This care process model (CPM) was created by a subcommittee of the Intermountain Healthcare (Intermountain) Primary Care Clinical Program, Behavioral Health Clinical Program, and Mental Health Integration (MHI) team. The goal of the CPM and supporting materials is to help providers deliver the best clinical care in a consistent and integrated way. The recommendations in this CPM build on guidelines from the Agency for Health Care Policy and Research (AHCPR),\(^1\) updated guidelines from the American Psychiatric Association,\(^2\) experience from implementation of this CPM, and recommendations from other published studies.

### Key points

- Depression is common and costly and makes other chronic conditions more difficult to manage. See pages 3 to 4 for more information.
- Treatment should be stratified based on symptom severity, and antidepressant therapy is a first-line treatment for moderate to severe depression. See pages 9 to 14.
- Full remission — not just partial resolution of symptoms — is the goal of treatment for depression. See pages 19 to 20 for information on the stages of depression and strategies to help achieve full remission.

### What’s new in this update?

- **Updates in suicide risk assessment.** The process recommended by the new *Suicide Prevention Care Process Model* uses the Columbia-Suicide Severity Rating Scale (C-SSRS) and a safety plan for patients at risk. See page 6.
- **Updates in substance use disorder screening.** The new *Substance Use Disorder Care Process Model* recommends use of the modified quick screen from the National Institute on Drug Abuse (NIDA). See page 8 for a summary.
- **Updates to medication information, including cost profiles,** based on new evidence and on cost information from SelectHealth. See pages 12 to 14.
- **Updates to screening and treatment in children.** See pages 22 to 23.

Watch for additional updates to this CPM in 2015.

### GOALS

- Increase the ability to identify and treat depression in the primary care setting.
- Improve patient adherence to treatment.
- Increase the percentage of patients who get well and stay well.
- 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.
WHY FOCUS ON DEPRESSION?

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

Problems

• **Prevalence.** In 2010, the U.S. Centers for Disease Control\(^3\) (CDC) reported a 12-month prevalence of depression at 9% based on an analysis of the Behavioral Risk Factor Surveillance System (BRFSS) survey data from 2006 and 2008. A 2012 CDC Morbidity and Mortality Weekly Report\(^4\) reveals that 8% of Americans over 12 years old (6% of males and 10% of females) report current depression. While this represents a small decrease, the prevalence continues to be significant.

• **Difficulties with diagnosis.** When they visit their primary care provider, 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 5–8).

• **Poor adherence to treatment.** A sampling of large studies over the past 10 years reveals that in primary care, treatment nonadherence was an average of 46.2% over a 6-month period.\(^5\) One large study (211,000 patients) showed that in patients who did not have previous antidepressant exposure, treatment nonadherence was 38% during the first 30 days.\(^6\) In the acute phase, barriers to treatment adherence are often caused by the condition itself such as poor motivation, pessimism about the chances of recovery, deficits in memory, or poor self-care. During the maintenance phase, a patient with improved mood may focus on the burdens of treatment rather than its value. In addition, some patients may face medication side effects and/or struggle with the economic burdens associated with continuing treatment.\(^2\)

• **Medical comorbidities.** Depression is more prevalent for persons with chronic medical conditions that include diabetes, heart disease, stroke, COPD, and cancer. Depression can exacerbate these conditions. For example, depression is associated with worse glycemic control in patients with diabetes, reduced survival for cancer patients, and higher mortality for patients after a heart attack.\(^7\)

Impacts

• **Economic burden.** The direct medical costs of depression have been estimated at over $26 billion annually.\(^3\) Patients with depression have been reported to take an average of 33.7 disability days every year\(^9\) in the U.S. and other higher-income countries. The estimated productivity loss due to depression in the U.S. has been estimated at $51.5 billion annually.\(^8\)

• **Human suffering.** Depression often interferes with normal functioning. According to the most recent WHO Global Burden of Disease report, unipolar major depression is the leading cause of disability-adjusted life years (DALY) in middle-income and high-income countries.\(^10\) 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. In office encounters, patients present with psychosocial problems and nonspecific physical complaints that require extra time to address.
Opportunities

- The primary care setting is preferred by patients. Roughly 74% of patients are treated for their depression in the primary care setting. In fact, primary care offices are often the first and only places where patients are screened or treated for mood disorders. Given this, it’s appropriate to focus on diagnosis and treatment in the patient’s preferred (primary care) 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. In one study that compared this approach to usual care, patients treated after the implementation of a quality protocol had improved mental health outcomes, better employment retention, and improved quality of life. Collaborative care models have been shown to result in 70% to 75% of patients showing a significant improvement in depression scores at a 4-month follow-up. Implementing this CPM in a MHI setting has significantly improved depression care at Intermountain (see the box below).

SUCCESES IN DEPRESSION TREATMENT

Mental Health Integration (MHI), Intermountain’s approach to collaborative care between primary care providers and mental health specialists (see page 10 for details), has proven to be successful in improving care for patients with depression. Implementing MHI at Intermountain has driven significant improvements in the following areas:

- Building an effective process for collaborative, team-based treatment. MHI has grown at Intermountain from one primary care clinic in 1998 to over 85 primary care clinics in 2014. Patients treated in MHI clinics report higher satisfaction in a range of measures, including the physician’s sensitivity, the physician’s communication, and overall quality of care. Physicians and staff at MHI clinics report improvements in their ability and confidence to detect mental health needs, work with patients with mental health problems (including difficult patients), and integrate the mental health team in the primary care setting.

- Tracking patients with depression across the Intermountain system. Depression-related data are incorporated into Intermountain’s electronic medical record and integrated in Intermountain’s enterprise data warehouse (EDW). Data in the EDW has been used to create a depression registry with over 154,000 active patients in 2013. Over 434,000 patients have been added to the depression registry between 1999 to 2013. The depression registry fosters research that can be used to improve care across the system.

- Using evidence-based tools for screening and diagnosis of depression. MHI packets have fostered increasing use of the PHQ-9 to screen patients for depression. A review of the depression registry showed that for over 37,000 unique patients, a PHQ-9 score was added to the patient record in 2013.

- Improving outcomes for patients with depression, at lower cost. For example, in the year following initial diagnosis of depression, patients with depression treated in MHI clinics have been shown to be 54% less likely to have ED visits than patients with depression treated in non-MHI clinics. In the year after a patient is diagnosed with depression, the growth in medical expenses was $670 less in patients treated in MHI clinics, compared with patients treated in non-MHI clinics, which is approximately 10% reduction in increased medical costs.
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, but the disorder may begin at any age. When age of initial onset is 25 or younger, the likelihood of developing bipolar depression increases. When an initial onset of depression occurs late in life, it’s correlated more with a degenerative disease than with a family history of mood disorders.

• 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 is often accompanied by comorbid conditions, such as heart failure, diabetes, asthma, chronic pain, other mental illness, and substance abuse — as well as character disorders. These conditions add to its disability and worsen its prognosis.

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).

• **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.
EVALUATION AND DIAGNOSIS

At any given time, 5% to 10% of patients will meet the diagnostic standard for a current episode of depression. However, without formal screening, depression will be detected in few of these patients. Therefore, this CPM recommends that every new patient be screened for depression and that certain patients be screened at regular intervals. In primary care, a patient’s risk of having a mood disorder is directly related to the number of somatic symptoms he or she presents with. The symptoms and conditions listed below are associated with a very high co-incidence of depression. Patients with any of these should be screened at routine intervals.

• Multiple unresolved somatic complaints (e.g., more than 3 unexplained symptoms)
• High healthcare utilization (e.g., thick chart or more than 6 visits/year)
• Chronic diseases (e.g., diabetes, heart failure, chronic pain)

ALGORITHM 1: SCREENING AND DIAGNOSIS

New patient appointment

Administer the Patient Health Questionnaire (PHQ-9), and review the 9 symptoms with the patient. (a)

Suicide risk (question 9) positive? → yes
Assess suicide risk, and take emergency action as necessary (see page 6).

Suicide risk (question 9) negative? → no

Administer and score Mood Disorder Questionnaire (MDQ) if predictive factors for bipolar disorder are present. (b)

MDQ positive? → yes
Assess and treat bipolar disorder (see page 21).

MDQ negative? → no

Review precipitating medical conditions. (c)
Review precipitating medications and abused substances. (d)
Screen for medical and psychological comorbidities. (e)

Suspect comorbidities? → yes
Do further medical and mental health evaluation.

Suspect comorbidities? → no
Diagnose and assess severity (see page 7).

Go to TREATMENT ALGORITHM (page 9)

ALGORITHM NOTES

(a) Patient Health Questionnaire (PHQ-9): The PHQ-9 is a free, patient-rated instrument that asks about the 9 symptoms of depression (see page 7). 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 21). Predictive factors for BD include sudden or severe depression onset, psychotic features, mood lability, onset younger than 25, and BD family history.

(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.

(d) Precipitating medications and abused substances: Use and/or abuse of some medications and other substances can also precipitate depressive symptoms (examples below). The modified CAGE or similar can be used to screen for substance abuse (see sidebar page 8).

(e) Comorbidities:

• Medical illnesses: Depression often occurs with heart disease, stroke, cancer, or diabetes, and can impair treatment.

• Other mental health disorders: MHI resources aid in screening (see page 10).

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**SUICIDE PREVENTION CARE PROCESS MODEL**

Intermountain’s Suicide Prevention Care Process Model, new in 2014, 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; 3–6 questions depending on patient responses. (Adult/Adolescent and Pediatric versions)
- **Lifetime/Recent Assessment**: Used for full assessment during the initial visit; 2-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**: 1-page list of suicide risks and protective factors

**RESOURCES FOR PATIENTS**

- **Suicide Prevention Safety Plan**: Collaborative safety planning is an important part of addressing suicide risk. Intermountain’s Safety Plan is a tool patients can use when suicidal thoughts arise.
- **Patient Education**: Krames Staywell provides several HealthSheets on suicide warning signs and how to respond. Clinicians can find and print patient education from the Krames patient education library at intermountain.net/pen.

**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 Care Process Model 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 local 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.

**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 9 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 22 for more information on diagnosing depression in children and adolescents.

The PHQ-9 provides a symptoms 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 based on PHQ-9 results.

FIGURE 1. Scoring and interpreting the PHQ-9

| 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). |

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.21
SCREENING FOR SUBSTANCE USE DISORDERS

When evaluating and diagnosing depression, it’s 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 Substance Use Disorder Care Process Model, new in 2014, provides practical strategies for effective SUD diagnosis and treatment.

The CPM recommends the SBIRT model: Screening, Brief Intervention, and Referral to Treatment. SBIRT is a comprehensive, practical, and integrated approach to SUD screening and treatment.

Screening for SUD

The Substance Use Disorder CPM recommends the following process:

- Start with the Intermountain-modified NIDA (National Institute on Drug Abuse) Quick Screen. This screen has 5 questions about use of the following in the past year: alcohol (≥5 standard drinks/day for men or ≥4 standard drinks/day for women), tobacco products, prescription meds for non-medical reasons, prescription meds outside prescribing instructions, or illegal drugs.

- If the NIDA screen is positive, administer Intermountain’s ASSIST-based assessment. The ASSIST is an interviewer-administered, 8-question assessment developed by the World Health Organization that assesses for all levels of problem or risky substance abuse. Screening takes 10 minutes for most patients.

See the Substance Use Disorder CPM, pages 16–17, for details on using these tools.

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. 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 as of 2015.

### Table 2. Possible diagnosis and treatment based on PHQ-9

<table>
<thead>
<tr>
<th>PHQ-9 Results</th>
<th>Possible Diagnosis</th>
<th>Treatment Approach (see Treatment section)</th>
</tr>
</thead>
</table>
| <5 symptoms of depression | Other — not depression | • Provide reassurance and/or supportive counseling  
| Questions A and B negative | | • Reassess if no improvement or condition worsens |
| | Atypical depression (depression not otherwise specified or minor depression) | • Watchful waiting; supportive counseling  
| Question 1 or 2 positive | | • If no improvement after 4+ weeks, use antidepressant or brief psychotherapy |
| Question A positive | | |
| 2 to 4 symptoms | Persistent depressive disorder (dysthymia) | • Antidepressant and/or psychotherapy |
| Question 2 positive | | |
| Question B positive | | |
| ≥5 symptoms | 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. |
| Question 1 or 2 positive | | |
| Question A positive | | |

#### Severity Treatment

<table>
<thead>
<tr>
<th>Severity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity score 10 to 14 — Mild</td>
<td>Antidepressant OR psychotherapy (patient preference)</td>
</tr>
</tbody>
</table>
| Severity score 15 to 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 |
**TREATMENT OVERVIEW**

The following algorithm presents a treatment approach 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 2: TREATMENT OVERVIEW (a)**

![Algorithm Diagram]

- **Diagnosis of major depressive disorder (MDD)**
  - Mental health emergency?
    - Yes ➔ Immediate consultation with psychiatrist (b)
    - No ➔ Arrange safe transport to emergency room if needed

- **Stratify treatment. (c)**
  - **MILD**
    - PHQ-9 severity score 10–14
    - Antidepressant (d) OR psychotherapy (e)
    - Patient education (f)
  - **MODERATE**
    - PHQ-9 severity score 15–19
    - Antidepressant (d) AND/OR psychotherapy (e)
    - Patient education (f)
    - Consider/offer care management or other Mental Health Integration (MHI) resources (g)
  - **SEvere**
    - PHQ-9 severity score ≥20
    - Antidepressant alone (d) OR antidepressant combined with psychotherapy (e)
    - Patient education (f)
    - Consider/offer care management or other MHI resources (g)

- **Treatment(s) selected?**
  - Antidepressant with or without psychotherapy ➔ Go to MEDICATION ALGORITHM (page 13)

- **GOOD RESPONSE (h1) or PARTIAL RESPONSE (h2)**
  - Continue therapy and follow up at 12 weeks with PHQ-9.
  - 12-week follow-up. Repeat PHQ-9.

- **NO RESPONSE (h3)**
  - Consider adding or changing to antidepressant therapy. (Go to MEDICATION ALGORITHM on page 13)

**ALGORITHM NOTES**

(a) Treatment goal is **full remission**! A PHQ-9 severity score of 5 or less can be used as the full-remission goal.

(b) Psychiatrist consultation: Consult with a psychiatrist for any patient with suicidal thoughts, especially if the patient has a plan, intent, or high anxiety. See page 10 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 10 for more information on psychotherapy.

(f) **Patient education**
  - Give Depression patient education handout describing the disease and treatment options (see page 11).
  - 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 pages 10 and 11).

(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
MENTAL HEALTH INTEGRATION

Mental health integration (MHI) is mental healthcare that is integrated into everyday primary care practice. It’s a team-based approach that promotes consultative and collaborative relationships between PCPs, care managers, and mental health specialists for appropriate patients. The collaborative MHI approach reduces the burden on PCPs, improves clinical decisions, and allows patients and their families to receive an array of needed services within the primary care setting.

MHI is a flexible approach that is subject to the discretion of the PCP. A PCP may choose to work with specialists and care managers in any phase of patient care, from diagnosis, treatment, and maintenance. Common scenarios for initiating the team-based approach include the following:

- High suicide risk or other mental health emergency (immediate access to a consulting psychiatrist is recommended for every PCP in this case)
- Comorbidities or severe psychological/physical problems
- Difficult family/relational complications
- Likelihood/evidence of poor adherence to treatment
- Nonresponse to standard treatment
- Difficult mental health conditions beyond the PCP’s level of comfort

PCPs may choose to work with team members in various ways according to the needs, circumstances, and preferences of the patient.

For example, a PCP may request ongoing education and supervision from the other team members, consult with them about a particular case, or establish a collaborative network of care for a patient and family.

Consult the Mental Health Integration (MHI) Care Process Model 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 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 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. It treats depression by helping patients identify, address, and solve life problems that contribute to their depression. It can also help patients identify and improve negative or distorted thinking patterns and explore other learned thoughts and behaviors that create problems and contribute to depression.

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

- With mild to moderate, non-recurrent 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

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. Patients who receive this type of care have much better results than those who don’t.

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
Patient education

Patient education is critical to successful treatment. 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 right.)
  - Adverse effects, if they occur, usually diminish within 1 to 4 weeks.
  - Antidepressant therapy may need to be changed, 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
- 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. Updated APA guidelines and expert consensus indicate several important ways to foster treatment adherence:

- Provide key patient education messages (see above and the sidebar at right).
- Discuss medication costs and copays openly, and factor these considerations into prescription choices. (Note: The medication tables on pages 14 to 17 now include cost information.)
- Encourage patients to express any fears or concerns they have about treatment, and correct any misconceptions that arise.
- Mobilize care management (see page 10) and family support.
- Talk with patients about medication reminder systems such as pill boxes or alarms.

Access this patient education handout and other patient education materials at:

- www.iprintstore.org (search for "depression," or use the Behavioral Health category in the menu)
- intermountainphysician.org/clinical/topics (browse to "D" in the A to Z menu, and select Depression)
DO ANTIDEPRESSANTS WORK?
A 2010 JAMA study\(^3\) suggested that, for people with mild or moderate major depression, the effects of antidepressants may be "minimal or non-existent."
However, it’s important to note the limitations of the JAMA article conclusions:

- The meta-analysis covered only 6 studies of just 2 medications (amitriptyline and paroxetine) that make up a limited portion of current prescribing.
- The studies were conducted over a brief period (6 to 8 weeks) in patients with limited comorbidities and had design features that make it difficult to extrapolate results to real-world settings.

More applicable to real-world conditions are clinical effectiveness trials such as the STAR*D study, which examined the effectiveness of medication and psychotherapy for 3,671 patients with mild to moderate depression in primary care and mental health outpatient settings for a full year. The results of STAR*D and many similar studies continue to support the use of antidepressants as first-line treatment for depression of any severity. While medications have costs and side effects that should be weighed against benefits, antidepressants should always be considered, given that untreated depression is a disabling and chronic illness.

TREATMENT-RESISTANT DEPRESSION (TRD)
While experts do not agree on a precise definition of TRD,\(^3\) this CPM recommends the following definition:

Moderate to severe depression (with diagnosis confirmed) that has not responded to 2 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 3 (on page 13) 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 depression of any severity, 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 14) 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 previous response, family history of response, safety and side effects, ease of use, and cost.

- **Monitor and manage side effects.** Monitor patients closely on a regular basis 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 at right and Table 3 (page 14) for guidance on dosing and trial duration.

- **In each trial, 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 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 or more failed antidepressant trials (each trial 8 to 12 weeks at an adequate dose), add a second medication\(^25-30\) and refer the patient to concurrent psychotherapy.\(^2\)

Key details about augmentation appear below.

- **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 higher likelihood of poor adherence. However, as demonstrated in the STAR*D effectiveness trial,\(^29\) remission rates drop sharply after two failed trials. This leaves a treatment population less responsive to medications and more likely to relapse.

- **Also consider augmentation** when raising the dose of a partially effective medication is not tolerated or desired or after initial remission with relapse.\(^26,27\)

- **Focus on the medication choices** for augmentation best supported by research\(^28-30\) and presented in more detail in Table 4 (page 15):
  1. Adding a second first-line antidepressant of a different class
  2. Adding a tricyclic antidepressant, lithium, other mood stabilizer, or thyroid hormone

- **Continue augmentation as long as it is effective.** Research on augmentation with lithium\(^31\) or atypical antipsychotics\(^32\) 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.
ALGORITHM NOTES

(a) General principles:
- Select from 1st-line medications (see Table 3). Choose generics first, when available. 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 to 12 months of remission achieved

(c) 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, 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 bipolar disorder (see page 21 and 22), active substance abuse, comorbid medical conditions like thyroid disease, and other precipitating factors.

(e) MHI resources: Care management, psychotherapy, psychiatric consult, etc. See page 10.

(f) Augmentation: After 2 failed antidepressant trials, consider one of these strategies:
- Add a second, first-line antidepressant of a different class
- Add a tricyclic antidepressant
- Add lithium, other mood stabilizer, or thyroid hormone
  See pages 15 and 16 for more details.

(g) Concurrent psychotherapy: Since remission rates drop precipitously after the first 2 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.
## Medication tables

**TABLE 3. First-line antidepressants for adults**

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dose ranges &amp; guidelines**</th>
<th>Notes (See Table 6 for further details on side effects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin-norepinephrine reuptake inhibitors (SSRIs)</td>
<td>citalopram (Celexa)</td>
<td>20 mg once daily</td>
<td>• Common side effects: sexual dysfunction, anxiety, insomnia or sedation, headache, nausea, and diarrhea</td>
</tr>
<tr>
<td></td>
<td>escitalopram (Lexapro)</td>
<td>10 mg once daily</td>
<td>• Citalopram precautions and monitoring:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Avoid doses greater than 40 mg daily due to dose-dependent increased risk for QTc prolongation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- ECG at baseline in patients with history of CHF, bradyarrhythmias, or concurrent administration of other QTc-prolonging medications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Check potassium and magnesium levels at baseline for patients at risk of electrolyte abnormalities</td>
</tr>
<tr>
<td></td>
<td>fluoxetine (Prozac)</td>
<td>20 mg once daily</td>
<td>• To avoid transient discontinuation symptoms, taper in patients taking fluoxetine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20–60 mg once daily</td>
<td>• May be discontinued abruptly if needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80 mg once daily</td>
<td>• May be decreased to 5 mg/day if patients are intolerant to higher doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weekly capsule: 90 mg once weekly</td>
<td>• Bupropion IR is not recommended due to seizure risk and poor tolerability.</td>
</tr>
<tr>
<td></td>
<td>paroxetine (Paxil, Paxil CR)</td>
<td>20 mg once daily</td>
<td>• Bupropion is contraindicated in patients with a history of seizure disorder or eating disorder (IR is highest risk).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 mg once daily (CR)</td>
<td>• 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)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20–50 mg once daily (IR)</td>
<td>• Common side effects: insomnia, headache, dizziness, nausea, and diarrhea; may also cause delirium or restlessness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25–62.5 mg once daily (CR)</td>
<td>• May improve sexual desire, arousability and orgasmic ease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg once daily (IR)</td>
<td>• No weight gain and may help with weight loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR 25–62.5 mg once daily (CR)</td>
<td>• Useful as a smoking cessation agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>225 mg once daily</td>
<td>• Avoid taking after dinner or at bedtime</td>
</tr>
<tr>
<td></td>
<td>venlafaxine XR (Effexor XR)</td>
<td>37.5–75 mg once daily</td>
<td>• Increased risk of liver damage for patients with substantial alcohol use or preexisting liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75–225 mg once daily</td>
<td>• Monitor blood pressure during dose titration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>225 mg once daily</td>
<td>• Duloxetine: hepatic function test at baseline</td>
</tr>
<tr>
<td></td>
<td>desvenlafaxine (Pristiq) (Generic NOT available)</td>
<td>50 mg once daily</td>
<td>• Taper to reduce risk of discontinuation syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50–100 mg once daily</td>
<td>• Levomilnacipran (Fetzima) is not used first-line</td>
</tr>
<tr>
<td></td>
<td>duloxetine (Cymbalta)</td>
<td>30–60 mg once daily</td>
<td>• Common side effects are similar to SSRIs: nausea, sexual dysfunction, activation, and dose-related increases in blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30–60 mg once daily</td>
<td>• Increased risk of liver damage for patients with substantial alcohol use or preexisting liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120 mg once daily</td>
<td>• Common side effects: diarrhea, nausea/vomiting, dizziness, weight gain</td>
</tr>
<tr>
<td></td>
<td>levomilnacipran (Fetzima)</td>
<td>20 mg once daily</td>
<td>• May improve sexual desire, arousability and orgasmic ease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>daily for 2 days</td>
<td>• No weight gain and may help with weight loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40–120 mg once daily (may increase by 40 mg every 2 days)</td>
<td>• Useful as a smoking cessation agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120 mg once daily</td>
<td>• Avoid taking after dinner or at bedtime</td>
</tr>
<tr>
<td>Serotonin-norepinephrine reuptake inhibitors</td>
<td>bupropion HCl (Wellbutrin SR or XL)</td>
<td>150 mg every morning (SR/XL)</td>
<td>• Bupropion IR is not recommended due to seizure risk and poor tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 mg twice daily (SR)</td>
<td>• Bupropion is contraindicated in patients with a history of seizure disorder or eating disorder (IR is highest risk).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR 300 mg once daily (XL)</td>
<td>• 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)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR 450 mg divided twice daily (SR)</td>
<td>• Common side effects: insomnia, headache, dizziness, nausea, and diarrhea; may also cause delirium or restlessness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR 450 mg once daily (XL)</td>
<td>• May improve sexual desire, arousability and orgasmic ease</td>
</tr>
<tr>
<td></td>
<td>mirtazapine (Remeron)³⁵</td>
<td>15 mg once daily, at bedtime</td>
<td>• No weight gain and may help with weight loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15–45 mg once daily, at bedtime (titrate to effect and tolerability)</td>
<td>• Useful as a smoking cessation agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45 mg once daily, at bedtime</td>
<td>• Avoid taking after dinner or at bedtime</td>
</tr>
<tr>
<td></td>
<td>vilazodone (Viibryd) (Generic NOT available)</td>
<td>10 mg once daily</td>
<td>• Mechanisms of action: SSRI, SHT₃ receptor antagonist, SHT₄ agonist</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 mg once daily</td>
<td>• Generally not used first-line</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 mg once daily</td>
<td>• May be decreased to 5 mg/day if patients are intolerant to higher doses</td>
</tr>
<tr>
<td></td>
<td>vortioxetine (Brintellix) (Generic NOT available)</td>
<td>10 mg once daily</td>
<td>• May be discontinued abruptly if needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–20 mg once daily</td>
<td>• To avoid transient discontinuation symptoms, taper in patients taking 15–20 mg/day; decrease dose to 10 mg/day for one week then discontinue</td>
</tr>
</tbody>
</table>

**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 B.
### TABLE 4. Other antidepressants and augmentation agents

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dose ranges &amp; guidelines*</th>
<th>Notes (See Table 6 for further details on side effects)</th>
</tr>
</thead>
</table>
| Tricyclic antidepressants (TCAs) | amitriptyline (Elavil) | Start: 75 mg per day, Maintenance: 50–100 mg per day, Max: 150 mg per day | • Tricyclics in combination with serotonergic medications can increase blood levels; adjust dosing based on the tricyclic blood level  
• May be given once daily at bedtime, if tolerated, or divided in 2–3 doses  
• 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: 
  – ECG at baseline 
  – Pregnancy test as clinically indicated 
  – Serum levels (trough) as clinically indicated |
|                              | nortriptyline (Pamelor) | Start: 25–50 mg per day, Maintenance: 75–100 mg per day, Max: 150 mg per day | |
|                              | desipramine (Norpramin) | Start: 25–50 mg per day, Maintenance: 100–200 mg per day, Max: 300 mg per day | |
|                              | imipramine (Tofranil) | Start: 75 mg per day, Maintenance: 50–150 mg per day, Max: 200 mg per day for outpatients | |
| Lithium preparations          | lithium carbonate (Eskalith, Eskalith CR, Lithobid) | • Range: 150 to 1,500 mg per day — immediate release generally divided 2 to 3 times daily; extended release may be given once daily as tolerated  
• Target: Serum level 0.4–0.8 mEq/L | • 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  
• Monitoring (as clinically indicated) AND: 
  – Electrolytes, UA, and pregnancy tests at baseline 
  – EKG and CBC at baseline and yearly 
  – Renal and thyroid function at baseline and every 6 months 
  – Serum lithium level 10 to 12 hours after last dose, 4 to 5 days after initiation or dose change, then every 3 months |
| Anticonvulsant                 | lamotrigine (Lamictal) | • Initiate at 25 mg once daily  
• Titrate per set schedule of:  
  – 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 | • Not FDA approved for the treatment of depression  
• Do not titrate more rapidly than recommended dosing schedule due to increased risk of potentially fatal rash  
• 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  
• 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  
• 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%  
• Monitor suicidality, pregnancy, renal and hepatic function tests baseline and yearly |
| Thyroid supplement            | liothyronine sodium (Cytomel) | • Initiate at 25 mcg once daily  
• Titrate by 12.5 to 25 mcg every 1 to 2 weeks  
• Goal range: 25 to 50 mcg once daily | • Not FDA approved for the treatment of depression  
• Risks are primary hyperthyroidism and its sequelae  
• Most effective in females with low-normal thyroid functioning  
• Monitor TSH and free T3 at baseline and at 3 months |

*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 8.*
### TABLE 4. Other antidepressants and augmentation agents (continued)

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dose range and guidelines*</th>
<th>Side effects and other comments</th>
<th>Monitoring for ALL atypical antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second-generation antipsychotics†</td>
<td>aripiprazole46, 41</td>
<td>• <em>Initiate</em> at 2–5 mg once daily</td>
<td><em>FDA approved as an adjunct for treatment of depression</em></td>
<td>• Pregnancy test</td>
</tr>
<tr>
<td></td>
<td>(Abilify) (Generic NOT available)</td>
<td>• <em>Titrate</em> by up to 5 mg every week</td>
<td><em>Common side effects: restlessness, stimulation, and nausea</em></td>
<td>• Initial BMI measurement, then every visit for 6 months and quarterly once dose is stable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <em>Goal range:</em> 2–15 mg once daily</td>
<td><em>Minimal risk of extrapyramidal side effects (EPS) other than akathisia</em></td>
<td>• Baseline hemoglobin A1c or fasting plasma glucose before initiating, then every year</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Minimal sedation</em></td>
<td>• Blood pressure at each visit</td>
</tr>
<tr>
<td></td>
<td>olanzapine42</td>
<td>• <em>Initiate</em> at 5 mg once daily, at bedtime</td>
<td><em>FDA approved for the treatment of treatment-resistant depression as a combination product</em></td>
<td>• Ocular evaluations every 2 years (yearly for ages 40+)</td>
</tr>
<tr>
<td></td>
<td>(Zyprexa)</td>
<td>• <em>Titrate</em> by up to 5 mg every 4 to 7 days</td>
<td><em>Significant sedation and weight gain, moderate EPS risk</em></td>
<td>• Baseline fasting lipid panel, then every 2 years (if normal) or every 6 months (if LDL &gt; 130 mg/dL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <em>Goal range:</em> 5–12.5 mg once daily, at bedtime</td>
<td><em>Potential for dyslipidemia and hyperinsulinemia</em></td>
<td>• Baseline extrapyramidal side effects (EPS) evaluation, then weekly until dose is stable; after any dose change, evaluate for EPS weekly for 2 weeks, then at each outpatient visit</td>
</tr>
<tr>
<td></td>
<td>olanzapine/fluoxetine (Symbyax)</td>
<td></td>
<td><em>May increase risk of type 2 diabetes</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>quetiapine43–45</td>
<td>• <em>Initiate</em> at 50 mg once daily, at bedtime</td>
<td><em>Only XR is FDA approved as an adjunct treatment for depression</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Seroquel, Seroquel XR)</td>
<td>• <em>Titrate</em> by 50 mg daily as tolerated</td>
<td><em>IR may be given once nightly if tolerated or divided over the day</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <em>Goal range:</em> 150–300 mg once daily, at bedtime</td>
<td><em>Significant sedation and moderate weight gain</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>risperidone46</td>
<td>• <em>Initiate</em> at 0.5 mg once daily, at bedtime</td>
<td><em>Lowest EPS risk of the atypical antipsychotics</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Risperdal)</td>
<td>• <em>Titrate</em> by 0.5 mg daily as tolerated</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <em>Goal range:</em> 1–3 mg once daily, at bedtime</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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.2

† Atypical antipsychotics: Antipsychotic medication should always be used in the treatment of major depression with psychosis.2
### TABLE 5. Medication choices for special circumstances

<table>
<thead>
<tr>
<th>Circumstance</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Anxiety or agitation                              | - Antidepressants will often improve anxiety in 1 to 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 to 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 to 2 weeks, monitoring for symptoms of benzodiazepine withdrawal. |
| Akathisia (atypical; antipsychotic-induced)       | - 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. Incrementally titrate up to 6 to 10 mg daily as needed to manage akathisia symptoms.  
- If benzodiazepines are ineffective, consider propranolol 10 mg twice daily, titrating up to 20 mg twice daily and finally to propranolol LA 60 to 120 mg daily. |
| Chronic pain                                      | - 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                                   | - 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                                       | - The following choices are energizing for some patients: bupropion, citalopram, sertraline, aripiprazole, fluoxetine, venlafaxine, duloxetine. |
| Insomnia                                          | - 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                       | - Use of antidepressants in pregnancy remains controversial, despite significant 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.  
- 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                | - Anticholinergic agents may be used for acute situations or as prophylactic/maintenance agents.  
- Elderly patients are prone to anticholinergic delirium. |
| Psychosis                                         | - Antipsychotic medication should always be used in the treatment of major depression with psychotic features. Consider consulting a psychiatrist. |
| Substance use disorder                            | - 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. (see page 8).  
- Give appropriate referral and treatment for substance abuse 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 antidepressant response even at low levels (one or two drinks a day). |
| Thyroid dysfunction                               | - Subclinical hypothyroidism — characterized by TSH 4 to 8 μIU/mL (micro International Units/milliliters) and normal Free T4 — correlates with poor antidepressant response; augmenting with liothyronine sodium has the best response with this population.  
- Clinical hypothyroidism or hyperthyroidism can be related to anxiety, depression, and treatment resistance. Optimize thyroid functioning while treating depression. |
| Weight gain >5 pounds or weight gain prevention   | - 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. 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. A meta-analysis of 6 trials showed an average 6-month weight loss of 6.5% with topiramate. Lorcaner, a selective serotonin receptor agonist, has recently been approved as long-term therapy for overweight/obese patients with at least one medical comorbidity. Long-term data are sparse, but current safety data suggest a beneficial effect on CV and diabetes risks. |
### TABLE 6. Potential side effects of antidepressants

<table>
<thead>
<tr>
<th>SSRIs</th>
<th>OTHER MEDICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal</strong>: 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.</td>
<td><strong>Bupropion (Wellbutrin)</strong>: 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 per 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.</td>
</tr>
<tr>
<td><strong>Activation/insomnia</strong>: SSRIs may precipitate or exacerbate restless, agitation, and sleep disturbances. These side effects often attenuate with time. Anxiety may be minimized by introducing the agent at a low dose.</td>
<td><strong>Duloxetine (Cymbalta)</strong>: 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.</td>
</tr>
<tr>
<td><strong>Sexual</strong>: 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.</td>
<td><strong>Mirtazapine (Remeron)</strong>: 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. 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.</td>
</tr>
<tr>
<td>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. SSRIs have also been associated with extrapyramidal reactions, including akathisia, dystonia, parkinsonism, and tardive dyskinesia. The occurrence of such extrapyramidal symptoms is generally very low but may be higher in older patients, especially those with Parkinson’s disease.</td>
<td><strong>Tricyclic antidepressants (TCAs)</strong>: Can cause weight gain that is often dose-dependent; weight gain is typically more significant with amitriptyline and less significant with desipramine.</td>
</tr>
<tr>
<td>Citalopram has been shown to cause dose-dependent QTc interval prolongation; the prescribing information has been modified to recommend against giving citalopram at doses above 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.</td>
<td><strong>Venlafaxine (Effexor)</strong>: 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.</td>
</tr>
<tr>
<td><strong>Weight changes</strong>: 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.</td>
<td><strong>Vilazodone (Viibryd)</strong>: 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.</td>
</tr>
<tr>
<td>Serotonin syndrome: SSRIs can cause nausea/vomiting, diaphoresis, tremor, myoclonus, rhabdomyolysis, renal failure, cardiovascular shock, and may result in death. 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.</td>
<td><strong>Levomilnacipran (Fetzima)</strong>: Side effects include nausea, vomiting, constipation, sexual dysfunction, increased heart rate, palpitations, and sweating.</td>
</tr>
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REMIS SION AND MAINTENANCE

Full remission — not just partial resolution of symptoms — is the goal of treatment for depression. Remission rates in primary care practices over a 2-year period are estimated at only 45%.64 Under-treatment of depression contributes to protracted suffering and impairments in work and interpersonal relationships and leaves patients with a heightened risk of suicide.65 Patients not in full remission (i.e., patients with residual symptoms) are also likely to have the following:

- 3 to 5 times higher relapse rate66-68
- 7 times higher likelihood of being less effective on the job69
- More severe and chronic courses of depression, with shorter well intervals and fewer symptom-free weeks70
- 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,25 which followed usual patients in both primary care and mental health clinic settings, provides a good estimate of how long is necessary to assess effectiveness. 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 5 or less 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 to 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 7 below.

TABLE 7. Phases of treatment for depression

<table>
<thead>
<tr>
<th>ACUTE</th>
<th>CONTINUATION</th>
<th>MAINTENANCE</th>
</tr>
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<tbody>
<tr>
<td>Usually 6 to 12 weeks&lt;br&gt;Effective treatment response is usually obtained during this phase, bringing the syndrome into initial remission.</td>
<td>Usually 9 to 12 months&lt;br&gt;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.</td>
<td>More than 9 months&lt;br&gt;- If this is the first depression episode, taper and discontinue medication. &lt;br&gt;- If this is a recurrent episode, consider long-term maintenance, generally with the same type and dosage effective in the previous acute stage. &lt;br&gt;- 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.</td>
</tr>
</tbody>
</table>

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.
Preparing to end treatment

Revised APA guidelines suggest two key steps when discontinuing treatment:

• **Schedule a follow-up.** The highest risk for relapse is in the first 2 months after treatment is discontinued; a follow-up visit within this period can be helpful in identifying relapse signs.

• **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 withdrawal 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. Though withdrawal symptoms are usually mild, they can be quite pronounced in a minority of patients. Antidepressant withdrawal symptoms may include acute onset of any of the following:

• Fatigue
• Myalgias
• Vertigo, dizziness, and/or lightheadedness
• Nausea
• Numbness/tingling
• Anxiety and/or agitation

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)**

Electroconvulsive therapy (ECT) may be considered for treatment-resistant depression (see sidebar on page 12 for a definition of treatment-resistant depression). Updated APA depression management guidelines include the following key points on ECT:

• **Effectiveness.** ECT has the highest rates of response and remission of any depression treatment; 70% to 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 6 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

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 bipolar disorder. Intermountain’s Bipolar CPM will be republished in late 2015. Refer to these guidelines: APA (2002; see Guideline Watch), NICE (2014), and VA DoD (2010).

Prevalence

Whereas bipolar disorder has a U.S. lifetime prevalence of 3.9%, those patients already diagnosed with depression have a higher risk. In a prospective study looking at 550 patients diagnosed with depression over 17 years, over 19% were diagnosed with bipolar disorder — 7.5% with bipolar type I (full mania and full depression) and 12.2% with bipolar type II (hypomania and full depression).

Screening

Most patients with bipolar disorder present with depressive symptoms, not manic symptoms. The strongest predictors of which depressed patients will eventually develop bipolar disorder are:

- Sudden onset of depressive symptoms or onset prior to 25 years of age
- Severe acute illness
- Psychotic features or mood lability
- Family history of bipolar disorder

Therefore, all patients who have these predictors should be screened for bipolar disorder. A good screening tool is the Mood Disorder Questionnaire (MDQ). The MDQ has 13 questions, and when 7 are answered positively, it has a sensitivity of 73% and a specificity of 90%.

If the MDQ is positive, further screening should include an interview for at least one lifetime episode of depression as well as of mania or hypomania, using DSM-5 criteria as well as the SADFIGS mnemonic (at right) to confirm diagnosis. Consider referral to a specialist.

Treatment

Studies have shown that use of antidepressants can actually induce mania and rapid cycling (4 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. Strategies for minimizing the risk of mania and rapid cycling for adults with bipolar depression include (see page 22 for information on children and adolescents):

- Using mood stabilizers alone or in combinations to minimize antidepressant therapy
- Discontinuing antidepressant therapy in patients who experience more frequent mania
- Avoiding tricyclic antidepressants and SNRIs or any antidepressant that has been destabilizing in the past
- Considering ECT for patients who are treatment resistant or pregnant, who have responded well to ECT in the past, or who experience psychotic features

DO NOT USE UNOPPOSED ANTIDEPRESSANTS.

Unopposed antidepressants can make the illness worse by inducing mania and mixed bipolar states, mood instability, and rapid cycling.
SUICIDE RISK IN CHILDREN, TEENS, AND YOUNG ADULTS

Suicide is the sixth leading cause of death in school-age children and the third leading cause of death in ages 14 to 25. Healthcare providers should carefully monitor children with mood disorders due to the severe risk of suicide 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 www.i-printstore.com and can be found on intermountainphysician.org/clinical/topics. See page 24 for information on finding resources.

DIAGNOSING BIPOLAR DISORDER IN CHILDREN & ADOLESCENTS

Screening tools for diagnosing BD in this population are the MDQ-A (Mood Disorder Questionnaire – Adolescent), Young Mania Rating Scale, and FIND guidelines83 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)

Children and adolescents

Prevalence and prognosis

It is estimated that 1% to 2% of children and 3% to 8% of adolescents have major depressive disorder (MDD).78 Depression in children and adolescents can result in severe adverse outcomes — including suicide, the 3rd leading cause of death in people aged 10 to 24 years.78 In 2009, 13.8% of students in grades 9–12 reported seriously considering suicide, 6.3% reported at least one suicide attempt, and 1.9% had made a suicide attempt that resulted in an injury, poisoning, or overdose requiring medical attention.79 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 to 2 months in community samples to 7 to 9 months in referred children. Recurrence ranges from 20% to 60% within 1 to 2 years.80 Some children are chronically depressed, with symptoms extending several years. In addition to MDD, watch for milder, chronic depression as well as bipolar depression, which often indicates referral to a specialist.

Screening and diagnosis

Major depression in children and adolescents can be quite different from major depression in adult patients, creating challenges for diagnosis.

- Mood and behavior. Children can present with an irritable rather than a depressed mood. Children express more anxiety, irritability, temper tantrums, and behavioral problems. Parents’ descriptions of a child’s mood (appears sad or tearful) are useful.

- Psychiatric and somatic symptoms. Assessment of weight changes is more difficult and should accommodate for normal growth. Preadolescent children present with a higher incidence of auditory hallucinations and somatic complaints. Children express more apathy and less psychomotor retardation or anhedonia.

Depression symptoms in children and adolescents often overlap with problems such as ADHD and bipolar disorder. In fact, comorbidity is estimated to be about 66%.81,82

Screening tools. The following are available through the Mental Health Integration program and are designed for use with children and adolescents (also, see the tools for diagnosing bipolar disorder 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.

Treatment overview

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 bipolar disorder under the age of 10. Refer to drugs@FDA.gov for the latest approved medications for ages 10 and up.
Use of antidepressants in children

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.

- The data remains conflicting on 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, other studies show an inverse relationship between suicide and antidepressant use. While no evidence proves that antidepressants cause an increase in actual suicides, untreated or inadequately treated depressive illness causes the majority of completed suicides in children and adolescents.

- If antidepressants are prescribed, follow these general guidelines:
  - Start at a low dose and gradually increase to an appropriate dose. 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 alternative treatment.
  - If a patient does not experience complete remission of symptoms after 12 weeks at an adequate dose, consider alternative treatments and evaluate the patient for factors that may be contributing to poor medication response.

### TABLE 8. Notes on antidepressants for children and adolescents

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dosage</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin-norepinephrine reuptake inhibitor (SNRI)</td>
<td>bupropion (Wellbutrin)</td>
<td>Start at 37.5 mg once daily; range 37.5–200 mg daily in divided dosing</td>
<td>Start at 75 mg; range 100–300 mg daily in divided dosing</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitor (SSRI)</td>
<td>fluoxetine (Prozac)</td>
<td>Start at 2.5–5 mg once daily; range 2.5–20 mg once daily</td>
<td>Start at 5–10 mg once daily; range 10–40 mg once daily</td>
</tr>
<tr>
<td></td>
<td>escitalopram (Lexapro)</td>
<td>Start at 5 mg once daily; range 5–10 mg once daily</td>
<td>Start at 10 mg once daily; range 10–20 mg once daily</td>
</tr>
<tr>
<td></td>
<td>sertraline (Zoloft)</td>
<td>Start at 12.5 mg once daily; range 12.5–50 mg once daily</td>
<td>Start at 12.5–25 mg once daily; range 25–150 mg once daily</td>
</tr>
<tr>
<td></td>
<td>citalopram (Celexa)</td>
<td>Start at 5–10 mg once daily; range 5–20 mg once daily</td>
<td>Start at 10 mg once daily; range 10–40 mg once daily</td>
</tr>
</tbody>
</table>

**General:**
- Obtain informed consent 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.

**SSRIs:**
- Fluoxetine is FDA-approved to treat pediatric depression (age 8 to 17).
- Escitalopram is FDA-approved to treat depression in adolescents (age 12 to 17).
- Paroxetine is currently not recommended for use in children/adolescents.

**Bupropion:**
- Bupropion is available as 12-hour sustained release (SR), 24-hour extended release (XL), 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.
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 www.iprintstore.org.

• Choose Patient and Provider Education Materials. Then search for items, or use the Category menu to browse.

• Click any item to see a description, then click View PDF to open the file, or click Add to Cart to order copies.

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.

  • Krames Staywell articles on a range of topics including mental health disorders.

  • A symptom checker to guide patients in evaluating symptoms and seeking care.

  • Krames Staywell videos on conditions and treatments.

  • View media animations on conditions and treatments.

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

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).