

DIAGNOSIS AND MANAGEMENT OF

Depression

2020 Update

This care process model (CPM) was created by a subcommittee of the Intermountain Healthcare Primary Care Clinical Program, Behavioral Health Clinical Program, and Mental Health Integration (MHI) team. The goal of this CPM and supporting materials is to help providers deliver the best clinical care in a consistent and integrated way. The focus of this CPM is on adults with a section on [page 25](#) for depression in children and adolescents. The recommendations in this CPM build on guidelines from the Agency for Health Care Policy and Research (AHCPR), updated guidelines from the American Psychiatric Association (APA), experience from the implementation of this CPM, and recommendations from other published studies.^{SCH, APA1}

► Key points

- **Depression is common and costly and makes other chronic conditions more difficult to manage** (see [pages 3 to 4](#)).
- **Treatment should be used based on symptom severity and antidepressant therapy as a first-line treatment for moderate to severe depression** (see [pages 8 to 17](#)).
- **Full remission — not just partial resolution of symptoms — is the goal of treatment for depression.** (See [pages 22 to 23](#) for information on the stages of depression and strategies to help achieve full remission.)

► What's new IN THIS UPDATE?

- **A broader focus on self-care** via a new section that provides guidance on mindfulness in treating depression (see [page 10](#)).
- **New sections** offering guidance on dealing with perinatal and geriatric patients (see Table 6 on [page 20](#)).
- **Updates in substance use disorder (SUD) screening based on the recommended CRAFFT screening tool for adolescents** (see [page 7](#) of the [Substance Use Disorder CPM](#)).
- **Updates to medication information**, based on new evidence (see [pages 15 to 21](#)).

► WHAT'S INSIDE?

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GOALS AND MEASUREMENTS

- Increase the ability to identify and treat depression in the primary care setting.
- Improve patient adherence to treatment by measuring ongoing PHQ-9 scores, medication compliance >3 months, and attending therapy >1 time.
- Increase the percentage of patients who have remission of depressive symptoms per DSM-V and PHQ-9 criteria.
- Increase the appropriate level of referral to and consultation with mental health providers.
- Improve overall quality of care and decrease medical spending in patients with severe medical problems and significant untreated/undertreated depression.



Indicates an Intermountain measure

OPPORTUNITIES

The primary care setting is preferred by patients. Roughly 74% of patients are treated for their depression in the primary care setting.^{MOJ} Given this fact, it's appropriate to focus on diagnosis and treatment in this setting. Primary care settings also present a unique opportunity to improve treatment adherence by reinforcing ongoing relational patient and family contact.

Primary care providers (PCPs) can coordinate proven, team-based strategies to improve care. Numerous studies indicate that the quality improvement measures captured in this CPM—enhanced by a collaborative MHI program like Intermountain's—can significantly improve care, lower costs, and increase satisfaction for both patients and PCPs. Implementing this CPM in an MHI setting has significantly improved depression care at Intermountain (see the [Mental Health Integration CPM](#)).

► WHY FOCUS ON DEPRESSION?

This CPM is a response to significant problems, impacts, and opportunities for diagnosis and treatment of depression in primary care.

Problems

- **Prevalence.** Nationally, depression in any given two-week period impacts between 8% and 10% of people ages 12 years and older. The 2018 [National Center for Health Statistics \(NCHS\) Data Brief](#) reports:^{BRO}
 - Women are almost twice as likely to have depression as men (10.4% vs. 5.5%).
 - A lower percentage of non-Hispanic Asian adults (3.1%) have depression compared with other groups (8.2% for Hispanic, 9.2% for non-Hispanic black, and 7.9% for non-Hispanic white).
 - The prevalence of depression decreases as family income increases.

In Utah, provider-diagnosed depression is more prevalent for women than for men (29.4% vs. 16.2%), and self-reported lifetime depression is consistently higher than the U.S. rate (24.2% vs. 18.6%).^{IBIS}

- **Underdiagnosis or misdiagnosis.** When they visit their PCP, very few patients actually identify depression as a formal chief complaint. Instead, most patients come prepared to describe their physical symptoms. Identifying depression in primary care is difficult unless standardized screening and diagnosis tools are used along with a formal diagnostic process (see [pages 4–7](#)).
- **Poor adherence to treatment.** Research studies indicate that in primary care, treatment nonadherence averages 46.2% over a six-month period.^{SAN} For 2017, the [National Institute of Mental Health](#) reported that the numbers of adults and adolescents not receiving treatment for depression were 35% and 60%, respectively.^{NIM} No matter how accurate the diagnosis and treatment plan, most patients won't improve if they don't adhere to treatment. (See [page 11](#) for specific methods to foster treatment adherence for depression, based on the 2010 [APA's Practice Guideline for the Treatment of Patients with Major Depressive Disorder](#).)
- **Medical comorbidities.** Depression is more prevalent for persons with chronic medical conditions that include diabetes, heart disease, stroke, COPD, and cancer and can exacerbate these conditions.

Impacts

- **Economic burden.** Each year in the U.S., the estimated direct medical costs of depression are more than \$26 billion, and productivity losses due to the illness are \$51.5 billion.^{GRE}
- **Human suffering.** Depression often interferes with normal functioning and is the leading cause of disability-adjusted life years (DALY) in middle-income and high-income countries.^{WHO} Depressive illnesses cause enormous pain and suffering to patients and to those who care about them.
- **Inefficiency and frustration.** When depression is not properly addressed, caring for patients can become time-consuming and frustrating for the PCP.

DEPRESSION IS NOT A PERSONAL FAILING

People often believe that, like the *mood* depression, the *disease* depression should be amendable by force of personal will alone. This is not true. Depression is a disease—not a personal failing or character flaw.

RISK FACTORS FOR DEPRESSION

- Family history
- Medical comorbidity
- Recent childbirth
- Substance abuse
- Bereavement
- Prior episodes or suicide attempts
- Female gender

DEPRESSION SYMPTOMS: SIG “E” CAAPS

Use SIG “E” CAAPS to help remember the nine symptoms of depression:

- **S**leep
- **I**nterest
- **G**uilt
- **E**nergy
- **C**oncentration
- **A**ppetite
- **A**ffect / mood
- **P**sychomotor retardation / agitation
- **S**uicidality

► UNDERSTANDING DEPRESSION

The mood versus the disease

- **Depression, the mood.** Depression, as the word is commonly used, is a persistent, distinctly unpleasant emotional state. Feelings of loss, disillusionment, despair, hopelessness, shame, or guilt often accompany or lead to depression. A depressed mood can occur when we feel trapped by unwanted life circumstances.
- **Depression, the disease.** Depression, the disease, is a disorder of personal and social functioning. It has a distinct behavioral syndrome with symptoms that affect the body’s normal functioning. Individuals with this disease are afflicted by excessive guilt, hopelessness, suicidal thoughts, and impaired memory. Depression can be examined from biological, developmental, social, economic, and even spiritual points of view. In primary care, it’s often useful to focus on the biological nature of depression—including symptoms, genetics, and medical treatment. This helps alleviate the sense of shame experienced by many patients.

Etiology

- **While depression symptoms typically develop over days, weeks, or months, a depressive disorder may develop suddenly,** particularly after a **psychosocial stressor** such as a loved one’s death, marital separation, or the end of a key relationship. Childbirth can also precipitate a sudden onset of depression.
- **Factors affecting major depression** include seasons of the year, intense light, sleep deprivation, structural damage to the brain, and concurrent medical illness. Early life trauma, style of thinking, and life stress may also affect the disease.
- **The average age at onset for an initial episode of depression is 30 years,** but the disorder may begin at any age. When the age of initial onset is 25 years or younger, the likelihood of developing bipolar depression slightly increases.^{CD1} When the initial onset of depression occurs late in life, it’s correlated more with a degenerative disease than with a family history of mood disorders.^{TE0}
- **Major depression has a strong inheritance pattern,** suggesting a multi-gene trait. The illness is 1.5 to 3 times as common among those with a first-degree biological relative affected with the disorder than among the general population.
- **Biochemically,** modern science has characterized extracellular / extraneuronal processes that correlate with the disease of major depression. The presumed intracellular etiology is currently only theorized and not experimentally known.
- **Major depressive disorder (MDD) is often accompanied by comorbid conditions,** such as heart failure, diabetes, asthma, chronic pain, other mental illness, and substance abuse—as well as personality disorders. These conditions add to its disability and worsen its prognosis. Patients in primary care with high utilization, multiple chronic conditions, or chronic pain have a particularly high prevalence.^{KAT1}

Symptoms

- **Psychological.** Depression can cause a depressed mood, feelings of worthlessness or excessive guilt, thoughts of hopelessness and suicide, and loss of interest or pleasure in activities (e.g., libido, leisure, etc.).
- **Somatic.** Physical symptoms are often the common chief complaint in a primary care setting. They include sleep changes (insomnia or hypersomnia), loss of interest in food, significant weight change (e.g., 5% gain or loss), low energy, and physical agitation or slowing, often accompanied by poor concentration.

ALGORITHM NOTES

(a) **Patient Health Questionnaire (PHQ-9):**

The PHQ-9 is a free, patient-rated instrument that asks about the nine symptoms of depression (see [page 6](#)). It is easy to complete, scan, and score. If positive, the PHQ-9 provides a baseline symptom score and severity score. It also screens for suicidal tendencies, impairment, and chronic depression. Adolescent and pediatric versions are available.

(b) **Bipolar disorder (BD):** Patients with BD often present with depression (see [page 24](#)).

- **Predictive factors** for BD include sudden or severe depression onset, psychotic features, mood lability, onset younger than 25, and BD family history.
- Use the Composite International Diagnostic Interview (CIDI) for screening.

(c) **Precipitating medical conditions:**

Many medical conditions can precipitate depressive symptoms. Evaluate for these conditions before diagnosing depression. Concurrent treatment of depression and coincident medical disorders is usually indicated.

- Thyroid disorders (even subclinical)
- Endocrinopathies
- CVA
- Viral illness
- Parkinson’s (even subclinical)
- Carcinomas (pancreas), lymphomas, carcinoid syndrome

(d) **Precipitating medications and abused substances:**

Use and/or abuse of some medications and other substances can also precipitate depressive symptoms (examples below). Use the NIDA (for adults) or CRAFFT (for children and adolescents) to screen for substance abuse (see SUD CPM sidebar [page 7](#)).

- Steroids
- Birth control pills
- Interferon alpha
- Opioids
- Alcohol
- Cannabis
- Hallucinogens
- Methamphetamines
- Cocaine

(e) **Comorbidities:**

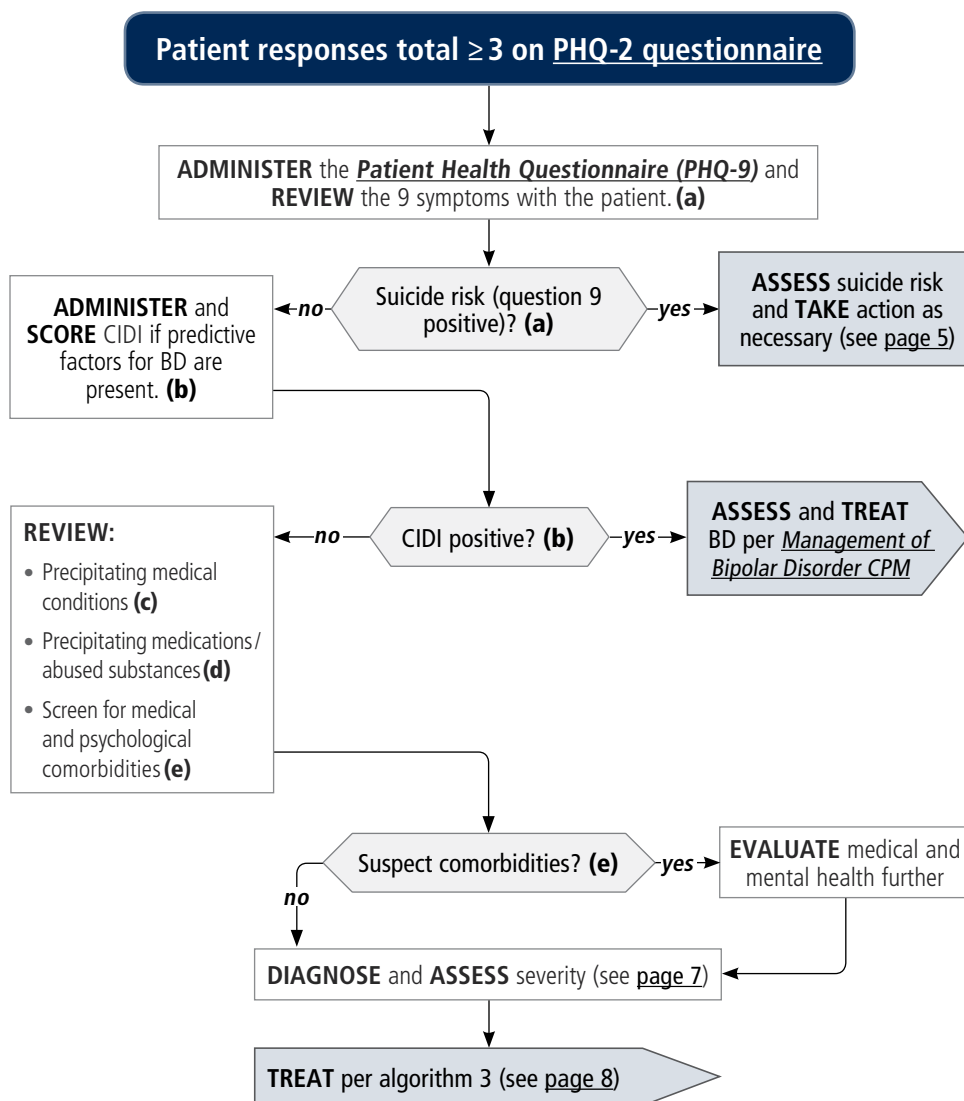
- **Medical illnesses:** Depression often occurs with heart disease, stroke, cancer, or diabetes, and can impair treatment.
 - Screen patients for BMI, diabetes, lipid abnormalities, smoking, and hypertension if not already screened.
 - Depression treatment may help improve overall outcomes by reinforcing treatment for medical conditions.
- **Other mental health disorders:** MHI resources aid in screening (see [page 9](#)).

► **EVALUATION AND DIAGNOSIS**

At any given time, 5% to 10% of patients will meet the diagnostic standard for a current episode of major depression.^{KAT2} However, without formal screening, depression will be detected in few of these patients. Therefore, this CPM recommends annual screening for all, more frequent screening for certain populations, and scheduled screening for those previously diagnosed with depression. In primary care, patients’ risk of having a mood disorder is directly related to the number of somatic symptoms with which they present.^{TRI1} These symptoms and conditions are associated with a very high co-incidence of depression and require screening at routine intervals:

- Multiple unresolved somatic complaints (e.g., more than three unexplained symptoms)
- High healthcare utilization (e.g., thick chart or more than six visits/year)
- Chronic diseases (e.g., diabetes, heart failure, chronic pain)
- Postpartum status
- History of depression or anxiety
- Family history of depression
- Active substance abuse

ALGORITHM 1: SCREENING AND DIAGNOSIS



SUICIDE PREVENTION CARE PROCESS MODEL

Intermountain's *Suicide Prevention CPM* provides guidance for prevention, assessment, and treatment for patients with suicidal thoughts, feelings, or behaviors.



C-SSRS SCREENING TOOLS

Intermountain uses several versions of the C-SSRS to consistently identify and track patient suicide ideation and behaviors across the continuum of care:

- **Quick Screen:** Used to quickly screen patients for suicidal thoughts and behaviors; three to six questions depending on patient responses. (**Adult/Adolescent** and **Pediatric** versions)
- **Lifetime/Recent Assessment:** Used for full assessment during the initial visit; two-page assessment (number of questions varies based on patient responses). (**Adult/Adolescent** and **Pediatric** versions)
- **Since Last Visit Assessment:** Used to assess patients at follow-up visits; same questions as Lifetime/Recent Assessment. (**Adult/Adolescent** and **Pediatric** versions)
- **Suicide Prevention — Risk Assessment Tool:** One-page list of suicide risks and protective factors

RESOURCE FOR PATIENTS

Collaborative safety planning is an important part of addressing suicide risk. Intermountain's *Suicide Prevention Adult Safety Plan* is a tool patients can use when suicidal thoughts arise.



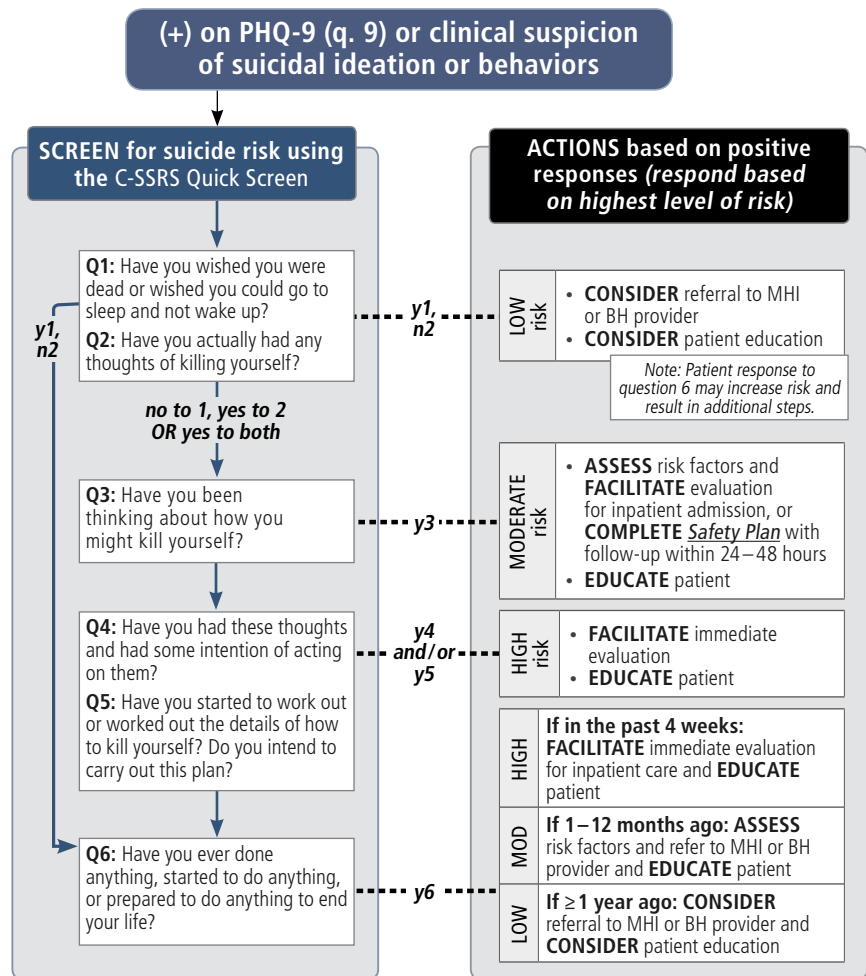
Suicide assessment

Every patient who responds positively to question 9 on the PHQ-9 (thoughts that you would be better off dead or of hurting yourself in some way) should be screened for suicide risk. Intermountain's *Suicide Prevention CPM* recommends screening with the *Columbia-Suicide Severity Rating Scale (C-SSRS)*.

While no instrument or person can predict suicide in the future, appropriate screening may identify patients at increased risk of suicide who need treatment. The C-SSRS helps clinicians classify a person's suicidal ideation and behavior, determine levels of risk, and make clinical decisions about care. It standardizes the assessment method and terminology across Intermountain and has become the standard in Utah.

Intermountain uses several versions of the C-SSRS (see the sidebar), but all the versions have consistent questions. See the algorithm below for guidance on using the C-SSRS for screening in primary care.

ALGORITHM 2: SUICIDE ASSESSMENT



Suicide prevention at Intermountain clinics

To reduce suicide risk, establish and communicate a clinic focus on suicide prevention:

- Discuss suicide screening and treatment at regular staff trainings.
- Review patient suicide cases with the team to determine what could be improved.
- Establish open communication with patients about suicide risk.
- Seek to reduce factors that increase the risk for suicidal thoughts and behaviors (see the *Suicide Prevention CPM*, page 12).

The PHQ-9

The *Patient Health Questionnaire (PHQ-9)* is a patient-rated tool that screens for the nine symptoms of depression. The PHQ-9 is simple for a physician to score and, along with other elements of patient assessment, can help evaluate and diagnose a major depressive episode. Pediatric and adolescent versions are also available (see [page 25](#) for more information on diagnosing depression in children and adolescents).

The PHQ-9 provides a symptom score that helps with diagnosis and a severity score that can be used to rate severity of illness (mild, moderate, or severe), which is useful in formulating a treatment plan. The PHQ-9 can also help screen for suicidal ideation, assess for level of impairment, and differentiate other subtypes of depression. The figure below describes how to score and interpret PHQ-9 results. [Table 2](#) on the following page summarizes possible depression diagnoses and treatment approaches for adults based on PHQ-9 results.

FIGURE 1. Scoring and interpreting the PHQ-9

Patient Health Questionnaire (PHQ-9) (page 1 of 1)

Today's Date: _____ Patient's Name: _____ Date of Birth: _____

Are you currently: on medication for depression? not on medication for depression? not sure? in counseling?

Over the last 2 weeks, how often have you been bothered by any of the following problems?	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/staying asleep, 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're 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 each column				

Question 1: A score of 2 or 3 is positive for **anhedonia** (loss of pleasure).

Question 2: A score of 2 or 3 is positive for **mood disturbance**.

Question 9: A score of 1 ("several days") or more is positive for **suicide ideation**.

Question A: A score of at least "somewhat difficult" indicates **functional impairment**.

Question B: YES is positive for **persistent depressive disorder** (dysthymia).

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?

A. Not difficult at all Somewhat difficult Very difficult Extremely difficult

B. **In the past 2 years**, have you felt depressed or sad most days, even if you felt okay sometimes?

Symptom score: The total number of positive symptoms for questions 1–9. A positive symptom is a score of 2 ("More than half the days") or 3 ("Nearly every day") for questions 1–8. For question 9, a score of 1 ("Several days") or more is positive.

Severity score: The total points from all questions 1–9 (i.e., the total number of points in the last 3 columns). Used to rate severity and measure progress.

The patient meets **diagnostic criteria** for a major depressive episode with at least **5 out of the 9 symptoms** of depression — **for the same 2-week period** — with one of the symptoms being **depressed mood or lack of pleasure** in doing things (anhedonia). These symptoms should **not be due to other medical conditions or substance abuse** and should be severe enough to **cause impairment** in a person's life.^{MCI}

SCREENING FOR SUBSTANCE USE DISORDERS

When evaluating and diagnosing depression, it is important to screen for substance use disorders (SUD) as well. Many patients have comorbid mental health conditions and SUD. For these patients, integrated care can improve outcomes and reduce cost more effectively than traditional care (separate, siloed primary care, mental health, and SUD treatment).

Intermountain’s [Assessment and Management of Substance Use Disorder CPM](#), provides practical strategies for effective SUD diagnosis and treatment.



Diagnosis

- **Using PHQ-9 results:** PHQ-9 scores, along with other elements of your evaluation, can help diagnose a major depressive episode, differentiate other subtypes of depression, and quantify the severity (mild, moderate, severe). See Table 2 below.
- **Meeting DSM-5 criteria:** The DSM-5 lists diagnostic criteria for a **major depressive episode** and **persistent depressive disorder** (previously referred to as dysthymic disorder). Major depressive episodes can be specified according to **remission, chronicity, postpartum onset**, and presence of **psychotic, catatonic, melancholic**, and/or **atypical** features.^{APA2} The DSM-5 also lists new disorders not considered in this CPM, including disruptive mood dysregulation disorder and premenstrual dysphoric disorder. Intermountain-employed physicians can access an online version of the DSM-5 via the e-resources page on www.intermountain.net.

TABLE 2. Possible diagnosis and treatment based on PHQ-9

PHQ-9 Results	Possible Diagnosis ^{APA2}	Treatment Approach (see Treatment section)
<ul style="list-style-type: none"> • < 5 symptoms of depression • Questions A and B negative 	Other — not depression	<ul style="list-style-type: none"> • Provide reassurance and/or supportive counseling. • Refer to behavioral health educational resources. • Reassess if no improvement or condition worsens.
<ul style="list-style-type: none"> • < 5 symptoms • Question 1 or 2 positive • Question A positive 	Depression not otherwise specified (depression not otherwise specified or minor depression)	<ul style="list-style-type: none"> • Watchful waiting; supportive counseling. • Educational resources • If no improvement after ≥ 4 weeks, use antidepressant or brief psychotherapy.
<ul style="list-style-type: none"> • 2 to 4 symptoms • Question 2 positive • Question B positive 	Persistent depressive disorder (dysthymia)	<ul style="list-style-type: none"> • Antidepressant and/or psychotherapy.
<ul style="list-style-type: none"> • ≥ 5 symptoms • Question 1 or 2 positive • Question A positive 	Major depressive episode (can be classified as mild, moderate, or severe — and recurrent or single episode)	See summary of suggested options based on severity score below. See algorithm on the next page for more detail.
	Severity	Treatment
	Severity score 10–14 = Mild	Antidepressant or psychotherapy (patient preference); watchful waiting in children.
	Severity score 15–19 = Moderate	Antidepressant and/or psychotherapy (patient preference). Consider / offer care management.
Severity score ≥ 20 = Severe	Antidepressant alone or antidepressant combined with psychotherapy. Consider / offer care management.	

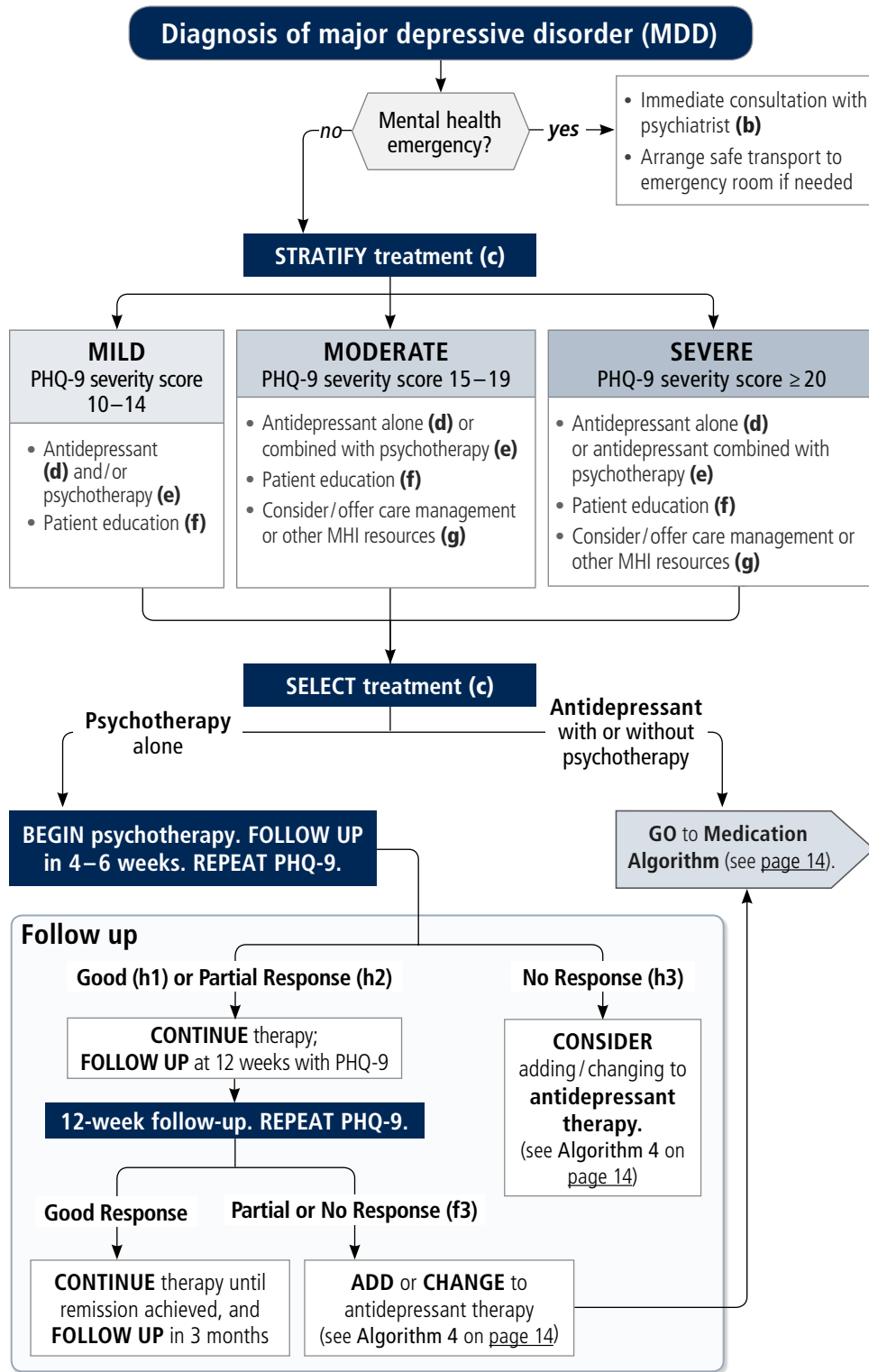
ALGORITHM NOTES

- (a) Treatment goal is full remission.**
A PHQ-9 severity score of <5 can be used as the full-remission goal.
- (b) Psychiatrist consultation:** Consult with a psychiatrist or psychiatric APP for any patient with suicidal thoughts (especially if the patient has a plan or intent) or high anxiety. See [page 9](#) for more indications for psychiatrist consultation.
- (c) Treatment stratification:** Disease severity is based not only on PHQ-9 symptom score, but also on other factors such as comorbidities, family coping skills, and past medical and mental health history.
- (d) Antidepressant therapy** should be considered first-line treatment for depression of any severity.
- (e) Psychotherapy** can be used alone or in combination with antidepressants. Combining psychotherapy with medication has a demonstrated advantage for patients with recurrent depression, with a history of nonadherence to treatment, or on multiple medications (see [page 9](#)).
- (f) Patient education**
Educate all patients and families:
 - Give *Depression* patient education handout describing the disease and treatment options (see [page 11](#)). Refer patient to other [Intermountain depression-related resources and education](#).
 - Emphasize adherence to treatment, especially adhering to prescribed medication regimen.
 - Help patient set self-management goals.
- (g) MHI resources:** A PCP may choose to work with specialists and care managers in any phase of patient care, based partly on patient preference (See [page 9](#)).
- (h) Response definitions:**
 - 1. Good Response:** PHQ-9 severity score improves by ≥ 25 %, or absolute score is < 5.
 - 2. Partial Response:** PHQ-9 severity score improves by < 25 %.
 - 3. No Response:** No or insignificant improvement in PHQ-9 severity score.

► **TREATMENT OVERVIEW**

The following algorithm presents a treatment approach for adults based on disease severity and patient preference. The PCP may choose to collaborate with specialists and care managers in any phase—from diagnosis to treatment and maintenance. Collaboration is especially helpful for patients who are non-compliant or have significant comorbidities.

ALGORITHM 3: TREATMENT OVERVIEW (a)



MENTAL HEALTH INTEGRATION

Mental health integration (MHI) is the Intermountain model of mental healthcare that is integrated into everyday primary care practice. MHI has also been referred to as **team-based care** for depression. Another model for integrated care is the **collaborative care** model from the University of Washington—the **AIMS model**. Consult the [Overview of Mental Health Integration \(MHI\) CPM](#) at www.intermountainphysician.org/clinical/topics under the “Mental Health Integration” topic.

Psychiatric consult

When added to an integrated mental health team, the expertise of a psychiatrist or psychiatric APRN — in the form of guidance, oversight, and/or direct patient care — can improve outcomes and provide a broader knowledge base to the PCP. Patients with the following conditions may warrant a psychiatric consult:

- Suicidal thoughts, especially if patient has a plan, intent, and/or high anxiety
- Bipolar history (e.g., history of mania, hypomania, or significant mood cycling)
- Comorbid drug or alcohol abuse
- Evidence of hallucinations or delusional thinking
- Failure after three trials of antidepressants

Psychiatric consultation may also be of help when treatment adherence issues intervene or treatment within the clinic becomes too problematic or time-consuming. However, patients who are having difficulty complying with treatment may not easily follow through with the recommendation to see a psychiatrist. Ideally, the PCP will remain involved and bring the psychiatrist or psychiatric APRN in as a consulting partner.

Many patients can be effectively treated in a primary care setting despite a severe PHQ-9 rating if the PCP is comfortable treating such patients and has access to a care manager. However, consultation is in order if the patient experiences repeated medication failures or presents with a significant short-term, self-harm risk.

Psychotherapy

Psychotherapy encompasses a variety of therapeutic approaches, such as cognitive-behavioral, interpersonal, behavioral, and short-term dynamic therapies.

When seeking psychotherapy, advise adult patients to find a therapist that practices cognitive behavior therapy (CBT) or interpersonal therapy (IPT) and sets specific goals and timelines. Psychotherapy can be used alone in the following situations:

- With mild to moderate depression
- When the patient requests it
- During pregnancy

Combining psychotherapy with medication has a demonstrated advantage for patients with recurrent depression or a history of poor adherence to treatment.

Care management

Patients who work with care managers (offering both knowledge and a supportive relationship) have much better results than those who do not.^{HUN}

With routine phone or clinic contact, care managers can educate patients regarding their care, set expectations, assist with social emergencies, and direct patients to return to the clinic sooner rather than later. Care managers offer both knowledge and a supportive relationship to patients—both of which are necessary for success. Working inside and outside the clinic, a care manager can assist a PCP by helping with:

- Treatment adherence, patient education, and self-management
- Reinforcement of ongoing physician, patient, and family contact
- Communication and coordination between mental health and primary care
- Support with requests for consultation
- Improving timely contact with patients and monitoring their responses

SUGGESTED MINDFULNESS READING FOR PATIENTS

- *The Mindful Way through Depression*, by Mark Williams, John Teasdale, Zindel Segal, and Jon Kabat-Zinn. This resource includes a CD for guidance which is very helpful.
- *10 Percent Happier*, by Dan Harris.
- *Hardwiring Happiness*, by Rick Hansen
- *Radical Acceptance*, by Tara Brach
- *Mindfulness for Beginners: A Simple Concise & Complete Guide to Mindfulness Meditation*, by Jeffrey Holloway
- *Mindfulness for Beginners: Practical Guide to Mindfulness Meditation & Productive Life*, by Martin Lippmann

MINDFULNESS APPS

- **Calm** (free)
- **Headspace** (initially free, then a charge to continue use)
- **Insight Timer** (free)
- **Stop, Breathe and Think** (free)

MINDFULNESS CLASSES

Intermountain Healthcare offers Mindfulness Based Stress Reduction (MBSR) classes at various sites. Online registration and more information are available at: <https://intermountainhealthcare.org/calendar/chc-mckay/mindfulness-based-stress-reduction-mbst/>. Contact the Behavioral Health Clinical Program (BHCP@imail.org).

Mindfulness

Mindfulness is most useful for chronic or recurrent depressive disorders and has been found to be as effective as medications in preventing relapse.^{KUY} It helps individuals to practice being fully present in the current moment without judgement. This means just being aware of what is happening right now without a focus on whether it's good or bad, what might make it better, how it compares to other moments, etc.

When it comes to depression, mindfulness helps in a variety of ways such as:

- Focusing on just this moment to reduce rumination on past and worry about the future (key features in depression)
- Reducing reactivity by placing current emotion / pain in a “bigger” emotional and life picture
- Developing a different way to relate to pain which tends to decrease suffering and distress
- Increasing self-compassion and ability to experience richness of life experience which tends to improve access to positive aspects of life

Mindfulness is most useful when it is part of a lifestyle. It is a skill that can be learned but is best learned when not in crisis. There are a number of ways to make mindfulness training available to patients (see sidebar at left).

Basic mindfulness exercise:

Awareness of the breath is a simple way to begin the formal practice of mindfulness.

Instruct patient to:

- Sit upright with the back a bit away from the back of chair, feet flat on the floor and hands resting comfortably in the lap or on the thighs.
- Allow the eyes to close and as the eyes close allow the mind to drop in and focus on the sensations of breathing. Allow the breath to be just as it is, avoid trying to control or manipulate the breath in any way.
- Follow the breath as well as they can. When the mind wanders (which it will) simply have them notice where the mind has gone and bring it back to the breath.
- Keep returning the mind to the breath over and over again, even if it wanders dozens or hundreds of times. Just keep coming back to this breath.
- Count the breaths. If they choose to do this they should simply count “one” on the in breath, “two” on the out breath, “three” on the in breath and so on until they reach “ten” then begin again with “one”. If they get lost, they should just come back and begin with “one” again. If they find they’ve kept going with the counting and are at “fifteen” or “twenty-seven,” just have they come back to “one” on the next in breath and begin again.
- Begin with 5 minutes twice a day and expand as they are able until they are sitting for 30 minutes a day.

EVIDENCE-BASED EDUCATION TIPS FOR PATIENTS

If a PCP emphasizes the following points, evidence demonstrates that a patient's adherence to medication treatment is greatly improved:^{UN}

- Take your medication daily.
- You must take your medication for 2–4 weeks before there may be a noticeable effect.
- Continue taking your medication, especially if you feel better.
- Do not stop taking your medication without checking with your physician.

For patient education resources, [see page 33](#).

Patient education

Patient education is critical to successful treatment. (Refer patient to Intermountain's [Depression website](#).) Key components include:

- Emphasizing the importance of reporting suicidal ideation, particularly if there is increased frequency or intensity.
- Countering the frequently held stigma that depression carries by explaining that it:
 - Is not a character flaw or weakness
 - Is a biologic disease with high heritability
 - May manifest as physical problems (e.g., fatigue, pain) and sleep disturbance
 - Has a high prevalence
- Providing patient education that emphasizes the following points:
 - When medication is a component of treatment, it must be taken consistently and as prescribed (see the evidence-based education tips at left).
 - Adverse effects, if they occur, usually diminish within 1–4 weeks.
 - Antidepressant therapy may need to be adjusted since only about half of patients respond to the first antidepressant prescribed.
- Encouraging patients to create a self-management plan in which they set one or more goals in the following areas:
 - Adhering to their treatment plan
 - Maintaining or building fulfilling relationships
 - Ensuring good nutrition and getting regular exercise
 - Scheduling enjoyable or relaxing activities daily
 - Developing realistic, rather than negative, perceptions of self
 - Dividing problems into smaller components and identifying ways to address them
 - Practicing mindfulness (see [page 10](#))
- Explaining therapy options and expectations and stressing the importance of adherence to the treatment plan (see additional notes below).

Fostering treatment adherence

Depression requires patients to participate in treatment for long periods of time, even though it can also pose multiple barriers to treatment adherence — including treatment side effects, depression-associated pessimism or lack of motivation, and logistical, economic, or cultural factors. Expert consensus and updated APA guidelines indicate several important ways to foster treatment adherence:^{APA1}

- Provide key patient education messages (see above and the sidebar at left).
- Discuss medication costs and copays openly, and factor these considerations into prescription choices.
- Encourage patients to express any fears or concerns they have about treatment, and correct any misconceptions that arise.
- Mobilize care management (see [page 9](#)) and family support.
- Talk with patients about medication reminder systems, such as pill boxes or alarms.

TREATMENT-RESISTANT DEPRESSION (TRD)

Experts do not agree on a precise definition of TRD.^{AHRQ} As such, this CPM recommends the following definition:

Moderate-to-severe depression (with diagnosis confirmed) that has not responded to two or more trials of appropriate medications of different classes, with adequate strength and duration. The patient must be taking the medications correctly, and other causes of depression should be ruled out.

Following Algorithm 4 (see [page 14](#)) can help ensure that antidepressants are given an adequate trial before concluding that depression is resistant to treatment.

▶ ANTIDEPRESSANT THERAPY

General principles

Antidepressants should be considered first-line treatment for major depression of any severity in adults, based on treatment effectiveness studies (see sidebar at left). General principles are:

- **Start with first-line medications.** The first-line antidepressants listed in Table 3 ([page 15](#)) were chosen because they have broad efficacy for depressive disorders, once-a-day dosing for much of the dosing range, favorable side-effect profiles, and safety in overdose. Using these first-line medications can prevent the need for complicated titration, which in turn allows for quicker response, better adherence, fewer visits, and lower overall cost. In general, no first-line antidepressant is more effective than another; choose based on a previous response, family history of response, safety and side effects, ease of use, and cost.
- **Monitor and manage side effects.** Monitor patients closely and regularly for increased suicidality, especially during the first few weeks. During the first week, transient side effects are likely. Reassure the patient. If the patient has significant side effects at any dose (nausea, insomnia, headache, agitation, diarrhea), consider cutting the dose in half for one week, then rechallenge. (For example, if sertraline [Zoloft] 100 mg causes nausea, try 50 mg for 1 week, then rechallenge at 100 mg.)
- **Treat with an adequate dose for an adequate duration.** Each medication should be tried for 8 to 12 weeks before being considered a failed trial; 4 weeks is the earliest to assess its efficacy. See the algorithm ([page 14](#)) and Table 3 ([page 15](#)) for guidance on dosing and trial duration.
- **When switching antidepressants, make a full transition from one medication to the next.** When patients are cross-tapered off one antidepressant onto another, patients often get a positive early result, which leads many clinicians to leave patients on the two-antidepressant combination. This CPM recommends the antidepressant cross-taper continue, and an adequate dosage of the second antidepressant be achieved. This strategy is likely to result in the lowest cost and side effect burden when successful.

Antidepressant augmentation

After two failed trials (8 to 12 weeks at an adequate dose), add a second antidepressant or **augmentation strategy**.^{RUS, FLE, MCI, TRI2, DEW, CAR2} Also, refer the patient to **concurrent psychotherapy**.^{APA1}

- **Wait until it is necessary — but don't neglect to augment when it is needed.** For patients treated during their first two antidepressant trials, augmentation risks are likely higher than their benefits — based on a higher side-effect burden, added cost, and a higher likelihood of poor adherence. However, as demonstrated in the STAR*D effectiveness trial, remission rates drop sharply after two failed trials.^{RUS} This leaves a treatment population less responsive to medications and more likely to relapse.
- **Also, consider augmentation** if raising the dose of a partially effective medication is not tolerated or desired or after initial remission with relapse.^{FLE, MCI}
- **Focus on the medication choices** for augmentation best supported by research.^{TRI3, DEW, CAR2} These are presented in more detail in Table 5 ([page 18](#)):
 1. Adding a second first-line antidepressant of a different class
 2. Adding a tricyclic antidepressant, lithium, a mood stabilizer, thyroid hormone, or ketamine (see [page 13](#))
- **Continue augmentation as long as it is effective.** Research on augmentation with lithium^{BAU} or atypical antipsychotics^{ALE} demonstrates that if successful, the augmenting agent should continue for the duration of treatment with the original antidepressant. It would also be prudent to continue other augmenting medications along with the initial antidepressant for the duration of efficacy.

INTERMOUNTAIN KETAMINE GUIDELINES

Intermountain ketamine guidelines can be found on the [Behavioral Health Clinical Program](#) website:

- [Ketamine Administration for Treatment in Behavioral Health with Outpatient Services](#)
- [Ketamine Administration for Treatment in Behavioral Health with Inpatient Services](#)
- [Ketamine Administration for Treatment in Behavioral Health within the Community/Home](#)

ESKETAMINE (SPRAVATO®)

Esketamine (Spravato®) is the S-enantiomer of racemic ketamine and may have a higher affinity for NMDA receptors; however, esketamine is only available for in-office administration through a Risk Evaluation and Mitigation Strategy (REMS) Program.

Esketamine has abuse potential and additional side effects include dysgeusia, vertigo, dissociation, somnolence, and dizziness. In addition, esketamine costs between \$600 and \$900 per dose, and ketamine is about \$3 per dose. Esketamine is FDA-approved for use in treatment-resistant depression but ketamine is considered off-label for this use. Esketamine is also currently not covered or is non-preferred by any major insurance payers.^{THA}

Ketamine

When major depression does not respond to first- or second-line treatment, it is often termed treatment-resistant depression. One approach to treatment when other modes have failed is the use of ketamine.^{THA}

Ketamine was developed as a sedative for surgical procedures and has since been discovered to have positive effects on treating treatment-resistant depression. The mechanism of action in reducing depressive symptoms is not known, but ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist. Ketamine is metabolized hepatically via CYP2B6 and CYP3A4 pathways, as are many other common medications. Due to this, drug interactions must be considered and monitored.

Possible routes of administration include intravenous (IV), oral, and nasal. Of these, IV has been the most extensively studied.

- **IV.** There is no set recommended dosage for IV ketamine. Studies found the minimum effective dose is 0.5 mg/kg infused over 40 minutes with the ability to adjust up to 0.75 mg/kg. Frequency of administration is suggested at once to twice per week for up to six weeks.
- **Oral** administration requires a higher dosing of 1 mg/kg but has poor bioavailability and a bad taste and is not usually recommended.
- **Nasal** administration is becoming a more popular route, especially with self-administration. The nasal route is not appropriate for those with swollen mucosa or a deviated septum. Typically, it is given in 5 mg doses to each nostril every 10 minutes for 5 administrations for a total of 50 mg (not weight-based). Recommended dosing is twice weekly for 1 month then once weekly. Self-administration requires monitoring by a responsible adult.

Refer patient to outpatient or home health infusion center for initiation. It is recommended that the first dose be given in a monitored environment where vital sign monitoring and patient teaching can be completed.

The efficacy of ketamine for treatment-resistant depression is short-term and lasts about 2 weeks with a single administration. Greater improvement has been seen in those with more intense depression. Ketamine also has greater effectiveness when combined with oral antidepressant therapy. Suicidal ideation can decrease within 1 hour of administration and last for up to 1 week. Longer-term effects are not known due to short duration of high-quality studies and lack of follow up.

Concerns related to use of ketamine for treatment resistant depression include abuse, addiction, neurotoxicity, bladder toxicity, hepatotoxicity, and tachyphylaxis (decline in efficacy with repeated use).

Ketamine's long-term benefit versus side effect profile is unknown. Clinical decisions regarding long-term use need to be made between the clinician and patient after reviewing the risks, benefits, side effects, and alternatives.

ALGORITHM NOTES

(a) General principles:

- Select from first-line medications (see [Table 3](#)). Choose generics first. Generics can result in significant cost savings for both the patient and the healthcare system.
- Treat with an adequate dose for an adequate duration.
- Monitor and manage side effects.

(b) Summary of follow-up schedule:

- 2 weeks: Phone call or visit
- Every 4 weeks with repeat PHQ-9 until GOOD RESPONSE (see response definitions below)
- Every 3 months until 9–12 months of remission achieved

(c) Response definitions:

- 1. GOOD RESPONSE:** PHQ-9 severity score improves by $\geq 25\%$, or absolute score is < 5
- 2. PARTIAL RESPONSE:** PHQ-9 severity score improves, but by $< 25\%$
- 3. NO RESPONSE:** No or insignificant improvement in PHQ-9 severity score

(d) For any failure to respond: Assess patient adherence and review for BD (see [pages 24 and 25](#)), active substance abuse, comorbid medical conditions like thyroid disease, and other precipitating factors.

Assess patient adherence and review for BD (see [pages 24 and 25](#)), active substance abuse, comorbid medical conditions like thyroid disease, and other precipitating factors.

(e) MHI resources: Care management, psychotherapy, psychiatric consult, etc. (See [page 9](#).)

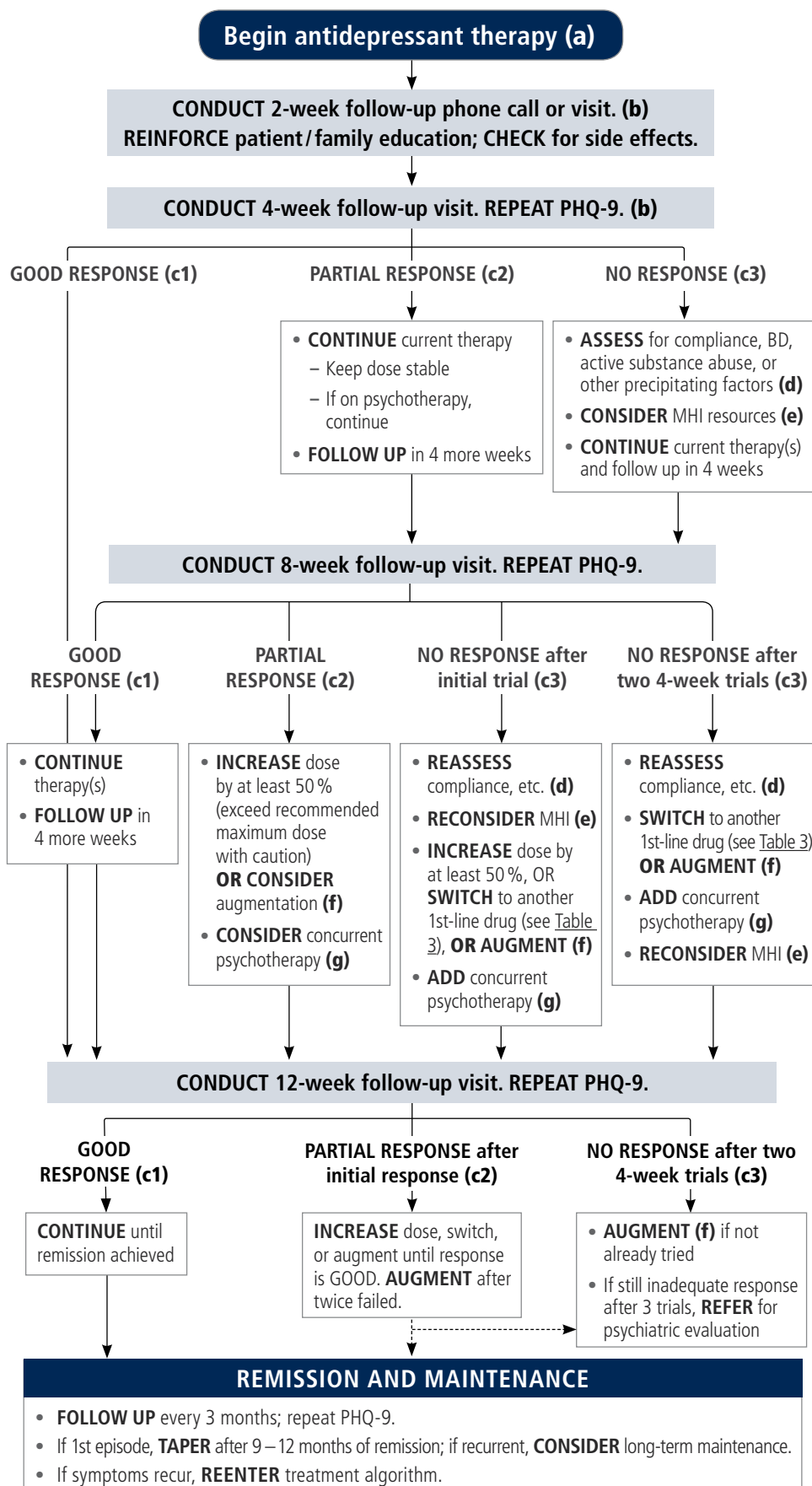
(f) Augmentation: After two failed adequate antidepressant trials, consider one of these strategies: ^{RUS, FLE, TRI2, DEW}

- Add a second, first-line antidepressant of a different class.
- Add a tricyclic antidepressant.
- Add lithium, another mood stabilizer, thyroid hormone, or ketamine.

See [pages 18 and 19](#) for more details.

(g) Concurrent psychotherapy: Since remission rates drop precipitously after the first two failed antidepressant trials, these patients are less responsive to meds, more likely to have side effects, and more likely to relapse. At this point, all patients should be referred for psychotherapy.

ALGORITHM 4: ANTIDEPRESSANT THERAPY



Medication tables

TABLE 3. First-line antidepressants for adults

Class	Drug	Dose ranges & guidelines*			Notes (see Table 7 for further details on side effects)
		Start	Maintenance	Max	
Selective serotonin reuptake inhibitors (SSRIs)	citalopram (Celexa)	20 mg once daily	20–40 mg once daily	40 mg once daily	<ul style="list-style-type: none"> • Common side effects: Sexual dysfunction, anxiety, insomnia or sedation, headache, nausea, and diarrhea. • Citalopram precautions and monitoring: <ul style="list-style-type: none"> – Avoid doses > 40 mg daily due to dose-dependent increased risk for QTc prolongation. – ECG at baseline in patients with a history of CHF, bradyarrhythmia, or concurrent administration of other QTc-prolonging medications. – Check potassium and magnesium levels at baseline for patients at risk of electrolyte abnormalities. • Taper to reduce the risk of discontinuation syndrome, particularly with paroxetine and sertraline (not necessary with fluoxetine). • Potentially lethal interaction with monoamine oxidase inhibitors (MAOIs). If MAOI treatment is considered, consult a drug information reference or psychiatrist for dosing, wash-out period, monitoring, and drug-drug and drug-food interactions.
	escitalopram (Lexapro)	10 mg once daily	10–20 mg once daily	20 mg once daily	
	fluoxetine (Prozac)	20 mg once daily	20–60 mg once daily	80 mg once daily	
	Weekly capsule: 90 mg once weekly				
	paroxetine (Paxil, Paxil CR)	20 mg once daily (IR) OR 25 mg once daily (CR)	20–50 mg once daily (IR) OR 25–62.5 mg once daily (CR)	50 mg once daily (IR) OR 62.5 mg once daily (CR)	
sertraline (Zoloft)	50 mg once daily	50–200 mg once daily	200 mg once daily		
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	desvenlafaxine (Pristiq) (generic NOT available)	50 mg once daily	50–100 mg once daily	100 mg once daily	<ul style="list-style-type: none"> • Common side effects are similar to SSRIs: Nausea, sexual dysfunction, activation, and dose-related increases in blood pressure. • Increased risk of liver damage for patients with substantial alcohol use or preexisting liver disease. • Monitor blood pressure during dose titration. • Duloxetine: Hepatic function test at baseline. • Taper to reduce risk of discontinuation syndrome. • Avoid administration of MAOIs concurrently or within 14 days of SNRIs.
	duloxetine (Cymbalta)	30–60 mg once daily	30–60 mg once daily	120 mg once daily	
	venlafaxine XR (Effexor XR)	37.5–75 mg once daily	75–225 mg once daily	225 mg once daily	
Atypical antidepressants	bupropion HCl (Wellbutrin) SR or XL	150 mg every morning (SR/XL)	150 mg twice daily (SR) OR 300 mg once daily (XL)	450 mg divided twice daily (SR) OR 450 mg once daily (XL)	<ul style="list-style-type: none"> • Bupropion IR is not recommended due to seizure risk and poor tolerability. • Contraindicated in patients with a history of seizure disorder or eating disorder (IR is the highest risk). • Mechanism of action: Dopamine-norepinephrine reuptake inhibitor; available as 12-hour sustained-release (SR), 24-hour extended-release (XL), or immediate-release (IR is preferred in gastric bypass patients). • Common side effects: Insomnia, headache, dizziness, nausea, and diarrhea; may also cause delirium or restlessness. • May improve sexual desire, arousability, and orgasmic ease. • No weight gain and may help with weight loss. • Useful as a smoking cessation agent. • Avoid taking after dinner or at bedtime.

* **Dosage ranges:** Consider lower doses (about half) for elderly patients. Consult drug information resources for dosing in patients with renal impairment, hepatic impairment, pregnancy, or who are taking medications that interact with antidepressants. For recommended medications and dosing for children, refer to [Table 9](#).

TABLE 4. Other antidepressants for adults

Class	Drug	Dose ranges and guidelines*			Notes (see Table 7 for further details on side effects)
		Start	Maintenance	Max	
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	levomilnacipran (Fetzima) (generic NOT available)	20 mg once daily for 2 days	20–40 mg once daily (may increase by 40 mg every 2 days)	120 mg once daily	<ul style="list-style-type: none"> Common side effects are similar to SSRIs: Nausea, sexual dysfunction, activation, and dose-related increases in blood pressure. Increased risk of liver damage for patients with substantial alcohol use or preexisting liver disease. Monitor blood pressure during dose titration. Taper to reduce risk of discontinuation syndrome. Avoid administration of MAOIs concurrently or within 14 days of SNRIs.
Atypical antidepressants	mirtazapine (Remeron) ^{CAR1}	15 mg once daily, at bedtime	15–45 mg once daily, at bedtime (titrate to effect and tolerability)	45 mg once daily, at bedtime	<ul style="list-style-type: none"> Mechanisms of action: Norepinephrine-serotonin release enhancer; 5HT₂ and 5HT₃ receptor antagonist. Common side effects: Sedation, dry mouth, increased appetite, weight gain. Less sedation at higher doses; minimal sexual dysfunction. Available as IR tablets or orally disintegrating tablets.
Serotonin modulators	nefazodone (Serzone)	100 mg twice daily	100–200 mg twice daily	300 mg twice daily	<ul style="list-style-type: none"> Mechanism of action: Postsynaptic 5HT_{2A} antagonist and down regulator; weak SNRI properties. Can cause irreversible liver damage. Monitor liver function at baseline and periodically and stop if AST/ALT increases to greater than 3 times upper limit normal. No risk factor predicts who will develop irreversible liver failure, and no clinical strategy has been shown to reduce the risk. Common side effects: Nausea, somnolence, dry mouth, dizziness, constipation, weakness, and blurred vision. May be discontinued abruptly if needed. Minimal sexual dysfunction and weight gain.
	trazodone	150 mg daily in divided doses (often dosed once daily at bedtime)	150–600 mg daily in divided doses (titrate to effect and tolerability)	400 mg per day (outpatients) 600 mg per day (inpatients)	<ul style="list-style-type: none"> Mechanism of action: Acts upon postsynaptic 5HT_{2A} and 5HT_{2C} receptors (antagonist at low doses, agonist at high doses), weak SSRI properties. Common side effects: Sedation, dizziness, dry mouth, nausea. Clinical practice guidelines recommend doses up to 600 mg without consideration of inpatient or outpatient status. 50–100 qHS may be effective for insomnia.
	vilazodone (Viibryd) (generic NOT available)	10 mg once daily	40 mg once daily	40 mg once daily	<ul style="list-style-type: none"> Mechanisms of action: SSRI and 5HT_{1A} partial receptor agonist. Common side effects: Diarrhea, nausea/vomiting, dizziness, dry mouth, insomnia. Avoid administration of MAOIs concurrently or within 14 days of vilazodone.
	vortioxetine (Trintellix) (generic NOT available)	10 mg once daily	10–20 mg once daily	20 mg once daily	<ul style="list-style-type: none"> Mechanisms of action: SSRI, 5HT₃ receptor antagonist, 5HT_{1A} agonist. May be decreased to 5 mg/day if patients are intolerant to higher doses. May be discontinued abruptly if needed. To avoid transient discontinuation symptoms, taper in patients taking 15–20 mg/day; decrease dose to 10 mg/day for one week, then discontinue. Avoid administration of MAOIs concurrently or within 14 days of vortioxetine.

* **Dosage ranges:** Consider lower doses (about half) for elderly patients. Consult drug information resources for dosing in patients with renal impairment, hepatic impairment, pregnancy, or who are taking medications that interact with antidepressants. For recommended medications and dosing for children, refer to [Table 9](#).

TABLE 4. Other antidepressants for adults (continued)

Class	Drug	Dose ranges and guidelines*			Notes (see Table 7 for further details on side effects)
		Start	Maintenance	Max	
Tricyclic antidepressants (TCAs) ^{AND1}	amitriptyline (Elavil) Tertiary amine	25–50 mg per day	50–100 mg per day	300 mg per day	<ul style="list-style-type: none"> • Tricyclics in combination with serotonergic medications can increase blood levels of tricyclics; adjust dosing based on the tricyclic blood level. • Except as indicated, may be given once daily at bedtime, if tolerated, or divided in 2–3 doses. • Mechanisms of action: TCAs are essentially SNRIs. <ul style="list-style-type: none"> – Tertiary amines are more potent at blocking reuptake of serotonin. – Secondary amines are more potent at blocking reuptake of norepinephrine. • Clomipramine is not FDA-approved for use in MDD. • Common side effects: Sedation, dry mouth, orthostatic hypotension, tachycardia, QTc prolongation, and sexual dysfunction. • More cardiotoxic in overdose than first-line agents; potentially dangerous in overdose. • Avoid administration of MAOIs concurrently or within 14 days of TCA. • Monitor for suicidal ideation or behavior AND: <ul style="list-style-type: none"> – ECG at baseline. – Pregnancy test as clinically indicated. – Serum levels (trough) as clinically indicated.
	clomipramine (Anafranil) Tertiary amine	12.5–50 mg per day	50–150 mg per day	250 mg per day	
	desipramine (Norpramin) Secondary amine	25–50 mg per day	100–200 mg per day	300 mg per day	
	doxepin (Sinequan) Tertiary amine	25–50 mg per day	100–300 mg per day	300 mg per day	
	imipramine (Tofranil) Tertiary amine	50 mg per day (outpatients) 100–150 mg per day (inpatients)	50–150 mg per day (outpatients) 100–200 mg per day (inpatients)	200 mg per day (outpatients) 300 mg per day (inpatients)	
	nortriptyline (Pamelor) Secondary amine	25 mg per day	75–100 mg per day	150 mg per day	
	protriptyline (Vivactil) Secondary amine	10–20 mg per day (in 3–4 divided doses)	20–60 mg per day	60 mg per day	

* **Dosage ranges:** Consider lower doses (about half) for elderly patients. Consult drug information resources for dosing in patients with renal impairment, hepatic impairment, pregnancy, or who are taking medications that interact with antidepressants. For recommended medications and dosing for children, refer to [Table 9](#).

TABLE 5. Augmentation agents

Class	Drug	Dose range and guidelines*	Notes	Monitoring
Lithium preparations	lithium carbonate ^{BAU, VAL, CRO} (Eskalith, Eskalith CR, Lithobid)	<ul style="list-style-type: none"> • Range: 150–1,500 mg per day (IR generally divided 2–3 times daily; XR may be given once daily as tolerated) • Target: Serum level 0.4–0.8 mEq/L 	<ul style="list-style-type: none"> • Not FDA-approved for the treatment of depression. • May be given once daily as tolerated. • Common side effects: Polydipsia, polyuria, acne, GI discomfort, hand tremor; most are serum-level related. • Moderate weight gain. • Multiple drug interactions (NSAIDs, ACE inhibitors, diuretics, etc.). • No significant sedation or stimulation; one of the best-studied augmentation strategies; helpful with suicidal behavior. • One of the only agents shown to prevent suicide in randomized trials. 	<p>Monitor (as clinically indicated) AND:</p> <ul style="list-style-type: none"> • Electrolytes, UA, and pregnancy tests at baseline. • ECG and CBC at baseline. • Renal and thyroid function at baseline and every 6 months. • Serum lithium level 10–12 hours after the last dose, 4–5 days after initiation or dose change, then every 3 months.
Anticonvulsant	lamotrigine (Lamictal)	<ul style="list-style-type: none"> • Initiate at 25 mg once daily • Titrate per set schedule of: <ul style="list-style-type: none"> – 25 mg once daily x 2 weeks, then – 50 mg once daily x 2 weeks, then – 100 mg once daily x 1 week, then – 200 mg once daily 	<ul style="list-style-type: none"> • Not FDA-approved for the treatment of depression. • Do not titrate more rapidly than recommended. • May provoke toxic dermal eruptions (Stevens-Johnson syndrome, toxic epidermal necrolysis), but markedly reduced risk when titrated as directed; patient should seek medical attention immediately if a rash appears. • If taking with divalproex, halve titration doses; if taking with carbamazepine, double titration doses (but no more than 100 mg/day increase). • Dose adjustment is needed if concomitant enzyme-inducing antiepileptic medication or valproic acid is discontinued. • Common side effects: Nausea and rash; if continuing therapy despite rash, reduce dose and titrate more slowly once rash resolves. • Estrogen-containing oral contraceptives may decrease lamotrigine levels by 50%. 	<p>Monitor suicidality, pregnancy, renal and hepatic function tests baseline and yearly</p>
Thyroid supplement	liothyronine sodium ^{RUS} (Cytomel)	<ul style="list-style-type: none"> • Initiate at 25 mcg once daily • Titrate by 12.5–25 mcg every 1–2 weeks • Goal range: 25–50 mcg once daily 	<ul style="list-style-type: none"> • Not FDA-approved for the treatment of depression. • Risks are primary hyperthyroidism and its sequelae. • Most effective in females with low-normal thyroid functioning. 	<p>Monitor TSH and free T3 at baseline and at 3 months.</p>

* **Dosage ranges:** Consider lower doses (about half) for elderly patients. Consult drug information resources for dosing considerations in patients who have renal impairment, hepatic impairment, are pregnant, or who are taking medications that interact with antidepressants. For recommended medications and dosing for children, refer to [Table 9](#).

TABLE 5. Augmentation agents (continued)

Class	Drug	Dose range and guidelines*	Notes	Monitoring
Second-generation antipsychotics†	aripiprazole ^{BER, MAR1} (Abilify)	<ul style="list-style-type: none"> • Initiate at 2–5 mg once daily • Titrate by up to 5 mg every week • Goal range: 2–15 mg once daily 	<ul style="list-style-type: none"> • FDA-approved as an adjunct for treatment of depression. • Common side effects: Restlessness, stimulation, and nausea. • Minimal risk of extrapyramidal side effects (EPS) other than akathisia. • Minimal sedation. 	Monitoring for ALL atypical antipsychotics: <ul style="list-style-type: none"> • Pregnancy test • Initial BMI measurement, then every visit for 6 months and quarterly once dose is stable • Baseline hemoglobin A1c or fasting plasma glucose before initiating, then every year • Blood pressure at least yearly • Baseline fasting lipid panel, then yearly if normal or every 6 months if LDL > 130 mg/dL • Baseline extrapyramidal side effects (EPS) evaluation, then at each outpatient visit
	brexpiprazole (Rexulti) (generic NOT available)	<ul style="list-style-type: none"> • Initiate at 0.5–1 mg once daily • Titrate by 0.5–1 mg every week • Goal range: 1–3 mg once daily 	<ul style="list-style-type: none"> • FDA-approved as an adjunct for treatment of depression. • Common side effects: Restlessness, dyslipidemia, and weight gain. • Minimal risk of extrapyramidal side effects (EPS) other than akathisia. • Minimal sedation. 	
	olanzapine (Zyprexa)	<ul style="list-style-type: none"> • Initiate at 5 mg once daily, at bedtime • Titrate by up to 5 mg every 4–7 days • Goal range: 5–12.5 mg once daily, at bedtime 	<ul style="list-style-type: none"> • FDA-approved for the treatment of treatment-resistant depression as a combination product olanzapine/fluoxetine (Symbyax). • Significant sedation and weight gain, moderate EPS risk. • Potential for dyslipidemia and hyperinsulinemia. • May increase risk of type 2 diabetes. 	
	quetiapine ^{ELK, WEI, DAT} (Seroquel, Seroquel XR)	<ul style="list-style-type: none"> • Initiate at 50 mg once daily, at bedtime • Titrate by 50 mg daily as tolerated • Goal range: 150–300 mg once daily, at bedtime 	<ul style="list-style-type: none"> • Only XR is FDA-approved as an adjunct treatment for depression. • IR may be given once nightly if tolerated or divided over the day. • Significant sedation and moderate weight gain. • Lowest EPS risk of the atypical antipsychotics. 	
	risperidone ^{EDW} (Risperdal)	<ul style="list-style-type: none"> • Initiate at 0.5 mg once daily, at bedtime • Titrate by 0.5 mg daily as tolerated • Goal range: 1–3 mg once daily, at bedtime 	<ul style="list-style-type: none"> • Not FDA-approved for the treatment of depression. • May be given once nightly if tolerated or divided over the day. • Moderate sedation and weight gain; increases prolactin. • Minimal risk of EPS below 4 mg daily. 	

* **Dosage ranges:** Consider lower doses (about half) for elderly patients. Consult drug information resources for dosing considerations in patients who have renal impairment, hepatic impairment, are pregnant, or who are taking medications that interact with antidepressants.^{APA1}

† **Atypical antipsychotics:** Antipsychotic medication should always be used in the treatment of major depression with psychosis.^{APA1}

TABLE 6. Medication choices for special circumstances

Circumstance	Recommendations
Anxiety or agitation	<ul style="list-style-type: none"> • Antidepressants will often improve anxiety in 1–3 weeks. Duloxetine, escitalopram, paroxetine, and venlafaxine have approved indications for generalized anxiety disorder (GAD). Citalopram, fluoxetine, and sertraline also have evidence supporting their use for GAD. Anxious or agitated depression is likely to respond as quickly to a stimulating antidepressant as to a sedating one. • For more immediate relief, consider adding a benzodiazepine. Low doses of clonazepam, diazepam, or lorazepam have demonstrated benefit. Titrate dose slowly as needed, based on response. When anxiety has decreased for at least 2–3 days, begin to taper. May titrate rapidly for short-term therapy; for benzodiazepine use in excess of 6 months, taper dosage by approximately 10% every 1–2 weeks, monitoring for symptoms of benzodiazepine withdrawal.
Akathisia (atypical; antipsychotic-induced)	<ul style="list-style-type: none"> • Consider a cautious antipsychotic dose reduction while monitoring for a recurrence of depression symptoms. • If a dose reduction is unfeasible or insufficient, consider adding a benzodiazepine. Two small trials suggest that lorazepam 0.5 mg twice daily may reduce symptoms compared to placebo.^{MAR2} Incrementally titrate up to 6–10 mg daily as needed to manage symptoms. • If benzodiazepines are ineffective, consider propranolol 10 mg twice daily, titrating up to 20 mg twice daily and finally to propranolol LA 60–120 mg daily.
Chronic pain	<ul style="list-style-type: none"> • Duloxetine is indicated for diabetic peripheral neuropathic pain, fibromyalgia, and chronic musculoskeletal pain. • Amitriptyline, imipramine, nortriptyline, and desipramine may be preferable to first-line antidepressants for patients with chronic pain.
Elderly patient	<ul style="list-style-type: none"> • Consider decreasing dose ranges by 50%. Older patients are more susceptible to lithium toxicity and at increased risk for other side effects. • Monitor for increased suicidality, more accidents, and self-neglect. • Atypical antipsychotic medications may increase the risk of death in elderly patients with dementia.
Hypersomnia	<ul style="list-style-type: none"> • The following choices are activating for some patients: bupropion, citalopram, sertraline, aripiprazole, fluoxetine, venlafaxine, duloxetine.
Insomnia	<ul style="list-style-type: none"> • Consider adding trazodone at bedtime. Doses from 25 mg up to 200 mg tend to be well tolerated. • Many patients find mirtazapine sedating and report more sedation at lower doses.
Pregnancy and breastfeeding	<ul style="list-style-type: none"> • Use of antidepressants in pregnancy should be carefully considered. Evidence indicating the overall risk to the neonate is low. • In patients with no history of antidepressant use and no suicidal ideation, consider psychotherapy only. • Medication choices: Fluoxetine and sertraline have the most evidence on safety during pregnancy. <ul style="list-style-type: none"> – Sertraline is the recommended antidepressant during pregnancy. Patients taking fluoxetine or another antidepressant prior to pregnancy should consider switching to sertraline, based on available safety data. – However, if a patient becomes pregnant while taking fluoxetine or another antidepressant, she should remain on that drug (if it is effective) to minimize risk and limit neonatal exposure to additional medications. – Consider bupropion if there is a history of ADHD, poor response to first-line agents, or concurrent smoking cessation efforts. • No evidence exists to support antidepressant tapering or discontinuation as term approaches; instead, many women on antidepressants will require increased doses in the third trimester to maintain euthymia. • Breastfeeding: The benefits of breastfeeding generally outweigh the small risks associated with antidepressant therapy. If antidepressants are needed, monotherapy with sertraline or paroxetine at the lowest effective dose is preferred. For women already on an antidepressant while pregnant, there is no need to change the agent while breastfeeding.
Pseudo-Parkinson's, acute dystonia	<ul style="list-style-type: none"> • Anticholinergic agents may be used for acute situations or as prophylactic/maintenance agents. • Elderly patients are prone to anticholinergic delirium.
Psychosis	<ul style="list-style-type: none"> • Antipsychotic medication should always be used in the treatment of major depression with psychotic features.^{APA1} Consider consulting a psychiatrist.
Substance use disorder	<ul style="list-style-type: none"> • Screen every patient with treatment-resistant depression for substance use disorder. Start with the Intermountain-modified NIDA (National Institute on Drug Abuse) Quick Screen. If the NIDA screen is positive, administer Intermountain's ASSIST-based Assessment. • Give appropriate referral and treatment for substance use issues. See Intermountain's Substance Use Disorder CPM for information. • Psychotropic medications are unlikely to be successful in the presence of significant substance use. Daily alcohol intake may interfere with an antidepressant response even at low levels (one or two drinks a day).
Thyroid dysfunction	<ul style="list-style-type: none"> • Subclinical hypothyroidism—characterized by TSH 4–8 μIU/mL and normal Free T4—correlates with a poor antidepressant response; augmenting with liothyronine sodium has the best response with this population.^{SAC} • Clinical hypothyroidism or hyperthyroidism can be related to anxiety, depression, and treatment resistance. Optimize thyroid functioning while treating depression.^{SAC}
Weight gain >5 pounds or weight gain prevention	<ul style="list-style-type: none"> • Consider a medication change. Mirtazapine and paroxetine may be associated with more weight gain than similar agents. Bupropion is not associated with weight gain. • Recommend a consult with a registered dietitian (RD). SelectHealth commercial plans cover up to 5 visits with \$0 copay. • Consider adding metformin or topiramate. One large trial showed an average 3-year weight loss of 2.5% (maintained over 10 years) with metformin.^{KRO} A meta-analysis of 6 trials showed an average 6-month weight loss of 6.5% with topiramate.^{HUS}

TABLE 7. Potential side effects of antidepressants

SSRIs	Other medications
<ul style="list-style-type: none"> • Gastrointestinal: SSRIs can cause nausea, vomiting, and diarrhea to a greater extent than TCAs. These adverse events are generally dose-dependent and dissipate after a few weeks. • Activation/insomnia: SSRIs may precipitate or exacerbate restlessness, agitation, and sleep disturbances. These side effects often attenuate with time. Anxiety may be minimized by introducing the agent at a low dose. • Sexual: SSRIs may cause loss of erectile or ejaculatory function in men and loss of libido and anorgasmia in both sexes. If the dysfunction is thought to be SSRI-induced instead of caused by the depressive disorder itself, try the following strategies: Continue treatment and assess for spontaneous symptom resolution, decrease the dose, discontinue the antidepressant, or switch to another antidepressant such as bupropion.^{APA1, WAL} Pharmacologic treatments that can be added for arousal or erectile dysfunction include sildenafil, yohimbine, or neostigmine. Treatment options for orgasmic dysfunction include sildenafil, cyproheptadine, or amantadine.^{BAL} Trazodone has also been implicated as a treatment option for SSRI-induced sexual dysfunction, particularly in female patients. • Neurological: SSRIs can initially exacerbate both migraine and tension headaches. These effects tend to be transient and improve within the first few weeks. There is some suggestion that with continued treatment, SSRIs may then actually help prevent and treat migraine headaches.^{DOU, SAC} SSRIs have also been associated with extrapyramidal reactions, including akathisia, dystonia, parkinsonism, and tardive dyskinesia.^{KOL, TRI1} The occurrence of such extrapyramidal symptoms is generally very low but may be higher in older patients, especially those with Parkinson's disease. • Cardiovascular: Citalopram has been shown to cause dose-dependent QTc interval prolongation; the prescribing information has been modified to recommend against giving citalopram at doses over 40 mg/day. While other agents have also been associated with QTc prolongation, no others have yet been deemed sufficiently significant to warrant similar warnings. • Weight changes: Fluoxetine has been shown to cause an initial weight loss, but weight tends to be gained back subsequently. While the literature differs as to whether SSRIs beyond the acute phase do or do not lead to weight gain, recent APA guidelines indicate paroxetine has a higher incidence of weight gain than other SSRIs.^{APA1} • Serotonin syndrome: SSRI use has been associated with the rare development of a syndrome due to excess of serotonergic activity. Serotonin syndrome features include abdominal pain, diarrhea, flushing, sweating, hyperthermia, lethargy, mental status changes, tremor, myoclonus, rhabdomyolysis, renal failure, cardiovascular shock, and may result in death.^{APA1} Although serotonin syndrome can occur with SSRIs alone, risk is increased with simultaneous use of additional serotonergic agents, such as MAOIs, SNRIs, TCAs, mirtazapine, vortioxetine, vilazodone, levomilnacipran, linezolid, tramadol, fenfluramine, dexfenfluramine, or MDMA. 	<ul style="list-style-type: none"> • Bupropion (Wellbutrin): Neurologic side effects have been observed, including headaches, tremors, and seizures. Seizure risk can be reduced by avoiding high doses (e.g., keep the dose less than 450 mg/day), using divided dosing (e.g., three times a day), and avoiding bupropion for patients with seizure risk factors. Bupropion has been associated with development of psychotic symptoms, including delusions and hallucinations; use bupropion cautiously in patients with psychotic disorders. Other side effects include insomnia and GI upset. • Duloxetine (Cymbalta): Closely monitor patients taking duloxetine for signs of liver damage, including itching, dark urine, jaundice, right-upper quadrant tenderness, and unexplained flu-like symptoms. Avoid duloxetine in patients who have liver disease or who use alcohol substantially. Other side effects are similar to those with SSRIs, such as nausea/vomiting, sexual dysfunction, and activation. • Mirtazapine (Remeron): The most common side effects from mirtazapine include sedation, dry mouth, and weight gain. These tend to occur early and may attenuate with continued treatment. Mirtazapine has also been shown to increase serum cholesterol levels in some patients.^{CRO} While agranulocytosis has been observed in patients taking mirtazapine, this has been very rare. Routine white blood cell (WBC) monitoring is not needed, although checking may be advisable in patients with signs or symptoms of infection. • Tricyclic antidepressants (TCAs): Can cause weight gain that is often dose-dependent; weight gain is typically more significant with amitriptyline and less significant with desipramine. • Venlafaxine (Effexor): Side effects have been linked to those seen with SSRIs, including nausea and vomiting, sexual dysfunction, and activation. Venlafaxine can cause a dose-related increase in blood pressure that may be resolved with dose reduction. As with SSRI side effects, venlafaxine side effects can attenuate with continued use. • Vilazodone (Viibryd): While side effects are similar to those of SSRIs, fewer sexual side effects are reported with vilazodone. The most common side effects include nausea and diarrhea, although as with SSRIs, these side effects can attenuate with continued use. • Levomilnacipran (Fetzima): Side effects include nausea, vomiting, constipation, sexual dysfunction, increased heart rate, palpitations, and sweating. • Vortioxetine (Brintellix): Side effects include nausea, vomiting, dry mouth, constipation, dizziness, and sexual dysfunction.

MHI FOLLOW-UP PACKETS HELP IN MONITORING PROGRESS

In addition to the PHQ-9, other components of Intermountain’s Mental Health Integration Follow-up Packets may be useful for monitoring progress during the continuation and maintenance phases, especially for patients with comorbidities. Find these tools at intermountainphysician.org/clinicalprograms under the “Mental Health Integration” topic.

► REMISSION AND MAINTENANCE

Full remission — not just partial resolution of symptoms — is the goal of treatment for depression. Remission rates in adult primary care practices over a two-year period are estimated at only 45%.^{YIE} Under-treatment of depression contributes to protracted suffering and impairments in work and interpersonal relationships and leaves patients with a heightened risk of suicide. Patients not in full remission (i.e., patients with residual symptoms) are also likely to have the following:

- Three to five times higher relapse rate^{JUD1, CHO, PAY}
- Seven times higher likelihood of being less effective on the job^{DRU}
- More severe and chronic courses of depression, with shorter well intervals and fewer symptom-free weeks^{JUD2}
- Worse outcomes for medical comorbidities
- Higher medical costs

Achieving full remission

Remission is achieved through treatment of adequate duration with sufficient doses of medication. Treatment failure is often due to inadequate dosage and/or insufficient time on medication.

The STAR*D trial, which followed usual adult patients in both primary care and mental health clinic settings, provides a good estimate of how long is necessary to assess effectiveness.^{RUS} In the first phase of the study, patients were treated with citalopram over a 12-week period. The average time to response (defined as a symptom improvement of 50% or more) was 5.5 weeks, and the average time to remission was 6.3 weeks. Changing a patient’s medication before 6 weeks would have missed more than half of all good responses and more than half of all remissions for these patients.

Using an outcome instrument like the PHQ-9 can assist in the process of achieving full remission. A severity score of less than 5 on the PHQ-9 can be used as the treatment goal. Once remission is achieved, patients should remain on the dose of medication that made them better for 9–12 months to prevent relapse. Medication can then be tapered and discontinued. For patients who have had recurrent episodes of depression, long-term maintenance should be considered. See Table 8 below.

TABLE 8. Phases of treatment for depression

Acute (usually 6–12 weeks)	Continuation (usually 9–12 months)	Maintenance (>9 months)
Effective treatment response is usually obtained during this phase, bringing the syndrome into initial remission .	During this phase, residual depressive symptoms can continue to impair patients socially and at work and complicate comorbid medical illness. Patients are also prone to relapse during this phase. Continue the full therapeutic dose during this time.	<ul style="list-style-type: none"> • If this is the first depression episode, taper and discontinue medication. • If this is a recurrent episode, consider long-term maintenance, generally with the same type and dosage effective in the previous acute stage. • Other factors that would extend a course of antidepressant treatment include patient preference, severity/disability of illness, family history of mood disorders, and ongoing psychosocial stressors.

CONTINUING PSYCHOTHERAPY

The revised APA practice guidelines recommend that, for patients who received depression-focused psychotherapy during the acute and continuation phases, continuing psychotherapy during the maintenance phase (perhaps with less-frequent appointments) can help to prevent relapse.^{APA1}

PATIENT EDUCATION FOR TRANSCRANIAL MAGNETIC STIMULATION (TMS)

Lexicomp has patient handouts available in [English](#) and [Spanish](#) to educate patients and families about the TMS procedure. The handouts describe why the procedure is performed; what happens before, during, and after the procedure; what the potential results may be; and potential side effects.



Preparing to end treatment

Revised APA guidelines suggest two key steps when discontinuing treatment:^{APA1}

- 1. Schedule a follow-up.** The highest risk for relapse is in the first two months after treatment is discontinued; a follow-up visit within this period can be helpful in identifying relapse signs.
- 2. Educate the patient.** Consider telling patients and families about the potential for relapse, describing early signs of relapse to watch for, and helping patients and families make a plan to seek treatment if it occurs.

Tapering antidepressants

To avoid discontinuation symptoms and the possibility of relapse, taper medications gradually when discontinuing treatment in a successfully treated patient. Both SSRIs and TCAs can have significant, but non-life-threatening, withdrawal symptoms. These symptoms are usually mild, they can be quite pronounced in a minority of patients. Antidepressant discontinuation symptoms may include acute onset of any of the following:

- Fatigue
- Myalgias
- Vertigo, dizziness, and/or lightheadedness
- Nausea
- Numbness/tingling
- Anxiety and/or agitation
- “Brain zaps” (subjective cerebral/cranial electrical sensations)

Symptoms are most common in shorter half-life compounds (e.g., venlafaxine, paroxetine, sertraline, and TCAs) and are uncommon or unreported in bupropion, fluoxetine, mirtazapine, and citalopram.

▶ ELECTROCONVULSIVE THERAPY (ECT) AND TRANSCRANIAL MAGNETIC STIMULATION (TMS)

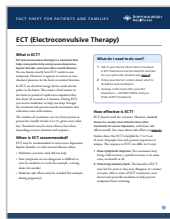
Many patients with unipolar major depression do not respond to standard treatment with pharmacotherapy and psychotherapy and are thus candidates for noninvasive neuromodulation procedures, including repetitive transcranial magnetic stimulation (TMS) and electroconvulsive therapy (ECT).^{RUS, HOL, APA1, MIL} Although ECT is more efficacious than repetitive TMS, patients may prefer repetitive TMS because it is better tolerated and unlike ECT, TMS does not require general anesthesia and induction of seizures.^{NIH, ERA}

See sidebar at left for a helpful patient education resource regarding TMS.

See [page 24](#) for APA’s updated depression management guidelines for ECT.

PATIENT EDUCATION FOR ECT

The Intermountain patient education fact sheet, [ECT \(Electroconvulsive Therapy\)](#), can be helpful in educating patients and families about the ECT process; its benefits, risks, and side effects; how to prepare; and self-care afterward.



This fact sheet can be viewed and ordered via [PrintIt!](#) and can be found at intermountainphysician.org/clinical/topics. See [page 33](#) for more information on finding resources.

DO NOT USE UNOPOSED ANTIDEPRESSANTS

Unopposed antidepressants can make bipolar depression worse by inducing mania and mixed bipolar states, mood instability, and rapid cycling.

Following key points on ECT

Updated APA depression management guidelines include the following key points on ECT:^{APA1}

- **Effectiveness.** ECT has the highest rates of response and remission of any depression treatment; 70–90% of patients treated with ECT show improvement.
- **Indications.** As noted above, ECT may be considered for patients whose symptoms have not responded to medication. It is also a potential option for patients who have psychotic or catatonic symptoms, who need a quick treatment response because they are suicidal or nutritionally compromised, who have medical conditions that preclude the use of antidepressants, and who are pregnant.
- **Side effects.** The most common side effect is anterograde amnesia, which typically resolves soon after the last ECT treatment, and retrograde amnesia, which improves over time and usually resolves within six months. Potential cardiovascular side effects can be managed by medication and/or modification in ECT administration.
- **Education.** If ECT is recommended, educating the patient and family can increase their confidence about this choice. See the sidebar for a helpful resource.

► SPECIAL POPULATIONS

Bipolar disorder (BD)

A small but important proportion of patients treated for depression in primary care will have bipolar depression rather than unipolar depression. This has important treatment and prognosis implications, and it is important to make the distinction clinically. The following is an overview of screening and treatment recommendations for BD. Refer to Intermountain's [Management of Bipolar Disorder CPM](#).

Prevalence

Whereas BD has a U.S. lifetime prevalence of 3.9%, those patients already diagnosed with depression have a higher risk.^{KES} In a prospective study looking at 550 patients diagnosed with depression when older than 17 years, more than 19% were diagnosed with BD—7.5% with bipolar type I (full mania and full depression) and 12.2% with bipolar type II (hypomania and full depression).^{FIE}

Screening

Most patients with BD present with depressive symptoms, not manic symptoms.^{KAT2} The strongest predictors of which depressed patients will eventually develop BD are:^{PER}

- Sudden onset of depressive symptoms or onset before 25 years of age
- Severe acute illness
- Psychotic features or mood lability
- Family history of BD
- Results from [Mood Disorder Questionnaire \(MDQ\)](#) or [CID-I](#)

Therefore, all patients who have these predictors should be screened for BD according to the guidance in the [Management of Bipolar Disorder CPM](#).

BARRIERS TO DIAGNOSIS OF DEPRESSION IN CANCER PATIENTS

Barriers to diagnosis may also include misconceptions such as:^{SNY}

- All cancer patients are depressed.
- Patients are just experiencing normal sadness.
- Depression is a normal part of the disease process.
- This is too vulnerable a time for the patient to fully explore psychological symptoms.

SUICIDE RISK IN CHILDREN, TEENS, AND YOUNG ADULTS

In Utah, suicide is the leading cause of death in children ages 10 to 17.

Healthcare providers should carefully monitor children with mood disorders due to the severe suicide risk with this disease state. Keep in mind, however, that 19% of teens have occasional suicidal thoughts and most do not take their own lives.

RESOURCES FOR CHILDREN AND ADOLESCENTS

- **Intermountain's Child and Adolescent Mental Health Integration packets** include tools for initial and follow-up evaluation of depression and other mental health comorbidities. These tools can be found at intermountainphysician.org/clinicalprograms under the "Mental Health Integration" topic.
- **Let's Talk About...Suicide Prevention.** This handout is available to view and order from [PrintIt!](#) and can be found on intermountainphysician.org/clinical/topics. See [page 33](#) for information on finding resources.



Treatment

Studies have shown that the use of antidepressants can induce mania and rapid cycling (four or more mood episodes a year). The antidepressants that seem most likely to cause these problems are TCAs, venlafaxine, and duloxetine. Bupropion seems least likely.^{LEV, KOS} Refer to the [Management of Bipolar Disorder CPM](#) for thorough guidance on treatment strategies for adults, children, and adolescents.

Cancer patients

The estimated incidence of depression in cancer patients is four times that of the general population, with the highest percentage of depression occurring in advanced stages and when the patient experiences disability and unrelieved pain. For cancer patients, depression adversely impacts their quality of life, compliance with treatment, caregiver relationships, and mortality.^{SNY} In addition, untreated depression can lead to more intense pain and other symptoms, which complicates treatment.^{NOO}

Diagnosis and treatment

Diagnosis and treatment are critical as depression is negatively associated with cancer survival. Underdiagnosis of depression in cancer patients has been difficult due to symptoms closely mirroring physiologic cancer symptoms, which can make the use of DSM criteria alone less predictive.^{SNY} Additionally, there is concern about misdiagnosis and subsequent antidepressant treatment that puts patients at risk for unnecessary side effects and potential adverse drug interactions.

Children and adolescents

Prevalence and prognosis

It is estimated that 0.5–2%^{MUL} of children and 13.3%^{NIM} of adolescents have MDD. Depression in children and adolescents can result in severe adverse outcomes—including suicide, the third leading cause of death in people aged 10–24 years.^{PRA} In 2009, 18.8% of students in grades 9–12 reported seriously considering suicide, 8.9% reported a suicide attempt, and 2.5% had made a suicide attempt that resulted in an injury, poisoning, or overdose requiring medical attention.^{CDC2} Untreated or inadequately controlled depressive disorders are the leading cause of completed suicides in children and adolescents.

The clinical course of depression in children and adolescents is variable, ranging from 1–2 months in community samples to 7–9 months in referred children. Recurrence ranges from 20–60% within 1–2 years.^{LEW} Some children are chronically depressed, with symptoms extending several years. **In addition to MDD, watch for milder, chronic symptoms of depression, bipolar depression, or symptoms of trauma. Symptoms of trauma can also frequently mimic or exist along with depression symptoms. A specialist referral should be considered.**

Screening and diagnosis

A screen for depression symptoms should occur at every encounter and at least once yearly with PHQ-2, PHQ-9, and/or CSSRS. Major depression in children and adolescents can be quite different from major depression in adult patients (as noted below), creating challenges for diagnosis.

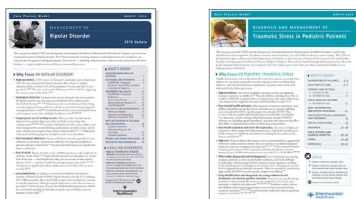
- Children and adolescents often present with irritable rather than depression mood.
- Children express more anxiety, irritability, temper tantrums, and behavioral difficulties.
- Children present more often with somatic complaints.
- Adolescents may present with school refusal, oppositional behavior, and substance use.
- Children may present with auditory hallucinations.
- Generally, children and adolescents express more apathy and less psychomotor retardation than adults.

DIAGNOSING BD AND TRAUMA IN CHILDREN AND ADOLESCENTS

Screening tools for diagnosing BD in this population are the MDQ-A (Mood Disorder Questionnaire – Adolescent), *Young Mania Rating Scale*, and FIND guidelines^{KOW} summarized below:

F	Frequency, symptoms occur most days of the week
I	Intensity, symptoms cause extreme disturbance in 1 domain or moderate disturbance in 2+ domains (school, home, etc.)
N	Number, symptoms occur 3–4 times a day
D	Duration, symptoms occur 4+ hours a day (cumulatively)

Refer to the *Management of Bipolar Disorder CPM* and the *Diagnosis and Management of Traumatic Stress in Pediatric Patients CPM* for detailed guidance.



ANTIDEPRESSANTS AND SUICIDE RISK

Starting in 2007, the Food and Drug Administration (FDA) required that all antidepressant medications carry an expanded black-box warning that identifies an increased risk of suicidal symptoms in young adults (18–24 years) during initial treatment. (The black-box warning on the increased risk of suicidal thinking, feeling, and behavior in children and adolescents has been required since October 2004.)

The FDA analyses that led to the warning showed an elevated risk of suicide and suicide ideation in patients age 18 to 24; however, the risk was not significantly elevated and was only elevated during the first few weeks of antidepressant therapy).^{FDA1} **Balancing the small increased risk of suicide in young adults against the clear risk of suicidality associated with depressive syndromes is critical to treatment.**

Screening and diagnosis (continued)

Depression symptoms in children and adolescents often overlap with problems such as ADHD, anxiety, and trauma symptoms. In fact, comorbidity is estimated to be about 66%.^{AND2, ANG}

Screening tools. The following are available through the Mental Health Integration program and are designed for use with children and adolescents (also, see diagnosing BD and trauma screening tools at left):

- **PHQ-A:** Designed for use with adolescents; the symptom-based questions are posed to fit their situation.
- **PHQ-C:** Designed to help parents report observed symptoms in non-verbal children.

Treatment

Most sources encourage a comprehensive treatment approach for children and adolescents, which should include the following:

- Cognitive-behavioral therapy or interpersonal therapy.
- Family relational support to promote adherence and ongoing self-management.
- Use of antidepressant medications if necessary. (PCPs should use caution in prescribing medications, following the guidelines on the next page.)

Consultation with a child psychiatrist may be indicated for clarification of the diagnosis and treatment plan. **At this time, there are no FDA-approved medications for treating children with depression under the age of 10. There are only two medications FDA approved for the treatment of depression in adolescents. Consensus guidelines recommend the use of any SSRI (other than paroxetine) as first line treatment. Refer to drugs@FDA.gov for the latest approved medications for ages 10 and older.**

Use of antidepressants

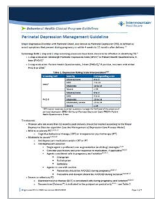
The American Academy of Child and Adolescent Psychiatry states that medication can be a helpful component of depression treatment for some children and adolescents when used within a comprehensive treatment plan that also includes psychoeducation, supportive management, and family and school involvement.^{BIR}

The data remain conflicting on the benefits versus risks of antidepressants for young people. It has been difficult to prove in trials that antidepressants other than fluoxetine are effective in children, partly because supportive therapy combined with placebo are also quite effective. As for risks in children, while some studies warn of a potential increase in self-harm or suicidal behaviors,^{FDA1-4, WAR} other studies show an inverse relationship between suicide and antidepressant use.^{OLF, PEL} While no evidence proves that antidepressants cause an increase in actual suicides, untreated or inadequately treated depressive illness causes the majority of completed suicide deaths among children and adolescents.

See [page 27](#) for general guidelines on prescribing antidepressants for children and adolescents.

PERINATAL DEPRESSION MANAGEMENT GUIDELINE

Refer to the [Perinatal Depression Management Guideline](#) for screening, treatment, and medication information.



Use of antidepressants (continued)

If antidepressants are prescribed, follow these general guidelines:

- Start at a low dose and gradually increase to an appropriate dose. Provide office check-in at 2 weeks to review treatment plan and assess for suicidal ideation. Maintain an adequate dose for 4 weeks before determining response, with assessments every 4 weeks. Increase the dose if you do not see adequate symptom improvement within these 4-week periods.
- After 8 weeks at an adequate dose, patients should experience some improvement. If symptoms don't improve, the patient needs a trial of a second antidepressant.
- If a patient does not experience complete remission of symptoms after 12 weeks at an adequate dose, consider medication adjustments according to treatment algorithm and evaluate the patient for factors that may be contributing to poor medication response.
- Overall side effects of antidepressant medications, including GI, increased irritability, etc., are more common the younger children are.
- If augmentation strategies are being considered, it would be reasonable to consult a child psychiatrist as no clear evidence exists.

Perinatal depression

Major depressive disorder with perinatal onset, also known as perinatal depression (PD), is defined as mood symptoms that present during pregnancy or within 4 weeks to 12 months after delivery. Refer to the [Perinatal Depression Management Guideline](#) for screening, treatment, and medication information.

Late-life depression

Depression is underrecognized and undertreated in the elderly, especially in men, African Americans, and Hispanics.^{UNU, HYB, FYF, CRY} Eighty percent of mental health treatment for older adults is delivered in the primary care setting.^{KAT3}

Risk factors

The risk factors for late-life depression include female sex, social isolation, widowed, divorced or separated, lower socioeconomic status, comorbid medical conditions, uncontrolled pain, insomnia, and functional or cognitive impairment.^{COL}

Screening and diagnosis

The PHQ-2 remains the screening instrument of choice.^{ARR} If positive, follow up with the PHQ-9.^{KRO} Evaluation of late-life depression should include an assessment of suicidality, psychotic symptoms, medication interactions, thyroid disease, diabetes, pain syndromes, cognitive functioning and family history.^{BEE, THI}

Treatment

First line treatment of depression consists of psychotherapy and somatic therapy. The choice of treatment will depend on the severity, type, and chronicity of depressive episode, contraindications to medication, treatment access, and patient preference. The overall effect size of either psychotherapy or medication was moderate to large, and roughly equivalent.^{PIN} Psychotherapy may be used singly or in combination. For moderate to severe forms of depression, pharmacotherapy is recommended. For chronic forms of depression, the combination of pharmacotherapy and psychotherapy are most effective.^{KEL1}

Electroconvulsive therapy can be particularly beneficial in the elderly.^{GED} Many elderly patients do not tolerate or respond to medications, cannot participate in psychotherapy or do not respond to it, or develop symptoms of depression that require immediate relief.^{KEL2} in the PRIDE Study, geriatric depression remitted in 62% of patients getting right unilateral ultra-brief pulse ECT in combination with venlafaxine.^{KEL3}

EATING DISORDERS

Refer to Intermountain's [Management of Eating Disorders CPM](#) for more detailed information about the diagnosis and treatment of eating disorders.



Eating disorders

Eating disorders may have a co-occurring diagnosis of depression but are often underdiagnosed. Primary care providers serve an important role in evaluating disordered eating and diagnosing eating disorders. Of adults with eating disorders, at least half were diagnosed by PCPs. If at any time during the diagnosis process you feel uncomfortable or unprepared to work with the patient, rely on other experts (e.g., MHI care manager, an on-site mental health provider, etc.) to support you.

Screening and diagnosis

The key principles of eating disorder diagnosis in primary care include:

- Patients with a suspected eating disorder may be more or less willing to reveal information based on your language and tone.
- Any time you feel uncomfortable working with the patient, bring in a mental health professional or another expert for support
- After diagnosis, a multidisciplinary team provides the best outcomes.
- If you rule out an eating disorder but still suspect the patient is at risk, provide patient/family education and follow up with the patient regularly.
- Consider referral to a registered dietitian for evaluation of dietary intake and recommendations for improvement.
- The diagnosis of eating disorders involves:
 - A comprehensive medical evaluation, including a medical history, review of systems, physical examination, and laboratory and diagnostic testing.
 - A patient and family conversation to assess whether an eating disorder is present.

These two steps can happen in any appropriate order. For example, if you notice a low heart rate and weight loss in a standard physical, you might begin a conversation about eating and dieting patterns with the patient.
- Patient and family conversation. The **Modified Eating Disorder Screen in Primary Care** (see [page 4](#) of the [Management of Eating Disorders CPM](#)) can help you determine whether an eating disorder is present, but it may not be enough. A conversation is helpful in determining diagnosis and/or the need for team-based treatment.

Treatment

Refer to Intermountain's [Management of Eating Disorders CPM](#) for treatment recommendations.

TABLE 9. Notes on antidepressants for children and adolescents

Class	Drug	Dosage		Notes
		Age 7–11 years	Age > 12 years	
Selective serotonin reuptake inhibitors (SSRIs)	fluoxetine (Prozac)	Start at 5 mg once daily Range: 5–20 mg once daily	Start at 5–10 mg once daily Range: 10–60 mg once daily	<p>General:</p> <ul style="list-style-type: none"> Obtain informed consent from a parent or legal guardian and explain the potential risks and benefits of antidepressants before starting pharmacotherapy. Monitor for side effects, increases in depression symptoms, and suicidality. Antidepressants not listed here have limited safety and efficacy data for the treatment of depression in pediatric populations and are not recommended first-line. <p>Typically, if treating anxiety or an anxiety-related disorder, start with a lower dose.</p> <p>SSRIs:</p> <ul style="list-style-type: none"> Fluoxetine is FDA-approved to treat pediatric depression (ages 8–17 years) and pediatric OCD (ages 7–17 years). Escitalopram is FDA-approved to treat depression in adolescents (ages 12–17 years). Sertraline is FDA-approved to treat pediatric OCD, but not depression (ages 6 years and up). <p>SSRIs in children may cause increased agitation, irritability, or decreased sleep; consider morning dosing, discontinuing SSRI or decreasing the dose.</p> <p>The half-lives of citalopram, escitalopram, and sertraline are shorter in children than in adults; monitor for withdrawal side effects when prescribing these once per day.</p> <p>Citalopram precautions and monitoring:</p> <ul style="list-style-type: none"> Avoid doses > 40 mg daily due to dose-dependent risk for QTc prolongation. ECG at baseline in patients with a history of CHF, bradyarrhythmias, or concurrent administration of other QTc prolonging medications. <p>Duloxetine</p> <ul style="list-style-type: none"> Duloxetine is FDA-approved to treat pediatric (ages 7–17 years) generalized anxiety disorder, but not depression. <p>Bupropion:</p> <ul style="list-style-type: none"> Bupropion is available as 12-hour sustained-release (SR), 24-hour extended-release (XR), or immediate-release (IR) tablets. The half-life of bupropion SR is shorter in children than in adults; monitor for withdrawal side effects when prescribing these once per day. Bupropion is contraindicated in patients with anorexia and bulimia due to an increased risk of seizure.
	escitalopram (Lexapro)	Start at 2.5–5 mg once daily Range: 5–20 mg once daily	Start at 5–10 mg once daily Range: 10–20 mg once daily	
	sertraline (Zoloft)	Start at 12.5–25 mg once daily Range: 12.5–200 mg once daily	Start at 25–50 mg once daily Range: 25–200 mg once daily	
	citalopram (Celexa)	Start at 5–10 mg once daily Range: 5–20 mg once daily	Start at 10 mg once daily Range: 10–40 mg once daily	
Serotonin-norepinephrine reuptake inhibitor (SNRI)	duloxetine (Cymbalta)	Start at 20 or 30 mg once daily Range: 20–120 mg	Start at 30 mg once daily Range: 30–120 mg	
Dopamine-norepinephrine reuptake inhibitor	bupropion (Wellbutrin)	<p>Immediate-Release (IR) Start at 37.5 mg twice daily Range: 37.5–150 mg twice daily</p> <p>Sustained-Release (SR) & Extended-Release (XR) There are no recommendations. May transition to SR/XR if stable on IR and dosage form of same total dose available.</p>	<p>Immediate-Release (IR) Start at 37.5 mg twice daily Range: 37.5–200 mg twice daily</p> <p>Sustained-Release (SR) 2 mg/kg up to 100 mg every morning (start with IR if lower dose needed) Range: 100–200 mg twice daily (0800 & 1700 hours)</p> <p>Extended-Release (XR) Start at 150 mg once daily Range: 150–400 mg/day</p>	

Note: Paroxetine (Paxil) is currently **not recommended** for use in children/adolescents.^{FDA3,WAR}

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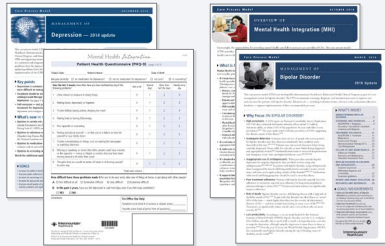
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PROVIDER TOOLS

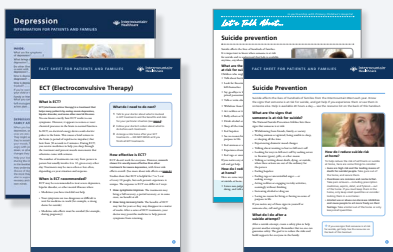
Tools available for providers (see the access information at right) include CPMs, and evaluation tools.



- **Depression:** This CPM, the [PHQ-9](#), [PHQ-A](#), and [PHQ-C](#)
- **Bipolar disorder:** [MDQ](#) (Mood Disorder Questionnaire) and the [CIDI](#) (Composite International Diagnostic Interview) for screening.
- **Suicide:** [Suicide Prevention CPM](#), C-SSRS assessment tools, and [safety plan](#)
- **Substance Use Disorder:** [CPM](#) and assessment tools
- **The MHI process:** [CPM](#), evaluation packets, and other tools
- **Comorbidities:** CPMs and evaluation tools for [eating disorders](#), [chronic pain](#), [diabetes](#), obesity, and other common comorbidities

PATIENT EDUCATION TOOLS

Patient education tools (see the access information at right) are available for the following areas:



- **Depression:** An 8-page [handout](#), plus fact sheets on [Suicide Prevention](#), [Mental Health and a Healthy Heart](#), and [ECT Therapy](#)
- **Bipolar disorder:** A 4-page [handout](#)
- **Comorbidities:** A range of booklets, trackers, handouts, and fact sheets focused on topics related to chronic pain, diabetes, obesity, etc.

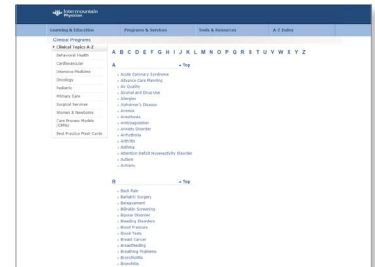
RESOURCES

See the information below on accessing resources for providers and patients such as those listed at left.

For providers:

Go to intermountainphysician.org/clinical/topics, and use the A to Z topic menu. For example, click “D,” and then click “**Depression**” to find a Depression topic page.

Each topic page links Clinical Guidelines and CPMs, Patient Education Tools, and Forms.



For patients:

Patient education materials are available at Intermountain’s [Print It!](#) online store.

Patients can be referred to intermountainhealthcare.org.

The Health Library on our public website allows patients to browse or search content from the following sources:

- **Intermountain handouts** as described on the left.
- **A symptom checker** to guide patients in evaluating symptoms and seeking care.
- **Media animations** on conditions and treatments.

Using the library, patients can choose from an alphabetical list of topics, such as “**Depression**” or “**Anxiety**,” or search by keywords.

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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to **Mark Foote, MD, Intermountain Healthcare, Behavioral Health Medical Director** (mark.foote@imail.org).