the need for continued treatment.

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- Escitalopram Oral tablet; Adults: 10 mg PO once daily is the initial and recommended dose. If needed, may increase to 20 mg once daily after a minimum of 1 week, but one trial suggested no additional benefit. Max: 20 mg/day PO. Periodically reassess the need for continued treatment.
- Escitalopram Oral tablet; Geriatric Adults: 10 mg PO once daily is the initial and recommended dose. Periodically reassess the need for continued treatment.

– Fluoxetine
- Fluoxetine Hydrochloride Oral tablet [Depression/Mood Disorders]; Children and Adolescents 8 to 17 years: 10 to 20 mg PO once daily. An initial dose of 10 mg/day may be appropriate in lower weight children; increase to 20 mg/day after 1 week. Usual effective dose: 10 to 20 mg/day. May increase by 10 to 20 mg increments if response not sufficient; full effect may take 4 weeks or longer. Max: 60 mg/day. May divide daily dose into 2 doses (e.g., morning and noon) if the dosage is 20 mg/day or more.
- Fluoxetine Hydrochloride Oral tablet [Depression/Mood Disorders]; Adults: 20 mg/day PO initially. May increase after several weeks by 10 to 20 mg as needed and tolerated. Consider lower dosages for geriatric adults. Max: 80 mg/day PO. May divide daily dose into 2 doses (e.g., morning and noon) if the dosage is 20 mg/day or more.

– Paroxetine
- Paroxetine Hydrochloride Oral tablet; Adults: 20 mg PO once daily initially, usually in the morning. May increase by 10 mg at weekly intervals. Max: 50 mg/day PO. DEBILITATED ADULTS: 10 mg PO once daily initially, with increases as needed by 10 mg at a minimum of weekly intervals up to a maximum of 40 mg/day PO. When discontinuing, taper the dose if possible.
- Paroxetine Hydrochloride Oral tablet; Geriatric Adults: 10 mg PO once daily initially. May increase by 10 mg at weekly intervals. Max: 40 mg/day PO. When discontinuing, taper the dose if possible.

– Sertraline [32]
- Evidence recommends that physicians use caution when prescribing sertraline in pediatric patients (if at all)
  - For children 6 to 11 years with major depressive disorder: do not recommend off-label sertraline; the harms of the drug outweigh any benefits [33]
  - For adolescents 12 to 17 years with major depressive disorder: [33]
    - First line treatment: to achieve a clinical response with minimal risk of suicidality, recommend cognitive interventions first
    - Second line treatment: if cognitive interventions fail and adolescents are closely monitored for sertraline-associated harms, may recommend off-label sertraline
- Sertraline Hydrochloride Oral tablet; Children 6 to 11 years†: 12.5 mg to 25 mg/day PO initially. Begin with a low dose and titrate gradually in 12.5 to 25 mg/day increments at 4-week intervals until clinical response is achieved; some studies report titration in 25 mg to 50 mg/day increments as often as every 1 to 2 weeks. A dose of 50 mg/day PO is considered effective in some patients. Max: 200 mg/day PO.
- Sertraline Hydrochloride Oral tablet; Children and Adolescents 12 to 17 years†: 25 to 50 mg/day PO initially. Begin with a low dose and titrate gradually in 12.5 to 25 mg/day increments at 4-week intervals until clinical response is achieved; some studies report titration in 25 mg to 50 mg/day increments as often as every 1 to 2 weeks. A dose of 50 mg/day PO is considered effective in some patients. Max: 200 mg/day PO.
- Sertraline Hydrochloride Oral tablet; Adults: 50 mg PO once daily. A lower initial dose (25 mg PO once daily) may be used to minimize adverse effects. If necessary, increase at intervals of not less than 1 week. Max: 200 mg/day PO. The length of treatment should be determined on an individual basis. Periodically reassess the need for continued treatment.

○ Serotonin-norepinephrine reuptake inhibitors

– Duloxetine
- Duloxetine Oral capsule, gastro-resistant pellets; Adults: Initially, give 20 mg PO twice daily or 60 mg/day PO as a single dose or in 2 divided doses (i.e., 30 mg PO twice daily). Alternatively, give 30 mg/day PO for 1 week, then increase to 60 mg/day. Target maintenance dose: 60 mg/day; dividing doses may increase tolerability. Max: 120 mg/day PO, but more than 60 mg/day has not been shown to have an additional benefit.

– Milnacipran
- Milnacipran Hydrochloride Oral tablet; Adults: Initially, 12.5 to 25 mg PO twice daily. Based on individual response, the dose may be titrated to 100 mg PO twice daily. Max: 200 mg/day. In one trial of adult patients with diabetes mellitus type 2 and co-morbid depression, 72.6% of treated patients fulfilled criteria for antidepressant response according to the Beck Depression Inventory scale.

– Venlafaxine
- Venlafaxine Hydrochloride Oral tablet; Adults: 75 mg/day PO, given in 2 or 3 divided doses, initially. If needed, may increase by 75 mg/day no less than every 4 days. Outpatient Max: 225 mg/day PO, given in divided doses. Institutional Max: 375 mg/day PO, given in 3 divided doses.

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- Noradrenergic and specific serotonin antidepressants
  - Mirtazapine[31]
    - Do not use concomitantly with MAOIs
    - Mirtazapine Oral tablet; Adults: 15 mg PO once daily at bedtime, initially. If needed, may titrate no sooner than every 1 to 2 weeks. Geriatric patients may need slower titration schedules. The effective dose range is 15 to 45 mg/day. Max: 45 mg/day PO.
- Noradrenergic and dopaminergic antidepressants
  - Bupropion
    - Bupropion Hydrochloride Oral tablet [Depression/Mood Disorders]; Children† and Adolescents† 6 years and older: Dosage not established. Suggested dosage ranges from 1.4 to 6 mg/kg/day PO, titrated upward slowly and administered in divided doses. In trials, the average effective dose is roughly 3 mg/kg/day PO; the maximum dosage is generally 250 to 300 mg/day PO. Safety data are not extensive; most patients have also been diagnosed with ADHD.
    - Bupropion Hydrochloride Oral tablet [Depression/Mood Disorders]; Adults: Initially, 100 mg PO twice daily; titrate after 3 days to 100 mg PO 3 times per day if needed; no single dose should exceed 150 mg.
- Tricyclic antidepressants[29]
  - Amitriptyline
    - Amitriptyline Hydrochloride Oral tablet; Adolescents: Begin at a low daily dosage, usually at bedtime, and titrate as needed and tolerated. Lower doses are used compared to young adults; 10 mg PO 3 times per day with 20 mg PO at bedtime may be satisfactory in adolescents who do not tolerate higher dosages. When satisfactory improvement has occurred, reduce to the lowest effective dose. Weight-based dosing has been used in clinical trials in adolescents for other indications. TCAs are not drugs of choice for pediatric patients with depression; there is lack of high-quality data to support efficacy and safety.
    - Amitriptyline Hydrochloride Oral tablet; Adults: Initially, 75 mg/day PO, given in divided doses, or, 50 mg to 100 mg PO once daily at bedtime. Hospitalized patients may require 100 mg/day PO initially. Titrate if needed, up to 150 mg/day PO, by increasing the daily dose 25 to 50 mg at weekly intervals, to response and tolerance. Max (hospitalized patients): 300 mg/day PO. Usual maintenance dose: 50 to 100 mg PO per day. In some patients, 40 mg/day PO is sufficient. For maintenance, give as a single dose, preferably at bedtime. Use lowest effective dose. It is appropriate to continue maintenance therapy 3 months or longer to lessen the possibility of relapse.
    - Amitriptyline Hydrochloride Oral tablet; Geriatric: 10 to 25 mg PO at bedtime initially. Titrate as needed and tolerated. Max: 150 mg/day PO, but such doses are not typically tolerated in the geriatric adult. Usual adult maintenance dosage: 50 to 100 mg per day. In some patients, 40 mg/day is sufficient. For maintenance therapy, give as a single dose, preferably at bedtime. Use lowest effective dose. It is appropriate to continue maintenance therapy 3 months or longer to lessen the possibility of relapse.
  - Clomipramine
    - Clomipramine Hydrochloride Oral capsule; Children and Adolescents 10 years and older: Initially, 25 mg PO once daily, gradually increasing up to a total of 100 mg/day PO given in divided doses; or 3 mg/kg/day given in divided doses, whichever is the smaller, over the first 2 weeks. In clinical trials in pediatric patients for OCD, the average effective dose range was 100 to 200 mg/day.
    - Clomipramine Hydrochloride Oral capsule; Adults: Initially, 25 mg PO once daily, may gradually increase in the first 2 weeks to 100 mg/day PO, given in divided doses. Max: 250 mg/day. After titration, the total daily dose may be given every night at bedtime to minimize daytime sedation.
  - Desipramine
    - Desipramine Hydrochloride Oral tablet; Adolescents: 25 to 50 mg PO at bedtime initially. May titrate at weekly intervals by 25to 50 mg, depending on response and tolerance. Usual Max: 100 mg/day PO, in single or divided doses. Max (hospitalized patients): 150 mg/day PO. Once at a maintenance dosage, administering the total daily dose at bedtime may minimize daytime sedation and improve compliance. TCAs are not drugs of choice for pediatric patients with depression; there is lack of high-quality data to support efficacy and safety.
    - Desipramine Hydrochloride Oral tablet; Adults: 50 to 75 mg/day PO initially, in single or divided doses. Titrate by 25 to 50 mg at weekly intervals according to response and tolerance. The usual adult dose is 100 mg to 200 mg PO per day, in single or divided doses. Max: 300 mg/day PO. Patients requiring up to 300 mg/day should generally be hospitalized for therapy initiation. Once at a maintenance dosage, administering the total daily dose at bedtime may minimize daytime sedation and improve compliance.
    - Desipramine Hydrochloride Oral tablet; Geriatric: 25 mg PO at bedtime initially. May titrate at weekly intervals by 25 to 50 mg, depending on response and tolerance. Usual max: 100 mg/day PO, in single or divided doses. Max (hospitalized patients): 150 mg/day PO. Once at a maintenance dosage, administering the total daily dose at bedtime may minimize daytime sedation and improve compliance.

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- Imipramine
  - Imipramine Hydrochloride Oral tablet; Adolescents: Initially, 30 mg to 40 mg/day PO once daily at bedtime to help minimize daytime sedation. If necessary, titrate upward based on response and tolerability. Usual Max: 100 mg/day PO. Use the lowest effective dose that maintains remission. TCAs are not drugs of choice for pediatric patients with depression; there is lack of high-quality data to support efficacy and safety.
  - Imipramine Hydrochloride Oral tablet; Adults: OUTPATIENTS: Initially, 75 mg/day PO; bedtime dosing may reduce daytime sedation. The, titrate to 150 mg/day as a single dose or divided doses based on response and tolerability. Optimal response may take 1 to 3 weeks of treatment at a given dose. Maintenance: 50 to 150 mg/day. Outpatient Max: 200 mg/day PO. HOSPITALIZED ADULTS: Initially, 100 mg/day PO in divided doses, gradually increased to 200 mg/day PO in divided doses as required. If no response after 2 weeks, increase to 250 mg/day to 300 mg/day PO. Hospitalized patient Max: 300 mg/day PO. Use lowest effective dose that maintains remission.
  - Imipramine Hydrochloride Oral tablet; Geriatric Adults: Initially, 30 mg to 40 mg/day PO once daily at bedtime to help minimize daytime sedation. If necessary, titrate to response and tolerability. Usual Max: 100 mg/day. Use the lowest effective dose that maintains remission.
- Nortriptyline
  - Nortriptyline Hydrochloride Oral capsule; Adolescents: Initially, 10 mg or 25 mg PO at bedtime.May increase as tolerated to 30 mg to 50 mg per day, given in divided doses or once daily at bedtime. TCAs are not drugs of choice for pediatric patients with depression; the quality of data to support efficacy and safety in adolescents is considered marginal.
  - Nortriptyline Hydrochloride Oral capsule; Adults: Initially, 25 mg to 50 mg PO per day, given in divided doses or at bedtime. May increase as needed and tolerated. Max: 150 mg/day PO.
  - Nortriptyline Hydrochloride Oral capsule; Geriatric Adults: Initially, 10 mg to 25 mg PO at bedtime. May increase as tolerated to 30 mg to 50 mg per day, in divided doses or at bedtime.

- MAOIs[34]
  - Avoid alcohol, tobacco, caffeine, and tyramine-containing foods (eg, aged cheeses, cured meats, fermented cabbage, soy sauce, fava beans) except when taking selegiline at the lowest dosage
  - Isocarboxazid
    - Isocarboxazid Oral tablet; Adolescents 16 years and older: In patients receiving contraindicated drugs known to interact with MAOIs, the interacting drug should be discontinued for at least 1 to 2 weeks before initiating isocarboxazid therapy. INITIAL DOSAGE: 10 mg PO twice daily. Carefully assess for drug efficacy and safety to individualize dosage. May increase by 10 mg/day PO every 2 to 4 days, up to 40 mg/day PO by end of first week. May increase further by up to 20 mg/week, if needed and tolerated. Max: 60 mg/day PO, given in 2 to 4 divided doses. Use caution if receiving more than 40 mg/day PO. MAINTENANCE DOSAGE: After maximum clinical response is achieved, reduce the dosage over several weeks to the lowest dosage that maintains effectiveness to limit cumulative MAOI effects and serious dose-related toxicity. Periodically re-evaluate for drug effectiveness and safety.
    - Isocarboxazid Oral tablet; Adults: In patients receiving contraindicated drugs known to interact with MAOIs, the interacting drug should be discontinued for at least 1 to 2 weeks before initiating isocarboxazid therapy. INITIAL DOSAGE: 10 mg PO twice daily. Carefully assess for drug efficacy and safety to individualize dosage. May increase by 10 mg/day PO every 2 to 4 days, up to 40 mg/day PO by end of first week. May increase further by up to 20 mg/week, if needed and tolerated. Max: 60 mg/day PO, given in 2 to 4 divided doses. Use caution if receiving more than 40 mg/day PO. MAINTENANCE DOSAGE: After maximum clinical response is achieved, reduce the dosage over several weeks to the lowest dosage that maintains effectiveness to limit cumulative MAOI effects and serious dose-related toxicity. Periodically re-evaluate for drug effectiveness and safety.
  - Phenelzine
    - Phenelzine Sulfate Oral tablet; Adults: 15 mg PO 3 times daily; may rapidly increase to 60 mg/day if tolerated. Individualize dosage based on careful observation. For some, an increase up to 90 mg/day may be necessary. Onset of maximum effect is 2 to 6 weeks. After the maximum benefit is achieved, reduce dosage slowly over several weeks to the lowest dose that maintains effectiveness. Maintenance dose may be as low as 15 mg/day PO or 15 mg PO every other day, continued as long as required. NOTE: In patients requiring a contraindicated drug known to interact with MAOIs, phenelzine should be discontinued for at least 2 weeks before initiating the interacting drug.
  - Selegiline
    - Selegiline Hydrochloride Transdermal patch - 24 hour; Adults: Initially, 6 mg/24 hours transdermally once daily. If clinically indicated, increase by 3 mg/24 hour at intervals of no less than 2 weeks. Effective dose range: 6 to 12 mg/24 hours. Max: 12 mg/24 hours. Inform patients to avoid tyramine-containing foods/beverages/dietary supplements beginning on the first day of selegiline 9 mg or 12 mg/24 hours treatment. Avoid tyramine for 2 weeks after dose reduction (to 6 mg/24 hours) or discontinuation of 9 mg/24 hours or 12 mg/24 hours.

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- NMDA (N-methyl-D-aspartate) receptor antagonists
  - Esketamine nasal spray[28]
    - First NMDA antagonist to receive FDA approval for major depression
    - Used as an adjunct to an oral antidepressant for treatment-resistant depression (those who have failed 2 or more standard antidepressant treatments)
    - Only available through a restricted distribution system, under a Risk Evaluation and Mitigation Strategy, owing to risk of serious adverse outcomes resulting from sedation and dissociation and the potential for drug misuse
    - Esketamine intranasal dosage (ie, Spravato nasal spray containing 28 mg per device); Adults: INDUCTION PHASE: On day 1, administer 56 mg intranasally. For subsequent doses during Weeks 1 through 4, administer 56 mg or 84 mg twice per week. Use 2 devices for the 56 mg dose and 3 devices for the 84 mg dose with a 5-minute rest between use of each device. MAINTENANCE PHASE: During Weeks 5 through 8, administer 56 mg or 84 mg once weekly. During Week 9 and thereafter, administer 56 mg or 84 mg every 2 weeks or once weekly. The dosing frequency should be individualized to the least frequent dosing to maintain remission/response.[35]
- Nondrug and supportive care
  - Music therapy
    - Music therapy (provided by a music therapist) has been found to decrease depressive symptoms, improve anxiety associated with major depressive disorder, and improve functioning[36]
  - Acupuncture[37]
    - Small to moderate reduction in the severity of depressive symptoms has been reported
  - Exercise[38]
    - Exercise has been shown to have significant effect in reducing depressive symptoms in patients with major depressive disorder,[39] especially regular, moderate-level, aerobic exercise
  - Procedures
    - Psychotherapy
      - General explanation
        - Includes cognitive behavioral therapy, behavioral activation therapy, interpersonal psychotherapy, problem-solving therapy, nondirective counseling, and psychodynamic therapy[10]
        - First line recommendations for acute major depressive disorder include cognitive-behavioral therapy, interpersonal psychotherapy, and behavioral activation therapy[40]
        - All types are known to be effective options[41, 10]
        - May be used as the initial treatment modality for patients with major depressive disorder, with or without concomitant medication therapy; often adequate as initial therapy, early in the course of the disease[10]
        - Cognitive behavioral therapy administered concurrently with medication may increase the rate of patient response[40, 42]
        - Cognitive behavioral therapy administered after medication is withdrawn may impart a protective effect against relapse[42]
      - Indication
        - Significant psychological stressors, intrapsychic conflict, or interpersonal difficulties
        - Mild to moderate depression[24]
          - Patients are more likely to respond to psychotherapy than to medication
    - Electroconvulsive therapy[43]
      - General explanation
        - Generalized seizures are intentionally induced using electrical impulses
        - Typically performed 2 to 3 times per week until clinical response is seen
        - Average course is 6 to 12 treatments, which are administered under anesthesia and with muscle relaxants
      - Indication[44, 24]
        - May be used as first line therapy for patients who have:
          - Psychotic depression
          - Catatonia
          - Previous response to this treatment method
          - Severe suicidality
          - Anorexia/rapidly deteriorating physical status
          - Treatment-resistant depression
          - Repeated medication intolerance
      - Contraindications
        - Relative contraindications
          - Age younger than 18 years
          - Space-occupying brain lesions

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        - Elevated intracranial pressure
        - Recent myocardial infarction
        - History of retinal detachment
        - Pheochromocytoma
    - Complications
      - Associated with transient postictal confusion and a period of antegrade and retrograde memory loss
      - Can cause a transient rise in heart rate, in cardiac workload, and in blood pressure
  - Repetitive transcranial magnetic stimulation [45]
    - General explanation
      - Magnetic fields stimulate nerve cells in the brain to improve symptoms of depression
        - Evaluate patients for seizure risk before repetitive transcranial magnetic stimulation, including: [46, 23]
          - Personal/family history of seizures or epilepsy
          - Previous head injury or stroke with neurologic sequelae
          - Current use of medications/substances that lower seizure threshold (eg, psychostimulants) or reduction in dose of medication with antiseizure properties (eg, benzodiazepine)
          - Presence of medical condition or neurologic disorder that may lower seizure threshold (eg, electrolyte imbalance, sleep deprivation, drug withdrawal)
      - Electromagnetic coil is held against the forehead and short electromagnetic pulses are administered through the coil
      - Left prefrontal repetitive transcranial magnetic stimulation repeated daily for 4 to 6 weeks is an effective and safe treatment in adult patients with unipolar major depressive disorder that has failed 1 or more antidepressant trials [47]
        - Typical session lasts 30 to 60 minutes and does not require anesthesia [46]
    - Indication
      - First line treatment for patients with major depression who have not responded to antidepressant drug therapy [44, 25]
    - Contraindications
      - Pregnancy
      - Aneurysm clips
      - Presence of other ferromagnetic material in the head, with the exception of the mouth
      - Deep brain stimulator use (unintended currents can result)
    - Complications [48]
      - Headache
      - Scalp discomfort
      - Seizures
- Comorbidities
  - Anxiety disorder
    - Approximately one-half of patients with anxiety disorders have other mood disorders (typically dysthymia or depression) [49]
  - Obsessive-compulsive disorder
    - Often produces additional depression symptoms [50]
  - Substance abuse disorder (eg, alcohol, opioids, amphetamine, cocaine, cannabis)
    - Associated with depression and suicide attempts
    - Impulsivity is heightened when under the influence of substances [51]
  - Coronary artery disease
    - Risk of future cardiac events is 2 to 3 times higher in patients with coronary artery disease and depression when compared to patients without depression [52]
  - Diabetes mellitus
    - Patients with diabetes and depression experience worse glycemic control and an increased risk of diabetic complications [53]
  - Obesity
    - Depression-associated low motivation, poor adherence, negative thinking, fatigue, and sleep problems reduce the success of early-treatment weight loss programs [54]
- Special populations
  - Pregnant women
    - Untreated major depressive disorder in pregnancy poses a risk to the mother and fetus (potential harm from malnutrition, poor prenatal care, substance abuse, or suicide attempts)

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- Treatment can include psychotherapy and medications determined by the patient's obstetrician and psychiatrist
  - Given the potential harms to the fetus and newborn child from certain pharmacologic agents, clinicians are encouraged to consider cognitive behavioral therapy or other evidence-based counseling interventions when managing depression in pregnant or breastfeeding women [25, 5]

MONITORING

- During the initial phase of treatment, monitoring can vary from once per week to multiple times per week depending on severity
- American Academy of Pediatrics guidelines recommend that adolescents are assessed in person within 1 week of treatment initiation [27]
- Frequency of monitoring can be based on severity, presence of suicidal ideation, patient adherence to treatment, social supports, and coexisting medical conditions

COMPLICATIONS AND PROGNOSIS

COMPLICATIONS

- Suicide
  - Majority of patients with completed suicide have major depression
- Substance abuse

PROGNOSIS

- There is a high risk of relapse after a depressive episode, especially in the first 6 months; risk declines with time in remission [24]
  - Risk factors for relapse include presence of residual symptoms, number of previous episodes, severity, duration, and degree of treatment resistance of the most recent episode
- Untreated depression increases the risk of self-inflicted injury or suicide
- Prognosis of major depressive disorder in elderly patients is poor, as the majority of cases remain undetected [5]

SCREENING AND PREVENTION

SCREENING

- At-risk populations
  - United States Preventive Services Task Force recommends screening adults for major depression; the optimum interval for screening is unknown [5]
  - United States Preventive Services Task Force recommends screening adolescents aged 12 to 18 years for major depressive disorder [55]
  - American Academy of Pediatrics guidelines recommend that adolescent patients aged 12 years and older should be screened annually for depression with a formal self-report screening tool [56]
  - United States Department of Veterans Affairs recommends screening for major depression annually [10]
  - American College of Obstetricians and Gynecologists recommends patients be screened for depression and anxiety symptoms at least once during the perinatal period, using a standardized, validated tool; screening for postpartum depression and anxiety is also recommended, using a validated instrument [57]
- Screening tests
  - Standardized depression inventory tests include Beck Depression Inventory, Major Depression Inventory, Hamilton Depression Rating Scale, and Patient Health Questionnaire-9 [5, 8, 7, 10]

PREVENTION

SYNOPSIS

KEY POINTS

- Major depressive disorder is a chronic and relapsing disease, characterized by a pervasive sad mood and the loss of pleasure in most activities (anhedonia)
- Rule out underlying physical illnesses that may mimic major depressive disorder (eg, hypothyroidism, dementia)
- Diagnosis relies on history and physical examination, as well as validated depression inventory tools [5] such as Beck Depression Inventory, [8] Hamilton Depression Rating Scale, [8] Major Depression Inventory, [7] and Patient Health Questionnaire-9 [6]
- Psychotherapy is often adequate as initial therapy early in the course of the disease [22]
- Use antidepressant medications for more severe or chronic disease [22]
- Consider combination therapy (psychotherapy and medication) when the response to a single therapy is inadequate [22]
- For severe disease, drug therapy is required, and for most patients combined therapy is more effective than either psychotherapy or antidepressant medication alone [22]

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- If patient has a high risk of suicide or if welfare is threatened (eg, lack of nutrition or fluid intake), electroconvulsive therapy will be necessary [22]
- Untreated depression increases the risk of self-inflicted injury or suicide

URGENT ACTION

- Suicidal ideation or suicide attempts require hospitalization and urgent evaluation by a psychiatrist

PITFALLS

- Even if major depressive disorder is diagnosed correctly, bipolar disorder may be present; treatment varies by disorder, so differentiation is required
- Always consider substance abuse as a potential contributor to major depressive disorder and a potential consequence of it
- Discontinuing medications that influence serotonin levels (particularly with short half-lives) can suddenly cause antidepressant discontinuation syndrome:
  - Flulike symptoms (eg, nausea, vomiting, diarrhea, headaches)
  - Sensory/movement disturbances (eg, vertigo, dizziness)
  - Cognitive symptoms (eg, hyperarousal, confusion)

SELECTED REFERENCES

1 González HM et al: The epidemiology of major depression and ethnicity in the United States. J Psychiatr Res. 44(15):1043-51, 2010
2 American Psychiatric Association: Depressive disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association; 2013:155-88
3 Romera I et al: Individual residual symptoms and functional impairment in patients with depression. Psychiatry Res. 220(1-2):258-62, 2014
4 Singh MK et al: The neuroscience of depression: implications for assessment and intervention. Behav Res Ther. 62:60-73, 2014
5 Siu AL et al: Screening for depression in adults: US Preventive Services Task Force recommendation statement. JAMA. 315(4):380-7, 2016
6 Pfizer Inc: Patient Health Questionnaire - 9 (PHQ-9). US Preventive Services Task Force website. Published 1999. Accessed April 25, 2019. http://www.uspreventiveservicestaskforce.org/Home/GetFileByID/218
7 Bech P et al: The sensitivity and specificity of the Major Depression Inventory, using the Present State Examination as the index of diagnostic validity. J Affect Disord. 66(2-3):159-64, 2001
8 Schneibel R et al: Sensitivity to detect change and the correlation of clinical factors with the Hamilton Depression Rating Scale and the Beck Depression Inventory in depressed inpatients. Psychiatry Res. 198(1):62-7, 2012
9 Glover J et al: Assessment of the person with late-life depression. Psychiatr Clin North Am. 36(4):545-60, 2013
10 Bentley SM et al: Major depression. Med Clin North Am. 98(5):981-1005, 2014
11 Andriopoulos P et al: Depression, quality of life and primary care: a cross-sectional study. J Epidemiol Glob Health. 3(4):245-52, 2013
12 Woo YS et al: A diagnosis of bipolar spectrum disorder predicts diagnostic conversion from unipolar depression to bipolar disorder: a 5-year retrospective study. J Affect Disord. 174:83-8, 2015
13 Zimmermann P et al: Heterogeneity of DSM-IV major depressive disorder as a consequence of subthreshold bipolarity. Arch Gen Psychiatry. 66(12):1341-52, 2009
14 Wakefield JC et al: Validity of the bereavement exclusion to major depression: does the empirical evidence support the proposal to eliminate the exclusion in DSM-5? World Psychiatry. 11(1):3-10, 2012
15 Bennett S et al: Depression and dementia: cause, consequence or coincidence? Maturitas. 79(2):184-90, 2014
16 Kamboj MK et al: Management of nonpsychiatric medical conditions presenting with psychiatric manifestations. Pediatr Clin North Am. 58(1):219-41, xii, 2011
17 Stanghellini G et al: Differential typology of delusions in major depression and schizophrenia. A critique to the unitary concept of "psychosis." J Affect Disord. 171:171-8, 2015
18 Wu EL et al: Increased risk of hypothyroidism and hyperthyroidism in patients with major depressive disorder: a population-based study. J Psychosom Res. 74(3):233-7, 2013
19 Hirschfeld RM et al: The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. JAMA. 277(4):333-40, 1997
20 Thase ME: Evaluating antidepressant therapies: remission as the optimal outcome. J Clin Psychiatry. 64 Suppl 13:18-25, 2003
21 Schoepf D et al: Comorbidity and its relevance on general hospital based mortality in major depressive disorder: a naturalistic 12-year follow-up in general hospital admissions. J Psychiatr Res. 52:28-35, 2014
22 Malhi GS et al: Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry. 49(12):1087-206, 2015
23 Qaseem A et al: Nonpharmacologic versus pharmacologic treatment of adult patients with major depressive disorder: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 164(5):350-9, 2016
24 Cleare A et al: Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2008 British Association for Psychopharmacology guidelines. J Psychopharmacol. 29(5):459-525, 2015
25 U.S. Department of Veteran Affairs et al: VA/DoD clinical practice guideline for the management of major depressive disorder. Version 3.0. U.S. Department of Veteran Affairs website. Published April 2016. Accessed April 25, 2019. https://www.healthquality.va.gov/guidelines/MH/mdd/
26 Kennedy SH et al: Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 3. Pharmacological treatments. Can J Psychiatry. 61(9):540-60, 2016
27 Cheung AH et al: Guidelines for adolescent depression in primary care (GLAD-PC): part II. Treatment and ongoing management. Pediatrics. 141(3), 2018
28 U.S. Food and Drug Administration: FDA news release. FDA approves new nasal spray medication for treatment-resistant depression; available only at a certified doctor's office or clinic. FDA website. Published March 9, 2019. Accessed April 25, 2019. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm632761.htm
29 von Wolff A et al: Selective serotonin reuptake inhibitors and tricyclic antidepressants in the acute treatment of chronic depression and dysthymia: a systematic review and meta-analysis. J Affect Disord. 144(1-2):7-15, 2013
30 Cipriani A et al: Escitalopram versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2:CD006532, 2009
31 Khoo AL et al: Network meta-analysis and cost-effectiveness analysis of new generation antidepressants. CNS Drugs. 29(8):695-712, 2015
32 Cipriani A et al: Sertraline versus other antidepressive agents for depression. Cochrane Database Syst Rev. 4:CD006117, 2009
33 Shamliyan TA et al: Evidence Review: Comparative Effectiveness and Safety of Off-label Sertraline for Major Depression in Pediatric Patients. Elsevier Evidence-Based Medicine Center
34 Amsterdam JD et al: MAOI efficacy and safety in advanced stage treatment-resistant depression--a retrospective study. J Affect Disord. 89(1-3):183-8, 2005
35 Janssen Pharmaceuticals Inc: Spravato - esketamine hydrochloride solution. Drug label information. DailyMed website. Updated March 11, 2019. Accessed April 25, 2019. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d81a6a79-a74a-44b7-822c-0dfa3036eaed

Published February 19, 2016; Updated April 30, 2019

36 Aalbers S et al: Music therapy for depression. Cochrane Database Syst Rev. 11:CD004517, 2017
37 Smith CA et al: Acupuncture for depression. Cochrane Database Syst Rev. 3:CD004046, 2018
38 Schuch FB et al: Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. J Psychiatr Res. 77:42-51, 2016
39 Paolucci EM et al: Exercise reduces depression and inflammation but intensity matters. Biol Psychol. 133:79-84, 2018
40 Parikh SV et al: Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 2. Psychological treatments. Can J Psychiatry. 61(9):524-39, 2016
41 Driessen E et al: The efficacy of short-term psychodynamic psychotherapy for depression: a meta-analysis update. Clin Psychol Rev. 42:1-15, 2015
42 Hollon SD et al: Enduring effects for cognitive behavior therapy in the treatment of depression and anxiety. Annu Rev Psychol. 57:285-315, 2006
43 Charlson F et al: ECT efficacy and treatment course: a systematic review and meta-analysis of twice vs thrice weekly schedules. J Affect Disord. 138(1-2):1-8, 2012
44 Milev RV et al: Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 4. Neurostimulation treatments. Can J Psychiatry. 61(9):561-75, 2016
45 Fitzgerald PB et al: Transcranial magnetic stimulation in the treatment of depression: a double-blind, placebo-controlled trial. Arch Gen Psychiatry. 60(10):1002-8, 2003
46 McClintock SM et al: Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. J Clin Psychiatry. 79(1):pii: 16cs10905, 2018
47 Perera T et al: The Clinical TMS Society consensus review and treatment recommendations for TMS therapy for major depressive disorder. Brain Stimul. 9(3):336-46, 2016
48 Janicak PG et al: Transcranial magnetic stimulation in the treatment of major depressive disorder: a comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. J Clin Psychiatry. 69(2):222-32, 2008
49 Yap K et al: Obsessive-compulsive disorder and comorbid depression: the role of OCD-related and non-specific factors. J Anxiety Disord. 26(5):565-73, 2012
50 Dhossche DM et al: The association of suicide attempts and comorbid depression and substance abuse in psychiatric consultation patients. Gen Hosp Psychiatry. 22(4):281-8, 2000
51 Rudisch B et al: Epidemiology of comorbid coronary artery disease and depression. Biol Psychiatry. 54(3):227-40, 2003
52 Gehlawat P et al: Diabetes with comorbid depression: role of SSRI in better glycemic control. Asian J Psychiatr. 6(5):364-8, 2013
53 Waring ME et al: Early-treatment weight loss predicts 6-month weight loss in women with obesity and depression: implications for stepped care. J Psychosom Res. 76(5):394-9, 2014
54 Chan LF et al: Are predictors of future suicide attempts and the transition from suicidal ideation to suicide attempts shared or distinct: a 12-month prospective study among patients with depressive disorders. Psychiatry Res. 220(3):867-73, 2014
55 Siu AL et al: Screening for depression in children and adolescents: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 164(5):360-6, 2016
56 Zuckerbrot RA et al: Guidelines for adolescent depression in primary care (GLAD-PC): part I. Practice preparation, identification, assessment, and initial management. Pediatrics. 141(3), 2018
57 ACOG Committee Opinion No. 757: screening for perinatal depression. Obstet Gynecol. 132(5):e208-12, 2018

Published February 19, 2016; Updated April 30, 2019